

Appendix A. Annotated Data Extraction Forms

The annotations (comments) are included to explain how the extracted data were used in the analyses of agreement across extractors.

Keep extracted data concise. Recognize that this is a generic form, not topic-specific.

Author, Year		PMID	
Extractor		RefID	
Language			

1. Eligibility criteria

Inclusion criteria: demographics	
Inclusion criteria: disease/conditions (generic, e.g. HTN)	
Inclusion criteria: disease/conditions (specifics, e.g. SPB >140)	
Inclusion criteria: other	
Exclusion criteria: comorbidity	
Exclusion criteria: other	

2. Interventions*

2(a) If interventions are drugs/supplements (other interventions that fit):

	Intervention drug name	Dose	Frequency	Route	Duration of intervention
1					
2					
3					

2(b) If interventions are not drugs*

	Intervention name	Concise Description	Frequency	Duration of intervention
1				
2				
3				

* If a cointervention (eg, education) is used in all patients, enter info in 4, not here.

If an intervention has multiple components (that are all different than in other study arms) enter each on a separate row and renumber the 1st column as needed.

3. Comparator

Type of comparator: (other drug, placebo, usual care, no treatment, etc.)	
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3a. If comparator is a drug/supplements (other interventions that fit):

	Comparator drug name	Dose	Frequency	Route	Duration of intervention
1					
2					
3					

3b. If comparator is not a drug:

	Comparator name	Concise Description	Frequency	Duration of intervention
1				
2				
3				

4. Co-interventions

	Co-intervention name	Description (include dose, frequency, and other details)
1		
2		
3		

5. Design

Maximum (Mean) Duration of Followup	Number enrolled (total all arms)	Number randomized (total all arms)	Number of centers	Washout period, if XO (y/n/NA, duration)

6. Quality issues

Was Randomization Technique Reported? (y/n)	Was Allocation Concealment Method Reported? (y/n)	Claimed Intention to Treat Analysis in Methods (y/n)	Power calculation in Methods (y/n)	Verifiable† difference in reported results between text and table (y/n, what?)	
Blinded Patient (y/n/nd)	Blinded caregiver (y/n/nd)	Blinded Outcome Assessment (y/n/nd)	“Double blinded” (y/n)	“Single blinded” (y/n)	Other blinding (describe)

† A discrepancy you can point to, not just this “seems” wrong.

7. Outcomes. List all outcomes reported in the article (abstract, Results section, tables, figures). In round 1 of extraction complete only the first 5 columns (w/o ‡).

	Outcome Name (Everyone)	In abstract? (y/n) (only non-English extractor)	Principal Timepoint for Outcome (only non-English extractor)	Dichot or Continuous? † (only non-English extractor)	Data/#s reported in text? (y/n) (only non-English extractor)	Chosen to extract results? (Y/N)‡ (EB/MC/NH/WY)	Definition of Outcome (only if chosen to extract results)‡ (Everyone)
1							
2							
3							
4							

† Answer this for any outcome that is not obvious.

‡ After round 1, we will choose two outcomes (at 1 timepoint) for you to extract results. Outcome definitions are needed only for these 2 outcomes.

Tables 8&9: Extract results only for those outcomes listed in Table 7 under “Chosen to extract results”

8. Results (dichotomized outcomes). Include only reported data. Do not calculate any values.

Outcome	Intervention (intervention or control)	n Event	N Total	Unadjusted (reported)				Adjusted (reported)				
				Metric§	Result	95% CI#	P btw	Metric§	95% CI#	P btw	Adjusted for:	
	Tx											
	Cx											

§ RR, OR, HR, RD

Change to SD or SE, if necessary.

9. Results (continuous measures) Include only reported data. Do not calculate any values. If adjusted & unadjusted analyses reported, extract adjusted only.

Outcome	Intervention (intervention or control)	Unit	Baseline			Final			Change (Final – Baseline)			Net Δ /Difference* (Δ test – Δ control)*				
			N	Value	SD/SE*	N	Value	SD/SE*	Value	SD/SE/CI*	P	Value	SD/SE/CI*	P	Adjusted for:†	
	Tx															
	Cx															

* Delete or correct the incorrect value/item. Replace with nd if necessary

† Complete only if analysis was adjusted (regardless of whether analysis was net change, difference of final values, or change from baseline). Otherwise leave blank.

10. Time. Only for those extracting from English translations

	A Lot	A Little	None
Extra time required to extract because of apparent poor translation:			

Appendix B. List of Articles Translated and Included

Chinese

Hu XY, Zhou YX, Xu SZ, et al. [Effects of probiotics on feeding intolerance in low birth weight premature infants]. [Chinese]. *Zhongguo Dangdai Erke Zazhi* 2010;12(9):693-5.

Li H, Dong L, Li Y, et al. [A randomized clinical trial of combination of Aidi injection with Gemcitabine and Oxaliplatin regimen or Go regimen only in the treatment of advanced non-small-cell lung cancer.]. [Chinese]. *Chinese Journal of Lung Cancer* 2008;11(4):570-3.

Liu X, Liu D, Li J, et al. [Safety and efficacy of carbon dioxide insufflation during colonoscopy]. [Chinese]. *Zhong Nan da Xue Xue Bao* 2009;Yi(8):825-9.

Tang FZ, Liu YL, Wen FQ, et al. [Comparison of therapeutic effects in severe nocturia: gradual versus immediate drug withdrawal]. [Chinese]. *Zhongguo Dangdai Erke Zazhi* 2010;12(3):198-200.

Wang P, Yang J, Liu G, et al. [Effects of moxibustion at head-points on levels of somatostatin and arginine vasopressin from cerebrospinal fluid in patients with vascular dementia: a randomized controlled trial]. [Chinese]. *Zhong Xi Yi Jie He Xue Bao/Journal of Chinese Integrative Medicine* 2010;8(7):636-40.

Xu JS, Yang JW, Gu MN, et al. [Effects of fentanyl on EC50 of ropivacaine for postoperative epidural analgesia after gynecological surgery]. [Chinese]. *Di Yi Junyi Daxue Xuebao* 2004;24(11):1326-7.

Xu XH, Chang YT, Li L, et al. [Effect of fructose-1,6-diphosphete on myocardial preservation during pulmonary operations]. [Chinese]. *Zhong Nan da Xue Xue Bao* 2008;Yi(10):966-9.

Yang MH, Li M, Dou YQ, et al. [Effects of Bushen Huoxue Granule on motor function in patients with Parkinson's disease: a multicenter, randomized, double-blind and placebo-controlled trial]. [Chinese]. *Zhong Xi Yi Jie He Xue Bao/Journal of Chinese Integrative Medicine* 2010;8(3):231-7.

Yi JH, Li RR. [Influence of near-work and outdoor activities on myopia progression in school children]. [Chinese]. *Zhongguo Dangdai Erke Zazhi* 2011;13(1):32-5.

Zhang GQ, Ge L, Ding W, et al. [The value of portal vein chemotherapy after radical resection in delaying intrahepatic recurrence of stage II primary hepatocellular carcinoma]. [Chinese]. *Aizheng* 2008;27(12):1297-301.

French

Aubin M, Vezina L, Maziade J, et al. [Control of arterial hypertension: effectiveness of an intervention performed by family practitioners]. [French]. *Canadian Family Physician* 1994;40:1742-52.

Aydin A, Karadayi K, Aykan U, et al. [Effectiveness of topical ciclosporin A treatment after excision of primary pterygium and limbal conjunctival autograft]. [French][Erratum appears in *J Fr Ophtalmol*. 2010 Jun;33(6):435]. *Journal Francais d Ophthalmologie* 2008;31(7):699-704.

Baillargeon L, Drouin J, Desjardins L, et al. [The effects of Arnica Montana on blood coagulation. Randomized controlled trial]. [French][Erratum appears in *Can Fam Physician* 1994 Feb;40:225]. *Canadian Family Physician* 1993;39:2362-7.

Devogelaere T, Beresniak A, Raymaeckers A, et al. [Clinical study of Supranettes pads in the treatment of seasonal or perennial allergic conjunctivitis in children]. [French]. *Journal Francais d Ophthalmologie* 2006;29(6):593-8.

Fekih M, Ben ZN, Jnifen A, et al. [Comparing two Prepidil gel regimens for cervical ripening before induction of labor at term: a randomized trial]. [French]. *Journal de Gynecologie, Obstetrique et Biologie de la Reproduction* 2009;38(4):335-40.

Gadioux-Madern F, Lelez ML, Sellami L, et al. [Influence of the instillation of two versus three eyedrops of cyclopentolate 0.5% on refraction of Caucasian nonstrabismic children]. [French]. *Journal Francais d Ophthalmologie* 2008;31(1):51-5.

Gosselin P, Verreault R, Gaudreault C, et al. [Dietary treatment of mild to moderate hypercholesterolemia. Effectiveness of different interventions]. [French]. *Canadian Family Physician* 1996;42:2160-7.

Lamouliatte H, Perie F, Joubert-Collin M. [Treatment of Helicobacter pylori infection with lansoprazole 30 mg or 60 mg combined with two antibiotics for duodenal ulcers]. [French]. *Gastroenterologie Clinique et Biologique* 2000;24(5):495-500.

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Rolachon A, Kezachian G, Causse X, et al. [Value of high-dose interferon-alpha in chronic viral hepatitis C patients non-responder to a 1st treatment. Pilot study prospective and randomized trial]. [French]. *Gastroenterologie Clinique et Biologique* 1997;21(12):924-8.

German

Bechdorf A, Pholmann B, Guttgemanns J, et al. Motivationsbehandlung für Patienten mit der Doppeldiagnose Psychose und Sucht Ergebnisse einer randomisierten Studie. *Nervenarzt* 2011;Epub ahead of print.

Birnbaum F, Schwartzkopff J, Bohringer D, et al. [Penetrating keratoplasty with intrastromal corneal ring. A prospective randomized study]. [German]. *Ophthalmologie* 2008;105(5):452-6.

Borner M, Burkle H, Trojan S, et al. [Intra-articular ketamine after arthroscopic knee surgery. Optimisation of postoperative analgesia]. [German]. *Anaesthesist* 2007;56(11):1120-7.

Langer C, Forster H, Konietschke F, et al. [Mesh shrinkage in hernia surgery: data from a prospective randomized double-blinded clinical study]. [German]. *Chirurg* 2010;81(8):735-42.

Marx S, Cimniak U, Beckert R, et al. [Chronic prostatitis/chronic pelvic pain syndrome. Influence of osteopathic treatment - a randomized controlled study]. [German]. *Urologe (Ausg 2009;A)*.(11):1339-45.

Meybohm P, Hanss R, Bein B, et al. [Comparison of premedication regimes. A randomized, controlled trial]. [German]. *Anaesthesist* 2007;56(9):890-2.

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Stoffels I, Wolter TP, Sailer AM, et al. [The impact of silicone spray on scar formation. A single-center placebo-controlled double-blind trial]. [German]. *Hautarzt* 2010;61(4):332-8.

Warlo I, Krummenauer F, Dick HB. [Rotational stability in intraocular lenses with C-loop haptics versus Z haptics in cataract surgery. A prospective randomised comparison]. [German]. *Ophthalmologe* 2005;102(10):987-92.

Wohlrab D, Droege JW, Mendel T, et al. [Minimally invasive vs. transgluteal total hip replacement. A 3-month follow-up of a prospective randomized clinical study]. [German]. *Orthopade* 2008;37(11):1121-6.

Hebrew

Gimelfarb Y, Natan Z. [Risk factors for suicide attempts in dual diagnosis patients]. [Hebrew]. *Harefuah* 2009;148(6):355-8.

Haimov I, Vadas L. [Sleep in older adults: association between chronic insomnia and cognitive functioning]. [Hebrew]. *Harefuah* 2009;148(5):310-4.

Kugelman A, Anabussi S, Sharon N, et al. [The association between pertussis during infancy and childhood asthma]. [Hebrew]. *Harefuah* 2009;148(2):80-3.

Oksenberg A, Arons E, Greenberg-Dotan S, et al. [The significance of body posture on breathing abnormalities during sleep: data analysis of 2077 obstructive sleep apnea patients]. [Hebrew]. *Harefuah* 2009;148(5):304-9.

Oliven A, Tov N, Odeh M, et al. [Electrical stimulation of the genioglossus to improve pharyngeal patency in obstructive sleep apnea: comparison of results obtained during sleep and anesthesia]. [Hebrew]. *Harefuah* 2009;148(5):315-9.

Otto O, Peleg R, Press Y. [Streptococcal pharyngitis among children: comparison of attitudes between family physicians and pediatricians]. [Hebrew]. *Harefuah* 2009;148(8):511-4.

Perlitz Y, Gtezer-Soltzman S, Peleg A, et al. [Correlation of maternal serum and amniotic fluid leptin and insulin levels with neonatal birth weight]. [Hebrew]. Harefuah 2009;148(7):420-3.

Rosenberg E, Elkrinawi S, Goldbart A, et al. [Obstructive sleep apnea syndrome in young infants]. [Hebrew]. Harefuah 2009;148(5):295-9.

Italian

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Japanese

Adachi Y, Sumikuma T, Kagami R, et al. [Improvement of patient adherence by mixing oral itraconazole solution with a beverage (orange juice)]. [Japanese]. *Rinsho Ketsueki - Japanese Journal of Clinical Hematology* 2010;51(5):315-9.

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Mochizuki M, Hatsugaya M, Rokujoh E, et al. [Randomized controlled study on the effectiveness of community pharmacists' advice for smoking cessation by Nicorette--evaluation at three months after initiation]. [Japanese]. *Yakugaku Zasshi - Journal of the Pharmaceutical Society of Japan* 2004;124(12):989-95.

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Korean

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Kim YG, Moon JT, Lee KM, et al. [The effects of probiotics on symptoms of irritable bowel syndrome]. [Korean]. Korean Journal of Gastroenterology/Taehan Sohwagi Hakhoe Chi 2006;47(6):413-9.

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Seo YJ, Yoon H. [The effects of preemptive analgesia of morphine and ketorolac on postoperative pain, cortisol, O₂ saturation and heart rate]. [Korean]. Journal of Korean Academy of Nursing 2008;38(5):720-9.

Portuguese

Amorim MM, Lippo LA, Costa AA, et al. [Transdermal nitroglycerin versus oral nifedipine administration for tocolysis: a randomized clinical trial]. [Portuguese]. Revista Brasileira de Ginecologia e Obstetricia 2009;31(11):552-8.

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Muller KR, Bonamigo RR, Crestani TA, et al. [Evaluation of patients' learning about the ABCD rule: A randomized study in southern Brazil]. [Portuguese]. *Anais Brasileiros de Dermatologia* 2009;84(6):593-8.

Pereira PP, Oliveira AL, Cabar FR, et al. [Comparative study of manual vacuum aspiration and uterine curettage for treatment of abortion]. [Portuguese]. *Revista Da Associacao Medica Brasileira* 2006;52(5):304-7.

Santos FM, Rodrigues RG, Trindade-Filho EM. [Physical exercise versus exercise program using electrical stimulation devices for home use]. [Portuguese]. *Revista de Saude Publica* 2008;42(1):117-22.

Simao AN, Godeny P, Lozovoy MA, et al. [Effect of n-3 fatty acids in glycemic and lipid profiles, oxidative stress and total antioxidant capacity in patients with the metabolic syndrome]. [Portuguese]. *Arquivos Brasileiros de Endocrinologia e Metabologia* 2010;54(5):463-9.

Spanish

Bonetto G, Salvatico E, Varela N, et al. [Pain prevention in term neonates: randomized trial for three methods]. [Spanish]. *Archivos Argentinos de Pediatria* 2008;106(5):392-6.

Ceriani Cernadas JM, Carroli G, Pellegrini L, et al. [The effect of early and delayed umbilical cord clamping on ferritin levels in term infants at six months of life: a randomized, controlled trial]. [Spanish]. *Archivos Argentinos de Pediatria* 2010;108(3):201-8.

de Luis DA, de la FB, Izaola O, et al. [Randomized clinical trial with a inulin enriched cookie on risk cardiovascular factor in obese patients]. [Spanish]. *Nutricion Hospitalaria* 2010;25(1):53-9.

Garcia-Talavera Espin NV, Gomez Sanchez MB, Zomeno Ros AI, et al. [Comparative study of two enteral feeding formulas in hospitalized elders: casein versus soybean protein]. [Spanish]. *Nutricion Hospitalaria* 2010;25(4):606-12.

Gomez-Garcia A, Hernandez-Salazar E, Gonzalez-Ortiz M, et al. [Effect of oral zinc administration on insulin sensitivity, leptin and androgens in obese males]. [Spanish]. *Revista Medica de Chile* 2006;134(3):279-84.

Lopez-De-Blanc SA, Salati-De-Mugnolo N, Femopase FL, et al. Antifungal topical therapy in oral chronic candidosis. A comparative study. *Medicina Oral* 2002;7(4):260-70.

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Perez-Barcena J, Barcelo B, Homar J, et al. [Comparison of the effectiveness of pentobarbital and thiopental in patients with refractory intracranial hypertension. Preliminary report of 20 patients]. [Spanish]. *Neurocirugia (Asturias, Spain)* 2005;16(1):5-12.

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Vasquez AM, Sanin F, Alvarez LG, et al. [Therapeutic efficacy of a regimen of artesunate-mefloquine-primaquine treatment for *Plasmodium falciparum* malaria and treatment effects on gametocytic development]. [Spanish]. *Biomedica* 2009;29(2):307-19.

English

Artinian NT, Flack JM, Nordstrom CK, et al. Effects of nurse-managed telemonitoring on blood pressure at 12-month follow-up among urban African Americans. *Nurs Res* 2007;56(5):312-22.

Binanay C, Califf RM, Hasselblad V, et al. Evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness: the ESCAPE trial. *JAMA* 2005;294(13):1625-33.

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Calo L, Lamberti F, Loricchio ML, et al. Left atrial ablation versus biatrial ablation for persistent and permanent atrial fibrillation: a prospective and randomized study. *J Am Coll Cardiol* 2006;47(12):2504-12.

Domagk D, Menzel J, Seidel M, et al. Endoluminal gastroplasty (EndoCinch) versus endoscopic polymer implantation (Enteryx) for treatment of gastroesophageal reflux disease: 6-month results of a prospective, randomized trial. *Am J Gastroenterol* 2006;101(3):422-30.

Gagnadoux F, Fleury B, Vielle B, et al. Titrated mandibular advancement versus positive airway pressure for sleep apnoea. *Eur Respir J* 2009;34(4):914-20.

Meador K, Loring D, Nichols M, et al. Preliminary findings of high-dose thiamine in dementia of Alzheimer's type. *J Geriatr Psychiatry Neurol* 1993;6(4):222-9.

Noel-Weiss J, Rupp A, Cragg B, et al. Randomized controlled trial to determine effects of prenatal breastfeeding workshop on maternal breastfeeding self-efficacy and breastfeeding duration. *J Obstet Gynecol Neonatal Nurs* 2006;35(5):616-24.

Schiele F, Meneveau N, Vuilleminot A, et al. Impact of intravascular ultrasound guidance in stent deployment on 6-month restenosis rate: a multicenter, randomized study comparing two strategies--with and without intravascular ultrasound guidance. RESIST Study Group. REStenosis after Ivus guided STenting. *J Am Coll Cardiol* 1998;32(2):320-8.

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Chinese. Example 1

- Clinical experience

Aidi injection combined with gemcitabine Gao oxaliplatin (GO) treatment of advanced non-small cell lung cancer

[Authors]

Lung cancer is one of the most common malignant tumor, non-small cell lung cancer (non-small cell lung cancer, NSCLC) accounts for 80% lung cancer, the majority of the time of diagnosis has been advanced (III B, IV period), except for a few to surgery, the chemotherapy is the primary means of treatment of advanced NSCLC. Most were older with advanced NSCLC, generally in poor condition, and chemotherapy, the body has significant multi-system adverse reactions, to explore improved efficacy, improved quality of life, reduce adverse reactions of chemotherapy, since February 2003 -2006 4 years Aidi injection combined with months of gemcitabine Gao oxaliplatin (GO) in the treatment of advanced NSCLC 53 patients, and single GO treatment of advanced NSCLC 51 例 do comparative observation, the results reported below.

1 Materials and Methods

1.1 ① inclusion criteria have to undergo a chest CT, confirmed by pathology, in line with NSCLC diagnostic criteria [1]; ② Department of recurrence after surgery or were inoperable III B-IV of the patients had measurable lesions; ③ KPS [2] score ≥ 60 ; ④ blood, liver and kidney function and normal ECG and no contraindication to chemotherapy; ⑤ expected survival of more than 3 months.

1.2 General information from February 2003 to April 2006 patients were treated 104 patients with advanced NSCLC over the same period were randomly divided into treatment and control groups. Treatment group 53 cases, 39 males and 14 females, aged 32 -79 years, median age was 58 years; III B of the 29 cases, IV stage 24; initial treatment in 26 cases, 27 cases of retreatment. The control group 51 cases, 34 males and 17 females, aged 31 - 77 years, median age of 57 years; III B in 26 cases, IV of 25 cases; initial treatment, 21 cases re-treated 30 cases. Differences in clinical data between the two groups was not significant (Table 1), comparable.

1.3 The treatment of patients in both groups using GO chemotherapy, usage: Gemcitabine (Gemcitabine, GEM, 200 mg / branch, Jiangsu Howson pharmaceutical company) 1000 mg/m², intravenous infusion, on days 1,8; Osage Lee Platinum (Oxaliplatin, L-OHP, 50 mg / support, Jiangsu Hengrui pharmaceutical company) 135 mg/m², intravenous infusion, day 1; 21 days to 1 cycle. Treatment group in this program based on Aidi injection (10 mL / support, from Guizhou Yi Bai pharmaceutical company, group, party is ginseng, astragalus, stabbed five tomato, cantharidin, the main components of ginseng saponin, astragalus saponin, thorn Five tomato polysaccharide to a cantharidin, crude drug per ml 0.3 g) 60 mL in 5% glucose injection 250 mL in intravenous infusion, day 1, once every 10 days, 21 days for a cycle. GO program the control group alone. Both groups during chemotherapy with symptomatic and supportive treatment.

1.4 Observation of indicators and evaluation criteria

1.4.1 Clinical Assessment of curative effect of solid tumors according to WHO criteria [3], complete remission (CR) for the visible lesions completely disappeared, more than 1 month; partial remission (PR) for the mass reduced by 50% or more, not less than 4 weeks; stable (SD) for the tumor size less than 50% or increased less than 25%; Progress (PD) for one or more lesions of more than 25% increase or new lesions; CR + PR was effective (RR) , CR + PR + SD for the disease control rate, complete at least 2 cycles were evaluated.

1.4.2 KPS score of [2], after treatment than before treatment score ≥ 10 points were added to improve, increase or decrease <10 points for the stability, reduce by ≥ 10 points for the decline.

1.4.3 Adverse reactions observed in accordance with the WHO anti-cancer drug side effects of acute and subacute standard [3] evaluation, sub-0 - IV degrees.

1.4.4 NK cells and T lymphocyte subsets in the 2 cycles before treatment and after treatment were detected by NK cells and T lymphocyte subsets, were collected.

Statistical analysis with SPSS10.0 version 1.5 statistical software, count data between the two groups using chi-square test, t test measurement data are used, the survival rate with survival analysis, $P < 0.05$ was considered statistically different.

2 Results

2.1 The effect of both groups can be evaluated in all patients. Treatment group were CR 2 例 (3.77%), PR 21 例 (39.62%), SD 19 例 (35.85%), PD 11 例 (20.75%), RR 23 cases (43.40%), disease control rate 79.25%; control group were CR 0 例, PR 18 例 (35.29%), SD 18 例 (35.29%), PD 15 例 (29.41%), RR 18 cases (35.29%), disease control rate was 70.59%. RR no significant difference between the two groups ($\chi^2 = 0.71$, $P = 0.398$).

2.2 KPS score of the two groups was 58.49% in treatment group increased (31/53), stable rate of 28.30% (15/53), decreased rate of 13.21% (7 / 53); the control group increased rate of 23.53% (12 / 51), stable rate of 45.10% (23/51), decreased rate of 31.37% (16/51); KPS score of the two groups was statistically significant difference ($\chi^2 = 13.10$, $P = 0.002$).

2.3 Comparison of two groups of adverse events (Table 2) mainly to reduce adverse reactions to blood cells, nausea, vomiting, peripheral neuritis, and abnormal liver function, the I - II degree-based, III - IV degree rare, the difference was statistically significant ($P < 0.05$).

2.4 The two groups of NK cells and T lymphocyte subsets in comparison after 2 cycles of treatment, NK cell activity and CD4 + / CD8 + ratio was significantly higher than before treatment ($t = 16.50$, $P < 0.001$; $t = 5.00$, $P < 0.001$), in the control group after 2 cycles of NK cell activity and CD4 + / CD8 + ratio were lower than before treatment ($t = -3.178$, $P = 0.002$; $t = -2.247$, $P = 0.025$), the two groups after treatment difference was statistically significant ($P < 0.05$) (Table 3).

2.5 Comparison of survival of the two groups were followed up to October 31, 2007, 7 patients were lost, 97 patients completed the follow-up, patients lost to follow-up time was recorded last censored data, the treatment group survival 9-27 months, median survival of 12.5 months and 1 year survival rate was 58.49% (31/53). The control group survival 7-26 months, the median survival was 10.5 months and 1 year survival rate 45.10% (23/51). No significant difference between the two groups ($\chi^2 = 1.87$, $P = 0.171$). Kaplan-Meier survival curve in Figure 1.

3 Discussion

Most older with advanced NSCLC, poor physical condition, weight loss, immune dysfunction, is difficult to successfully complete the cycle of chemotherapy. Find a chemotherapy effect can not only improve, but also side effects of chemotherapy drugs, cancer chemotherapy is one of the directions, traditional Chinese medicine in improving immune function, reduce symptoms and prolong survival, improve quality of life and so on show greater advantage, combining Chinese and Western Medicine in achieving this goal has good prospects [4]. Aidi injection is the application of modern technology from ginseng, astragalus, stabbed five 筋 and spot beetle and other traditional Chinese medicine extracted from the processing, ginseng, astragalus and stabbed five Jiayou righting solid, qi, soothe the nerves of the effect, can improve the body Shi Ying, enhanced immunity and detoxification Liver, with a wide range of biological activity; cantharidin poisoning attack erosion are sore, Poxue Sanjie function by inhibition of protein synthesis, hormone levels and reduce the impact of cancer drugs nucleic acid metabolism of cancer cells induce apoptosis of cancer cells [5]. Aidi injection can significantly improve patients with advanced cancer CD3 +, CD4 +, NK cell ratio, decreased CD8 + cells, thereby enhancing the immune function of patients, inhibition of tumor cell activity, improve quality of life and prolong survival [6].

Gemcitabine is a new synthetic pyrimidine nucleoside analogue, is the treatment of advanced NSCLC in recent years, an effective drug, alone over 20% efficiency, can significantly improve the tumor-related symptoms, toxicity, well tolerated [7]. Platinum drugs and gemcitabine, the inherent mechanism of inhibition of DNA replication and repair has obvious synergy [8]. Cisplatin in the treatment of advanced NSCLC, is considered one of the most active agents, monotherapy 14% efficient, due to its renal toxicity and less intense vomiting, subject to certain limited clinical application [9]. And vomiting, renal toxicity of carboplatin compared with cisplatin for the light, and serious blood toxicity, 50% of the patients had grade III - IV neutropenia, 40% of the patients had grade III - IV reduced red blood cells were not easily advanced patients [10]. Oxaliplatin belongs to the third-generation platinum agents, popular clinical concern, it has high water solubility, low toxicity, broad spectrum anti-tumor, a significant effect characteristics, and DNA binding in vivo than the rate 10 times faster than cisplatin, and the combination of solid, has a stronger cytotoxic effect, no renal toxicity, gastrointestinal reactions and blood toxicity light, with cisplatin, carboplatin, no cross-resistance, especially for poor general condition of patients with advanced NSCLC [11]. Faivre et al [12] reported that gemcitabine and oxaliplatin (GO) in the treatment of 35 patients with poor prognosis in advanced NSCLC, CR 1 例, PR 11 例, RR 33.3%, resistant to cisplatin were also effective. Buosi [13] reported that gemcitabine and oxaliplatin in the treatment of Gao's advanced NSCLC is 46.2% efficient. Crino et al [14] reported that gemcitabine and oxaliplatin in first-line treatment of advanced NSCLC is 56% efficient.

Select the test GO Aidi injection combined with the treatment of advanced NSCLC 53 patients with single-use treatment of advanced NSCLC 51 GO to do the same period 例 contrast, recent results were satisfactory, KPS score improved significantly reduced side effects, improved immune function, survival prolonged, is worthy of further study and promote the use of.

Table 1 treatment group and control group comparison of patients with general information

Tab 1 Comparison of patient characteristics between the treatment group and control group

Characteristics	Treatment Group (n=53)	Control Group (n=51)	χ^2 value	P value
Gender			0.595	0.441
Male	39	34		
Female	14	17		
Age (Year)			1.567*	0.124
Median	58	57		
Range	32–79	31–77		
Histological Subtype			0.630	0.582
Squamous	21	19		
Adenocarcinoma	27	29		
Large cell cacinoma	5	3		
Disease Staging			0.146	0.703
III B	29	26		
IV	24	25		
KPS			0.936	0.333
90–100	16	20		
60–80	37	31		
Treatment Condition			0.652	0.420
First–lineChemotherapy	26	21		
Second–lineChemotherapy	27	30		

* t value

Table 2 the treatment and control groups adverse reactions

Tab 2 Comparison of toxicities between the treatment group and control group

Type of toxic effect	Treatment Group (n=53)					Control Group(n=51)					χ^2	P
	I	II	III	IV	rate (%)	I	II	III	IV	rate (%)		
Leucopenia	9	6	2	0	32.08	14	11	5	2	62.75	9.81	0.002
Anemia	6	2	0	0	15.09	11	6	1	0	35.29	5.66	0.017
Thrombocytopenia	1	1	0	0	3.77	7	4	2	0	25.53	9.93	0.002
Nausea/vomiting	10	5	1	1	32.08	17	7	2	2	54.90	5.52	0.019
Stomatitis	9	4	1	0	26.42	12	7	1	0	39.22	1.94	0.164
Peripheral neuritis	7	1	1	0	16.98	16	4	3	0	43.40	9.65	0.002
Transaminase abnormalities	2	1	0	0	5.66	7	3	1	0	20.75	5.65	0.017
Urea nitrogen abnormalities	1	0	0	0	1.89	3	0	0	0	5.88	0.30	0.583
Electrolyte abnormalities	1	0	0	0	1.89	2	0	0	0	3.92	0.00	0.973
Alopecia	9	3	1	0	24.53	11	3	2	0	31.37	0.61	0.437
Constipation	10	4	1	0	26.42	13	6	1	0	39.22	0.39	0.239
Diarrhea	7	1	0	0	15.09	9	2	1	0	23.53	1.19	0.275

Table 3 before and after treatment NK cells, T lymphocyte subsets

Tab 3 The changes of NK cells, T-lymphocyte sub-group between the two groups after treatment (Mean \pm SD)

Type of cells	Treatment Group (n=53)		Control Group (n=51)		t	P
	Before treatment	After treatment	Before treatment	After treatment		
NK	20.3 \pm 3.7	35.9 \pm 5.8	21.2 \pm 5.2	17.8 \pm 5.6	41.57	<0.001
CD ₃ ⁺	38.6 \pm 10.1	48.2 \pm 9.8	39.2 \pm 7.9	34.9 \pm 9.2	30.46	<0.001
CD ₄ ⁺	33.2 \pm 11.2	34.7 \pm 7.1	32.9 \pm 7.7	31.2 \pm 8.1	2.33	0.019
CD ₈ ⁺	25.9 \pm 12.4	22.3 \pm 9.6	26.6 \pm 4.8	29.4 \pm 8.6	4.56	<0.001
CD ₄ ⁺ /CD ₈ ⁺	1.3 \pm 0.5	1.7 \pm 0.3	1.3 \pm 0.4	1.1 \pm 0.5	3.96	<0.001

Figure 1 treatment group and control group Kaplan-Meier survival curves

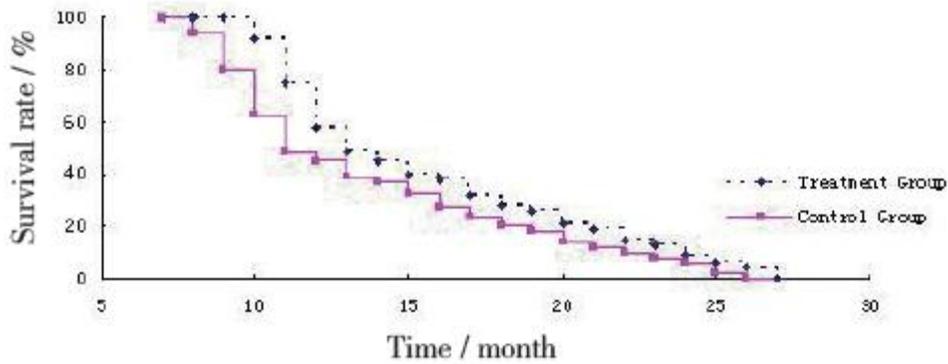


图 1 治疗组与对照组Kaplan-Meier生存曲线

Fig 1 Kaplan-Meier survival curves of treatment and control groups

Chinese. Example 2

See original for English words, numbers, and figures and full tables.

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Application of carbon dioxide colonoscopy evaluation of the safety and effectiveness

[Authors]

! Summary! "# Evaluate the purpose of carbon dioxide, \$ F_{CO_2} % colonoscopy is the safety and effectiveness of "Methods to% & \$ # patients were randomly divided into F_{CO_2} Group \$ \$ j6] &% \$ \$, and air group j6] 5%! were injected F_{CO_2} colonoscopy or air" before the colonoscopy examination and inspection & measurement in patients with end-tidal carbon dioxide partial pressure * 8 \$ HM F_{CO_2} % +! to understand the in vivo F_{CO_2} retention of the situation," using a visual analog rating scale \$ nEZ% at the end of colonoscopy and examination 6!%! _ and "& (abdominal pain severity score" before colonoscopy examination is not routinely used & sedatives and analgesics "results # F_{CO_2} group and air group in the average age & gender composition & operating time of colonoscopy and the percentage to reach the ileocecal no significant difference in terms of \$ are: i # / # 5% "of two colonoscopy between groups and at different time points after 8 \$ HM F_{CO_2} % \$ were no significant differences between the value of: i # / # 5%! but F_{CO_2} group after colonoscopy every point The average nEZ scores were significantly lower than the air group, were: d # / # 5% " F_{CO_2} group checked 6!%! _ and "& (score of abdominal pain nEZ # significantly higher than the percentage of those air group \$ are: d # / # 6% "Conclusion # into F_{CO_2} for either a colonoscopy does not cause patients F_{CO_2} retention! can significantly reduce the pain," so it is a safe and effective method "

! Keywords! "Colonoscopy #! CO #! Clinical randomized controlled trials #! Abdominal pain

! CLC "! R5]&/_!! Document code"! E!! Article number "! 6_]" I] % &] \$ "## \$% # 'l #'" 5l # 5

About \$,*%-")/%! Liuxiong Xiang, MD # # # Master of Digestive Endoscopy is mainly engaged in the research clinic # now working in Xiangtan Central Hospital -

Colonoscopy in the diagnosis and treatment of colorectal diseases are playing an increasingly important role - the application of air colonoscopy has become the standard method of most parts of the world - but # colonoscopy in the air is led into the intestine of patients surgery. postoperative abdominal pain and abdominal discomfort of the main reasons - in recent years has been reported that the application of carbon dioxide #! F_{CO_2} " colonoscopy can reduce colonoscopy and examination of abdominal pain and abdominal discomfort '6 l' (- but in laparoscopic surgery into the F_{CO_2} often lead to arterial carbon dioxide partial pressure '8! F_{CO_2} "(elevated '\$ l6 # (- so # need to understand the colonoscopy injection F_{CO_2} will lead to the body F_{CO_2} the retention - the air as a control in this study in colonoscopy # injected F_{CO_2} if patients can reduce pain and cause the body F_{CO_2} to evaluate the retention -

HI Materials and Methods

6 / 6! Study

The "# #] years \$ month" to "# #] # 6 in the period from 66 months in the Second Xiangya Hospital of endoscopy room in patients undergoing colonoscopy as a research subject - one of the following patients were excluded from the \$ outside of this study under the age of 6 & & not relevant to the study completed the questionnaire & have serious chronic obstructive pulmonary disease. heart disease or known to have F_{CO_2} retention by -% & \$ patients by colonoscopy Check Order # by pre-programmed randomly divided into F_{CO_2} group! \$ j6] &" with air group! \$ j6] 5 "# respectively F_{CO_2} and the air colonoscopy -

6 / "! Colonoscopy

All tests were the Second Xiangya Hospital Ethics Committee approved the implementation - before testing on the basic conditions of this experiment are explained to the patient and signed informed consent was # Book - colonoscopy using F @ .1 * 90 electronic colonoscopy! Japan "and made F_{CO_2} gas injection equipment - conventional oral examination before the castor oil in patients with intestinal # chosen cleaning "of experienced endoscopists colonoscopy and seek to plug # mirror to the ileocecal - preoperative not routinely intraoperative sedation - preliminary animal experiments in this study group showed # application made F_{CO_2} gas injection equipment into F_{CO_2} colonoscopy is safe and effective - in order to ensure double-blind trial colonoscopy host and # F_{CO_2} gas injection equipment valves are covered with black cloth by the person responsible for control # F_{CO_2} valve and pump switch # colonoscopy host operator and the patients were checked I do not know the type of gas used -

6 /%! Detection of end-tidal carbon dioxide partial pressure

Normal adults showed end-tidal carbon dioxide partial pressure of 8! HM F_{CO_2} " and the arterial carbon dioxide partial pressure 8! F_{CO_2} " is very similar so the # 8! HM F_{CO_2} " is often used to replace blood 8! F_{CO_2} "

"CO₂" # test is an ideal noninvasive method for '66 (- this test using hand-held F-CO₂ analyzer! a7M18 # T:) 3, IF (13B: # Finland," Detection of 8! HM F-CO₂ "- measured by nurses in some patients randomly selected in the following time points & 8! HM F-CO₂ "\$ start colonoscopy. ileocecal or reach the nearest place. to return to the rectum and 6 # 1 After the inspection, > 2 -

6 / &! Abdominal pain score

6 # # 11 with visual analogue rating scale! W> 09: @: 2: @ <A 0 =: @ 3 # nEZ "pain severity score '6 (# nEZ scale scores for the # f6 # # # # left-most scores are representative of the far right without pain score was 6 # # # 11 # representatives can not stand the pain - Patients at the end of the endoscopy and examination, and 6 # % # _ "& (on to assess pain severity # # and fill out the questionnaire is completed questionnaire by mail to the Second Xiangya Hospital of endoscopy room -

6 / 5! Statistically

By ZUZZ6% / # statistical package was used for statistical analysis - the number of measurement data are the standard deviation of h! Bh4 "between groups that use% # test - the value of each period was used to compare the average score nEZ nonparametric two-sample rank sum test # on scores between groups at each time point nEZ the percentage of applications for the # chi-square test - 8! HM F-CO₂ " values at each time point using repeated measures analysis of variance to compare -: d # / # 5 for the difference was statistically significant -

OI Results II results

"/ 6! F-CO₂ group and the baseline characteristics between the air group

A total of% 5 'outpatients and hospitalized patients were randomly assigned according to the principles of research into this case # where \$ sedation for endoscopy were excluded from the remaining # % & \$ cases according to requirements for the return of the questionnaire - % & \$ case using F-CO₂ as a medium of gas injection, 6] & # the use of air in 6 cases] 5 patients - average age in both groups. gender composition. physique! body mass index." endoscopy operation time. get the percentage of the ileocecal etc. There was no significant difference!: i # / # 5 # Table 6 "-

"/! 8 \$ HM F-CO₂ % value

Randomly selected in the test "# 5 patients were HM F-CO₂ # to learn to monitor arterial blood before and after endoscopy, 8! F-CO₂ " # where the change F-CO₂ group of 6 #" 6 # Example # Air Group % patients - "check in and check group after 8! HM F-CO₂ "value before the test than their own air group, particularly dropped down # # but the difference was not statistically significant! are: i # / # 5 # Figure 6 "- the average at each time point between the two groups of 8! HM F-CO₂ "no significant difference between the value of comparison! are: i # / # 5 # Figure 6" -

"/%! Abdominal pain

Although the two groups at the end of the examination have different degrees of pain and discomfort # VAS but no significant difference in scores nEZ: + # / # 5 - P>0.05- F-CO₂ after the test group and 6 # % _ (abdominal pain scores were on average nEZ significantly lower than the air group! are: d # / # 6 # map "" # Check after "& (between the two groups remained statistically significant difference!: d # / # 5 # map" "- F-CO₂ group of pain after inspection mitigation inspection faster and # 6 (compared with the check at the end of nEZ score significantly!): d # / # 6 # map "" - on the score of each time point nEZ the percentage of # # using chi-square test results showed that [F "6 # % inspection group _ and #" & (score of abdominal pain nEZ #! no pain, "the percentage of those groups were significantly higher than the air! are: d # / # 6 # Figure%" -

Discussion II on PI

Current injected into the air colonoscopy has become the standard method of most parts of the world - because the air is easy access to simple low-cost # # # while fully reveal the intestinal wall to reach the required brightness of the observed effective observation of the intestinal wall # mucosa - its biggest shortcoming, however # the intestine is continuing expansion will lead to abdominal pain. distension in patients with fear, not # This is the main reason for colonoscopy colonoscopy # hinder the promotion and application & followed by #, serious cases can cause or induce intestinal perforation & also # when air into the blood when the risk of thrombosis - in recent years has been a small number of applications # F-CO₂ as a medium for gas injection colonoscopy reported in the literature # but its safety and effectiveness has yet to be further evaluation -

The results of this study show # F-CO₂ group and air group, the average arrival time and colonoscopy percentage ileocecal & between the two groups were similar to colonoscopy and at different time points after 8! HM F-CO₂ "value-free statistics However, differences in study # F-CO₂ in the colonoscopy group at each time point after the end! 6 # % # _ and" & ("average nEZ scores were significantly lower than the air group, # This is consistent with the reported '6 I' (# prompt application of F-CO₂ colonoscopy patients will not cause either F-CO₂ # retention can significantly reduce the pain -

Applications F-CO₂ instead of air colonoscopy can reduce the patient's abdominal pain # This is mainly because F-CO₂ has a different physical and chemical characteristics of air due to - F-CO₂ colorless. Odorless. Is not flammable. Easily soluble in blood and other body fluids # # can rapidly absorbed from the intestine also easy to be excreted through the lungs - Z) 3W320 <2, etc. "(found in the application of randomized controlled trials F-CO₂ colonoscopy in patients with end _ and # check "& (later than the air group significantly reduced abdominal pain &

After the inspection, 6 (abdominal e # air line photos showed significant group continued expansion of # the intestine F^{CO_2} group of the gas residual lumen diameter of few # intestine were significantly higher than the air reduced - suggesting that F^{CO_2} in the intestine has the characteristics of fast absorption and thus reduce the # colonoscopy abdominal pain after the expansion of the intestine. distension - for further study F^{CO_2} # this feature can be quickly absorbed and intestinal blood flow in their # k: 091:0: '6 other "(to the rat model were injected into the F^{CO_2} or the comparative study of air into the intestine # found F^{CO_2} has a fast absorption characteristics # minimal disturbance of the intestinal blood flow at the same time # when there is a small dose of the role of promoting blood flow to increase this further indicates that the application # F^{CO_2} when colonoscopy is less chance of potential complications caused by intestinal ischemia may be # Smaller # of clinically relevant symptoms such as abdominal pain and bloating are less likely to -

Ideal for colonoscopy inert gas should be a # but Shangmo found - although F^{CO_2} is the normal body metabolism # but F^{CO_2} will affect the absorption of the normal physiological metabolism of the body so it is not # ideal gas colonoscopy - showed in laparoscopic surgery into the F^{CO_2} will result in blood 8! F^{CO_2} "elevated '\$ I6 # (# Therefore evaluation F^{CO_2} in the safety of colonoscopy is necessary - research shows that healthy adults # 8! HM F^{CO_2} " and arterial blood 8! F^{CO_2} " is very similar so the # 8! HM F^{CO_2} " can replace blood 8! F^{CO_2} " # test is considered an ideal noninvasive method for '66 (- this study used 8! HM F^{CO_2} " As the body to determine whether the F^{CO_2} # retention index colonoscopy was found in the injected F^{CO_2} will not cause patient examination and check in after 8! HM F^{CO_2} " level rose higher than before the test # # On the contrary there is a certain decline in # particular group is more obvious in the air, but were not statistically significant # - F^{CO_2} of the group and air group point average of 8! HM F^{CO_2} " no significant difference between the value: i # / # 5 "- and \; 3) (: 93; such as '6 (reported consistent - 8! HM F^{CO_2} "reduction in the level may be associated with stress. check hyperventilation caused pain and injection-related # F^{CO_2} in a way not compensate for the hyperventilation-induced 8! HM F^{CO_2} " drop -

To sum up # into F^{CO_2} for either a colonoscopy does not cause patients F^{CO_2} # retention can significantly reduce the pain - so it is a safe and effective method -

Sign! Issued! Kail Things

% Of Central South University! Medical Sciences formerly known as% # & Hunan Medical University, "first published in 6 \$ 5 'years," the Ministry of Education Head (Central South University, Advanced Medicine and Health sponsored a comprehensive academic journal + journal of the medical literature by the U.S. and on-line retrieval system! YHT78PH # and% of Medical Index &! 3 - # "Dutch% EMBASE &! M-#" American% Chemical Abstracts &! "H # " the Russian% Digest Magazine &! H! "O3F3S3 #" Chinese Science Citation Database! core library #! [Z [T # and other important domestic and foreign, and authority of the abstracts database is in Chinese core journals included \$ (Source Journals Chinese Articles and Chinese periodicals matrix) double-effect * \$ multiple journals times by the national and provincial press and publication departments as the outstanding scientific and technical journals ""##" was named) the first "session of the China Science and Technology University Journal of Quality * () * Chinese Journal of Quality Technology and Hunan) Top Ten Science and Technology Journals * + has been successfully achieved with] 3BF \$ 2 of the text link (Commentary magazine Piyou (on the (review (Case Report (Research Letters and other columns + is now facing higher medical institutions (medical and health research systems and institutions of foreign Excellent collection (in English manuscript "particularly welcomes the national research project (funded key research projects and major research papers on the subject "provision of the relevant studies have been reported magazine column," and for the creation of high-quality manuscripts) green channel * + magazine interview magazine website draft, D))*,+,- ./., 01/23

Address, Xiangya Road, Changsha, Hunan Xiangya Medical College, No. 66 #] 5 mail!!!! PC, & 6 # # ']

Table 1

Group	n	Sex! Male + Female "	Age! years old "	Body mass index	Operating time	To reach the ileocecal (%)
CO2 group						
Air group						

reviews from \$ to! \$ Indicating the most pain from the pain (5 (!) For the town Pain satisfaction!
effective analgesia "(c! valid # for the pain

!; A,, anesthesia

Patients were tested before surgery A \$, 17: intramuscular injection of atropine \$; #, 13, and stability! \$, 13 # into the operating room after the d! - "or d"-A line of epidural space puncture \$ to the head-end epidural catheter A, Y1 \$ epidural!;%> # after lidocaine anesthesia of patients satisfied with reservations \$ epidural catheter back to the ward patients lost consciousness when the anesthesia pain \$ two groups were not tolerate epidural catheter after injection of different preset concentration of local anesthetic, "\$, # 12 for epidural analgesia

!; C,, experimental methods

Sequential changes in accordance with law & A 'the basic principles of administration of \$ starting from the high concentration of \$ \$ if effective analgesia is next! Cases of drug concentration to reduce the \$ \$ is higher if the invalid # ie! Patients were given the default concentration! \$; # "" \$ local anesthetic after treatment !"#\$\$%&! to '() score, "said'()!*! used as an effective drug concentration! the following * cases of drug concentrations used a ladder down * #! +""\$, % the contrary! as'()-*! and additional "+./, bupivacaine or ropivacaine * "# \$ 0 after the'()!*! that anesthesia success! that in this case the town pain is invalid! the patients under * the drug concentration using a ladder% * If additional again after bupivacaine or ropivacaine analgesia is still valid! epidural catheter may prolapse or anesthesia failed! this case removed ! following * cases or ropivacaine with bupivacaine concentration of the same & By 1% 23 & '! (The method of calculating cross there were effective and ineffective analgesia of ropivacaine used in the average concentration! Is the bupivacaine or ropivacaine 45 / "value &

*+### Statistical

In) 6))**+" statistical software using two samples! Inspection &

. # # Results

.+*## Analgesic effect of ropivacaine

Group 7!! Cases! For them! Cases of prolapse of the epidural catheter was removed! The remaining eight cases effective analgesia *) *. patients with pain is invalid! Analgesia with ropivacaine concentration! And effective and ineffective analgesia cases shown in Figure 1% * & 23 & under way there will be cross-listed as valid and invalid data calculated object! calculated ropivacaine 45 / "to" + "98, # &

.+## Ropivacaine combined with fentanyl !.#!; \$ 0 "of the analgesic effect

7 <group!. Cases! For them. Epidural catheter with blood or catheter back off! Been removed & 7 <group of analgesic drug concentration and analgesic effect) case shown in Figure invalid. & 23 & under 1% of the method to calculate the fentanyl #.#!; \$ ropivacaine = 45 0 \$ / "value" + "> 9! 7 group was significantly lower than the 45 /" value #?"+"*\$ &

! # # Discussion

In this study, the improvement of 1% 23 & @ ABC3D & Determination of ropivacaine for epidural analgesia after gynecological 45 / "& Its characteristics are in accordance with ropivacaine epidural analgesia effective concentration near the start the experiment! subjects according to the order of drug concentration! so that the concentration of drug concentrations used in the / ", RMS near '! (& This study measured ropivacaine for postoperative epidural town of gynecological pain 45 / "to" + "98, & 5EA3: & E and other 'F (painless childbirth in the study measured ropivacaine 45 /" for the "+*/>!, different reasons with which this study may lie in * # * \$ gynecologic postoperative pain and the nature of labor pain, pain)% # of varying intensity. \$ epidural puncture different! epidural spinal cord sections of varying the volume! uneven thickness of the nerve root! Ropivacaine may also 45 / "affect% #! \$ subjects with different tolerance to pain & The study also found that post-secondary application .#!; \$ 0 fentanyl! Ropivacaine 45 / "down" +

"> 9! Was significantly lower than in the ropivacaine group, 45 /"! That opioid medicines composite local anesthetic in the epidural analgesia in a synergistic effect ' / (& has been reported to "+*. , ropivacaine combined with fentanyl G. #!;\$ 0H hard lower abdominal surgery extracellular cavity analgesia superior to bupivacaine combined with fentanyl for postoperative pain ""(&, but if it is different parts of) the different nature of the best post-operative pain and how best to achieve both good ratio! remains to be further research &

Chinese. Example 4 (html)

Moxibustion head points based on cerebrospinal fluid of patients with vascular dementia of somatostatin and arginine vasopressin levels of the randomized controlled trials

Background: Vascular dementia (vascular dementia, VaD) patients with a variety of plasma and cerebrospinal fluid neuropeptide substances change significantly; effectively intervene neuropeptide levels, the prevention and treatment of VaD is very important.

Objective: Treatment with acupuncture moxibustion head VaD, improve clinical symptoms observed in cerebrospinal fluid and regulation of learning and memory associated with the substance of neuropeptide somatostatin (somatostatin, SS) and arginine vasopressin (arginine vasopressin, AVP) level role.

Design, setting, participants and interventions: 65 patients were VaD Anhui Traditional Chinese Medical acupuncture in patients with hospital outpatient or inpatient cases. Were randomly divided into the moxibustion group (33 cases) and western medicine group (32 cases). Moxibustion group were treated with monkshood pressure moxibustion, moxibustion repeated 20 min; western medicine group were treated with piracetam tablets 0.8 g, 3 times / d. Both groups were treated for 4 cycles, 4 weeks for a course of treatment.

Main outcome measures: To compare the two groups before and after treatment Hasegawa Dementia Scale Smart Check (Hasegawa's Dementia Scale, HDS), Mini Mental mental state examination (Mini-Mental State Examination, MMSE) and ADL (Activity of Daily Living Scale, ADL) points change, and SS and AVP levels in CSF.

Results: The total efficiency and moxibustion medicine group, the difference was statistically significant ($P < 0.01$). Before and after treatment HDS, MMSE and ADL points, the difference was significant ($P < 0.05$, $P < 0.01$), moxibustion group HDS, MMSE and ADL scale score difference before and after treatment has improved compared with the western medicine group ($P < 0.05$, $P < 0.01$). After treatment, cerebrospinal fluid levels of SS and AVP significantly increased than that before treatment ($P < 0.01$), moxibustion group after treatment SS and AVP levels increased significantly compared with group B ($P < 0.01$).

Conclusion: The clinical relevance of moxibustion can improve symptom score, control and learning and memory-related neuropeptide substance is an effective method of treatment of VaD.

Vascular dementia (vascular dementia, VaD) is a chronic progressive disease, the clinical manifestations of damage to the nervous system targeting the main symptoms and signs, patients can cause significant memory, cognition, thinking, numeracy and emotional and behavioral disorders, severely affected the patient's work and life. Recent studies show that, VaD plasma and cerebrospinal fluid of patients with a variety of neural peptides changed significantly, such as somatostatin (somatostatin, SS), arginine vasopressin (arginine vasopressin, AVP) and β -endorphin peptide (beta-endorphin, β -EP), etc., and these changes in neuropeptide involved in cerebral ischemia and brain damage caused by the process of learning and memory processes is an important factor, and effective intervention in the changes of neuropeptide levels, Prevention and treatment of VaD is important [1]. Our department from 2005 to 2007, with circulation collaterals moxibustion, and acupuncture to moxibustion Treatment of head and VaD, and related materials from the changes of neuropeptides point to explore the possible mechanism of action, and through the cerebrospinal fluid in the SS AVP levels were controlled study achieved the expected results.

1 Materials and Methods

1.1 Clinical data

1.1.1 study 65 cases were diagnosed as VaD patients from January 2005 to December 2007 Anhui Traditional Chinese Medical acupuncture outpatient or inpatient cases.

1.1.2 Diagnostic criteria used by the U.S. Academy of Neurology, "Neurology Diagnostic and Statistical Manual" (DSM-IV) [2] on the diagnostic criteria for VaD, the use of modified Hachinski Ischemic score method [3] distinguish between Alzheimer's disease (Alzheimer disease, AD) and VaD; degree of mental retardation based on improved intelligence check Hasegawa dementia scale (Hasegawa's Dementia Scale, HDS) [3]. HDS score by grading standards VaD were divided into four grades: normal 31 to 32.5 points; mild dementia (margin status) 22 ~ 30.5; moderate dementia (suspected dementia) 10.5 to 21.5 points; severe dementia (dementia) 0 10.0.

1.1.3 Inclusion criteria consistent with American Academy of Neurology, "Neurology Diagnostic and Statistical Manual" (DSM-IV) [2] on the diagnostic criteria for VaD; Hachinski ischemic score [3] > 7 points; modified HDS score [4] < 29.5 points.

1.1.4 Exclusion criteria in place prior cerebrovascular disease, has dementia symptoms; imaging studies (CT or MRI) not confirmed cerebrovascular disease; cerebrovascular disease within 5 months; with sports and mixed aphasia or mental illness; addition to knowledge barriers, without other focal signs of cerebrovascular disease.

1.2 Research Methods

1.2.1 Methods 65 patients were randomized to VaD patients were randomly divided into the moxibustion group and western medicine group, 33 cases in which moxibustion and western medicine group of 32 cases.

1.2.2 moxibustion group interventions: the main points to take Baihui, the Court of God, Ojo. Acupoints with the disease: liver and kidney deficiency with liver Yu, Shenshu; phlegm blocking orifices with Zhong Wan, Hong Leong; deficiency with the sea air. Point positioning based

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on "national standard Meridian area" (GB 12346-1990) [5]. With the pressure of the main points Baihui moxibustion, acupuncture points on the order by the preparation of 4 ~ 6 mm thick tuber slices as intervals, ignited the Qing Ai, moxibustion moxibustion fire direct pressure on the spacer, to the point of local hot flush skin immediately instituted, Immediately the pressure again moxibustion, moxibustion repeated 20 min; God tribunal, Dazhui use up moxa moxibustion 20 min. Points for using acupuncture needles. 1 day, weekly rest, 1 d, 4 weeks for a course of treatment, were treated with 4 courses, one week rest between courses. Western group: oral piracetam tablets (each 0.4 g, Shanghai Pharmaceutical Co F, approval of the text as Zhunzi H31021433), each 0.8 g, 3 times / d, treatment with moxibustion group.

1.2.3 Detection of observed indicators and

1.2.3.1 Scale and grading before and after treatment were calculated HDS, mini mental state examination Mental (Mini-Mental State Examination, MMSE) [6], and ADL (Activity of Daily Living Scale, ADL) [7] points. To reduce the score differences between operations, questions and record the completion by the same person, and in patients under conscious state.

1.2.3.2 Detection of cerebrospinal fluid index before treatment were treated 1 day after treatment, 4 the next morning for routine lumbar puncture, cerebrospinal fluid specimens from 2 mL, into the special test tube and mix sealed, -20 °C refrigerator. SS and AVP levels were measured by radioimmunoassay, kit purchased from the Department of Neurobiology, Second Military Medical University, operating strictly according to kit instructions.

1.2.3.3 Clinical standard reference Ministry of Health "Guidelines for clinical research of Chinese medicine drugs" [8]. the MMSE score as the main index, calculated using the formula of nimodipine: efficacy index = (post-treatment score - baseline score) / pre-treatment score × 100%, is divided into markedly effective, effective, ineffective, and worse 4. Markedly: efficacy index ≥ 20%; effective: efficacy index ≥ 12%; invalid: efficacy index < 12%; worse: efficacy index ≥ -20%, after the treatment efficiency evaluation.

1.3 The SPSS 12.0 statistical methods used statistical software to process data, all results are expressed by $\bar{x} \pm s$, the group compared with paired t test, comparison between groups using two sample t test, $P < 0.05$ was considered statistically significant.

2 Results

2.1 General Information moxibustion group of 33 patients, including 18 males and 15 females, aged 51 to 77 years, average age (64.58 ± 4.28) years, duration 0.5 to 3.9 years, mean disease duration (2.49 ± 0.95) years. Degree of dementia by HDS integral grading division, 14 cases of mild dementia, moderate in 16 cases, 3 cases of severe brain CT showed multiple infarction in 21 patients, single infarction in 4 cases, 28 cases of hypertension, hyperlipidemia 21 cases of disease, brain atrophy in 5 cases. Western group of 32 cases, including 19 males and 13 females, aged 53 to 75 years, mean age (66.42 ± 6.57) years, duration 0.5 to 4.3 years, mean disease duration (2.61 ± 1.30) years. Degree of dementia by HDS division of grading points, mild dementia, 11 cases, moderate in 17 cases, severe in 4 cases, CT showed multiple brain infarction in 19 cases, solitary infarction in 6 cases, 26 cases of hypertension, hyperlipidemia disease in 17 cases, brain atrophy

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in 4 cases. The statistical test, two groups of gender, age, duration and associated complications, the difference was not significant ($P > 0.05$), comparable. The two groups during the experiment completed the treatment, no drop-outs and loss to the situation, the subjects flow chart shown in Figure 1.



Figure 1 Flowchart subjects

Figure 1 Flow diagram of this randomized trial

2.2 Clinical Efficacy of moxibustion group of 33 patients were cured, 15 cases (45.5%), effective in 13 cases (39.4%) and 3 cases (9.1%), deteriorated in 2 cases (6.1%), total effective rate was 84.8% (28/33). Group B 32 patients were cured, 9 cases (28.1%), effective in 12 cases (37.5%), 8 cases (25.0%), deteriorated in 3 cases (9.4%), total effective rate was 65.6% (21/32). The total effective rate, the difference was statistically significant ($P < 0.01$).

2.3 scale score before and after treatment both groups before treatment HDS, MMSE and ADL points the difference was not statistically significant ($P > 0.05$), comparable. Compared with before treatment, after treatment, HDS, MMSE and ADL improved in varying degrees points, the difference was statistically significant ($P < 0.05$, $P < 0.01$). Moxibustion group HDS, MMSE and ADL points difference before and after treatment with the western group, the difference was statistically significant ($P < 0.05$, $P < 0.01$), tips moxibustion improve HDS, MMSE and ADL points more effective than western medicine. Table 1.

Table 1 before and after treatment HDS, MMSE and ADL points

Table 1 Scores of HDS, MMSE, and ADL in two groups before and after treatment



2.4 SS and AVP before and after treatment in both groups before treatment, the two groups SS and AVP in cerebrospinal fluid levels of the difference was not statistically significant ($P > 0.05$). After treatment, CSF SS, AVP level was significantly higher than that before treatment, the difference was statistically significant ($P < 0.01$). Moxibustion group SS and AVP difference before and after treatment with Western medicine group, the difference was statistically significant ($P < 0.01$), tips moxibustion increased cerebrospinal fluid levels of SS and AVP effective than western medicine. Table 2.

Table 2 before and after treatment level of SS and AVP

Table 2 Levels of SS and AVP in two groups before and after treatment

** $P < 0.01$, vs before treatment; $\Delta \Delta P < 0.01$, vs Western medicine group.

3 Discussion

The occurrence of VaD and stroke is closely related to blood stasis after stroke, brain network blocked, the five internal organs by the gas shortage on the wing "element of the House of God" and gradually induced dementia.

Prophylactic treatment of VaD focuses on the control of vascular risk factors, namely, primary and secondary prevention of stroke; symptomatic treatment consists mainly of microcirculation, neurotrophic and neuroprotective based, but the effects are still not sure. Previous studies found that acupuncture treatment in improving clinical symptoms of VaD and reduce mortality has a positive effect [9]. The use of moxibustion treatment of VaD in our hospital has accumulated many years of clinical experience in long-term clinical practice, summed up the main acupoints to head the moxibustion, the main point Baihui pressure with monkshood moxibustion, the Court of God, Dazhui with clear moxa moxibustion, the effect is satisfactory. Baihui for the Du Meridian, is the bladder of the intersection points with the Du channel, and the bladder through the hole "into the network brain", "Qian Jin Fang" more "Hundred will be the main evil evil cry out hi forget the wind," said ; Dazhui transferred through the head with blood, promoting blood brain operation of the power network; God tribunal may refreshing tune God. So moxibustion Baihui, God court, Ojo can Huayu network, fill marrow puzzle. The study found that after 4 cycles after treatment, clinical symptom score, intelligent integration and activities of daily living scale score were significantly improved; comparison with the western medicine group found that moxibustion improve the HDS, MMSE and ADL scale score highlights the efficacy of , is superior to conventional western medicine.

Neuropeptide neurotransmitters can play SS or nerve modulators involved in learning and memory processes, and AVP addition to regulating cardiovascular function in temperature regulation, maintenance of circadian rhythms and other functions, or learning and memory controller, and could have rationally processing information, memory consolidation and the formation of conditioned reflex, etc. [10]. The tests showed that the two groups before the cerebrospinal fluid of VaD patients with SS, AVP was significantly lower than after treatment with HDS, MMSE and ADL scale score was positively correlated, suggesting that patients with VaD central SS, AVP concentration is low, a series of interference and learning and memory associated with central neurotransmitter metabolism, which led to the occurrence of VaD and development. After treatment, HDS, MMSE and ADL scale score change significantly, SS, AVP levels were significantly increased, while moxibustion therapy in the head point increase SS, AVP levels more significant role, much better than Western medicine. The results show that the head of acupuncture moxibustion patients by regulating the central SS, AVP concentration to improve the function of the brain vital part of learning and memory may be made --of its better efficacy in patients with VaD treated one of the main. We believe that the treatment of clinically relevant in terms of improved symptom scores or in the regulation of learning and memory associated with the material aspects of

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French. Example 1

The effects of Arnica Montana on blood coagulation •

Randomize clinical trial

[Authors]

SUMMARY

(ETFE study under fGnt of Eshi li Randomized double-blind study plan AOLS, deyait yirfler a sl mickllllllf honaiopathique, Anka Montana eu le sigli6catement time scignement (Silllplate II) and its effects dialre sw diffirents Hngulne coagulation tests. Il was that prodllt Inll .. on various parameters of coagulation la Hngulne among yolontales ss Gll cows minutes Sliva ... Sin administration.

Like many European countries, homeopathy is gaining popularity in Canada. This therapeutic approach is based on the "law of similars)) that a patient can be treated with low doses or infinitesimal substances that cause symptoms similar to those of the disease in healthy subjects. 1 The effectiveness of homeopathy is still hotly contested by the entire scientific community. 2 Considering that rigorous clinical trials are essential to evaluate this therapeutic approach, we began a program of clinical research on homeopathy .3,4 The second study evaluated the effectiveness of treatment of bleeding.

The Arnica Montana is a homeopathic product derived from a plant of my name I owned li family Compositae. I n particular is used to prevent bleeding during or after abdominal surgery, dental or ear, nose and throat and to promote the resorption of blood effusions. It is also used in post-partum period in order to promote hemostasis and bleeding for low or medium abundance such as epistaxis. 1.5 • 8

Unlike many homeopathic medicines whose effect varies, after the theory, according to host characteristics, Arnica Montana would be effective in all individuals. I, 5.8 This product is effective in homeopathic dilutions at or below the fifth "Hahnemann centesimal" (5 CH or dilution 1 OI ~. 1,5,8,9

Although I Arnica Montana is a drug of urgency, the action will begin in the minutes following its administration, studies that evaluated its effects on hemostasis have not documented this aspect.7, 9,10

The objectives of this study were to verify if l'Arnica Montana le shortens bleeding time (Sirnplate II) within a period of 30 minutes after its administration and to describe its effects on various coagulation tests sanguine.

METHOD

This trial randomizes it dinique double-blind study plan cross was made at the Centre Hospitalier de l'Universite Laval with leave of the Ethics Committee of this institution. In group A, subjects received <; u first of Arnica montana 5 CH-saying-it is it the 10/10 dilution during the first experimental session. Two weeks later, they re <; u placebo. In group B, the order of treatment administration was reversed. I I

Eighteen healthy male volunteers were selected. To be improper in the study, subjects should not show any symptom or sign suggesting coagulopathy, suffer from chronic illness, being a smoker or have drug consumption or vitamin during the two weeks before I study.

During the experimental session, a technician in hematology efTectuait bleeding time and collect tubes of blood for further analysis. The subject then took it sublingually and 15 minute intervals two tubes-doses of Arnica montana 5 CH or placebo. The tubes doses prepared by Dolisos Laboratories under the rules of the Homeopathic Pharmacopoeia, eraient identical in appearance. Thirty minutes after taking the second dose tube, the technician again efTectuait bleeding time and collect tubes of blood.

Measures

The main variable studied Hait le bleeding time (Simplate 11) .12 The subject was seated for 15 minutes, his forearms being discovered. le after having gonfte chon man of 40mm Hg sphygmomanometer, eraient made two incisions parallel to the axis of the forearm with the aid of a Simplate II (Organon Teknika). At intervals of 30 seconds, a drop of blood was collected it with the aid of a filter paper. The length of each incision for bleeding was noted and the average of these two values was taken as the bleeding time.

Were also studied platelet count, APTT le, le thrombin time, ie prothrombin time (Quick), ie fibrinogen, factor VIII coagulant and le l'agregation with platelet l'ADP of epinephrine and collagen. To prepare plasma le, le venous blood was first levied in an era of plastic syringe with the aid of a needle Vacutainer (Becton Dickinson). Then he delicately ere pour into a glass tube coated with silicone or mix it with Heb sodium citrate 3.8% in the proportion of neufvolumes for. After 1000 RPM spin it for 10 minutes it 22 ° C, ie platelet-rich plasma (PRP) was first obtained ere used for the platelet count by Coulter STKS. A second centrifugation of the pellet, it 3000 RPM, le yielded platelet-poor plasma (PPP). It is from this substrate efTectues What was the partial thromboplastin time, prothrombin (Quick), thrombin and determinations of fibrin and Ogen faeteur VIII coagulant IL ACL 810 with the reactive Plate flax Excel LS(Organon Teknika), Simplastin (Organon Teknika), Thrombostat (Parke-Davis) and

factor VIII deficient (Organon Teknika). The platelet aggregation in vitro were effected by a PAP-4C aggregometer (Bio Data Corporation) with ADP, epinephrine and collagen (Bio-Data). In order to demonstrate a possible hyperaggregability platelet four concentrations were tested for each of the reagents, or ADP (5,0,2,5, 1.0 and 0.5 $\mu\text{m} / \text{L}$), epinephrine (50.0, 5.0, 2.5 and 1.0 $\mu\text{m} / \text{L}$) and collagen (0.95, 0.48, 0.24 and 0.12 g / L). To the aggregation platelet, 0.45 ml PRP prior adjustment to $250 \times 10^9 \text{L}$ with the aid of autologous PPP was mixed with 0.05 ml of reagent in a silicone pan (diameter = 0.8 mm) with a magnetic bar (1.0 mm x 0, 5 mm) at 1200 RPM and 37°C . The percentage transmittance and slope were recorded. These tests were performed in hematology laboratory of the Centre Hospitalier de l'Universite Laval participant Interlab of quality control and that of the College of American Pathologists.

Analysis

For both periods, the difference between IE and bleeding time of each subject 30 minutes after the treatment (f 30) and the initial bleeding time (TB) was used as the dependent variable. These variables are presented in columns Y1 and Y2 in Table 1. To quantify the difference between the Arnica and placebo, the differences Y1-Y2 (DA) and Y2-Y1 (DB) were calculated respectively for groups A and B. The treatment effect is the average effects obtained for each group. This method of calculation takes into account a possible effect of the period, that is to say the possibility that there is systematic variation between periods 1 and 2 which are separated by an interval of two weeks. Beforehand, it was responsible for the lack of interaction between the treatment and the period, that is to say that no residual effect of treatment remained during the first period was present at the beginning of the second period. Treatment effects for all variables and confidence intervals were calculated following the appropriate method for clinical study plan with crosses. 15

RESULTS

Eighteen men aged 22 to 46 years and whose average age was 32 years completed the study. One subject was excluded from the analysis because the length of time of initial bleeding during the first experimental session was longer than 9.5 minutes, which is higher than normal (2.3 to 9.5 minutes) after the monograph Simplate II. Individual differences between the bleeding time as Arnica montana and placebo for both groups are presented in Table 1. For group A, one observes that the effect of Arnica montana is an increase in bleeding time (T30-To) of 0.59 minutes, while for group B, the effect is to reduce this difference 0.28 minutes for an average effect of 0.16 minutes (95% CI -0.70 to 1.02) (Table 2).

Fibrinogen decreased significantly as Arnica montana, the difference being of -0.16 g/L (95% CI -0.27 to -0.04) (Table 2). The treatment had no statistically significant effect on the partial thromboplastin time, prothrombin time, the thrombin time, platelet count and factor VIII coagulant (Table 2). Finally, no significant change in platelet aggregation is demonstrated for the four dilutions of collagen, epinephrine and ADP (Table 3).

DISCUSSION

The evaluation of homeopathic treatment is usually complicated by the fact that the therapeutic response, after a theory, depends on the characteristics of individuals. To avoid this pitfall, we selected a treatment deemed effective for all individuals and several dilutions. 1, 5, B, 9 The choice of a high concentration of Arnica montana (5 CH OR $\cdot 1 \sim 10$) was chosen because at this dilution there is more substance called active molecules in homeopathic medicine.

Unlike the original hypothesis, this study demonstrated no decrease in bleeding time in Arnica montana compared to placebo in 17 healthy men. Bleeding time is usually used to detect an abnormal hemostasis may prolong the duration of bleeding in an individual. In this research, however, it was expected a shortening of bleeding time in subjects with normal haemostatic as observed previously after administration of desmopressin (DDAVP). In effect, a randomized double-blind study showed it in patients normal haemostatic a decrease of 22.4% in bleeding time in the group treated with DDAVP compared with the control group (-1, 3 min. CI 95%: -1.8 to 0, 8) .16

Given the lack of significant difference between the bleeding time as Arnica montana and placebo, no one has redone the computation of statistical power. The mean baseline bleeding time was 6.25 minutes. By asking the hypothesis a difference of about 20% of this variable could be observed as in the study on DDAVP, we calculated the statistical power to detect this difference is 80% which is satisfactory. 1G, 1i

This study has shown no change in other hemostatic parameters that may suggest a biological effect of Arnica montana. The only statistically significant difference observed in this study is a decrease in fibrinogen Arnica montana g/L of -0.16 (95% CI -0.27 to -0.04). The clinical significance of this observation is doubtful since the difference is small and is isolated. Indeed, no changes in other parameters of blood coagulation suggesting an effect of Arnica montana has been demonstrated.

Study it in a double-blind study of 39 patients hospitalized in a surgical ward for various diseases, we observed an increase in platelet aggregation with collagen, epinephrine and ADP after three weeks of treatment with Arnica montana 5 CH. These results should be interpreted with caution because this study had significant methodological problems. Indeed, the nature of the diseases suffered by participants and subjects taking drugs capable of altering the coagulation tests are not described in the article. Furthermore, the aggregation technique used is not specified and the results are not subjected to statistical analysis. If these findings were replicated in a methodologically rigorous, they suggest a long-term effect of Arnica montana on hemostasis.

CONCLUSION

This study in healthy men has not shown that Arnica montana has a clinically or statistically significant effect on bleeding time in minutes after administration. In addition, no clinically significant difference between observed Arnica montana and the placebo for other blood coagulation tests evaluated in this research. •

Requests for reprints may be sent to share Lucie Baillargeon, Clinical Research Unit midécine family, Centre Hospitalier de l'Université Laval, 2705 Blvd. Laurier, QC SainteFoy GI V 4G2

ReIDercielDents

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Table 1: Values of individual tern.ps saignern.ent (Sirn.plate II) of 17 subjects in Arnica Montana and placebo.

GROUPE A (ARNICA/PLACEBO)							
SUJET	PERIODE 1			PERIODE 2			DA
	T ₁ *	T ₃₀ **	Y ₁ ***	T ₀	T ₃₀	Y ₂ ***	Y ₁ -Y ₂
1	7,5	6,0	-1,50	10,5	7,0	-3,50	2,00
2	6,5	5,0	-1,50	6,5	6,0	-0,50	-1,00
3	7,5	6,5	-1,00	6,0	5,0	-1,00	0,00
4	6,5	5,8	-0,75	6,5	6,5	0,00	-0,75
5	5,8	8,0	2,25	3,5	4,3	0,75	1,50
6	7,0	6,5	-0,50	6,0	5,8	-0,25	-0,25
7	5,8	6,0	0,25	6,0	7,3	1,25	-1,00
8	3,5	6,8	3,25	5,5	4,5	-1,00	4,25
MOYENNE	6,25	6,31	0,06	6,31	5,78	-0,53	0,59
GROUPE B (PLACEBO/ARNICA)							
SUJET	PERIODE 1			PERIODE 2			DB
	T ₀	T ₃₀	Y ₁	T ₀	T ₃₀	Y ₂	Y ₂ -Y ₁
9	5,0	6,5	1,50	5,5	5,5	0,00	-1,50
10	8,0	8,0	0,00	7,0	6,0	-1,00	-1,00
11	5,0	5,5	0,50	4,0	4,5	0,50	0,00
12	5,5	6,5	1,00	6,5	7,5	1,00	0,00
13	5,0	4,0	-1,00	8,0	6,0	-2,00	-1,00
14	6,3	5,3	-1,00	5,0	7,0	2,00	3,00
15	6,0	7,5	1,50	9,5	9,0	-0,50	-2,00
16	5,0	5,8	0,75	4,5	4,8	0,25	-0,50
17	7,5	6,8	-0,75	8,8	8,5	-0,25	0,50
MOYENNE	5,92	6,19	0,28	6,53	6,53	0,00	-0,28

Groupe = group

Moyenne = average

Periode = period

* T: Time of initial bleeding

** T3: Bleeding time 30 minutes after treatment

*** Y₁ and Y₂: T₃-T₀

Table 2: Effect of Arnica montana on le bleeding time (Simplate II), ie partial thromboplastin time, prothrombin time le, le thrombin time, platelet count la, le and le fibrinogime factor VIII coagulant.

VARIABLES DIFFÉRENCE*	ARNICA-PLACEBO	(I.C. 95%**)
T.saignement (min.)	0,16	(- 0,70 à 1,02)
T.céphaline (sec.)	0,28	(- 0,05 à 0,62)
T.prothrombine (sec.)	0,05	(- 0,04 à 0,13)
T.thrombine (% du témoin)	0,57	(- 0,75 à 1,89)
Plaquettes (x10 ⁹ /L)	-5,44	(-12,99 à 2,04)
Fibrinogène (g/L)	-0,16	(- 0,27 à -0,04)
Facteur VIIIc	-0,06	(- 0,13 à 0,01)

VARIABLES DIFFERENCE "

T.saignement (min.)

T.eephaline (sec.)

T.prothrombine (sec.)

T.thrombine (% of control)

Platelets (x 09 l / L)

Fibrinogen (GIL)

Faeteur VIIIc

* Différences between variables (T30 - T1 as Arnica Montana and placebo

** Interval confidence 95%

Table 3: Effect of Arnica montana on platelet aggregation with collagime, adrenaline and l'ADP.

	PENTE* (I.C. 95%)**		% TRANSMITTANCE* (I.C. 95%)**	
COLLAGÈNE (g/L)				
0,95	5,32	(-3,57 à 14,21)	8,29	(-1,15 à 17,73)
0,48	-0,08	(-7,99 à 7,83)	-0,56	(-20,89 à 19,77)
0,24	1,23	(-6,69 à 9,16)	-2,94	(-21,04 à 15,16)
0,12	3,91	(-2,84 à 10,65)	12,41	(-8,92 à 33,74)
ADRÉNALINE (um/L)				
50,00	1,39	(-2,71 à 5,48)	5,03	(-6,07 à 16,13)
5,00	0,07	(-2,18 à 2,32)	4,13	(-3,38 à 11,63)
2,50	-1,15	(-3,01 à 0,71)	6,72	(-6,11 à 19,56)
1,00	-0,46	(-2,91 à 2,00)	8,43	(-7,40 à 24,26)
ADP (um/L)				
5,00	0,10	(-4,46 à 4,65)	0,94	(-9,60 à 11,49)
2,50	0,88	(-2,51 à 4,26)	0,35	(-3,11 à 3,80)
1,00	-0,51	(-1,88 à 0,86)	1,19	(-0,51 à 2,90)
0,50	-0,31	(-2,09 à 1,47)	0,69	(-0,40 à 1,78)

Pente = slope

* Differences between variables (Tif / TJ as Arnica Montana and placebo

** Intervalle corifiance of 95%

French. Example 2

Dietary treatment
1'hypercholesterolemie slight
has mo6eree
Efficacite d? Ffrentes interventions
[Authors]

Objective To compare 1'efficacite in the treatment of hypercholesterolemia 1egere to moderate, a brief dietary intervention made by a family physician or group sessions that taught individually by a dietitian.

DESIGN Randomized clinical trial.

BACKGROUND Clinic family medicine in remote areas. TOPICS lcr Between September 1991 and September 30, 1992, 135 hypercholesterolemic men and women between 20 and 60 years were recruited and randomized into three groups to learn hypocholesterol6miant regime of the American Heart Association. Participants had to submit a higher LDL cholesterol levels at desirable rate according to the criteria of the Canadian Consensus Conference on Cholesterol.

INTERVENTIONS Three m6thodes teaching the Plan have an assessed: 1'enseignement individual by the family doctor has his office (Phase I), group sessions with a dietitian and a m6decin (phase II) and individual instruction by aDietitian (Phase II). All participants were followed for six months e four games with educational and blood samples every 2 months.

MAIN OUTCOME MEASURES s6riques reduction rates of total cholesterol, LDL cholesterol, HDL-cholesterol and triglycerides ae measured after 2, 4 and 6 months of dietary intervention. The amendment of certain risk factors (smoking, weight, physical activity) and the index of cholesterol / saturated fatty acids, were evaluated.

RESULTS 99 subjects completed the 6 month diet. The average reduction in LDL-cholesterol was 0.08 mmol / L (1.8%) in group doctor, 0.07 mmol / L (1.6%) in group sessions and 0.28 mmol / L (6.3%) in the dietary groups ($p = 0.94$). A reduction of 10% or more of the initial rate of LDL-cholesterol was observed in 27% of subjects in the doctors and almost 40% of subjects in both groups ($p = 0.4$ 1). The intervention also resulted dietetiquc decreased weight, smoking and dietary intake of fat and increased physical activity.

CONCLUSION The dietary approach is the method of classical education is most effective. The family physician should focus on detection and contr6le other risk factors for cardiovascular disease rather than teaching the Plan.

DTH Gaudreault and Gosselin are doctors and Mtm Guillemette is dieteiste Health Centre in Port-Cartier. OF Verreault is an assistant professor in the Department of Social MAdecine etpre'venitive UniversiM of Laval.

The HYPERCHOLESTEROLEMIA ES'T A MAJOR risk factor for heart disease and affects nearly half of Canadians. " The different agencies nationauxx2-6 involved in the treatment of lipid disorders recommend that physicians detect and treat high cholesterol. For family physicians practicing in certain areas eloigne'es as the North Shore is a challenge because there is a high prevalence of hypercholeste'rolemie and insufficient resources Dietary.

This study compares the degree of lowering of plasma lipids after 6 months of teaching dietetics, provides individually by the family physician in his daily practice or in groups by a dietitian and a doctor, that obtained by an intervention di ' tetique standard.

METHODOLOGY

This randomized clinical trial was held in Port-Cartier, a community of 8713 inhabitants, located 900 km northeast of Montreal. lcr between September 1991 and September 30, 1992, men and women of the region aged 20 to 60 years who consulted their family physician were offered their serum total cholesterol blood (TB), if n 'had not had during the last year. A lipid control, including TB, triglycerides and measurement of lipoprotein cholesterol and low high-density (HDL-C and LDL-C) was performed if the initial level of CT exceed 4.6 mmol / L among people aged 20 to 29 years or 5.2 mmol / L in those aged 30 and over, according to the criteria of the Canadian Consensus on the second cholesterol.2 A complete lipid profile has been 'performed when the difference between first two results of CT was greater than 0.6 mmol/L.7

The subjects eligible for the study were to sign a consent form and have a level of LDL-C located in the boundary zone (3.4 to 4.2 mmol / L for persons aged 30 and over, or 3, 0 to 3.7 for those between 20 and 29 years) or high (greater than 4.2 or 3.7 depending on age). For all subjects, the low-fat diet was the first stage of treatment. The exclusion criteria were severe hyperlipidemia (LDL-C > 7 mmol / L or triglycerides > 4.5 mmol / L), secondary hypercholesterolemia, body mass index greater than 35, pregnancy, heart surgery or most during the last 3 months and participated in a scheme for other reasons (eg. the diab'ete).

Randomization of participants was performed sequentially in one of three treatment groups dietetics in order of entry into the study, by stratifying by age (20-29 years, 30-60 years) and sex. Between May and August, in 1992, no group session has been organized and recruited new subjects were randomized into two groups.

The two phases of the diet of the American Heart Association⁴ were used as part of the study. Phase I is to reduce daily energy intake total fat less than 30% of total calories and that saturated fats to less than 10% and reduce consumption of cholesterol below 300 mg. Phase II, more severe, aims to further reduce intake of saturated fat to less than 7% of total calories and cholesterol less than 250 mg. The two regimes are a total number of calories to achieve or maintain weight associated with good health.

Each treatment group had four meetings on education SPREAD 6 months. Physician group had individual meetings of 20 minutes every two months with the treating physician. A leaflet containing the main components of the Phase I was then given to the participants. Simpler than the regime of phase II, the Phase I could be more easily adaptable to the daily practice of family physicians. All physicians attended at baseline at a meeting to standardize the teaching of the Plan. The group sessions were facilitated by a dietitian and a physician and the regime of phase II was taught. It was attended by eight participants's accompanying their spouses. In a period of 2 hours per week, sessions were held for 3 consecutive weeks followed by one last meeting after four months. In the dietary groups, individual instruction, classical (phase II diet) was provided by the dietitian. The first meeting lasted 45 minutes and others 20 minutes. One dietitian involved in the project and met all the subjects of his group. At each meeting, adherence to dietary recommendations was checked by the doctor in revising the Plan with the patient or by the dietitian by revising the food diary.

A self-administered questionnaire on the ant & familial history and personal risk factors for cardiovascular disease (CVD), lifestyle and diet has been given to each participant at the beginning and the end of the study. Food consumption of fat in patients was estimated using the index of cholesterol / saturated fatty acids (ICS) ⁸ according to data from food frequency questionnaires. An estimate of the average size of the portions was used for men and women.

For each participant, a complete lipid profile was performed after 2, 4 and 6 months of diet. The base level of lipids was established using the results of the full dose of serum lipids or the average of assays when more than a full lipid profile had been performed initially. The average reduction of fat was calculated by averaging the differences between the core and the lipid content of each participant. The blood samples were collected at fasting by a nurse qualified respecting the criteria of prelevement.⁷ Blood tests were performed using a device type Cobas Mira - certify the provincial standardization of lipid analysis. CT, HDL-C and triglycerides were determined by enzymatic method. LDL-C was calculated using the equation of Friedwald⁹ when the triglyceride level was below 4.5 mmol / L. Analysis of variance was used to compare the mean reduction of lipids and the X² test or Fischer to compare proportions.

RESULTS

Of the 135 subjects recruited, 36 (27%) did not complete 6 months of planned follow-up and were excluded from the study. Subjects who dropped are distributed equally in the three treatment groups. They differ from participants by the following characteristics: more men, more often smokers and drinkers, less physically active and presenting initial rates of TC and LDL-C slightly higher.

Table 1 shows a similar distribution of baseline characteristics between groups. The average level of TC are at 6.38 mmol / L for the ensemble groups and the level of LDL-C 4.43 mmol / L.

In the dietary groups we found the most marked reduction in mean TC with 0.47 mmol / L (95% CI, 0.23 to 0.71 mmol / L) or 7.4% after 6 months of dietary intervention (Table 2). The reduction in LDL-C was also more marked in the dietary groups with 0.28 mmol / L (95% CI, 0.03 to 0.52 mmol / L) or 6.3%. In the physician group, the mean reduction in LDL-C has been of 0.08 mmol / L (95% CI, 0.16 to 0.33 mmol / L) and in group sessions of 0.07 mmol / L (95% CI, -0.26 to 0.40 mmol / L). In all groups, the mean level of HDL-C was a slight reduction of less than 0.1 mmol / L after 6 months of the regime. The average triglyceride level was only in the doctor group. For the ensemble groups, subjects initially presenting a level of LDL-C limit has increased by an average rate of LDL-C by 0.19 mmol / L (2.8%), while those of high rate of have reduced from 0.35 mmol / L, or 7.3% (p <0.001).

In all groups, the reduction of serum lipid levels was maximal after the second month of dietary intervention (Figures 1 and 2). After 4 months of diet, the average reduction in LDL-C was less important in all three groups and remained stable until the sixth month.

After 6 months, a reduction of 10% or more of the initial rate of LDL-C was obtained in more participants dietary groups (41.7%) and group sessions (37.5%) than in group doctor (27.0%) (Table 3). For all groups, 20.6% of subjects had an initial level of LDL-C limits have reduced their rates by 10% or more after 6 months of diet. This proportion has s'leeve more than double (44.3%) when the initial level of LDL is eevee ($p = 0.04$).

At the end of monitoring, some lifestyle changes were observed among participants (Table 4). In all three groups, the average weight was lower (1.2 kg) and the average consumption of fat (reduction of ICS to 18.6). A decrease in smoking was obtained in 10 of 24 smokers. Over a third of people said they had increased their physical activity.

DISCUSSION

In our study, a rather modest average reduction in the rate of TC and LDL-C was observed in all three groups. Of the three studied methods of teaching, the traditional dietary approach seems to be the best to correct the lipid profile of subjects with hypercholesterolemia slight, to moderate. In all groups, l'efficacite the regime was at its maximum after the first 2 months of dietary changes. The improvement of lipid profile in the diet was mainly observed in subjects with initially high rate of TC and LDL-C, while the response was minimal in those rate limits. The intervention has also effected to reduce risk factors for CVD

Subjects who abandons l'etude during follow-up had an average TC and LDL-C over high, and a greater number of risk factors for CVD than subjects who completed the study. Despite these withdrawals, the basic characteristics of participants who completed the study remained similar in all three groups, limiting selection bias. The size of each group was calculated initially has 60 individuals, but recruitment of participants slower than expected and the loss of subjects during follow-up have reduced the size of groups, thus affecting the power of our study is that a 0, 70, fixing the error oc 'was 0.10 and the diff6-ence to be detected by 0.5 mmol / L. The low power of the study allows only for patterns for the majority of the measures presented and proves the main weakness of the study.

The reduction of CT obtained after 6 months of diet in the three groups is comparable to the results of some previous studies in which a reduction is observe'e TB from 0% to 4% with the diet phase I and 5 to 15 '0 o % for the phase 1.j10-20 Over a third of study participants showed a reduction of 10% or more of their initial rate of LDL-C. Such a reduction could lead to long-term reduction of 16% has 19% risk MCV2 '

The subjects in our study with a baseline LDL-C limit have not improved their lipid profile with the follow dietetics. This suggests that dietary intervention should target individuals who have high levels of LDL-C, as recommended by the Canadian Task Force on the Periodic Health Examination. "3 The people with hypercholesterolemia and two factors limit risk could benefit more from changing any other dietary habits.

The dietary treatment of hypercholesterolemia remains l'etape initial therapeutic preferred by the majority of physicians famille.²² "2 The results published in 1990 by Tannenbaum²⁵ have shown that half of Canadian physicians surveyed's choosing to give themselves the dietary advice has 40% of their patients with lipid disorders. Our study suggests, however, that dietary intervention by the family physician, Fagon effected by short in the context of his office practice, has a limited impact on towards the betterment of profile lipid.

Dietetics education in group sessions did not show as good as the individual intervention by the dietitian. The distribution of different teaching encounters in this group has probably done more quickly lose the motivation to follow the diet. Optimizing this method would quickly and effectively disseminate information dietetics. o

Correspondence to: OF Peter Gosselin, Health Centre in Port-Cartier, 103 Boulevard. Rochellais, Port-Cartier QC G5B 1K5

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Table 1. Distribution of basic characteristics by treatment group under consideration in early

(CHARACTERISTICS)	TREATMENT GROUPS			P
	PHYSICIAN (N = 38)	GROUP SESSIONS (N = 25)	DIETARY (N = 36)	
Average age	43	46	45	0,21
Strata of age (n)				
20 -29 years	4 7	2 6	2 6	0,42
30 -39 years				
40 -49 years	17	5	16	
50 -59 years	10	12	12	
Men (%)	47	32	44	0,46
Mari6 (%)	92	83	83	0,44
Average tuition	10	11	10	0,91
IMCT average	27	26	28	0,60
ICS * Average	53	56	51	0,68
Smoking (%)	29	21	26	0,78
Consum. alcohol (%) (> 1 consom. / wk.)	32	25	20	0,53
Activitephysique (%) (> 1 time / wk.)	45	50	49	0,91
TC (mmol / L)	6,34+0,71	6,43+0,64	6,38 +0,83	0,65
C-1, DL (mmol / L)	4,44+0,70	4,40 +0,64	4,44 +0,70	0,84
HDL (mmol / L)	1,15 +0,28	1,20 +0,34	1,18 +0,41	0,55
LTriglyc6rides (mmol / L)	1,66+0,79	1,82+0,84	1,68 +0,63	0,43

* Index of cholesterol / saturated fat = (1.01 * saturated fat) + (0.05 * mg cholestMrol)

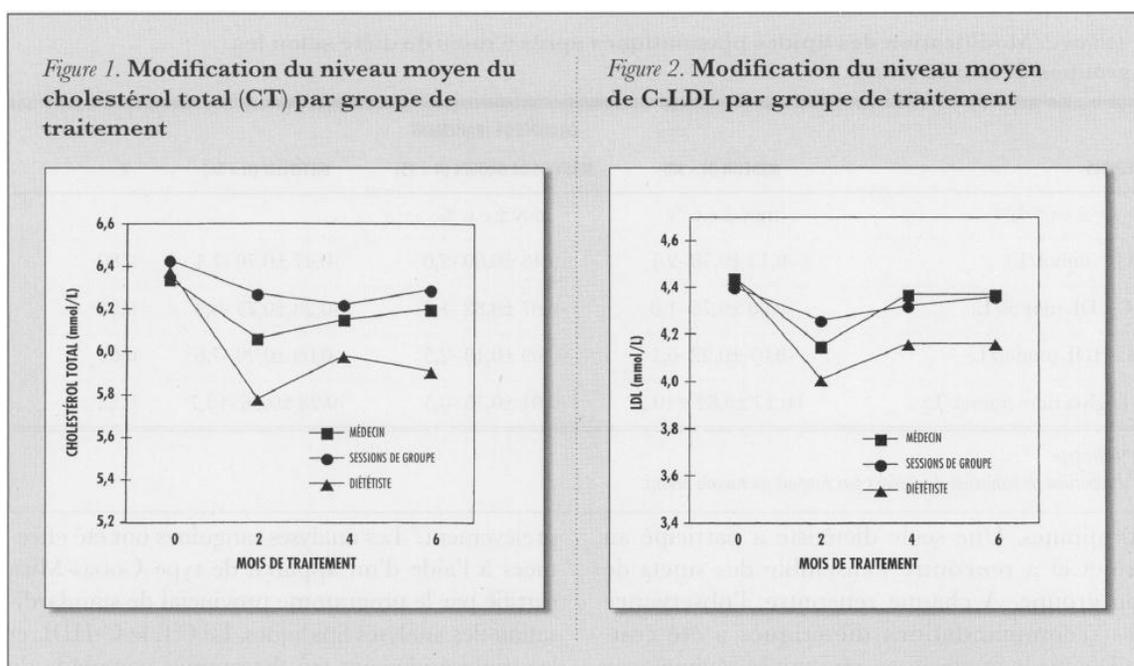
t Body Mass Index

Table 2. Modification of serum lipids after 6 months of diet according treatment groups

LIPID	TREATMENT GROUPS			P
	PHYSICIAN (N = 38)	GROUP SESSIONS (N = 25)	DIETARY (N = 36)	
Avg ± SD *% t	Avg ± SD %	Avg ± SD %		
TC (mmol / L)	-0,13 +0,78 -2,1	-0,13 +0,80 -2,0	-0,47 +0,70 -7,4	0,80
LDL (mmol / L)	-0,08 +0,76 -1,8	-0,07 +0,82 -1,6	-0,28 +0,75 -6,3	0,94
HDL (mmol / L)	-0,07 +0,22 -6,1	-0,03 +0,18 -2,5 l.....	-0,09+0,26 -7,6	0,63
Triglycerides (mmol / L)	+0,17 +0,82 + 10,2	-0,01 +0,75 -0,5	-0,23 +0,56 -13,7	0,22

* standard deviation

t Percentage of fat reduction from the initial level.



Can't translate. Sorry.

Table 3. Proportion of participants who have reduced by 10% and their level of TC and LDL-C, by treatment groups and according to the initial level of LDL-C

TREATMENT GROUPS	CT REDUCTION OF 10% AND MORE			REDUCTION OF LDL BY 10% AND MORE		
	N*	%	P	N	%	P
Médecin	38	26,3	0,79	37	27,0	0,41
Group Sessions	25	33,3		24	37,3	
Diététiste	36	28,0		36	41,7	
ORIGINAL LEVEL OF LDL						
Limit	41	26,8	0,65	36	20,6	0,04
Pupil	58	31,0		61	44,3	
Total	99	29,3		97	35,1	

| *. gloomy subjects in each group.

Table 4. Weight change, consumption of fat, smoking and physical activity at the end of 1'etude, by treatment group

	WEIGHT		ICS *		TOBACCO		PHYSICAL ACTIVITY	
					(SMOKERS ONLY)			
TREATMENT GROUPS	LOW AVERAGE		LOW AVERAGE		REDUCTION (CONSUMPTION)		INCREASE ACTIVITY	
	Nt	KG	N		N	%	N	%
M6decin	35	0,76	32	17,1	9	33,3	35	34,3
Group Sessions	20	0,73	22	22,5	6	66,7	24	37,5
Dieteiste	33	2,01	23	18,1	9	33,3	35	42,9
p	0,78		0,36		n.d.-		0,76	
Total	88	1,20	77	18,6	24	41,7	94	38,3

* Index of cholesterol / saturated fatty acids = (1.01 * saturated fat) + (0.05 * mg cholestirol)

tj number of results available

- Not available

French. Example 3 (html)

■ Summary

Treatment of acute maxillary sinusitis in adults Comparison of cefpodoxime proxetil- amoxicillin-clavulanic acid and

Objective> The WAS loved to Demonstrate The equivalence of the clinical efficacy and safety of cefpodoxime proxetil-(200 mg/50 mg) for 5 days to amoxicillin-clavulanic acid (1 g/125 mg b.i.d) for 5 days in acute maxillary sinusitis Adults with.

Method> In this prospective, multicenter, centrally-randomized, open-label study, 73 General Practitioners and 11 ear, nose and throat Specialists included 512 patients With acute unilateral maxillary sinusitis.

Results> The clinical success at day 12-19 in the per-protocol population (primary analysis) were 92.3% (215/233) in the cefpodoxime-proxetil group and 93.6% (204/218) in the amoxicillin-clavulanic acid group. The 95% confidence interval of [6.5%, 3.9%] to conclude non-inferiority of cefpodoxime-proxetil versus amoxicillin-clavulanic acid. Cure Rates at follow-up (day 25-30) were 90.6 and 92.7%, respectively. Similar results were in the intention-to-treat population. Compliance WAS Significantly Better In The cefpodoxime-proxetil group (99.2% versus 95.5%, $p = 0.011$). Tolerability was confirmed by analysis in the population

Volume 35> No. 1> January 2006> Book 1

■ Summary

OBJECTIVE: The objective of this study was to compare the clinical effectiveness and tolerance of cefpodoxime proxetil, at the daily dose of 400 mg in 2 doses for 5 days *versus* amoxicillin-clavulanic acid at a dose of 2 g/250 mg per day in 2 doses in the treatment of acute maxillary sinusitis

Method: In this prospective, multicenter, randomized, open, 512 adult patients with maxillary sinusitis were included according to criteria established by the French Agency for Safety of Health Products (AFSSAPS) and 11 specialists (ENT).

Results: The clinical success rate between J12 and J19 in the population per-protocol population (primary analysis) were 92.3 (215/233) and 93.6% (204/218) in the cefpodoxime-proxetil group and amoxicillin-clavulanic acid, respectively. The confidence interval was [6.5%, 3.9%] to conclude non-inferiority of cefpodoxime-proxetil *versus* amoxicillin-clavulanic acid. The clinical cure rates at follow-up visit (J25-J30) were 90.6 and 92.7% in the cefpodoxime-proxetil group and amoxicillin-clavulanic acid, respectively. These results were confirmed by analysis in the population

33

Significantly better: 1.2% (3 / 247) of cefpodoxime proxetil versus amoxicillin-clavulanic acid (99.2 versus 95.5%, p = 0.011) and similarly, tolerance was significantly better in the cefpodoxime-proxetil versus amoxicillin-clavulanic acid group (p < 0.001). In this study, a 5-day course of cefpodoxime proxetil was significantly better in the cefpodoxime-proxetil versus amoxicillin-clavulanic acid with a rate of patients reporting an adverse event related to treatment of 1.2% (3/247) and 10.7% (26/244) respectively (p < 0.001). The majority of adverse events related to treatment order was gastrointestinal and mild to moderate.

Polonovski JM, El Mellah M. Treatment of acute maxillary sinusitis in adults. Efficacy and safety of cefpodoxime proxetil versus amoxicillin-clavulanic acid. Presse Med. 2006, 35: 33-8. © 2006, Masson, Paris

CONCLUSION: In this study, a 5-day-per cepodoxime-proxetil 400 mg / day is clinically as effective as 8-day treatment with amoxicillin-clavulanic acid 2 g/250 mg / day with a better tolerance and compliance.

L

has acute infectious sinusitis is an infection or more sinus cavities by a viral or infectious agent bacterial and often occurs with the waning of viral respiratory, such as nasopharyngitis. Inadequately treated or untreated, acute bacterial sinusitis may develop to chronic or complicated by orbital cellulitis, bone-téomyélite with bacterial meningitis or life-threatening important for the patient [1, 2]. The diagnosis of acute bacterial sinusitis is formal in the case of isolation of the bacterium this isolation is rarely performed routinely. In addition, radiography of the sinuses is indicated in cases of clinical doubt diagnosis is mainly clinical and antibiotic probabilistic. The goal of antibiotic therapy is twofold: to reduce intensity and duration of symptoms and decrease the incidence of locoregional complications.

The bacterial epidemiology and the evolution of resistant antibiotic resistance, led to limit the choice of antibiotic in-1 rfor the treatment of acute sinusitis. The duration of antibiotic treatment, established empirically, conventionally is 7 to 10 days. However, changing regimens favors shorter duration of treatment for infections of moderate severity, treatment short could have several advantages: better compliance, better tolerance, lower impact on bacterial ecology [3].

In The activity of cefpodoxime in the two main agents pathogens causing acute sinusitis (*Streptococcus pneumoniae* and *Haemophilus influenzae*) is stable over time [4, 5]. In addition, the cefpodoxime-pimtil has proved effective in treating short 5 days in the treatment of acute sinusitis [6] and is recommended by treating ment of 1 rfor this indication [1, 2]. It was therefore interesting to evaluate the effectiveness of cefpodoxime proxetil in acute maxillary sinusitis and this in a context of practical with current policy, in particular, the involvement of doctors GPs, so the choice of the population was made to include according to criteria recommended in the clinical recommendations AFSSAPS (French Agency for Safety health products) [1]. The comparator was amoxicillin-clavulanate (1 g/125 mg) in 2 doses per day, for new-formulation marketed in France since 2000 [7]. This antibiotic is also one of those recommended by Afssaps [1, 2]. The objective of this study was pragmatic comparing cefpodoxime proxetil 200 mg-x 2/day for 5 days versus amoxicillin-clavulanate 1 g/125 mg x 2/day for 8 days in the treatment of maxillary sinusitis lar acute.

What was known

- An authorization for placing on the market (AMM) with a short pattern for most of the antibiotics recommended in the maxillary sinus acute (SMA).
- The diagnosis of SMA is mainly clinical in general practice.

What does this article

- The demonstration that a short regimen (5 days) cefpodoxime proxetil, is significantly effective as a schema Conventional (8 days) with amoxicillin clavulanate.
- A short regimen promotes adherence and tolerance.
- The rhinoscopy using an otoscope would strengthen the diagnosis clinical practice of general medicine.

Patients and methods

French study of phase IV, prospective, multicenter, randomized (1:1), open, was conducted between October 2000 and June 2004 by 73 GPs and 11-otorhinolaryngological (ENT). The main objective of the study was to evaluate the non-inferiority clinical effectiveness of cefpodoxime proxetil at a dose of 200 mg x 2 daily for 5 days versus amoxicillin-clavulanate at a dose daily of 1 g/125 mg x 2 for 8 days in the population *per* protocol for the evaluation visit between J12 and J19 in acute maxillary sinusitis in adults. The study protocol received the favorable opinion of the Advisory Committee of persons undergoing biomedical St. Germain-en-Laye, September 29, 2003.

Patients

Eligible patients must be aged 18 and over having acute maxillary sinusitis characterized by pain unilateral character associated with one of the following symptoms evolving for more than 72 hours but less than 10 days: Augmentation of rhinorrhea and its purulence, persistence or infraorbital sinus pain increased despite symptomatic treatment taken by the patient for at least 48 hours. Were excluded from the study patients had 3 episodes of acute maxillary sinusitis in the year or more preceding, patients with non maxillary sinusitis, a sinus Site subacute or chronic sinusitis of dental origin probable, sinusitis justifying or warranting puncture drainage or other surgical procedure, sinusitis or rhinitis allergic as well as patients with lesions anatomique obstructive nasopharyngeal known.

Treatments

According to the order of randomization centrally patients received either cefpodoxime proxetil-, 200 mg x 2 per day during for 5 days, or amoxicillin-clavulanate, 1 g/125 mg x 2 daily for 8 days. Taking another antibiotic for topical or general well an anti-inflammatory topical, inhaled or general was not allowed. Were allowed only the vasoconstrictors (Local corticosteroid without partner) during the first 3 days after inclusion, acetaminophen or other non-analgesic anti-inflammatory and nose washes with serum physical Physiology.

Conduct of the study

Patients were evaluated at three visits made: the inclusion (V1), the assessment visit between J12 and J19 (V2) and the difference in clinical success rates between the cefpodoxime proxetil and amoxicillin-clavulanic acid in the V2 population *per* protocol. A lower bound of the confidence interval > -10% To conclude non-inferiority of cefpodoxime-

Effectiveness evaluation

The primary endpoint was clinical response (success / failure) determined to V2 in the *per* protocol. This population includes patients randomized who received at least 80% of treatment, meeting the criteria for inclusion and non-inclusion and showing no major breach of protocol.

Clinical success was defined as:

- the disappearance of clinical signs of maxillary sinusitis acute or persistent nasal obstruction alone;
 - improvement of symptoms or clinical signs without administration of any antibiotic V2.
- Clinical failure was defined as:
- administering an antibiotic to V2 because of the persistence or worsening of pain and / or character of purulent rhinorrhea and / or nasal obstruction and / or persistence fever;
 - the emergence of an infectious complication of sinusitis maxillary acute;
 - the administration of an antibiotic other than salaries of the test prescribed for the disease being studied for failure efficiency or when an adverse event leading to arrest early treatment;
 - conducting a puncture-drainage between V1 and V2 lack of efficacy;
 - lack of information after V1.

The secondary endpoint was clinical response (cure / failure) to V3. Healing was defined as a success without relapse V2 the waning and without antibiotics administered for sinusitis and / or its complications. Clinical failure was defined by failure to V2 or relapse between V2 and V3. A scientific committee evaluated each observation without the knowledge of assigned treatment.

Evaluation of tolerance and compliance

Safety was assessed by adverse event report were described by their nature, frequency, gravity, duration, and accountability (possible or probable) to the antibiotic taken. Compliance was assessed from the comp-Tag tablets reported. It was considered correct if were taken $\geq 80\%$ of theoretical taken.

Statistical methods

Two populations were defined to evaluate the clinical effectiveness technique: the intention to treat population comprising all randomized patients who received at least one dose of treatment, and the *per* protocol described above. The analysis of the primary was conducted using an approach Non-inferiority was based on the confidence interval 95% difference in clinical success rates between the cefpodoxime proxetil and amoxicillin-clavulanic acid in the V2 population *per* protocol. A lower bound of the confidence interval > -10% To conclude non-inferiority of cefpodoxime-

Original article

proxetil vs. amoxicillin-clavulanate at the threshold of 2.5% (One-tailed test). The calculated number of patients evaluable for the protocol was 410 in total with a success rate of clinical expected 90% in each group.

Results

Population

In total, 512 patients were enrolled by 73 general practitioners and 11 ENT specialists. Twenty-one patients were excluded from the ITT population (1 for lack of randomization, 2 for treatment assigned unknown, having taken a treatment in the ITT population (1 for lack of randomization and 7 no treatment for non-verified sources in cefpodoxime-proxetil group: CPD, 5 had taken no treatment and 5 for non-verified sources in the amoxicillin-clavulanate: AAC) and 40 patients additional excluded from the *per* protocol population (14 patients in the PCD group and 26 in the AAC). The reasons are shown in *Table I*. Thus the intent-to-treat process consisted of 491 patients (247 patients in the

PCD group and 244 patients in the AAC) and the population included in the ITT protocol in 451 patients (233 patients in the PCD and 218 patients in the AAC).

Patients in the ITT population were mean age 44.6 years with a median of 42 years; 62.7% were women. Twenty-six patients in each group had a predisposing factor (diabetes, rhinitis, sinusitis, asthma). Smoking was found in only 22.7% (56/247) of patients in the cefpodoxime-proxetil group and 31.6% (77/244) of patients in the amoxicillin-clavulanate group.

The first signs of acute maxillary sinusitis were apyrexia with a median of 4 days before inclusion. Characters such as pain, the signs and symptoms as well as data from the examination of the nasal cavity were similar in the 2 groups (*Tables II and III*).

Clinical Efficacy

In the *per* protocol population, the success rate of J12-19 (Primary analysis) was 92.3% (215/233) in group PCD and 93.6% (204/218) in the AAC group. The interval 95% confidence was [-6.5%, 3.9%]. The lower bound of the confidence interval was > -10% and concluded non-inferiority of cefpodoxime-proxetil *versus* amoxicillin-clavulanate.

The cure rate at D25-D30 were respectively 90.6% (211/233) in the PCD and 92.7% (202/218) in the AAC group, success rates and recovery observed in the ITT population confirmed the results obtained in the *per* protocol (*Table IV*).

Tolerance

Among the 491 patients evaluable for safety, 4.4% (11/247) patients in the PCD group *versus* 14.8% (36/244) patients in the AAC group reported at least one event reaction ($p < 0.001$). In total, 29 patients had a Bishop-related adverse treatment: 3 patients (1.2%) in PCD group *versus* 26 patients (10.7%) in the AAC group. The percentage of patients with adverse event treatment was significantly higher in group AAC in the PCD group ($p < 0.001$). The majority of Bishop adverse events were gastro-intestinal tract (*Table V*). Eleven patients discontinued treatment due to Bishop Adverse events (2 in the PCD group and 9 in the AAC group). No serious adverse events were observed during the test.

Compliance

Adherence assessed in 491 patients was considered good in 99.2% of cases in the PCD group *versus* 95.5% in the AAC group ($p = 0.011$).

Table I
Major protocol deviations - ITT

Grounds for exclusion	CPD n = 247	AAC n = 244	Total n = 491
Number of patients excluded PP population	14 (5.7%)	26 (10.7%)	40 (8.1%)
Self-inclusion of the investigator	1 (0.4%)	1 (0.4%)	2 (0.4%)
Randomization procedure not respected	3 (1.2%)	1 (0.4%)	4 (0.8%)
Unilateral absence of pain	0	1 (0.4%)	1 (0.2%)
Sinusitis, frontal, fronto-ethmoidal	0	1 (0.4%)	1 (0.2%)
Anatomic obstructive lesion discovery under study	0	1 (0.4%)	1 (0.2%)
Unilateral pain without treatment symptomatic within 48 hours	1 (0.4%)	0	1 (0.2%)
More than 3 episodes of SMA in the year	1 (0.4%)	0	1 (0.2%)
Time evolution of signs = 0 days and symptoms	1 (0.4%)	0	1 (0.2%)
Disease duration of 1 day and the mucoid rhinorrhea	1 (0.4%)	1 (0.4%)	2 (0.4%)
Unilateral pain and increase of the mucoid rhinorrhea	5 (2.0%)	10 (4.1%)	15 (3.1%)
<6 consecutive shots from the making and adherence <80%	4 (1.6%)	4 (1.6%)	6 (1.2%)
Adherence <80%	0	6 (2.5%)	6 (1.2%)
Absence of V2	0	1 (0.4%)	1 (0.2%)

AAC: amoxicillin-clavulanate; CPD: cefpodoxime proxetil; PP: *per* protocol; SMA: sinusitis acute maxillary

Table II
Character of pain and clinical signs at baseline -
Per protocol population

	CPD n = 233	AAC n = 218
Pain		
Unilateral n (%)	233 (100)	218 (100)
Infraorbital sinus n (%)	202 (86,7)	178 (81,7)
Pulsating character n (%)	128 (54,9)	114 (52,3)
Increased pain head bent forward n (%)	187 (80,3)	168 (77,1)
Acme in the late afternoon night or n (%)	94 (40,3)	81 (37,2)
No increase in rhinorrhea n (%)	228 (97,9)	216 (99,1)
Mucopurulent rhinorrhea purulent or n (%)	227 (97,4)	215 (98,6)
Feeling Flow posterior nasal n (%)	173 (74,2)	155 (71,1)

Table III
Examination of the nasal cavity to the inclusion
Per protocol population

	CPD n = 233	AAC n = 218
Missing	2	2
Flow		
Unilateral n (%)	123 (53,2)	125 (57,9)
Bilateral n (%)	106 (45,9)	88 (40,7)
Absent n (%)	2 (0,9)	3 (1,4)
Aspect of the side of pain		
Purulent n (%)	95 (41,1)	81 (37,5)
Mucopurulent n (%)	130 (56,3)	124 (57,4)
Mucous n (%)	3 (1,3)	8 (3,7)
Absent n (%)	3 (1,3)	2 (0,9)

Original article

AAC: amoxicillin-clavulanate; CPD: cefpodoxime proxetil-

Discussion

Cefpodoxime proxetil and amoxicillin-clavulanic acid were demonstrated efficacy in the treatment of sinusitis acute [6, 7] and are recommended by Afssaps [1, 2] pre-first intention in the treatment of maxillary sinusitis acute. The conventional duration of treatment is from July to October. However, cefpodoxime proxetil, obtained a modification of the wording for a treatment duration of 5 days. Our study aimed to compare the clinical efficacy of a short 5-day treatment with cefpodoxime proxetil (2 times 200 mg daily) versus amoxicillin-clavulanic acid (2 times 1 g/125 mg per day) for 8 days in the maxillary sinus-alar acute in general practice. The study was conducted using a rigorous methodology. The willingness to conduct this study in the conditions most close to the actual practice led to the choice of a study "open" with its potential limits. However, to ensure reliability of results, all observations

been reviewed and validated by a scientific committee, without the knowledge of treatment received. The criteria for patient selection were purely ment clinics, as recommended by Afssaps [1, 2]. The unilateral nature of pain, the mandatory inclusion allowed to exclude acute congestive rhinitis, spontaneously. This pragmatic approach was facilitated by-participation of GPs in the study. The setting-evidence of a rhinorrhoea is unilateral or endoscopic using an otoscope has also helped strengthen the diagnosis of acute sinusitis. Rhinoscopy using an otoscope is a test easy and accessible to the general practitioner and should be encouraged. However, bacteriological documentation has not been researched in this study since, in practice, sampling at the middle meatus are not or little practiced. Similarly, radiographic confirmation of the sinus-alar acute maxillary site was not required for inclusion. The Results showed that clinically, both treatments are

Table IV
Clinical response - Per protocol and intention to treat

	CPD n (%)	AAC n (%)	95% the difference
Per protocol analysis			
Success V2	215/233 (92.3%)	204/218 (93.6%)	[-6.5%, 3.9%]
Healing V3	211/233 (90.6%)	202/218 (92.7%)	[-7.7%, 3.5%]
Intention to treat analysis -			
Success V2	228/247 (92.3%)	227/244 (93.0%)	[-5.7%, 4.3%]
Healing V3	224/247 (90.7%)	224/244 (91.8%)	[-6.5%, 4.3%]

AAC: amoxicillin-clavulanate; CPD: cefpodoxime proxetil-

Table V
Adverse events related to treatment

	CPD n = 247 (%)	AAC n = 244 (%)	p
At least one event			
adverse treatment-related	3 (1,2)	26 (10,7)	<0.001 *
Gastrointestinal Disorders	1 (0,4)	21 (8,6%)	<0.001 *
Infections	-	5 (2,0%)	N / A
Respiratory Disorders	1 (0,4)	-	N / A
Skin and mucous	2 (0,8)	3 (1,2%)	0,684 *

* Fisher exact test
AAC: amoxicillin-clavulanate; CPD: cefpodoxime proxetil.

have proven effective, the clinical success rate at J12-J19 were 92.3% and 93.6% for the cefpodoxime-proxetil and amoxicillin-clavulanic acid respectively, in the *per* protocol. This study demonstrated non-inferiority of cefpodoxime proxetil-Treating 5 days *versus* amoxicillin-clavulanic acid for 8 days the threshold of 10%.

Current recommendations are in line with an antibiotic brief therapy in acute non-bacterial infections

severe. The goal of treatment duration is shortened attenuate the environmental impact in terms of selection of resistant

tives while facilitating compliance. Maintaining a high rate distant healing (J25-J30) (90.6%) in group-cefpodoxime-proxetil, similar to that seen with amoxicillin-clavulanate in treatment of 8 days, the interest of a valid treatment by short-cefpodoxime proxetil in this indication.

In addition, compliance in the cefpodoxime-proxetil group was significantly better *versus* amoxicillin-clavulanic acid (p = 0.011). Finally, the 491 patients analyzed in tolerance insurance, 1.2% (3 / 247) of patients in the cefpodoxime-proxetil and 10.7% (26/244) in the amoxicillin-clavulanate (p <0.001) had presented an event independent sirable treatment-related, most of digestive origin. No serious adverse events were reported.

Conclusion

In this pragmatic study, the efficacy of cefpodoxime-proxetil 400 mg in 2 doses for 5 days is equivalent to that of amoxicillin-clavulanate 2 g/250 mg 2 catches for 8 days. In addition, cefpodoxime proxetil, prehas the advantage of a short treatment in maxillary sinusitis lar adult acute with statistically better tolerance and better compliance.

Funding and conflict of interest: MEGEOR study was conducted with the support from Sanofi-Aventis France.

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French. Example 4 (html)

Aim: To Study the Efficacy and Safety of topical cyclosporine A (CsA) as an adjuvant to the center of the cornea. It Treatment after surgical excision of primary pterygium and limbal conjunctival autograft (ACL) With respect to bread and Postoperative Complications.

Patients and Methods: A prospective randomized clinical study in 60 consecutive eyes was conducted. Its pathogenesis is still poorly understood. Because of its distribution in the sclera and its location in the area of the sclerolimbic fissure, several authors assume that exposure to UV is a factor in the pathogenesis [2-4]. Other factors include age factors [5], microlesbian or viral [6], inadequate cellular immunity [8, 9], and

Results: The average VAS WAS Significantly Lower In The CsA group ($p = 0.004$). There Was Only one recurrence (3.4%) In The CsA group ($n = 28$) and five recurrences (17.9%) in The Control group ($n = 29$). The Other complications Were "substantial graft scarring (One in The CsA group, Three In The Control Group), Tenon's granuloma (0 / 2), and fibrovascular proliferation (One in The CsA group, Two in The Control Group). The Ratio Of The boxes With No complications WAS statistically Significant ($P = 0.017$).

Conclusion: This study shows That topical CsA therapy after pterygium surgery May Reduce Postoperative Pain and Complications Including aussi recurrences.

Key-words: Pterygium, cyclosporin A, limbal conjunctival autograft.

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Efficacy of topical treatment with cyclosporin A after excision of pterygium primary and autologous connective-limbic

Objective: We evaluated the efficacy of topical cyclosporine A (CsA) after surgical treatment of primary pterygium excision and combined autologous connective-limbic (ACL) on postoperative pain and complications.

Patients and method: A case-control study, randomized, prospective was performed on 60 patients with primary pterygium. Sixty eyes were operated consecutively using the same surgical technique includes excision and LCD. Thirty eyes randomisi were treated with 0.05% CsA for 3 months after the operation, as supplement to standard topical treatment. All patients were followed for pain postoperatively using visual analogue scale (VAS) to a week and for complications including recurrence at one year.

Results: The mean value of VAS was statistically lower in the CsA group ($P = 0.034$). At the end of the year follow-up, one recurrence was observed in group CsA (3.4%, $n = 28$) and 5 in the control group (17.9%, $n = 29$). Other complications found were excessive scarring (one case in group CsA / three cases in the control group), granuloma of Tenon's capsule (two cases in the control group) and

The treatment of pterygium is always surgical [1]. Several technical surgical techniques have been proposed because of the high frequency of recurrences, the exposure of the sclera and the amniotic membrane transplantation [11]. Among these techniques, limbal conjunctival autograft (ACL) has emerged as an alternative surgery with little reciprocal dives (a recurrence rate of 5.3% 12.5%) [12-14].

Cyclosporin A (CsA), a peptide isolated from a fungus, has a immunosuppressive and anti-inflammatory effect by inhibiting the synthesis of cytokines and thus inhibit

fibrovascular proliferation (one case in group CsA / three cases in the control group). The rate of success without complications was significantly higher in the CsA group ($p = 0.017$).

Discussion: Autologous limbal connective is a promising technique in the treatment of pterygium. However, the problem of complications and recurrences (5-12% in literature) remains the major problem of this technique.

Conclusions: This study shows that topical treatment of cyclosporine A after pterygium operation significantly reduces the postoperative pain and complications including recurrences.

Keywords: Pterygium, cyclosporin A, autologous connective-limbal.

the action of T helper and cytotoxic lymphocytes [15]. CsA eye drops has been proposed in many contexts; its ocular surface diseases: k ratoconjontivite quickly dry k ratoconjontivite allergic conjunctivitis muco-synechia, Mooren ulcer, stromal keratitis herpetic keratitis, immune adjuvant a surgical corneal transplant [16]. We sem- Wheat possible that the use of topical CsA could limit inflammation and re- reduce recurrences and complications of treatment pterygium surgery, through its immune effects suppression and anti-inflammatory.

In this study, we evaluated the effectiveness of Topical CsA treatment after surgical treatment cystitis involving primary pterygium excision and self-limbal-conjunctival graft (ACL) on pain, postoperative inflammation, recurrent and complications.

PATIENTS AND METHODS

This prospective study was performed on 60 eyes 60 patients operated consecutively for primary pterygium Mayor of August 2006 to November 2006. We obtained Committee approval and a local ethics free and informed consent of all participants this study.

All patients underwent ophthalmologic examination complete before the intervention, including an evaluation functional signs using a questionnaire a measure of visual acuity, an examination of the bio-microscopic examination of pterygium (size, location, vascularization), a Schimer test (with anesthesia topical), a measure of the film rupture time lacrimal (break-up time t), AIM) and a measure of tone Eye to applanation.

All eyes were consecutively operated by the same ophthalmologist using the same technique including surgical excision and the ACL. The technique operation included the following: 3 drops a topical anesthetic (proparacaine hydrochloride 0.5% Alcaine $\text{\textcircled{R}}$) Were instilled. The hydrodissection of pterygium and conjunctiva was supero-temporal performed by injecting a local anesthetic (chloro-

using a scalpel (Beaver No. 64), resection of body was performed, leaving at least 5 mm scleral naked from the limbus. The limbal-conjunctival graft bed was sutured with vicryl pterygium 8 / 0 by sutures, following the removal of the graft supero-temporal quadrant of the eye. The site donor was sutured by two points limbal.

After surgery, all eyes were occluded for 24 hours. Topical treatment includes of prednisolone acetate 1% (Pred Forte $\text{\textcircled{R}}$) And 0.3% tobramycin (Tobrex $\text{\textcircled{R}}$) Was started the next day hand of response at 4 times daily for 4 weeks.

Thirty randomized eyes were treated with CsA (Eye drops to 0.05% in oil, castor Restasis $\text{\textcircled{R}}$) At 2 times daily for 3 months after surgery as a supplement to treatment Topical Standard (CsA group). The group of other 30 eyes were considered the control group. The Postoperative monitoring was performed on the first day, to 3 e day to 1 week, 2 weeks, 1 month, 3 months and 12 months after intervention by another ophthalmologist.

To assess postoperative pain, the visual scale analog (VAS) was used. The EVA is in the form of a strip length of 10 cm focused lr. On the far left, is marked "No pain". It is connected by a line in the distal mit  right marked "worst pain imaginable." He was asked patients to score the level of pain on the scale every day for a se-week after surgery. The pain level was measured in millimeters, and the average value of EVA 7 days was calculated.

A Schimer test (with topical anesthesia) and a measure AIM has been made in control of 12 e months. All patients were followed for recurrence and Other complications for one year. We considered a recurrence, recurrence of tissue fibrovascular pterygium in bed with an encroachment 1 mm or more on the cornea.

The comparison of patient characteristics and data pre-and postoperatively was done by following tests: Student t test, the test of Chi Square, the Mann-Whitney U, Paired t-test, the test

RESULTS

Sixty patients were enrolled in this study. There were 30 patients in each group (group CsA and control group). Two patients in the CsA group and patient control group did not come to control 12 months. Both groups were homogeneous and comparable. No significant differences were re-found between the two groups in terms of age, sex ratio, percentage of side eye, size pterygium, Schirmer's test or measurement of BUT preoperatively (Table I).

A significant difference was found between the Will their average VAS of both groups: 22.4 ± 11.0 mm for the CsA group, 28.5 ± 11.7 mm for group witness. $p = 0.034$, Mann Whitney U test (Table II).

In all cases, epithelialization of the cornea was obtained at 7^e postoperative day. No complications or tolerance problems were observed for the use of CsA, except for a sensation burning ocular instillation in 9 of 28 patients (32%).

At the end of follow-up of 12 months, 1 recurrence was observed in the CsA group (3.4%, $n = 28$) versus 5 in the control group (17.9%, $n = 29$) ($p = 0.19$, result non-significant, Fisher exact test). During follow-up, excessive scarring occurred (1 case in group CsA / 3 cases in the control group) (Fig. 1), granuloma of Tenon's capsule (2 cases in group control) (Fig. 2) and a fibrovascular proliferation (1 case in group CsA / 3 cases in the control group)

(Fig. 3). Two cases in the control group had a Tenon's granuloma and scarring excessive same time. There was no significant difference between the two groups in terms of these complications ($P = 0.25$, Chi Square test). The success rate without complications was significantly higher in CsA group (25 cases in the CsA group versus 18 cases in the control group, $p = 0.017$, Chi test Square).

Table I
Patient characteristics according to groups.

	Group CsA (N = 30)	Group witness (N = 30)	P
Age (Mean \pm SD)	32.63 ± 18.9	35.13 ± 14.0	0,49
Sex (F / M)	5 / 25	9 / 21	0,22
Side (L / R)	9 / 21	10/20	0,78
Encroachment on cornea (mm \pm SD)	3.13 ± 0.78	3.00 ± 0.67	0,47
Schirmer test (Mm \pm SD)	15.93 ± 3.71	16.10 ± 4.28	0,87
PURPOSE (Seconds \pm SD)	18.37 ± 4.21	17.43 ± 4.85	0,43

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SD: standard deviation, F / M: female / male, L / R: left / right;
PURPOSE: break-up time^a (time of rupture of the tear film) CsA: ciclo-
cephalosporins A.

February 1

Figure 1: Patients who received cyclosporine A, with excessive scarring to the contour of the graft connective-limbal in bed pterygium. Postoperative appearance at 12 months.
Figure 2: Patient control group, showing a granuloma of Tenon's capsule along the connective-limbal autograft. Appearance postoperative 3 months.

Table II
Clinical outcomes and complications between groups.

	CsA group	Control group	p
VAS (mm, mean ± SD):	22.4 ± 11.0	28.5 ± 11.7	0,034
- Day 1	59.2 ± 23, 8	64.9 ± 21, 9	0,25
- Day 2	41.5 ± 21, 7	45.2 ± 16, 7	0,16
- Day 3	25.3 ± 17,0	35.2 ± 15, 9	0,015
- Day 4	13.8 ± 12, 9	24.2 ± 13, 8	0,003
- Day 5	8.1 ± 9, 2	16.6 ± 11, 4	0,002
- Day 6	5.1 ± 7, 2	9.3 ± 8, 8	0,02
- Day 7	3.8 ± 6, 7	4.3 ± 6, 5	0,66
Uncomplicated cases (12 months)	25 (89.3%, n = 28)	18 (62.1%, n = 29)	0,017
Complicated cases (12 months):	3 (10.7%)	11 * (37.9%)	
- Recurrence	1	5	
- Excessive scarring	1	3	
- Tenon's granuloma	0	2	
- Fibrovascular proliferation	1	3	
Schirmer test (mm ± SD) (12 months)	17.57 ± 2.62	16.07 ± 4.88	0,16
GOAL (seconds ± SD) (12 months)	21.36 ± 3.63	19.00 ± 4.06	0,03

* Two cases in the control group showed both a Tenon's granuloma and excessive scarring. VAS: visual analogue scale; CsA: cyclosporin A; SD: standard deviation; AITM: break-up time (time of tear film break).

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The values of Schirmer test and BUT were normal in both groups at 12 months postoperatively (Table II).

DISCUSSION

CsA is a 11 amino acid peptide, isolated from a fungus, *Torulopsis inflatum* Gans. It has an acting intracellular inhibition of the synthesis of cytokines (including IL-2, IL-3, IL-4, G-CSF and TNF). At the same time, it inhibits the action of lympho-T helper and cytotoxic lymphocytes, and thus influences efferent phase of immune response. Thus, CsA reveals an anti-inflammatory, reducing production of proinflammatory cytokines. It also reduces the allergic reaction by inhibiting the release of mediators from mast cells, and cytokine cascade [15]. Since the first test published in 1985 on the topical use of CsA in corneal transplant [17], several studies have been conducted in many inflammatory diseases or immune of the ocular surface, keratoconjunctivitis Mooren ulcer dry [16, 18, 19].

In some studies, inflammation and immunity were cited as factors the etiopathogenic

pterygium [2, 10, 20, 21]. Beden *et al.* [20] observed in patients suffering from pterygium, infiltration significant T cell CD4 and CD8. And an increase in mentation of HLA DR expression in epithelial tissue LiAl and subepithelial pterygium excised. Pinkerton *and al.* [10] and Velogianni-Ioachim *et al.* [21] reported similar results, supporting the hypothesis of the role played by immunity in the etiology of pterygium.

Despite these findings, few studies have been published on the effectiveness of CsA in the treatment of pterygium. In one such study, Wu and Chen [22] compared the efficacy of CsA and thiotepa in Prevention of postoperative recurrence in 50 patients with pterygium. After simple excision, half the patients received topical 1% CsA and the other half of thiotepa 0.05%. After declining average of 10 months, the recurrence rate was 5% in CsA group and 10% in the thiotepa group. These results are very satisfactory, since recurrences are frequent with simple surgical techniques, ranging 23% to 75% in different studies [23]. In another recent study, Hercules *et al.* [24] showed that the 0.05% CsA inhibited the proliferation of fibroblasts culture from Tenon's capsule.

In our study, the success rate without complications was significantly higher in patients with received CsA (Fig. 4), with follow-up after one year

April 3

Figure 3: Patient control group, with a proliferation of fibrovascular connective-limbal autograft in pterygium bed. Appearance postoperative 12 months.

Figure 4: Patients who received cyclosporine A, with good healing without complication. Postoperative appearance at 12 months.

number of cases without complication in 25 CsA group (89.3%, n = 28) versus 18 in group control (62.1%, n = 29). The topical treatment with CsA after pterygium operation has also a significant decrease in postoperative pain CsA group, with an average value of EVA statistically lower, and significant values of EVA-tion below for four days (between days 3 and 6 postoperative) (Table II).

Despite new surgical techniques and the use of corticosteroids, the problem of recurrences and complications remains the major problem of treatment pterygium. Until now, many post-treatment procedures were used to avoid such occurrences and complications of brachytherapy for contact irradiation α - β [25], 5-fluorouracil [26], mitomycin C [27], the thiotepa [28]. The authors using these treatments report satisfactory rates of recurrence of 0 to 38% [23], but also some serious complications type of scleral or corneal ulceration, perforation globe, secondary glaucoma, lens opacity, uveitis, scleritis, corneoscleral, palpebral depigmentation.

In our study, the recurrence rate was 3.4% in CsA group (0.05% eye drops in castor oil) with a total rate of complications of 10.7%. These results are comparable to those published by other authors using different products to prevent recurrence postoperative [25-28]. No safety concerns have been observed in patients using CsA, apart from the sensation temporary burning ocular instillation.

CONCLUSION

In this study, we evaluated the effectiveness of topical treatment of CsA on postoperative pain

surgery and complications after treatment Primary pterygium surgery including excitatory sion and limbic-conjunctival autograft. This study shows that topical treatment of CsA after pterygium operation significantly reduces postoperative pain and complications including recurrences. No side effects been found in the use of CsA, except for a burning ocular instillation. Nevertheless, due to small sample size, these re-sults should be confirmed by studies including a larger number of patients and conducted a longer evaluation time.

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German. Example 1

[Authors]

Penetrating keratoplasty with intrastromal corneal ring

A prospective randomized study

Background

Because today the majority of projects implemented in the industrial nations for visual acuity and corneal transplants are not blind patients, and the expectations of the functional and refractive results have risen significantly. One of the main problems after penetrating keratoplasty is the occurrence of a significant part of regular and often irregular postoperative astigmatism. The causes for the appearance of Transplantatastigmatismus are shortcomings of trepanation (decentralization, vertical tilt), the sewing of the graft (horizontal torsion by asymmetry of the second situation seam, uneven tension of the continuous seams), the astigmatism of the donor and the cure behavior of the host cornea search [13, 14, 17]. The latter is in part because it softer in host corneal areas, especially in vascularized corneas, the filament migration is likely to cause a strong Transplantatastigmatismus. The average astigmatism after penetrating keratoplasty in most studies from 2.5 to 7 diopters [1, 3, 4, 5, 6, 9, 11, 12, 15, 16]. One approach to minimize postoperative Transplantatastigmatismus is the development of alternative Trepanationsverfahren.

Previously, the trephination with Handtrepanen (eg after Franceschetti) standard. They are still in special circumstances (keratoplasty limbo, very large or very small Trepanationsdurchmesser, penetrating keratoplasty à chaud, Autorotationskeratoplastik) requires [2]. The trephining of the graft is of endothelial, the trephination of the host cornea epithelial. The size of the graft usually 0.2 mm is selected to be greater than the host trephination of the cornea (positive disparity).

The "guided Trepanssystem" after Krumeich (GTS) is now widely used. There are studies that a lower postoperative astigmatism compared to Handtrepanen confirm [1, 8, 15]. The main advantage of this procedure is carried out by epithelial side trephination of donor and host cornea. This is made possible by the trephining of the graft by producing an artificial anterior chamber with an infusion pressure in the closed system. This results in congruent cut surfaces and angles, and which account for trephination with Handtrepanen required positive disparity.

The Erlangen technique of nonmechanical excimer laser trephination leads according to a study by Seitz et al. also at a lower Transplantatastigmatismus than penetrating keratoplasty with Handtrepanen [16].

All-new expectations can be subject to the femtosecond laser technology, as this may keratoplasty for the key-lock principle are almost even allows seamless and, therefore, may also better refractive results can be achieved. To what extent this new technology can meet these expectations, but is still completely uncertain.

Another possible solution is to attempt to stabilize the corneal wound between the graft and host cornea by a so-called intrastromal corneal ring. By introducing such a corneal ring during corneal transplantation, the different force vectors could be caught of the seam loops in the postoperative period, and it may be a more consistent wound healing allows.

In a pilot study carried out in advance and in a prospective study showed a reduced astigmatism with corneal ring [5, 9]. Corneal ring-related complication that occurred in

these studies do not. The results were not statistically significant. Therefore, we conducted a prospective, randomized study with the aim of the effectiveness and safety of intrastromal corneal ring after Krumeich checked.

Study design and methods

It is a single-center, prospective, randomized study.

After obtaining the approval of the Ethics Committee of the Albert-Ludwigs-Universität Freiburg, only patients with Fuchs' endothelial dystrophy or keratoconus were included in the study. It was randomized by drawing lots, whether the intervention should take place with or without intrastromal corneal ring. Per group with 10 patients were operated on. To participate in this study, the patients gave their written consent after a thorough prior oral and written information. Only patients who are older than 18 years, enrolled in this study.

Excluded were patients who already operative procedures were performed on the eye, or where further operations were planned to the eye (cataract or vitreous surgery). Furthermore, patients were excluded who had systemic diseases, often associated with a Transplantateinschmelzung or ideal for a complicated corneal surgery are (tissue diseases, rheumatoid arthritis, Wegener M.), patients with eczema and okulomukokutanen syndromes and patients with known allergic diathesis. Also excluded were patients who underwent corneal transplantation before the scheduled already a refractive laser surgery on the cornea or a cornea inzisionalen surgical, astigmatismuskorrigierenden intervention.

All penetrating keratoplasty were from the same surgeon with the guided Trepannsystem (GTS) operated on. The operations were performed in retrobulbar anesthesia or general anesthesia. The Trepanationsdurchmesser was 8.0 mm both in the graft and the host cornea. The grafts were analyzed by the double continuous cross-stitch suture according to Hoffmann and possibly with Einzelknüpfnähten to waterproof sewn [7]. In 10 patients after insertion of the graft was placed in an intra-stromal corneal ring into the wound gap and sutured. If necessary, simultaneously a peripheral iridectomy was performed.

The intrastromal corneal ring is made of a cobalt-chromium-molybdenum-titanium alloy (69.5% cobalt, 24% chromium, 4.5% molybdenum, 2% titanium). It has a diameter of 8 mm (outside diameter 8.1 mm, inner diameter 7.95 mm) and a thickness of 0.15 ± 0.02 mm (Fig. 1).. The intrastromal corneal rings have been provided by the company Human Optics available.

The planned follow-up checks were made after 6 weeks, 4, 12 and 18 months. In any study, best corrected visual acuity, a slit lamp examination, tonometry, a determination of the endothelial cell density and an Orbscan topography was performed. Here, the simulated K-value was recorded as a cylinder boundary. The mean values of astigmatism were compared with ANOVA test.

Statistical analysis was performed with SPSS 12.0 (Microsoft Corp., Redmond, USA).

Results

The group of patients with intrastromal corneal ring consisted of 4 patients with Fuchs' endothelial dystrophy, and 6 patients with keratoconus. In the group without ring 6 patients had Fuchs endothelial dystrophy and 4 patients keratoconus. The follow-up time is 18.9 ± 2.8 months.

The Orbscan determined astigmatism in the last survey. Table 1 below. There was no statistically significant difference between patients with and without intrastromal corneal ring (ANOVA: $p = 0.944$).

In both groups of patients at time of last examination in the median or a continuous thread.

The endothelial cell loss was 18.0% in the group with corneal ring and 7.3% in the group without a ring. This difference is not statistically significant (ANOVA: $p = 0.29$).

The complications are. Table 2 shows. In a patient with corneal ring led to a severe acute endothelial rejection. This patient also showed marked deep vascularization in the graft, which had grown into the graft below the ring. In this patient, an anterior chamber lavage was performed with dexamethasone, a steroid drip intense local and systemic steroid therapy initiated (fluocortolone 1 mg / kg body weight). In this therapy, it came to a complete recovery of the immune response. The graft remained clear centrally.

In a total of 5 patients with intrastromal corneal ring, there was spontaneous rupture of the continuous threads. In these cases, the broken threads were completely removed. In 2 patients ruptured within the first 4 months of either continuous threads. This was decided not to Fadennachlegung. One of these patients also showed spontaneous Fadenruptur the second continuous suture after 14 months. In 3 patients there was a rupture of the remaining second continuous filament. In one of these 3 patients Fadennachlegung was necessary because the rupture occurred within the first postoperative year. It was reloading a continuous suture with 8 punctures. Immediately after Fadenruptur or Fadennachlegung no Orbscan topography was performed, but it was to keep the regular check-up appointments for follow-up.

A patient with intrastromal corneal ring was excluded from the study because he suffered by a missile blast with Fadenruptur graft and bending of the corneal ring. In these patients Fadennachlegung was performed (new continuous suture). Due to the bending of the ring, the patient was excluded from the study. The graft recovered in the course, and the patient achieved a visual acuity of 0.4 currently with rigid contact lens, and would initially be carried out any further operations.

In 2 patients with intrastromal corneal ring, the ring was the 18-month follow-up to each one point very superficially just under the epithelium.

The. Table 3 shows the data of all patients at a glance.

Table 1 keratometric astigmatism in diopters (Orbscan)

	Without ring n = 10 dpt	
With ring n = 9 dpt		
Mean ± SD	3,9±2,5	4,0±2,1
Span	1,5–9,4	1,9–8,1
Median	3,2	3,1

Table 2 Complications

	With ring	Without ring
Rejection	1	—
	With deep vascularization in the graft	
Fadenrupturen	5	—
	1 with Fadennachlegung	
Study exclusion	1	—
	Graft demolished by missile, bending of the ring, Fadennachlegung	

Table 3 Summary of all patients with history of astigmatism (Orbscan), number stilllying threads Fadenrupturen and Fadennachlegungen, rejection, dropping out

Patient	Ring	Fadenrupturen first or 2 run away, the third	Fadennachlegung	Rejection	Dropping out	Astigmatism 6 week s / even lying threads	Astigmatism 4 months / still lying threads	Astigmatism 12 months / still lying threads	Astigmatism 18 months / still lying threads
1	-		-2		-2	2,6/2		3,2/0	
2	-		-2		3,5/2	4,3/2		2,9/0	
3	+	2.	+		7,0/2	-1	2,2/1		1,5/1
4	+		7,0/2		-7,0/2			5,2/0	
5	-		3,0/2		-2	3,0/2		2,7/2	
6	-		-2		-2	-2		3,3/2	
7	+	1.+2.		-2	2,2/2		5,6/1		9,4/0
8	-		3,1/2		7,0/2	7,0/1		6,6/1	
9	-		6,7/2		-2	6,1/1		7,5/0	
10	+	1.	+	+	2,2/2	1,8/2	15,0/2		-2
11	-		0,7/2		2,1/2	-2		1,9/2	
12	+	1.	+		-2	3,5/2	3,2/1		-1
13	+	2.		-2	3,2/2		-1		4,4/1
14	+		7,8/2		-2	-1		3,1/1	
15	+	2.		3,1/2	2,4/2		5,9/1		1,9/1
16	+		4,3/2		4,3/2	5,0/1		5,2/1	
17	+		4,8/2		1,8/2	1,4/2		1,6/2	
18	-		1,0/2		2,5/2	-1		2,2/0	
19	-		-2		5,2/2	5,5/1		6,8/1	
20	-		2,3/2		-2	3,4/1		3,1/1	

- Messung nicht möglich

Discussion

The use of intrastromal corneal ring resulted in this prospective, randomized study is not to minimize the postoperative Transplantastigmatismus. This result may be influenced by that of the many Fadenrupturen and the need for a patient Fadennachlegung was a stronger astigmatism and so the possibly positive effect of the corneal ring was destroyed. In addition, it involves only a relatively small number of patients (n = 20). In the study by Ehrich and Duncan [5] showed in the group ring, a lower astigmatism than in the control group, this result was not statistically significant. In a recently published retrospective study of 179 Duncker Krumeich and Perforating keratoplasty with corneal ring was operating was a historical control group consisting of 101 corneal transplants, compared with no ring. In this nonrandomized study, the different indications included (for example, Rekeratoplastiken and vascularized corneas). This showed no reduction of Transplantastigmatismus [10].

The reasons for the Fadenrupturen in our study are unclear. The surface of the ring was polished smooth in industrial production. It is likely that the filaments lie directly in some places the ring and that will be exerted by pressure on the eyeball (eg at night, unconsciously) through the ring excessive forces on the threads. Krumeich and Duncan

[10] reported in the retrospective study, however, only 4 at 179 Fadenrupturen eyes. Our surgical technique similar to that found in these studies. The trephination was carried out with the GTS, and it was a double continuous suture used by Hoffmann [7].

In the above study, the authors also report a statistically significant reduction of immune reactions by the intrastromal corneal ring. However, the only rejection reactions were taken into account, treat those who were not through systemic and local immune suppression. Another positive effect in the study by Krumeich is the reduction of vascularization [10]. So described the authors 'bending' of vascular ingrowth curves along the ring. In our study, there was only one patient in the group with intrastromal corneal ring to pronounced deep vascularization and to a high endothelial rejection. Due to the small sample size is a statistical evaluation with respect to a difference in the incidence of rejection is not possible.

The difference in endothelial cell loss (with ring 18%, without a ring 7.3%) showed no significance.

In 2 patients with corneal ring, the ring was the last examination in each case a very superficial location just below the epithelium. Whether this "go forward walking" of the ring, a progressive process remains to be seen.

Conclusion for practice

In summary, one can say that the main objective criterion of intrastromal corneal ring, the minimization of Transplantatastigmatismus, in this prospective, randomized study, and in all other previously published studies, is not met.

Penetrating keratoplasty with intrastromal corneal ring. A prospective randomized study

Abstract

Background. The purpose of the study was to evaluate the efficacy and safety of Krumeichs' intrastromal corneal ring following penetrating keratoplasty. Postoperative astigmatism and occurrence of complications were the main criteria of this study.

Material and methods. A total of 20 patients were included in this prospectively randomized study (10 patients with and 10 patients without corneal ring). Follow-up examinations were performed 6 weeks, 4, 12, and 18 months postoperatively, including best corrected visual acuity and Orbscan corneal topography.

Results. The mean follow-up time is currently 18.9 ± 2.8 months. The mean astigmatism (Orbscan) is 3.9 D in the group with ring and 4.0 D in the group without a ring. Spontaneous suture rupture occurred in five patients with corneal ring.

Conclusions. The use of the intrastromal corneal ring following penetrating keratoplasty caused no reduction of postoperative astigmatism. The reason for the spontaneous suture ruptures is unclear.

Keywords

Penetrating keratoplasty · Astigmatism · Intrastromal corneal ring

German. Example 2

Motivation for treatment of patients with dual diagnosis of psychosis and addiction

Results of a randomized study

[Authors]

Summary

Background. Patients with dual diagnosis of psychosis and addiction often have a particularly unfavorable course of disease and are difficult for post-hospital outpatient utilization, integrated treatment programs to motivate. The present study compares the effects of a first time on this issue tackle the problem of treatment motivation ("motivational interviewing", MI) with a non-specifically-supportive intervention (ST) same time scale. The primary outcome measure was the participation in a post-inpatient integrated treatment. Were additionally examined the possible post-interventional effects on substance use, disease progression, and stage of medication compliance. **Material and methods.** A total of 60 inpatients with dual diagnoses were randomized to 4 sessions of MI or ST treatment. The blinded data from surveys found, immediately after, 3 and 6 months after the respective intervention **statt. Ergebnisse.** 70.0% of the MI (n = 30) and 40.0% of ST patients (n = 30) took part in the postinterventional integrated outpatient treatment (p = 0.020). Regarding the secondary objectives (drug use) were found in the exploratory analysis no **Gruppenunterschiede.** **Schlussfolgerung.** The study design allowed for the first time a clear reduction of the positive effects regarding the inclusion of outpatient follow-up treatment to the specific intervention type of MI and underscores its efficacy. The establishment of the presented treatment concept in inpatient settings may mean therefore a key step in the supply of contaminated dual diagnosis clientele.

Keywords

Motivational Interviewing · Dual diagnosis · schizophrenia · substance abuse · Substance dependence

The course of schizophrenic illness → He is additionally containing a substance use negatively be influenced →. Thus, patients show with the dual diagnosis of a schizophrenic → NEN disorder and one Substanzab → usus or a substance dependency of in comparison to schizophrenic patients without proper co → for example, morbidity one out → impressed psychotic symptoms [1], higher re-admission rates [2], a poorer response to neuroleptic medication [3], a lower drug compliance [4] and a higher Suizidri → siko [5]. This is all the more weight to the total →, as countries do so at the Komorbidi → of substance abuse and schizophrenia or substance dependence by no means a sel → → tenes phenomenon: With a lifetime prevalence of 47% is the risk of substance abuse or

a substance dependence, patients with schizophrenia have Zophres about 4 times higher than in the general population [6].

These facts make it clear that a great need for interventions that may improve the disease course of patients with dual diagnoses. In addition to new developments in the psychopharmacological treatment (see [7]), which always forms an essential constituent of the treatment of patients with dual diagnosis of psychosis and addiction, have in recent years, different so-called integrated therapy concepts strengthened and receive attention in the treatment of psychiatric illness or substance abuse and substance dependence is the main by a team of therapists Samesky's model (eg [8, 9, 10, 11]). Despite encouragement in terms of warning on the effectiveness of treatment programs (eg [11, 12]) shows a large proportion of patients with low readiness for commissioning a part of such assistance and reduction of substance use [13].

To counteract this problem, there are now a stronger commitment to the development of specific treatments for patients with motivation dual diagnoses, the treatment offered to patients should pave the way for further treatment. Its theoretical foundation is one motivation understanding, the motivation is not considered as time-stable property ("trait"), but as a changeable dynamic state ("state"), which can over various time points and situational conditions vary across different and through interpersonal processes affected by them [14, 15]. Important impulses newer treatments represent concepts for patient diagnoses with double diagnosis originate mainly the trans-theoretical model of Prochaska and DiClemente [16] and the technology of Miller and Rollnick [15] developed "motivational interviewing". To building upon the approaches is keen research interest. Are so informed by several review articles [17, 18, 19] before, where so far is through a few evaluation studies on the motivational treatment of patients previously experiencing for some time, the comorbidity of schizophrenic illness and a substance abuse or there is a substance dependency. One problem is that the available randomized, controlled studies in this research field [20, 21, 22, 23, 24] in their validity limited in part by German-insoluble methodological limitations. In addition to very small numbers of 30 [21] and 23 participants [22] and a missing or unclear blinding of raters [21, 22, 23, 24], especially the problem of heterogeneous diagnostic groups. Furthermore, in none of these studies, the effectiveness of the motivational interviewing compared with a control condition, which controls the factor of non-specific grant an unspecific supportive intervention with an appropriate temporal scope [20, 21, 22, 23, 24].

The earnings situation in terms of active compound effectiveness of motivational strategies in the treatment of patients with dual diagnosis is in trials with higher numbers of cases previously regarded as inconsistent [20, 24]. Patients in the study by Swanson and coworkers [24] investigated after a single-blind on the principles of motivational interviewing-based individual treatment significantly more outpatient treatment than patients who received no intervention. Baker and coworkers [20] found no differences in terms of first session and it is at the

average of the perceived number of outpatient treatment sessions over a period of 3 months.

Question

→ to these inconsistent findings on his bright, examines the present study the effects of their own in the work → group developed Motivationsbehand → ment on the first participation in an integrated outpatient störungsspezi → treatment [9], fishing on the subs → dancing consumption and → Krankheitsver the course of the patient. Placed special emphasis were → de in the present study on the Ver → avoidance of the above metho → denkritischen aspects (eg, by implementing a sufficiently high number of cases, diagnostic homogeneity of the sample and comparing the motivation → tion treatment with a nonspecific-supportive intervention equal duration).

The motivation for treating pa → tients in the experimental group based on the strategies of Motivational → ivering In [15] and is often one of the Crossed → cognitive performance and concentration of the target group adapted → [25]. Thus, all contents → he worked at the end of a session by the therapist, and summarized at the beginning of the next meeting re → outdated. In addition, the patients received repeat and deepen the hold → In written records of all exercises in the course of treatment → ment will be carried out.

Checks are the primary hy → hypothesis that patients of the experimental group should be re → compared to the intervention with the control group fre → figer an integrated, patient-specific treatment record → trouble. Were studied additionally to possible dif → → ferenzielle effects of substance use conditions, disease progression, Me → dikamentencompliance stage of abstinence and motivation.

Study design and methods

The study was approved by the ethics committee → sion of the University Hospital of the University of Cologne, approved (04-159).

Patients

Patients were treated between April 2004 and March 2006 in the Department of Psychiatry and Psychotherapy at Cologne University Hospital → therapy in sta → tionary treatments recruited. Wa → ren aged between 18 and 65 years and he completed both the diagnostic criteria → an → ner schizophrenic, schizoaffective, or substance-induced psychotic disturbances → tion (F20.0-.5, F20.8-.9, F25.0-.2, F25.8-.9, F10-19.5) and the criteria Diagnosekri → a substance abuse or substance dependence (F10-16.1, F10-16.2, F19.1-.2). Were rejection criteria impacts pa-tients with severe physical diseases →, patients who are not sufficiently remitted psychopathology appeared to men at 50-minute sessions of increas →, suicidal patients patients, patients without sufficient knowledge of German and Pa →, who stood so close to release that no meeting date has been more identified.

Study design

It was a randomized parallel study with blinded → te raters. During the recruitment period from April 2004 to March 2006 were released just before the patient standing on the wards informed orally and in writing about the study and point-insoluble inclusion criteria screened. Ge → → Einschlusskrite nügten patients the criteria, there were no exclusion criteria and agreed to by the undersigned → tion

of informed consent to participation in the study, the AGREE \bar{n} , was the baseline survey conducted by \bar{n} . After completing the baseline survey, patients were He \bar{n} stratified by gender (m / f) and \bar{n} Substanzkonsum (single / multiple) were randomly assigned to experimental or control group pointed to \bar{n} . The patients were informed enter the result of randomization before treatment. The four individual sessions of the respective \bar{n} \bar{n} tion Studieninterven were offered primarily stationary, but could be continued outpatient at discharge.

Data collection

Data collection in the form of self-and external ratings were before, immediately after, 3 and 6 months after the interven \bar{n} tion instead. The ratings were blind by independent third-party, with respect to \bar{n} the condition of the patient study visits conducted specifically trained and experienced raters (physicians in advanced specialist training, CG, CF). The correla \bar{n} tions of the raters estimated and actual study conditions in which the patients were located, were not significant ($\chi^2 = 0.538$, $p = 0.463$), so that \bar{n} \bar{n} a successful blinding is to go out.

Objective parameters and measuring instruments

Participation or non-participation in the integrated outpatient trouble \bar{n} specific treatment that is offered in the \bar{n} ins titutsambulanz the Department of Psychiatry and Psychotherapy, University Hospital of Cologne, was recorded during the 6-month follow-up period. An evaluation of integrative treatment \bar{n} ment according Gouzoulis-Mayfrank [9] ge \bar{n} 's plans, actionable results have not heretofore [26]. It takes into account the per \bar{n} but common in the reviews as we assessed \bar{n} strategies significantly [27, 28]. Participation in development of a stationary \bar{n} wohnungsbehandlung was regarded as one of the integrated treatment of similar in-ventions.

The consumption pattern of the last 30 days was based on the two subs \bar{n} Kalen alcohol and drug use of the ASI (Addiction Severity Index) [29] He asks \bar{n} . The stage of Abstinenzmotiva \bar{n} tion was collected on the German version of the self-assessment scale Utica (Univer \bar{n} sity of Rhode Iceland Change Assessment) [30]. She is an internationally standardized \bar{n} Customary procedures for collecting the various "stages of change" sensu Prochaska and DiClemente [16] and captured the four motivational stages Absichtslo \bar{n} reliability, intention formation, action and maintenance using 32 items, each of which 8 items one of the 4 describe Stadi \bar{n} en. The level of support to the individual items is measured by a 5-point rating scale. Although the scale and its underlying \bar{n} following trans-theoretical model [16] are discussed in some very critical [31], there are numerous studies which indicate that these satisfied \bar{n} vice related test quality scale supply (eg, [32, 33, 34]). For this reason, in the present pilot study was not necessary to use additional methods of assessment of abstinence motivation (eg, [35] or medical decisions).

The psychopathology was assessed by the PANSS (Positive and Negative Syn \bar{n} drome Scale) [36] and the GAF (Global Assessment of Functioning) scale [37]. Furthermore, the current medication and the Medikamentencom \bar{n} pliance collected [38]. Rehospitalisie \bar{n} tion as a 36-hour vollstatio \bar{n} ary or 5-day-care was at \bar{n} contains [39] evaluated.

Study interventions

The meetings of the respective intervention lasted 50 minutes and found one to two times a week, rather than under stationary conditions. In the case of dismissal under of the intervention were the remaining outpatient sessions Benden perceived to be men.

Stage-dependent motivational pretreatment for patients with dual diagnoses
The four individual sessions comprehensive stage serving dependent motivation treatment for dual diagnosis patients (MI, [40]) is based on the strategies of motivating leaders interviewing [15] and correspondingly maintains adaptations that often turned limited cognitive ability and concentration ability of schizophrenes patients consider [25]. All content is developed on the En de summarized a meeting with the therapist and the beginning of the session following repeated after. All exercises are given on worksheets in writing and given to the patient for as repetition and deepening.

1st Session: Positive feedback and effects. In the first Session, the patients about the concept of motivation onsbearung cleared, received message on the back Current status of the term substance use and the subjective-selective positive effects of Substanzkonsums to be developed.

2nd Session: negative consequences. In the second Session, the negative consequences of substance use in looking outward on health, family, work, leisure time, personality, contacts, financial and legal consequences [41] beitet erar.

3rd Meeting personal goals and Ambivalence prevalence. In the first part of the 3rd meeting who asked the patient, benche personal goals and the principal nutrients. In the second part of the session, the personal ambivalence is worked out in terms of abstinence project. For this purpose, the individual pre- and post parts of abstinence discussed [42].

4th Session: realistic goals and alternative behaviors / relapse plan. In the fourth session of the patients judged to be realistic goals in respect of the consumption of substance determined over a period of three and six months. In the second part of the meeting with patients in the motivational stages of intention and purpose of education (within the meaning of the URI CA scores at the baseline survey, [30]) developed alternative behaviors and patient motivation stages of action and maintaining residue contingency plans drawn up [42].

Bechdolf and Pohlmann have the in manualized intervention and specific worksheets developed [40].

Supportive therapy

Patients in the control group erhielt nonspecific intervention in the form of 4-non-specific supporting estimates Sit (supportive therapy, ST). The patients were able to determine the contents of the Sit estimates free. Significant emotional Unter The rapeutenmerkmale were Afghanistan as therapeutic attention speed, empathic listening, transfer of therapeutic optimism, heat is now present, openness and cooperation. The establishment and maintenance of good therapeutically Atlantic Alliance and talking about neutral topics such as leisure activities, sports, but also current, the patients continued the stressful topics under the supportive therapy. discussed the contents were in the

meetings usually to discuss current problems of the patients (including those outside of substance use) and a general recommendation on the commissioning of an integrated outpatient care to be pronounced. MI strategies, teaching materials and homework benefits were not used. A Manual to the implementation of the intervention was not available.

Both interventions were offered by the "Motivational Interviewing" qualified psychologists trained in advanced therapeutic behavioral psychotherapy to participate in the continuing education (BP, CL). Evidence of formal adherence or competence testing by the therapist did not take place.

Determining the sample size

The present estimate of the sampling was related to the sample sizes to reach the primary goal of participation in specific continuation treatment. The other hypotheses were investigated in exploratory fashion. Starting with the findings of Swanson and colleagues [24], the methodological approach with our study different from theirs, we went from a "participation in the integrated treatment" of 10% in the control group and from 40% in the experimental group. With such a participant at the rate of the study intervention (motivation vs. Supportive treatment) following treatment in the integrated total of 60 patients were required to statistically with a power of 80% difference at the 0.05 level of significance secure.

Data Analysis

All statistical analyses were led by intention-to-treat conditions carried out. The primary hypothesis was tested by a χ^2 test. The significance level was mentioned above and set at 5%. Discontinuations of the study were intervention conservative as "non-participation in the integrated treatment" scored. In two cases the patients were postinterventional. A complete cessation treatment to shareholders. Thus it was considered analogous to "participation in the integrated treatment."

The secondary hypotheses were examined with exploratory repeated measures of analysis of variance with treatment. The significance level was also set at 5%. To test the effects of the intermediate time points of each time point was selected before the intervention as the reference category. Was at "loss to follow-up" after the Studienintervention in relation to "participation in an integrated treatment" is assumed conservatively no participation, concerning the disease and the Motivationsstadien the last available information were used ("case observation carried forward" COCF).

Results

Stichprobencharakteristik und participation in study interventions

At the study included 60 patients (see Fig. 1). The sample consisted mostly of men, mainly cannabis and alcohol were comorbid. The duration of psychotic illness was on average 4.8 years and the number of hospital stays averaged 3.7 (see Table 1). 50 patients suffered from schizophrenia or schizoaffective disorder. Only a relatively small patient population with a substance-induced psychotic disorder had ($n = 10$, including patients of 4 patients with comorbid with cannabis or by multiple drug use induced psychotic disorder and one patient each with an alcohol or stimulant induced psychotic

disorder). Regarding demographic and disease progression were the data concerning him there were no significant differences between the groups. This also applies to the medication. The groups in both investigations were the wide following percentage of patients predominantly antipsychotics (MI: 83.3%, ST: 93.3%), followed by Ben-benzodiazepines, mood stabilizing and subsequently antidepressants.

No patient discontinued participation due to a non-desired result portraits of the randomization. A total of four patients less than 4 Therapies were true (1, ST: Behandlungsabbrüche, MI 3). All affected patients broke the whole duck. There was no significant difference between treatment groups with regard to the treatment by perceived average number of sessions (MI: 3.97, ST: 3.73).

Participation in an integrated outpatient treatment. Within a period of 6 months, the patients of the MI group were significantly more frequent in the inpatient treatment offered integrated outpatient treatment for some patients [9] or on a stationary cessation treatment than patients that has previously gone through the non-specific supportive treatment ($p = 0.020$). While 70.0% of patients in the experimental group, the patients in the integrated treatment visited or participated in an inpatient weaning took, of the patients in the control group only 40.0% took part of the integrated action part. A total of two patients participated in a stationary weaning, these were seen as a specific absorption treatment and added to the integrated treatment.

Substance use

In both intervention groups increased both the incidence and the men from the consumption of both alcohol and cannabis. Here, however, showed no significant differences between groups, neither for the number of days on which in the previous 30 days of alcohol or cannabis were consumed, nor for the amount of consumption of alcohol or cannabis during the preceding 30 days.

Within the intervention groups showed in the experimental group a significant decrease in drinking days at 3 months ($p = 0.013$) and after 6 months ($p = 0.003$) and a significant reduction of the amount needed to 3 months ($p = 0.022$) and after 6 months ($p = 0.019$). When cannabis use was a significant decrease in consumption after 3 months showed ($p = 0.017$) and after 6 months ($p = 0.018$), regarding the amount showed no significant reductions after 3 months ($p = 0.104$) and after 6 months ($p = 0.089$).

For the patients who proved when alcohol consumption is a non-significant decrease in the consumption daily after 3 months ($p = 0.069$) and after 6 months ($p = 0.357$), a significant reduction of fluid intake after 3 months ($p = 0.021$) and a non-significant reduction after 6 months ($p = 0.264$). In cannabis use showed a non-significant decrease in consumption per day at 3 months ($p = 0.082$) and a significant decrease after 6 months ($p = 0.013$). When the amount consumed, a significant reduction was not after 3

months ($p = 0.112$) and a significant reduction after 6 months ($p = 0.039$).

Disease

A significant difference between treatment and the motivation of the supportive treatment on psycho-pathology, medication compliance and Rehospitalisierungshäufigkeit (MI: 0.50, ST: 0.76) did not appear.

Abstinence motivation

Abstinence motivation was both in the experimental group than in the control group before treatment in the middle in the "action stage". Effects on the motivational state were evident in both groups as a whole. When analyzing only those patients who had seen before the motivation of treatment have a low motivation stage aufgewie ("intentionality" and "down - supervisory training"), was found in the experimentalgruppe ($n = 15$) a significant edge raising Abstinenzmotivati - one immediately after ($p < 0.001$), 3 months ($p = 0.003$) and 6 months ($p = 0.023$) after treatment motivation. In the control group con - no comparable effect could be discerned (. Table 2).

Discussion

The investigation could prove that a motivating treatment amounting to four sessions in patients with the double - a schizophrenic disturbances - tion and a substance abuse or a substance dependence peldiagnose compared to a non-specific, supportive treatment - ment of the same length significantly more motivated to post stationary one - on outpatient, integrated gruppentherapeuti - ments can to take advantage (70.0% vs. 40.0%). In studies with suffi - spondingly large number of cases was the so - relevant superiority of the principles of motivational interviewing-based intervention to date only in comparison to standard treatment nachtage after 3 months ($p = 0.069$) and after 6 months ($p = 0.357$), a significant reduction of fluid intake after 3 months - months ($p = 0.021$) and a nichtsignifikan - te reduction after 6 months ($p = 0.264$). In cannabis use showed a nonsignificant decrease in consumption - day at 3 months ($p = 0.082$) and a significant decrease after 6 months ($p = 0.013$). When the amount consumed, a significant reduc - tion was not after 3 months ($p = 0.112$) and a significant reduction after 6 months ($p = 0.039$).

Disease

A significant difference between treatment and the motivation of the supportive treatment on psycho-pathology, medication compliance and Rehospitalisierungshäufigkeit (MI: 0.50, ST: 0.76) did not appear.

Abstinence motivation

Abstinence motivation was both in the experimental group than in the control group before treatment in the middle in the "action stage". Effects on the motivational state were evident in both groups as a whole. When analyzing only those patients who had seen before the motivation of treatment have a low motivation stage aufgewie ("intentionality" and "down - supervisory training"), was found in the experimentalgruppe ($n = 15$) a significant edge raising Abstinenzmotivati - one immediately after ($p < 0.001$), 3 months ($p = 0.003$) and 6 months ($p = 0.023$) after treatment motivation. In the control group con - no comparable effect could be discerned (. Table 2).

Discussion

The investigation could prove that a motivating treatment amounting to four sessions in patients with the double diagnosis of a schizophrenic disturbance and a substance abuse or a substance dependence compared to a non-specific, supportive treatment of the same length significantly more motivated to post stationary one on outpatient, integrated grouptherapeutic treatments can to take advantage (70.0% vs. 40.0%). In studies with sufficiently large number of cases this was the superiority of one regard to the principles of motivational interviewing-based intervention to date only in comparison to the standard treatment for

Conclusion for practice

Overall, it succeeded the present exemplary study using the first time, the significant positive effects of motivation treatment for patients with dual diagnosis of psychosis and addiction to participate in a carry on the outpatient treatment offered in comparison with a non-specifically-suppressing intervention same time scale clearly demonstrated.

From this perspective, it appears to clinical practice - even against the background of the difficult engaged typically forecast of the clients - recommended, to structure appropriate treatment established. It should be on the production of the frame conditions to be respected, the students are prepared for an smooth and low-threshold transition to outpatient follow-up treatment to ensure the effects of treatment on motivation to addiction

unterstützen. Korrespondenzadresse

PD Dr. A. Bechdorf

Department of Psychiatry and Psychotherapy, University Hospital of Cologne
Kerpener Str 62, 50937 Cologne

andreas.bechdorf @ uk-koeln.de Interessenkonflikt. The corresponding author states that no conflict of interest.

NOTE: To refer to [original document](#) for tables and figures.

German. Example 3 (html)

Ro tati ons sta bi li ty no-Mon

focal in trao ku lar sen lin

C-Hap-Hap tics Ver sus Z tics

Kata raktchir metallurgy

Per spec ti Ver ran Do Mi Galvanized comparison

A
llein in German agricultural annual pens... investigations of toric IOL su-ha... point of the study was to develop speaking
Lich approximately 550,000 patients from... that the astigmatism astigmatism... the occurrence on Ner rotation of the IOL to
raktepe rati on. Twice as can NEN-... Ner an IOL rotation of 30 ° and more on... than 10 degrees set firmly.
Ren patients benefit from having a pre-... Compared to the pre ope rative astigmatism
ope rative Astig mus sen widening mat... has still to be strengthened [12]. Rotates... Al materials and the Me tho
the NEN ih a toric intraocular lens in-... Toric IOL by 15 °, so has the pre-
is implanted. In addition to the implantat... Astig matis mechanism to half... For the students who were in the design equi-
Ner toric intraocular lens (IOL) is... reduced [4], in an Ner on rotation by 10... va equivalents MS 612 S lenses with C-haptics
there are other possibilities, a be-... The third is a knotty matis mus reductiv... and MS 6120 Z-haptic (in de IOL
ste Hen mechanism to reduce the astigm... is in der Akt [12]. It can be closed... from Human Optics, He long) and Ver-
as the specific set of zen limba Len dev... he decided that a toric IOL on no-... available. IOL possess at kie de Mar zen changes
las tung cut. The SE method alone... by more than 30 ° rotating case should... the NEN optical system, similar to those found in
However, the only AI can with low astigm... En tes Ope rationsergeb on... toric Intrao sen lin they face similar use det. It
tis men suffizi be used develop. Also... nis to ENSURE, so it should the post-... han Delt here in order spherical IOL
Combinations in the process were Ren... surgical rotation as small as possible... the patients were employed patients in de-
the ben described [6].
höhergra Tues GE Astig matis for mem... antiprimal postoperative rotation... korrekur existed. In the case of de IOL up to
particular de re at the same lie to premat... lergab lie fe position the lens de sign... here feel of building the same: Your total flow-
ope rati ons evaluating the overall gene... natsent feel Naptics of the IOL dar. the... aris at ater is 12 mm, the lens diameter
Thus, the nerve implantation on an histo... CAL pros prospectively ran collective... d... The margins of the optics
IOL on. It can be expected while that aro... l... ugen should because of her Haptik... 2nd Gene rati on (di-me thyldiphe
2 □ al learning Kataraktati patients, wh... ised ere Sp... d... derkonventionel Len nyl si lox on) are sharp-edged mini-chemistry for
about the patients in with a NEM-Astig... C-feel with regard to the postoperative... r... of Ri si kos an Ner after tain on ductile
matis mechanism of more than 4 D, of ar... Rot... tional stability-ons in an nerve-cont... led. Figure 1a, b who the scanning electron
generic IOL benefit authors [3, 8]. This... clinical study compared the ni's are Chen.
but he took aim on the knotty Re ductile... he aim of the study was to evaluate... For n nis se, the resulting water Ar were cooperation as a pre-
served, it is of utmost importance,
that the toric IOL ope rative be the pre-... generic IOL in a rotation on to de NEN... between Oph thal Mon lo gi between Ge sell community DOG
count th axis in reserves and not in... 10 ° or more well si Cher as possible VER... (Sep tem ber 2002 in Ber lin) and are pre sen benefits
Cape sack rotates sel. should be avoided. As a primary end... Mainz developed hal ten.

Figure 3 Three-Stücki GE Si li con-IOL with a C-Hap tics (Ras terelek tro-NEN microtip sko pi Scheme close to me). b Three Stücki GE Si li con-IOL with Z-Hap tics (ras terelek tro NEN microtip sko pi-Scheme to close me)

Figure 4 Box plots for the distributional ro tati on [degree] In the plan tati ons Mon ebe ne 3 natenach The plan ta-Mon ti on an Ner no focal IOL with a C-or Z-Hap tics, strati fi for under the front came Merti fe of the operations operate Eye; Ho ri zon ta Len be signed NEN Me dia ne and Quar-ti le of the ro tati on, Verti calendar Wed xi ma ni times and times oh be ended if Ro tatio NEN, chalk and star se ne be signed NEN statis tic barrels and extreme values from rei

NEN micro-scopic recording of the presented and the positive water-shonLee has just been re Cape sel if Vis koelas ti-the C-IOL haptics and with Z-haptics the. The study was completed under the cumulative injected.

Cli ni cal grade of Good Prac-ce by With an Ner Faltpin zette, the IOL

A total of 50 eyes of 50 patients out. GE in the folded to stand in the Cape sel sack

th Strati fikati were without one and oh- implanted. There she developed with

ne Blockbil training in a ratio of 1:1 to the IOL plan tati on and the haptics si consumers in the Cape sel sack. The

at the sign Haptikde groups ran domi- According to be, observing whethe IOL was turned far to the Mar-kie

Siert, the dominant Ran sati ons te lis was ments on the optical lenses on the de NEN

the SAS software 6.12 for insurance on Operati on the front with a NEM was Horv haautent Languages added. At the end of the opera-

Windows) issue. Exclusion criteria for tati ons controlled AGAINST Mar keurati fied and the seat of the IOL through the

the part close to me in the study were The drip anesthesia with Tetracaine 1 Operatung microscope documented photographically-

liferative diabetic retinopathy, corresponding at 0 ° and 180 ° on the corneamented.

He zündli surface diseases of the eye, Appropriate. All Ope rations were un- Nachunter deviations below the one fan

blyopie or wet macular edema, traumatic standardized conditions catalyzed by Di phra fene surgery and one and

matic cataract, pronounced horn- Chen tors may Ope (BD) performed. Bimonths after ope rative instead. The calculation

the skin damage, Pseu dOax foliatio leflia was a sclerocorneal tion of the IOL rotation was based

Vorope as rations to the to be investig That nel cut open the sides, 2 a slit lamp photography in Re Troil lu-

Chen the eye. ne small parameter set zentesen. Posit Wed culeton, dripped the most eye in

To the ordinary surface of the presentati on the front was a vis-koelas Was sitting.

Mark-IOL post ope rative on ti kum (Healon, AMO) graces injected. The pae left to the respective gene investigation

ENSURE NEN can to have a Pu-te the Cape sel was circularly ventricular Capie ppenisat rates of the Lich un-corrected

pil lenweite in Mydria sis of at least thä or he opened xis. The lens nucleus wa alloyed and the corrected visual acuity objectively

3 mm can be achieved NEN. The pre- Crushed by phacoemulsification determined. Furthermore, the spherical

have been mis si on the ethics of and vacuumed. The Cape was back sel and the cylindrical dri Scheme Re frac determined on

Lan desärz tekam Rheinland-Pfalz mer Thoroughly polished as possible Sun Inat calculates the spherical equivalent.

Ro sta bi li tati ons Mon ity no focal in trao ku lar sen lin C-Hap-Hap tics Ver sus Z tics Kata raktchir to metallurgy. Ver ti prospective ran Do Mi Galvanized comparison

Together men fas sung

The aim of the study was to compare the rotation of IOLs with C-loop haptics and Z-loop haptics. The study was conducted in a prospective manner. The primary finding of the study was that the rotation of IOLs with C-loop haptics was significantly greater than that of IOLs with Z-loop haptics. The rotation was clockwise. This was 40% (IOLs) with C-loop haptics and those with Z-loop haptics ($P = 0.33$).

Tively were 50 pros pek Kata Rakas fifteen-and 3 months months in ordination from the implant tati ons ach se, it can Chen Tei Len th same to the De signifirotiert. Ten the show zi ell th in the long running time delays from TEN zi ell the higher equi va Len th IOL MS 612 S (C-Hap) and Z-Hap tics IOL was on 1 Day. The average only Mi Ma Len deviation was 15.5 degrees clockwise after 3 months. The rotation of IOLs with C-loop haptics was significantly greater than that of IOLs with Z-loop haptics. The rotation was clockwise. This was 40% (IOLs) with C-loop haptics and those with Z-loop haptics ($P = 0.33$).

In the group of group C-Hap tics IOL rotated 40% in the raktchir metallurgy an IOL-ro tati on the tu di of 0° at then ($p = 0.33$).

Ro tation al sta bil i in trao cu lar Tyn lens it with C-loop hap tics Ver sus Z hap tics in a cat ractsurgery. A prospectiveran dom is ed com par i son

From abstracts

The aim of the study was to compare the rotation of IOLs with C-loop haptics and Z-loop haptics. The study was conducted in a prospective manner. The primary finding of the study was that the rotation of IOLs with C-loop haptics was significantly greater than that of IOLs with Z-loop haptics. The rotation was clockwise. This was 40% (IOLs) with C-loop haptics and those with Z-loop haptics ($P = 0.33$).

A total of 50 patients with cataracts were included in the study. The study was conducted in a prospective manner. The primary finding of the study was that the rotation of IOLs with C-loop haptics was significantly greater than that of IOLs with Z-loop haptics. The rotation was clockwise. This was 40% (IOLs) with C-loop haptics and those with Z-loop haptics ($P = 0.33$).

Table 2

Author (s)	Random number of follow-up	In the implanted IOL type	Frequently fig strength [%] clinical technically relevant ter ro tatio NEN
Till et al. (2002, [15])	100	Tori Scheme Plat th hap ties - Si li con 10.8 mm or 11.2 mm	11% > 15 °
Patel et al. (1999, [10])	23	Plat th hap ties - Si li con 10.8 mm	67% ≥ 10 °
Whipp (2001, [4])	26	Folding ba re C-Hap ties - PMMA	41% ≥ 10 °
Chang (2003, [1])	50	Rigi de C-Hap ties - Si li con	23% > 10 °
Was lo et al.	25	To ri Scheme Plat th hap ties - Si li con 10.8 mm	60% > 10 °
	25	Folding ba re C-Hap ties - Si li con	6% > 10 °

The tegibi letzte Spal the genes from each wei li profit decreased to be rich ere th eru ba larger share clinically relevant electronically van ter ro tatio NEN by 10 or 15 ° from the plans ta ti ons to ebe ne

Stratification along a gradual un- tive astigmatism matis mechanism and The C-haptic display th 59 de a mil, differences in the front was between Mepanrefative composition men hang [432] a mode-rate and 9 a Swedish re between the banks at the haptic-group On a 30 ° rotation has a knotty matis C-rotation. So the total was 41 of Top Ten described tendency of the haptics for GE, of the pre ope rative haptic Glamin of the maximum of 10 degrees rotated. On the rotation against the show Clockwise corresponds, ie, a COMPLETE the IOL with plate haptic display ken th a Effect of the repeal bungdes toric IOL at what worse outcome with 67 al- The observation observations of Shi M IOL cleaning, the latest minutes of the 10 ° rotated to ers th Kol selectively toric IOL confir the th 36). The late Ermittlung der rotational For a postoperative rative rotation on the Cape the sethoretic conditions A book from 6 months postoperatively rative. Here- sel can sack NEN meh several causes Ven investigated IOL sen as 20 a ro-schnittidie plates in haptics table statistically sig- ant sible be: is such a temple of tati on of over 30 °. When the patient rately better water (p < 0.01), it proved Not feel si consumers in the Cape sack FIB was induced astigmatism in a strong wavy stable once it one time a cer- it comes to an inevitably lauter fig Ver die tis ben described so that the author stiele in the Cape sel sack sat [10]. tion centering and an Ner rotation of the KOL at a rotation on more than 30 ° Till et al. retro prospectively studied 100 [7, 11]. Also, a tongue of the Cape Vefletic IOL was to avoid the [13]. Eyes nach Implantati on: r-folding line sacks pre-or intra ope rative can be used fischer et al. investigated in an NEMen [15]. There were plates IOL haptics in- Vermin tion de ne the stability of the IOL from 1994-1999 prospectively investigated, the water through a measure of ant- Ver wortlichsein ant. If a failure has VERes with a nervous rigi the toric IOL or 10.8 mm (Staar AA-4203 TF) or nis ba tween Cape sel-through bag and FOMMA [4]. The gene se einstiecki IOIStaar AA-4203 11.2 mm TL), so as: sen (before, so these were heaped measure rind op stit these Stiecki gene of IOL 62 of the water IOL sen as a postoperative rative Rative observed rotations of the IOL [8] in modifi ed C-haptic ken, the Deviations of ± 5 ° and less of the ger similar rates Lich li che Undul requirement opacit astigmatism planned, 27 wa- The frequently figs te reason for a rati on of the genes lie before the study, rind rati on up to 15 ° Lich rotates and 11 of IOL is a post-operational rative Kap sel sen. Of the 26 IOL rotated in the first the IOL was rotated through 15 °, 6 of sack-contraction on [9]. The changes IOL a weeks 6 th (23 of) by more than 14 ven over 30 °. These five the IOL, the more Cape of sel gene sacks fin the main Phab of which as many as 15 to oo. All stiecken IOL from the planned Ah se differed in the first ten 3 months after implantati on an NEM period of 3-6 weeks have been in half an egg Ner weeks postoperative ra- held on [14]. A rotation on more than by means of a rotation parameters zen time repositioned [15]. 90 hättieher in theory, a doubling of under anesthesia, the Drip they reposition d rati on able examined 2003, the country- pre ope rative lungdes Astig matis algom it h tices to an NEM th stop in the fere drives IOL haptics [1]. He implanted Fol GE. The IOL would be more then Cape sel sack led [4]. te the Staar AA-4203 TL is the total of 50 the axis of the weakest, but countries with Patel et al. Chen compared 1999 in Eye and studied the postoperative rative of the TENs cylindrical refractive powder in the study catalyzed the rot rati on able they hold ons. After 1 postop- parallel to the cylinder derfehler the TEN intermediate foldable IOL with plate rative month as the sen se IOL with a Cornea. The cylinder at derstärken C-haptic ken of silicon con, the feel- here at the Z-haptics vorgefun NEN de would then ad the REN, instead of like loops of the C-haptic IOL waren from rati on able rotational stability [1] to ben he planned on each other. polypropylene [10]. Early on after ro (Zoll) to ma xi rotated by 5 °, 18 of to Gerten et al. calculate the influence in ficks he said in mild conditions (10 ma xi by 10 °, 8 of to ma xi by 15 °, 2 of to tion of the IOL rotation for the post- opacit rat (10-30 degrees) and heavy (over 30 °).

The study described here shows that the Z-haptics are compatible with the current literature. The correct response result in favor of the Z-haptics, which is consistent with the current literature. The correct response result in favor of the Z-haptics, which is consistent with the current literature.

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Correspondence: Prof. Dr. HB Dick

Klinik für Ophthalmologie, Poliklinik für Ophthalmologie, Universität Mainz, Lan Gen beck strategic size 1, 55131 Mainz, Germany
E-mail: bdick@mail.uni-mainz.de

Hebrew. Example 1

Risk factors for suicide attempts in patients with Comorbidities
[Authors]

Partially presented at the annual meeting of the services
Mental Health) Ministry of Health (Prevention
Suicidality, March 2007, Jerusalem and gathering
15th Annual European Association of
Psychiatry, March 2007, Madrid, Spain.

Background: This article reports on patients with mental disorder to substance abuse while
Abuse - especially of drugs or alcohol. Substance abuse related behavior
Suicidality. Despite increased knowledge about substance abuse and suicidal behavior,
Information about suicide lacking comorbidities.

Goals: 1 (compare the rates of suicide attempts of patients with comorbidities
And the mentally ill did not consume drugs or drug addiction; 2 (determine risk factors for attempts
Suicidal double-morbidity among patients.

Methods: Analysis of 3433 consecutive hospital admissions: men and women aged 65-18 years Health
Center

Mind) between the 6.2003-to 5.2005-(.

Results: Of 848 hospital admissions of patients with comorbidities, 197) 23.2% (they were after
Making suicide attempts, and in 2558 hospitalizations of patients with mental disorder

No drug addiction, 403) 15.8% (there were after suicide attempts), odds ratio =

1.6; 95% from 1.9 to 1.3 (. After adjusting odds ratio = 1.4; CI 1.8 to 1.1,

I mean did not change significantly. Based on multivariate regression, urinalysis with

THC (Tetrahydrocannabinol (a protective factor, while the diagnosis of personality disorders and
behavior

) By classification of psychiatric disorders from the International Classification of Diseases, version)
ICD - 10 (10

Is a risk factor for suicide attempts.

Conclusion: Patients with comorbidities are at increased risk for suicide attempts

Compared with the mentally ill without drug addiction. An expanded training program is required to
order Rabbi

Professional, to reduce the rate of suicide attempts with morbidity patient population

Double.

Scientific background

Suicide is a leading cause of mortality in Israel. Suicide rate

Adjusted for age among men in Israel is 13.0 to 100,000 and in

Women - 3.2 to 100,000 between the years 2000 to 1998 [1]. Morbidity

Mental is one of the factors related to suicide [2]. It is known that consumption

Drugs is a risk factor for suicide] 3, 2 [among the mentally ill] 9-4 [.

Gossop et al] 10 [check scale and common causes of death for 4

Years cohort study included 1075 subjects drug addicts, who

Recruited in England during 1995 - 54 rehab treatment programs] 10 [.

The researchers found that the annual mortality rate was higher among subjects

6 times more than the general population, categorized by age. About 40.0% of

Deaths were attributable to deliberate self-injury.

In recent decades indicates the proportion of patients with comorbidities

Dual Diagnosis Patients - DDP (, and now stands for 25% of

Hmtaszim] 11 [. Dual problem of suicidal morbidity increases

Present unpredictable effects of addictive substances against integration

With medications. Both men and women with comorbidities are

Higher risk of suicide compared with patients of both sexes who do not mind

Drug needs] 12 [.

Beautrais et al] 13 [found that the risk of attempted suicide among patients
People with addiction disorders) Substance use disorders (2.6 times higher
) CI 95% ranged between 1.6 and 4.3 (compared to people without
Mental disorders. One of the factors related to suicide is making
Attempted suicide in the past. Therefore, knowledge of past suicide attempt may
Help prevent future suicide attempt or suicide.

Dalton et al [14] attempted to determine clinical predictors of attempts
Risk of suicide among 336 patients with schizoaffective disorder, bipolar
Bipolar I (I (or bipolar Bipolar II (II (. The researchers found a
Only a single predictor: diagnosis) at least once in a lifetime (of Mental Disorders
As the consumption of addictive substances) Lifetime co-morbid substance
) Use disorders

Information on attempted suicide in the past may prevent attempted suicide
Future or suicide. Dual problem of suicide increases morbidity
Present unpredictable effects of substance abuse against a combination with
Medications. To date no scientific evidence as an answer to the question,
Are there comorbidities population sub-groups with increased risk for
For suicide attempts?

The current work aims to compare the rates were attempts
Suicidal patients with comorbidities and the mentally ill who
Consumed drugs or drug addiction, and attempts to determine risk factors
Risk of suicide among patients with comorbidities.

Method

Sample: watch all 3433 hospitalizations) men and women aged 65-18
Years (from June 2003 to May 2005, Mental Health Center
Abarbanel.

Tools:

1 (a mental disorder was determined by classification of psychiatric disorders
International Classification of Diseases, Version 10.

2 (addiction collected information on self-reported and / or by testing
Aimonomocrumtografit urine drug), THC, Opioids, Cocaine, Methadone
Amphetamines, MethylenDioxyaMphetAmine - MDMA (laboratory
) When receiving a patient hospitalized (. A urine drug was to 1794
) 52.2% (Nbdkim.

3 (Information about suicide attempts the two months prior to hospitalization
Mental Health Center, received self-reported by patients as part
An integral part of their examination in the emergency room.

Procedure: After receiving approval and the Institutional Ethics Committee for
This study, conducted computational Reports Analysis Center of hospitalized
Abarbanel Mental Health, Bat - Yam.

Statistical analysis: was performed using SPSS-PC software and all the
All subjects in the sample. Odds ratio) [Odds Ratio [OR (and CI
Within 95% confidence interval [95% CI] (95.0% (calculated for
Suicide attempts than among patients with comorbidities and
Mental patients without substance abuse.

CI of odds ratio, which did not include a value of 1.0, considered
Statistically significant. CI of the odds ratio included the value of
1.0, was considered as statistically significant.)) NS = Non significant

Results

The scope of suicide attempts before hospitalization in two months: During the study
period reported 600 suicide attempts) 17.5% (

From 3406 hospitalization of the mentally ill, as follows:

- 197 suicide attempts) 23.2% (of 848 hospitalizations of patients
Comorbidities;

• 403 suicide attempts) 15.8% (of 2558 hospitalizations of patients
People without substance abuse.

Therefore, the rate of suicide attempts hospitalizations of mentally ill
Without comorbidities two months prior to hospitalization was 15.8%, but
Hospitalizations of patients with comorbidities ratio is OR = 1.6; (23.2%
) Unadjusted 95% CI = 1.3 - 1.9

To neutralize possible confounding factors, analysis was conducted using
Logistic regression) Logistic regression model (. Final model included variables
Age) 29-18; 39-30; 49-40; 65-50 years (gender) men and women (where
Birth) in Israel, the former USSR, then (, marital status) were married, then (,
Determining psychiatric diagnosis according to ICD-10) mental and behavioral disorders
Due to the consumption of addictive substances] F 19-10 [, schizophrenic disorders) F 29 -
20 [, Affective Disorders] F 39-30 [, neurotic disorders, disorders
Related - stress) Stress-related (and interference Somatoformiot[,] F 48-40
Personality disorders and adult behavioral, psychiatric observation, then (,
Determining at least one physical diagnosis) Yes, no (, length of hospitalization) 12-0; -13
59, 60 days or more (. Based on the model OR did not change significantly
) Adjusted OR = 1.4, 95% CI = 1.1 to 1.8 (

Risk factors for suicide attempts among Patients with comorbidities

Associations between suicide attempts and age, gender, place of birth,
Marital status, determination of psychiatric diagnosis by ICD-10, Set
At least one physical diagnosis, results of urine tests each type
Drugs, and several types of drugs at the same time the results of urine tests.
Association between suicide attempts and each variable

Following:

Following:

- Set a psychiatric diagnosis); Likelihood ratio = 58.1; df = 60
) P <0.001
- urine tests for THC: suicide attempt risk among patients with morbidity
Double with explicit testing positive compared to 2.5 times lower
Patients with comorbidities explicit as negative tests) = OR
) 0 0.4, 95% CI = 0.3 to 0.6
- opioid urine tests: suicide attempt risk among patients
Comorbidities with positive explicit tests 1.6 times higher
Compared to patients with comorbidities explicit as negative tests
) OR = 1.6, 95% CI = 1.01 to 2.5 (
- urine tests cocaine: a risk to attempt suicide in patients with influenza
Double-positive with explicit tests 1.9 times higher compared to patients
Comorbidities with explicit tests as negative), OR = 1.9
) 95% CI = 1.1 to 3.2

To determine risk factors for suicide attempts among patients
Comorbidities, were analyzed by logistic regression model) Logistic
regression model (. a variable depends on the chosen variable 'suicide attempts
Two months prior to hospitalization "with two sub - categories" yes "and" no ".

The analysis was conducted in the following steps:

1 (tested relations between the variable "suicide attempts" and each
Variables found significant association with him before regression analysis: those
Variables were associated with suicide attempts even regression.

2 (all these variables were tested joint model. Two variables were
Risk factors:

- Set a psychiatric diagnosis)) OR = 0.4, 95% CI = 0.2-0.6
Some groups of diagnoses (Table 1).
- urine tests for THC: patients with comorbidities urine tests
Positive low-risk suicidal attempt by 2.22 compared with patients
Comorbidities with explicit urine tests as negative) = OR
) 0.45, 95% CI = 0.3-0.7

Table 1 is that OR attempted suicide among patients morbidity

Dual diagnosed as having schizophrenic disorders) F 29-20 (though low 2.77 compared with patients with mental and behavioral disorders due Substance abuse) F 19-10 (. Also, OR attempted suicide among patients Comorbidities diagnosed as having personality disorders and behavior) F 69-60 (2.41-fold higher compared with patients with behavioral disorders And mental health as a result of substance abuse) F 10-19 (. Analysis of the entire model X2 index was $n = 772$; $df = 3$, $P < 0.001$ (76.83 (and the index 2 Log - Likelihood = 761.8 3 (these two variables were tested model interactions between them) Table .) 2

Table 2 is that OR attempted suicide among patients with morbidity Double, one with a diagnosis of schizophrenic disorders, in combination with Positive urine test result for THC at the same time, the low was 3.33 Double morbidity compared with patients with behavioral and mental disorders As the consumption of drugs, combined with the explicit result of a urine test Positive for THC at the same time. Analysis of the entire model X2 index was 22.1 $n = 772$; $df = 6$, $P < 0.001$ ((and the index 2 Log Likelihood = 816.4 -

Discussion

his research work mainly focused on attempts to determine the risk factors Morbidity risk of suicide among those taking a double. The main finding of This study shows that demographic factors do not predict Suicide attempts in patients treated with double-morbidity. Two Only clinical variables were risk factors for suicide attempts. The first variable is the psychiatric diagnosis is established. More Probably schizophrenic disorders) F 29 - F 20 (are as protective against Suicide attempts, and personality disorders and behavior)) F 69 - F 60 Constitute a risk factor for suicide attempts. Patient diagnosed in Lucca Schizophrenic disorders with consumption of addictive substances, is 2.77 times less likely to attempt suicide than do patients with disorders Behavioral and mental health as a result of substance abuse) F 19 - F 10 (. Risk Of a patient diagnosed with personality disorders and consumption behavior with Substance abuse-to attempted suicide, compared with 2.41 times higher than untreated With behavioral and mental disorders as a result of substance abuse) F 10 F 19 - (. Do not deny that the range of services) are hospitalized and in the community (Available to patients with schizophrenia) with or without comorbidities (Ensure close monitoring of other, more mental, including early detection More suicidality) thoughts / plans, suicide attempts (. The second variable is urine tests for THC. Morbidity in patients with Double and a positive urine test result for THC, the risk-to attempt Low losses by 2.22 compared with patients with a score comorbidities Negative urine test for THC. Probably caused by a syndrome Lack moved) Amotivational syndrome (, expressed a sense Adshon) Apathy (lack of energy, lack of ability and desire to complete tasks Etc.] 2, 15, 16 [. However, do not ignore the interaction between diagnosis Psychiatrist with the results of urine tests for THC at the same time: as of Patient diagnosed in one schizophrenic disorders in combination with the result Positive urine test for THC at the same time, his risk-to attempt 3.3 times lower losses compared to being diagnosed with behavioral disorders And mental health as a result of substance abuse in combination with urine test results Positive for THC at the same time. No scientific evidence on examination of a link between cannabis consumption Cannabis ((in which THC is the active material, and suicide attempts: No population of adult patients with mental disorders and Population of patients older comorbidities. Wilcox et al] 17 [claimed that there is very limited information about prospective Estimated relationship between suicide and cannabis consumption among the general population. Therefore, the analysis - the researchers could not determine mortality rates

Revised following the consumption of cannabis compared with alcohol or opioids. Hence, should not be denied the protective effect of hashish from attempted Suicidal population with comorbidities, but studies in Extended cohort to get more information about the phenomenon. With However, reported a link between suicide attempts and the frequency] 18 [and Age Beginning of the consumption of cannabis] 19 [. No form study Can recover data on the frequency of consumption of cannabis and pulled, And get a more complete picture about the phenomenon. To prevent both suicide and suicide attempts, you should identify Population at risk] 2, 20 [. The findings indicate The essential need for an expanded training program multidisciplinary team, the To reduce the rate of suicide attempts in the population at risk with Comorbidities.

Summary

Comorbidities in patients at increased risk of attempts Suicidal mental patients compared with no drug abuse or addiction Them. Positive urine test for THC is a protective factor, while the diagnosis Personality and behavior disorders) according to classification of psychiatric disorders Of the International Classification of Diseases) ICD - 10 (a risk factor Suicide attempts. Patients with comorbidities urine tests which drugs were discovered Increased risk of serious suicide attempts compared with patients With comorbidities with urine tests that were discovered in which soft drugs. With However, urine tests found them hard drugs were not found to cause Predictors of suicide attempts. Requires an expanded staff training program Multidisciplinary in order to reduce the rate of suicide attempts in the population Comorbidities.

Author author: Yuri Gimlfrb
Abarbanel Mental Health Center
Bat Yam, affiliated to Sackler Faculty of Medicine
Tel Aviv University
Email: ystatist@gmail.com

Table 1:
Suicide attempt risk and determining the psychiatric diagnosis

קביעת מבחנה פסיכיאטרית (לפי ICD-10)**	OR	95% CI	
		גבול עליון	גבול תחתון
Mental and behavioural disorders due to substance use* (F 10-19)	1.00		
Schizophrenic disorders (F 20-29)	0.36	0.55	0.24
Affective disorders (F 30-39)	0.84	1.81	0.39
Neurotic, stress-related and somatoform disorders (F 40-48)	2.82	8.74	0.91
Disorders of adult personality and behavior (F 60-69)	2.41	4.58	1.27
הסתכלות פסיכיאטרית	0.87	2.02	0.37
אחר	0.98	3.00	0.32

* Reference category*
** ICD - 10: International classification of diseases and health related problems, 10th revision (1992)

Table 2:
Suicide attempt risk and determining the interaction of psychiatric diagnosis with a score
Urine tests for THC

קביעת מבחנה פסיכיאטרית (לפי ICD-10)**	OR	95% CI	
		גבול עליון	גבול תחתון
Mental and behavioral disorders due to substance use* (F 10-19)	1.00		
Schizophrenic disorders (F 20-29)	0.30	0.53	0.16
Affective disorders (F 30-39)	0.82	2.09	0.32
Neurotic, stress-related and somatoform disorders (F 40-48)	0.91	8.86	0.09
Disorders of adult personality and behavior (F 60-69)	1.22	4.02	0.37
הסתכלות פסיכיאטרית	0.61	2.85	0.13
אחר	0.69	6.18	0.08

* Reference category*
** ICD - 10: International classification of diseases and health related problems, 10th revision (1992)

Hebrew. Example 2

Link between whooping cough in infancy and childhood asthma

[Authors]

Abstract:

Background: The past decade has seen an increase in frequency as she groaned. View of the relationship between asthma Bronchiolets infancy, the question arises whether a similar relationship exists between pertussis asthma. Objective: To determine whether there is a connection between the disease as she infancy) age > 6 months (childhood asthma) 9-3 years (. .

Methods: Two groups were compared with children who applied to the emergency room before age 6 months due to a cough. The study group was diagnosed with whooping cough in the control group denied pertussis) testing PCR-Polymerase Chain Reaction (. Asthma diagnosed in childhood questionnaire filled by parents.

Results: Out of 393 children referred to the emergency room, responded to the questionnaire were identified in 44 children in the study group and 52 children in the control group. There was a significant difference between groups in terms of epidemiological data) Age] median and range [when checking when she came 2.2) 6-1 (months with 3) 6-1 (months, sex and area of residence (except for more children of Arab descent in the study group) with 38% $P < 0.05$, 15% (. more children in the study group were hospitalized because of cough when referred to the emergency room) 75% with $P < 0.01$, 46% (. There was a significant difference between groups in the percentage of children immunized as she or environmental or genetic variables that can affect the incidence of asthma. no significant difference between the study group prevalence of asthma control group) 18% vs. $P = 0.24$, 9.6% (or atopic diseases), allergic rhinitis, hay fever, inflammation Lhmioat, or atopic dermatitis (. Similarly, the population of children hospitalized in infancy did not This study found a significant difference in prevalence of asthma in the future between the study and control group) 18.2% vs 8.3%, respectively $P = 0.44$ (. However, the combination of asthma or atopic in this population was significantly higher in the study group) 33% against.) $P = 0.03$, 8.3% In summary, the present study found that pertussis in infancy significantly increases Prevalence of childhood asthma.

Introduction

The prevalence of asthma) Asthma (in Western countries is on the rise 1. One possibility to explain this phenomenon is the theory of proofs.) Hygiene ie, following the "Key world" more due to better sanitary conditions, immunization and breastfeeding, caused fewer infections in infancy. Certain infections known Mshpalym the system Th1) T helper type 1), which causes the immune response to suppress the development of Th2 (T helper type 2). In their absence, a system the Th2 activated and may develop asthma 2,1. At the same time found that certain infections in infancy as Bronchiolets against Respiratory RSV (Syncytial Virus (may actually cause asthma in childhood. These children, due to interference with a Th1 defensively, morbidity by RSV is more difficult while no suppression of the development axis direction 3-1 Th2.

With the rise in asthma prevalence, there is actually a renewed outbreak of when she came. The question arises whether there is a connection between the two phenomena? When she's disease, similar to RSV, particularly affects infants and infancy, and ask whether this infection can also lead to asthma? Since 1999, there was an increase in frequency when she came, even though there was no change if the national vaccine 4. Main victims are children aged less than or children aged 15-5 years, mainly or partially immune children who are not immune. An infectious disease caused by the bacterium as she's immune response officers Thai Th1. Recovery from the disease depends on Specific response) specific (the Thai Th1, which secrete interferon- γ , if cleaning is important respiratory bacteria 5. In light of immune system activation in response when she came - mainly Th1 mechanism, but also mixing with a Th2 - which may be incurred may be) at infancy (an imbalance in the development of the immune system as on RSV increased incidence of asthma.

Information in the literature regarding the relationship between pertussis in infancy childhood asthma is limited and based largely on retrospective work 6-8. Most of them were made when the diagnosis as she made many years ago, the diagnosis of pertussis was based on an interview parents about symptoms when she came not on proof of infection in infancy. Today Testing is done primarily through the method - PCR Polymerase Chain Reaction (, (, which Ahatvssanv this work for pertussis diagnosis 9.

In conclusion, given the proximity of the symptoms of asthma prevalence increased in parallel with the explosion when she came, it is assumed that significant respiratory morbidity due to whooping cough in infancy, similar to RSV, can cause childhood asthma. The goal in this study was to examine whether there is a link between the disease as she infancy) age > 6 months (the development of childhood asthma) aged 9-3 years (. .

Research Methods

Study compared two groups of children who applied to the emergency room Bnai Zion Medical Center in Haifa before the age of 6 months due to cough) between the years 2004-1998 (. In the study group was diagnosed with whooping cough in the control group deprived of pertussis by PCR test 9. Determining the diagnosis of childhood asthma was made according 10,1 standardized questionnaire to answer the parents when the children were aged

9-3 years, after the explanation given to them by one of the authors) S. A. (. not included in the study: children with respiratory tract disease or against the heart, with abnormal development when referral to the emergency room, and children could not be detected when the questionnaire or whose parents did not respond to fill the questionnaire. The study was not hidden, but checking the questionnaires did not know when processing the data which of the children belongs to the study and control group.

Collected data about pertussis diagnosis by PCR test, symptoms of whooping cough based on a standardized questionnaire (11) relating to clinical disease manifestations ie cough, Whooping, shortness of breath, pauses in breathing, as a window, vomiting, fever (data on vaccination against whooping cough when you contact sorting infancy asthma diagnosis based on standardized questionnaire 10,1) allows to check the incidence of asthma, A family or family of atopic asthma, environmental factors such as smoking, stuffed animals at home, atopic background could be a risk factor for asthma. A positive answer to the question of asthma diagnosis by a pediatrician or a doctor lung was considered diagnostic. In addition, diagnostic treatment were permanent or seasonal asthma attacks by the treating physician, hospitalization for asthma or more than five positive answers to questions about asthma diagnosis (. .

Statistical processing: variables Aktegorieleime χ^2 or notice made Fischer's notice Continuous variables were Unpaired t-test or notice Paired t-test, depending on the groups were examined. Data are presented as mean and standard deviation or median with range. A P value of 0.05 was considered statistically significant.

Results

The initial study group included 353 children who applied to the emergency room Bnai Zion Medical Center due to cough and went as she suspected PCR test. The study group consisted of 106 children diagnosed as she blocks, while the control group included 247 children without pertussis. Two out of all the children who applied to the emergency room were not included in the study, due to chronic lung disease such as Alipat Achstiat Cystic fibrosis (. Two died - one from each group - as causes of death were unrelated to asthma or as she. In total, 41%) 44/106 (The study group versus 21%) 52/247 (the control group had responded to the questionnaire are provided for.) P <0.0001

Table 1 presents the demographic data, as well as environmental and genetic variables that can affect the prevalence of asthma. Groups were similar, except for a higher rate of children of Arab descent in the study group.) P = 0.01

No significant difference was found between the percentage of children with asthma in the study group) 8 / 44] 18.1% [(compared with the control group) 5 / 52] 9.6% [, P = 0.24 ((. There was a significant difference between the two groups in terms of prevalence of atopic diseases) hay fever or atopic dermatitis (or a combination of asthma prevalence and / or atopic) 13/44] 29.5% [with 8 / 52.) P = 0.13,] 15.4% [

When you emerge of cough in infancy were hospitalized significantly more children in the study group 33/44 (75%) compared with control group P = 0.006), 46% (24/52. The population of children hospitalized, suffering from more severe morbidity, higher rate was not significant asthma research group) 6 / 33] 18.2% [compared.) P = 0.44,] 8.3% [2 / 24, however, is more the combination of asthma and / or atopic) 11/33] 33% [compared.) P = 0.03,] 8.3% [2 / 24

No significant difference was found by immune against whooping cough) at least one dose (the control group - 40/52) 77% (study group - P = 0.65)) 73% (32/44 (. In addition, no difference was found among all children) groups Research and Control (unvaccinated children by children with asthma when she came 2 / 13 (15%) and children without asthma.) P = 0.53 () 29% (24/83

Discussion

In a retrospective study that tracked children who applied to the emergency room because of cough in infancy), age > 6 months (. No significant difference in childhood asthma prevalence among children that occurred as she and the children that occurred as she.

Following the recent increase in incidence of whooping cough equivalent asthma, the question of whether whooping cough in infancy is a risk factor for asthma development, similar to RSV? Many studies proved that inflammation Ahsimponunim Bronchiolets (from RSV in infancy 12,3,1 asthma prevalence increases. It is unclear whether the pollution itself causes asthma or whether children who suffer at an early RSV have a tendency to obstructive airway disease, the infection is only a factor which stimulates the development. the relationship between inflammation and asthma Ahsimponunim genetic theories have been proposed 13 key body inflammatory reaction disrupts the normal development process of the airways 15,14, the balance between Type 1 responses and Type 2 of the immune system Legg 0.3 to 1 Vahab, showed that the poor response to Type 1 or Type 2 response increased related to RSV and inflammation Ahsimponunim, and can disrupt the balance [between the two systems contribute to the development of asthma.

Previously conducted several studies trying to demonstrate that children develop pertussis asthma patients in old age frequently than other children. But mostly, this contact has not been proven clearly 8-6, 16. We analyzed these studies to determine how the new coupe in the "research" may add up to date information to help answer this question. In one study 6 examined whether increased incidence of asthma in children that occurred between the years 1979 to 1977 on Whooping cough before age compared to age and gender match controls from the same class at school. Families completed a questionnaire about asthma cough, and each child had respiratory function test. Both groups matched in terms of epidemiology, but differed in several variables. Principal of which was only about 6% of the study group are fully vaccinated against pertussis compared with about 32% of control group. Perhaps this difference was due to address parental asthma against vaccine against whooping cough, and

it is unclear which came first - asthma or whooping cough. Prevalence of asthma and diseases that make contact parents to the hospital, such as respiratory diseases and fevers, hay fever, pneumonia, severe ear infections (and other diseases) such as measles and chicken pox, was higher in the study group relative to the control group. Processing results without children's family background and asthma, patients still had more asthma research group. Respiratory function in the study group tended to be less good than those of the control group, but without statistical significance. In this study demonstrated that there is more respiratory morbidity in children in the past as she. But this study several Limitations: 1 (The fact that he was a relatively early period, and 2 (the fact that when she came up to a year in retrospect was diagnosed clinically based on only 3 (the fact that there is a difference between the two groups the number of types of morbidity and immune against pertussis. Such differences may suggest the initial bias, and influence the reported incidence of atopic asthma 17.

Another retrospective study conducted in 1990 and seventh in both German. This study examined about 26 000 children aged 10 years or so. East German children vaccinated against whooping cough, in western Germany children were not vaccinated. The study was based on questionnaires to parents allergy tests. Was predictably higher incidence of pertussis in western Germany. Were no differences in asthma prevalence between the two groups, but found a slight increase at the rate of allergic rhinitis in West Germany versus East Germany. However, it seems as she was not related, but other environmental allergens. In this study, a relatively early period, pertussis diagnosis made retrospectively using a questionnaire and at the age of infancy and environmental components are completely different between the groups.

The study of Johnston Vahab 8 was conducted in England due to the increasing incidence of pertussis in the early eighties, in light of vaccines in the mid-seventies. This study was a continuation of research conducted by the same group of researchers published three years earlier, determined that children with pertussis line Aananze more of respiratory morbidity, but their spirometry indices were identical control group 18. In the second study the researchers focused on long-term follow-up for that group. The average age of morbidity as she was four months. Testing is done by a questionnaire that parents fill clinical indices. Respiratory disease assessment was carried out by three components: a questionnaire for parents about respiratory symptoms of children last year, respiratory function notice skin allergy. Groups were consistent with epidemiological terms, the average age when the study was 9.9 years. Aananze or family of atopic asthma in the child were higher in the study group. The study group suffered more colds and there were more positive allergy skin notice. Had a tendency to more respiratory complaints in the study group, but not significantly, and there was no difference between the respiratory function tests in both groups), including over-reactivity test (. Some limitations to this study: The study period is relatively early, as she was determined mainly by clinical symptoms and was possible to determine that children of control group did not apply as she ever. In addition, due to the problem of response was tracking only 36 of 360 pairs) Research and Control (children included in the initial study. researchers conclude that pertussis does not cause respiratory future morbidity, but may have whooping cough occurs or is diagnosed in children with a genetic predisposition or environmental encourages respiratory morbidity.

Sundqvist Vahab 16 compared 12 children that occurred before age when she came with a control group by age and sex) 56 children (not ill when she came. Pertussis diagnosed by interview with the parents, tests Sarology culture tests. Being of children aged 4 years completed a questionnaire to diagnose atopic parents or asthma. The results yielded no difference in incidence of asthma or atopic between the two groups.

Johnston Vahab 19 followed 1392 children born in March 1958, aged 7, 11, 16, 23 and 35 years. Reporting wheezing or coughing fits as she made by parents included advanced age. Was a significant difference between parents' reports and included. Impact When she was examined in this study group of 215 children suffering from their past when she came before the age of 7 years. It was found that these children line lung function decline in relation to the control group, but this decrease was less than that observed in children who otherwise pneumonia in childhood. Adults suffering from the past as she no significant change in exhaled volume first second, but a significant decrease at $P = 0.04$ (Forced vital capacity (compared with the control group. Is a difference between the sexes: men suffering from the past as she affected than women suffering from this disease. This study was different from other studies: is prospective, as she examined him in childhood influence) and infancy (the respiratory morbidity in elderly) and childhood (.

A review of this literature indicates that as she has not been proven causes asthma in infancy childhood or adult age. These studies included were characterized by several large, comprehensive tests to diagnose asthma and as long surveillance. However, shortcomings were: demonstrating as she was on the basis of symptoms by parents and memory based on laboratory evidence of pertussis, since most of them retrospective morbidity was many years ago. Children's growth environment and incidence of asthma morbidity as she was different from today. Although follow-up was long term, but is difficult to prove the past pertussis and contained information about the exact date, there have been. In addition, children were exposed over time other environmental variables that may affect the development of asthma in elderly.

This study is unique in that he edited, so the results are relevant to answer the question recently raised relationship between asthma when she came, and diagnosis when she came it was clear) PCR test (. Pertussis proof of the first six months of life, which is a significant development period the immune system. Part time We chose to follow close proximity allows tracking whooping cough in infancy and childhood asthma, with relatively few additional variables in a child's life. However, this is a significant time period) at least three years of follow-up (that can allow an answer to the question of research. Nevertheless, the findings in our study are not different from those reported in the past, and they confirm the lack of association between whooping cough in infancy childhood asthma.

You can ask, then, why pertussis behaves differently from RSV in infancy. Answer to this question is complex. Pertussis acting like other apparently unlike infections from RSV, especially a risk factor for asthma

depends on factors and mechanisms that affect the immune system because they have not yet clarified.

Current work limitations: 1 (there was a difference in terms of origin in both groups. There are no known additional jobs are reported on a population average over an Arab. This bias may influence the other blur - asthma research group, since asthma is less common among Arabs toward the Jews in Israel 20 . in the control group had a tendency to more urban males - which could result in more - asthma in this group a blur possible effect of pertussis; 2 (not tracked another group of healthy children, matching age, sex, origin population that line section at infancy morbidity of airways. control group in our study was the group turn to the emergency room with cough and whooping cough. This control group has a limit, because we do not have full information about the cause of cough when you emerge. However, we know according to the follow-up, that background did not differ between atopic asthmagroups that were not significant background problems) such research landscape (. But if the cause of cough was RSV, may create bias that would actually increase the incidence of asthma in the control group. However, the prevalence of asthma research group in the control group similar to the general population) 18% 10% (1. Therefore, one can conclude that an appropriate control group; 3 (number included in the study was relatively small due to the problem of locating and responsiveness. According to the dispositions found Abmhakarino not reached statistical significance) than atopic asthma and research group in relation to the control group (there can not be ruled out beta error) Beta error (. ie, it does have more atopic asthma in infants suffering as she infancy, but the number included in our study is too small for the delay phenomenon; 4 (degree of responsiveness between the control group study group was significantly different. made it probably more inclined to admit Children with pertussis, allowing on the one hand is easier to find on the other hand has created more interest, concern and commitment among parents of those children; 5 (hospitalization over the study group can itself create a bias due to the possibility of more significant morbidity requiring hospitalization in infancy. However, analysis of developments in asthma only among patients in both groups did not raise significant difference in the development of childhood asthma), 18.2% and 8.3%, respectively, $P = 0.44$ (. However, the incidence was also found over the combination of asthma and / or sickness as she atopic group compared with patients in the study group) 33% against.) $P = 0.03$, 8.3%

Conclusion

Our study did not find that pertussis in infancy significantly increases the incidence of childhood asthma. However, the observed trends suggest that the observed prevalence of a combination of other asthma and / or sickness as she atopic group compared to children in their study was more severe illness and were hospitalized in infancy. Our study, similar studies published in medical literature, there were some limitations. Therefore, to answer the research question more significantly, there is room for research prospective, with a larger number included over time. Such research has to diagnose asthma and allergies according to the notice respiratory function tests and allergy, and fill out a questionnaire and perform a physical examination, with matching control group of children without influenza respiratory background infancy. •

Table 1:
Demographic variables, genetic and environmental factors

Variable	Control group	Study group	P value
Number of children	52	44	-
Age at emerge	1.7 ± 2.8 months *	1.4 ± 2.7 months	0.07
	3) 6-1 (months)	2.25 from 6 to 0.06 (months)	Age when filling out a questionnaire
4.8 * ± 1.6 years	1.9 years 4.3 ±	0.13	
	4) 9-3 (years **	5) 9-3 (years	Male / female
22/30	26/18	0.15	
Jewish / Arab	8 / 44	17/27	00:01
City / Village	13/39	19/25	0.08
Parents asthma	7	8	0.83
Asthma brothers	6	11	0.15
Smoking at	18	16	0.91
If smoking pregnant	6	5	0.79
Stuffed animals at	4	3	0.84

טבלה 1:

משתנים דמוגרפיים, גנטיים וסביבתיים

משתנה	קבוצת בקרה	קבוצת מחקר	ערך P
מספר ילדים	52	44	-
גיל בעת ההסתמנות	1.7±2.8 חודשים*	1.4±2.7 חודשים	0.07
	3 (6-1) חודשים	2.25 (6-0.06) חודשים	
גיל בעת מילוי שאלון	4.8±1.6 שנים*	4.3±1.9 שנים	0.13
	4 (9-3) שנים**	5 (9-3) שנים	
זכר/נקבה	22/30	26/18	0.15
יהודי/ערבי	8/44	17/27	0.01
עיר/כפר	13/39	19/25	0.08
גנחת להורים	7	8	0.83
גנחת לאחים	6	11	0.15
עישון בבית	16	18	0.91
אם עישנה בהריון	5	6	0.79
חיות פרווה בבית	3	4	0.84

* ממוצע+סטטיית תקן, ** חציון וטווח בגיל ההסתמנות

Hebrew. Example 3

Importance of body position on the interference Sleep apnea: evidence from 2077 patients
With obstructive sleep apnea

Abstract:

In the current study examined demographic characteristics of patients suffering
Vpolisumanugerfeim attention
Obstructive sleep breathing) Ednge"Q (1 related to body position) Tanvahtiyim
(not related position
Body) did not Tanvahtiyim (. Excluded in this study 2077 adult patients diagnosed
that blocks Bdnge"
Sleep Disorders Unit at Loewenstein during a period of a decade. If a subject is
under
Two or more sleep breathing disorders) and sub apnea - Sleep apnea (lying back
than
Lying down side is set in Lucca Bdnge"that my position.
Of 2077 subjects diagnosed"that blocks Bdnge, 1118) 53.8% (were tested
Tanvahtiyim
And 959) 46.2% (subjects were not Tanvahtiyim. No differences were found
between the two populations at
These. In contrast, respondents were not Tanvahtiyim higher weight and higher
BMI
Subjects Tanvahtiyim. Subjects with Ednge"that my position had fewer sleep
breathing disorders
Severity was mild in comparison to subjects with Ednge"that is not my
position. Therefore, respondents
Tanvahtiyim slept better, with higher rates of sleep stages 2, 4 and 3 +4,
Fewer short compared Awakenings Tanvahtiyim not checked.
In addition, respondents Tanvahtiyim were less sleepy during the day.MSLT test
results
multiple sleep latency test ((revealed that subjects did not Tanvahtiyim fell asleep
faster than any nap
Compared to subjects Tanvahtiyim. The - apnea hypoapnea index (AHI (and -),
body mass index (BMI
Were related to independently reverse the effect of body position on breathing
disorders
Sleep; as rising severity of the AHI and - BMI, the subject's chances diminished
with
Ednge"s be my position. Subjects were not Tanvahtiyim many breathing disorders
are followed
Sacheveat back and after Sacheveat Party, for continuous positive airway
pressure (CPAP (He
Clearly the preferred treatment solution.
Refraining from lying on your back can significantly improve the bedroom
followed by the

Level of alertness of a significant portion of patients Ahtanvahtiyim. Therefore, it is very important to qualitative research
To determine whether such treatment can be an alternative for patients suffering from Bdnge"s my position.

[Authors]

Key Words:

Sleep disturbances; sleep apnea syndrome; sleeping body posture; position back.

Introduction

Considerable importance to body posture, sometimes critical, and their frequency severity of disordered breathing during sleep. Strict component of back posture. The degree sleep breathing disorders has been one of the first articles published about Ednge's 1. Even so, it is surprising that this issue has been investigated enough so far, since Shlmhakar that could be important therapeutic. Great. In most patients suffering from Bdnge disorders that are respiratory mainly due to lying on your back. If a subject has over times two disordered breathing while lying back than the side, it is set as suffers from sleep apnea my position) PP-Positional Patient (compared Tested for which no major differences between the frequency of respiratory disturbances position Ms. position side [(NPP)] Non - Positional Patients. Effect of body position on breathing disorders during sleep became years one of the main research subjects in sleep disorders unit Loewenstein Hospital. First work on two paper authors tested this demographic data Vpolisumanugerfeim night and two days in 574 stick to blocks Bdnge's diagnosed. In the present study are summarized data related to this subject in 2077 adult subjects. These are blocks Bdnge's subjects diagnosed sleep disorders unit at Levinstein during the decade.

Methods

The subjects in this study were Aliahidtanv for suspected sleep apneasnores sleep between 2000-1991. During this period, 2300 patients were diagnosed with Q Ednge's syndrome. Subjects in this study included men and women with Apnea AHI > 5 (Hypopnea Index (AHI) (, over 18 years, underwent testing Polisumanugerpit total control of their sleep time it was at least 4 hours during the test. 2077 patients met the criteria in group research.

Were calculated for each tested the AHI position back) Sup AHI (and the AHI Party position) Lat AHI (, all tested with Sup AHI times 2 or more from Lat AHI set) according to the criterion of Cartwright 3) as a person with attention sleep apnea my position) PP-Positional Patient (, subjects with Sup AHI lower by 2 What Lat AHI subjects were defined not Tanvahtiym]) - N Positional Patients ([. Details about registration Polissumanugerperia, decoding settings and other details can be found in an earlier article the authors this article 2. Precise record of changes in body position during testing Polissumanugerfiut done by watching the video recording and monitoring all subjects, before decoding of the stages of sleep disordered breathing.

Statistics:

For comparison of demographic data Vpolisumanugerfeim, including data on nocturnal sleep breathing disorders in sleep and two days between the subjects Tanvahtiym and not Tanvahtiym - aided by the authors of this article on two sample student t test, including Bonferroni correction values are significant. To examine how BMI, AHI and age related effect of posture the body of sleep breathing disorders, statistical processing was performed in two stages: one processing - change) you will notice variables Aktogoreime x2 (processing Multi - variable) Multivariate logistic regression (to estimate the simultaneous contribution - a time of these three variables influence of body position on sleep breathing disorders. Today test data MSLT ((tested using Two-way analysis of variance with repeated ANOVA (measurements. (in order to compare the variability over time between the two groups.

Results

Of 2077 subjects diagnosed blocks Bdnge's, 1118) 53.8% (there were subjects Tanvahtiym) PP (and 959) 46.2% (subjects were not Tanvahtiym NPP ((. classification of PP and NPP by degree of hardware Ednge's stable presents 1. Regardless of the setting to determine the severity of Doom

Sleep apnea, in patients with mild severity Ednge"s, respondents Tanvahtiyim constitute 63% -60% of all subjects. In contrast, Among patients with sleep apnea severity is difficult, respondents Tanvahtiyim constitute between 45% -40% of patients.

Demographics:

Table 2 are concentrated in the demographics of the subjectsAhtanvahtiyim Compared with non Tanvahtiyim subjects. Slightly younger subjectsTanvahtiyim Than patients not Tanvahtiyim, but the difference did not reach significance Statistically. The significant difference is the weight of course the. BMI Subjects are not Tanvahtiyim higher weight and high BMI More subjects Tanvahtiyim.

Nocturnal data Polisumanugerfeim

Table 2 also concentrated nocturnal Polisumanugerfeim data subjects' Suffering Bdnge"that Tanvahtiyim compared with subjects that do notEdnge" Tanvahtiyim. Subjects Tanvahtiyim slept better, reflected On the one hand at a higher rate of sleep stages), SWS (3 +4, 4, 2 On the other hand - the other number or the number of short AwakeningsAwakenings / bedtime Significantly smaller compared to patients not Tanvahtiyim.

Indices of nocturnal breathing test Polisumanugerpia

Table 2 data are concentrated nighttime breathing of test Polisumanugerpit Subjects with Ednge"that Tanvahtiyim compared subjects with non-QEdnge" Tanvahtiyim. The data is very clear: all the respiratory indices Sleep were significantly more severe among non-respondents Tanvahtiyim.

Polisumanugerpia test data daily)) MSLT

The data is very clear: patients not Tanvahtiyim) n = 571) fall asleep Faster than subjects Tanvahtiyim (n = 618)) a nap in a nap $P = 0.003$ 8.7 ± 5.9 vs 9.8 ± 6.3 , 1 [, nap 5.9 vs 8.6 ± 5.9 , 2 ± 9.3 $P = 0.043$ [, $P = .080$ sleep [8.2 ± 5.5 vs 7.7 ± 5.5 , 3 [nap $P < 0.0001$ [10.0 ± 6.5 vs 11.5 ± 6.4 , 4 [, the average value), Av MSLT $P > .0001$ [8.7 ± 4.5 vs 9.7 ± 4.7 [(. two groups of subjects were demonstrated Similar changes throughout the day. Shortest sleep latency was asleep 3 after lunch Latency was asleep long sleep 4 - Last sleep before the test.

Impact of BMI, AHI and age on the effect of that position Bdnge"

Table 3 illustrated the prevalence of subjects Tanvahtiyim not Tanvahtiyim According to different categories of BMI, AHI and age. Inverse is Among BMI, AHI and the chance to be tested with Ednge"that my position.Among Younger respondents checked the incidence of higher Tanvahtiyim Than other subjects. The prevalence of subjects Tanvahtiyim decreases With a rise in severity of sleep apnea. Subjects with degree Hardware and easy) AHI = 10 - 19.9 (62.1% prevalence is decreasing To 40.1% in subjects with Ednge"that hard) $40 > \text{AHI}$ (. A similar phenomenon Demonstrated the effect of BMI on the prevalence of subjects Tanvahtiyimnot Tanvahtiyim. There is a gradual decrease of the prevalence of subjectsAhtanvahtiyim The larger the degree of obesity based on BMI. In lean subjects) = BMI -20 25 (comes Tanvahtiyim prevalence of respondents to 65.1%, patients Obese) $40 > \text{BMI}$ (reduced incidence of subjects Tanvahtiyim To 41.1%. Effect of age on the prevalence of subjects Tanvahtiyim not Tanvahtiyim more moderate than the two previous indices. In addition, there has been Decrease the frequency of subjects Tanvahtiyim with age, but decline More moderate and does not reach statistical significance. Amongsubjects Young people aged 39.9 to 20 years, the prevalence of subjectsTanvahtiyim comes To 56.1% down to to 50.6% in patients over 60 years. Multivariate regression model) Table 4 (allows to test the effect Each of the different variables given the effect of variables Others. Found with the help, that the BMI and - AHI significantly affect,

But the opposite, the prospect of being tested Edge"that position, compared with age, Found that is not a significant factor.

Discussion

This work demonstrated that% 53.8 of 2077 patients with diagnosed Edge"Q Unit during the decade are examined Tanvahtiyim. Ie, the number Full and partial outages of breath while lying back twice or More than following the party position. In addition to this work data revealed that Those with Edge"that my position as disorders suffer from sleep apnea, And that gravity is easier than subjects with Edge"that will not rest. As a result, the quality of sleep of patients was found as the best Tanvahtiyim More, so the degree of daytime alertness in relation to subjects better No Tanvahtiyim.

The prevalence of subjects Tanvahtiyim slightly smaller proportion was Of 55.9% in the first work in 1997 which included 574 Subjects 2. In the present study included only subjects that there is at least 4 hours Changed during Testing Polisumanugerpia. This figure is not taken into account Previous work: It includes subjects with AHI above 10 vs. AHI Over 5 In the present study.

In this study found that 54% of patients with 10> AHI were Tanvahtiyim. Therefore, no major differences on a definition based on AHI Natvsas:

Results will be very similar anyway. Table 1 shows This expression also for different categories of severity of the syndrome.Data These also clearly shows the prevalence of subjects Tanvahtiyim High, especially in mild severity of the syndrome Edge"Q, frequency Gradually decreases the higher the severity.

Previous review article authors found that subjects Tanvahtiyim Young had two other subjects did not Tanvahtiyim. This time, with Larger population, found that subjects Tanvahtiyim are younger, But no statistically significant difference. However, similar work Earlier, respondents Tanvahtiyim thinner than subjects not Tanvahtiyim) The higher their BMI (.

Nightly data Ahpolisumanugerfeim mainly demonstrated, among Subjects Tanvahtiyim better sleep continuity due to a lower number Awakenings Awakenings short and bedtime. In addition, low rates More of a deep sleep stage 2 among subjects not Tanvahtiyim express Well sleep quality differences between two groups of subjects. No matter what parameter breath tested, data interference Sleep apnea and data on oxygen saturation during sleep between patients Tanvahtiyim not Tanvahtiyim clearly suggest that patients Tanvahtiyim Respiratory disorders suffer from mild severity than subjects No Tanvahtiyim. The explanation is clear: Achsnbdakim Tanvahtiyim sleep on the side Did not develop respiratory disorders, or only a few questions; contrast, No patients developed respiratory disorders Tanvahtiyim lying back and Lying side. Therefore, the severity of Edge"that is more difficult, regardless of CPI respiratory tested. Hence, not hard to see the results for Quality of sleep that degree, that the quality of sleep in patients Tanvahtiyim good Than in patients not Tanvahtiyim.

Daily test results) MSLT (not surprising, since Respondents Tanvahtiyim produce better sleep quality and level Arnotam Better than patients not Tanvahtiyim. Interesting tendency of the imagination This test data in both these populations. A short time before falling asleep More slumber 3, which occurs after eating lunch. In addition, the time until Falling asleep asleep 4 is the longest in both populations. May This outcome reflects the expectation that the end of the test before releasing home. These data, obtained a large number of patients diagnosed unit Sleep disorders Loewenstein Hospital during a decade, strengthening the Importance of body position as an important component of exacerbation or relief Edge"s syndrome.

Important limitation of this work is the lack of data on differences Sex. All data processing were made without regard to sex of subjects. As in recent years has evidence relating to differences Significant aspects, between men and women suffering from Bdnge"n. The future will be necessary to test this issue in studies on the influence of Body position on sleep breathing disorders. Importance of body position over the years has become one of the issues Tenets of clinical work and research in sleep disorders unit at Loewenstein Hospital.

After initial work in 1997 2, published a review article About 4. Work, tested in a therapeutic aspect related to body position, Tested whether through a simple method to avoid putting behavior Back during sleep can improve blood pressure values. The method is called "Tennis ball technique" - wearing a cloth belt with a pocket on the back In which a tennis ball. When a person lies on his back and feels the ball is Rotates on its side. For one month, 13 patients diagnosed Tanvahtiy Sleep Disorders Unit at Loewenstein Hospital, resorted to "technique Tennis ball "every night to avoid putting the back 5. The results were Definitely good. Among subjects with high blood pressure) Hiprtanceime (And with normal blood pressure) Normotanceime (values significantly decreased Systolic diastolic blood pressure, both during 24 hours and during the day. At night, these values decreased, but systolic pressure values Did not reach statistically significant reduction. Thirty percent of the value Subjects with the other - Press - Blood Dan"s syndrome also suffer, of which Over 50% are tested Tanvahtiy. If similar data obtained This initial study will be study with a larger number of subjects, Against the control group was not addressed - then refraining from lying back in time Sleep can be a good treatment option for large numbers of subjects With hypertension.

Body position is also important in determining the maximum pressure device. CPAP Of patients who underwent calibration) Titration (CPAP 6, in 60 subjects Were subjected to maximum pressures are back and side position. Among 52) 87.2% (of which, the maximum air pressure) pressure overcomes breaks Full and partial breath, straighten the levels of the SaO2 overcomes Most snores (lying down was higher than Sacheveat back side. This figure indicates a significant obstruction of upper airway Lying in the back during sleep in patients with syndrome Ednge"n. In addition, it was found Maximum of CPAP pressures were higher in REM than In NREM, obese subjects are higher than not fat though BMI, higher among subjects with a more difficult level compared Hardware Those with Ednge"n that a lesser level of hardware. All comparisons always Ms. position pressures were higher than third position.

Another seven were working characteristics of sleep apnea breaks Apneas ((lying on your back than those that appear while lying side. Goal It examined 30 patients with Ednge"n that hard severity) 40> AHI (, Each with breathing pauses were 30) 10 in one-third of the night (Lying back and side following indices: duration of cessation of breathing, decrease in SaO2, changes of slowing and acceleration of the pulse, the duration of waking up late Cessation of breathing intensity of snoring at the end of most of cessation of breathing. Results showed that for each of the indices examined, breathing pauses Lying back were always more severe than those party position. Breaks Breathing while lying back are longer, causing severe Ldstoartzioat More, it's over a longer wake, changes pulse) Berdyckeredia / Tachycardia (snores were larger at the end of these events stronger The other party position of breath pauses. From this we can understand that position Back, not only the prevalence of sleep breathing breaks higher, but Severity of respiratory pauses harder than third position. In follow-up 8 tested efficiency of the tennis ball technique " Avoid putting back treatment Ldnge"n that my position. Excluded study

Those with Ednqe"refusing treatment that my position on preferring CPAPexperience Treatment "tennis ball technique. Among 78 patients who received Belt with a tennis ball were sent questionnaires containing questions related to This treatment. Fifty) 64.1% (subjects returned the questionnaire. which 19 (38%) respondents reported that they still strap the belt, 12 (24%) Wore it for a while and learned to avoid lying on your back, but Stopped, 19 (38%) stopped to strap the belt after a period of About a month, but have not learned to avoid putting the back and 28)35.9% (subjects Not returned the questionnaire.

Vpolisumanugerfim demographic data were examined, and found that ageis The only measure that separates the participants still learned a belt orstrap Avoid putting back) older age (compared to those who have not learned or not Returned the questionnaire) younger (. subjects wearing seat belt orlearned Avoid putting back reported improvement in sleep quality, improved levels Alertness during the day and reduced the intensity of snores. The main reason Times assistance to stop the tennis ball technique "was uncomfortable. In conclusion, this treatment can be good for 30% to 50% of patients With Ednqe"that my position especially for older patients. However, there Need to improve the system, because similar events with CPAP deviceshere Discomfort is also a significant limitation for this treatment. Therefore, any More qualitative research will not be a large number of subjects, controlled, Randomized, prospective and long-term treatment, this treatment option Shall be limited 9.

In recent years published important studies on the effect of Body position on sleep breathing disorders. Mador Vahab 10 found in the group A similar incidence of subjects reporting data in this article For patients Tanvahtiy 2, and a higher incidence in subjects with Ednqe"s mild severity. Richard Vahab 11 found on 120 patients with Ednqe"s that 55.8% of them were Tanvahtiy 2, and they were also youngerat 6.7 Years, but there were no differences on AHI and BMI between subjectsTanvahtiy 2 And Tanvahtiy 2.

Endoscopic examination was held, there were no differences between the two Groups instead of upper respiratory obstruction. Isono Vahab 12 Shown on eight subjects with Ednqe"that under anesthesia, that the side position improves The airway anatomically, and thus avoids a tendency chess Different areas of the upper airway. In children under Anesthesia showed Litman Vahab 13, that region has seen more than an extension position The other side is the back end Hafigalots and vocal cords. Ono Vahab 14 showed on 12 healthy subjects, the side position with back posture Prime alongside increases in the airway behind the tongue. Were Two important new studies: Chang) 1 and 15 Shiao found in research Cplomatri on 32 subjects Tanvahtiy 2 and 43 did not Tanvahtiy 2 that distance More on - Pharyngeal Airway Space (PAS (subjects Tanvahtiy 2 is It distinguishes anatomically between subjects and subjects Tanvahtiy 2 No Tanvahtiy 2; 2 (recently shown Walsh Vahab 16 imaging system A new and accurate) Optical coherence tomography (, that the change in position Brings back next morphological change of the upper respiratory tract: Beyond Air passes elliptical shape more circular shape without changing the Circumference of the airway. The round shape of the airways Prevents the collapse of the side walls of the airways, thus Maintains a more open air passage. Hence, considerable improvement snorting) Most strongly and frequently (intervals of breath full and partial Achsshuachevim the other side on the back. These researchers examined 11 patients With Ednqe"that my position. You may not Tanvahtiy 2 subjects beyond the scope of The air is so narrow, that change the position of the back side might change the Shape of the airways, but does not allow to prevent the collapse of Airway walls.

Two important studies with remarkable therapeutic aspect: Szollosi) 1 Vahab, 17 have shown that the side position improves sleep respiratoryfunction

) lowered the AHI in all sleep stages and improved the level falls Oxygen (in patients with heart failure and central respiratory pauses CSA - CSR (Cheyne Stoke Respiration (. This research was based in part On our article, which demonstrated the possible effect of body position Respiratory disorders such patient CSR brain after event 18. Researchers Hypothesized that the improvement is due to changes in health and oxygenbases Respiratory changes Tanvahtiyim; Skinner) 2 Vahab 19 compared study New treatment on CPAP with care to prevent back position on Thoracic(TASB anti-supine band) on 20 subjects Tanvahtiyim. Treatment on CPAP resulted Better results, but on 13 patients of 18 treated with -, TASB This treatment was successful. Also, no differences were observed in the indices of quality of life, The response was better at TABS than on. CPAP

Conclusion

The data of this work a large population of patients with Ednge"Q My position and my position once again show that subjects Tanvahtiyim areover Half the population of patients with Ednge"h. These subjects lean More suffer from the syndrome with the severity easier than subjects No Tanvahtiyim, both the number and severity of respiratory disorders and In harm the quality of sleep. Subjects not Tanvahtiyim breathing disorders Many are lying back and lying down side, for whom CPAP is undoubtedly Preferred treatment solution. As refraining from lying on your back can Significantly improve the bedroom followed by the level of alertness Of a significant portion of patients Ahtanvahtiyim, great significance editing Qualitative research to examine whether this treatment option as an alternative should be Therapy in patients suffering from Bdnge"s my position.

Author author: Arie Auxnberg
 Sleep Disorders Unit
 Loewenstein Hospital - Rehabilitation Center
 A. D 3, targeting 43 100
 Fresh Email: arieo@clalit.org.il

Table 1:

Distribution of patients with Ednge"s Tanvahtiyim not Tanvahtiyim accordingseverity

Difficult (severe)		Moderate		Easy (mild)		AHI
> 40	> 30	20-40	15-30	10-20	5-15	
215 (40.4%)	323 (44.9%)	309 (57.6%)	328 (56.2%)	390 (62.4%)	468 (60.4%)	Positional Patients (PP)
317 (59.6%)	396 (55.1%)	227 (42.4%)	256 (43.8%)	235 (37.6%)	307 (39.6%)	Non-Positional Patients (NPP)
532	719	536	584	625	775	Total

Table 2:

Demographic data on breathing disorders, nocturnal Polisumanugerfeim ofpatients Ednge"s				
Tanvahtiyim not Tanvahtiyim				
	Positional Patients n = 1118	Non- Positional Patients n = 959	P value	P value after Bonferroni correction
Age	51.6±11.2	52.5±10.9	0.063	
Weight	86.7±15.0	90.7±19.6	<0.0001	<0.0001
Height	170.9±8.6	170.3±8.5	0.124	
Bml	29.7±4.6	31.1±5.1	<0.0001	<0.0001
Total Recording Time	423.7 ± 39.0	422.0 ± 34.9	0.301	
Total sleep Time	359.9 ± 47.5	357.6 ± 53.5	0.288	

sleep. Efficiency	84.7 ± 8.9	84.5 ± 9.1	0.513	
Latency stage 1	10.8 ± 14.2	10.6 ± 13.3	0.722	
REm latency	90.0 ± 52.3	94.1 ± 56.3	0.083	
No of REms	3.6 ± 0.9	3.5 ± 1.0	0.018	0.108
REm Length	24.2 ± 12.7	25.6 ± 22.5	0.095	
% sT1	5±3.6	5.3±4.3	0.107	
% sT2	57.8±10.6	59.4±11.7	0.001	0.006
% sT3	4.5±2.9	4.4±3.1	0.298	
% sT4	12.4±8.1	11±8.2	<0.0001	<0.0001
% REm	20.1 ± 6.0	19.7 ± 6.5	0.115	
% sWs	16.9 ± 9.0	15.3 ± 9.4	0.001	0.006
WAsO	49.8 ± 31.4	50.7 ± 33.0	0.523	
# of arousals >15 s	28.6 ± 13.1	28.3 ± 14.0	0.627	
# of arousals < 15 s	171.7 ± 96.0	224.4 ± 145.6	<0.0001	<0.0001
Arousal Index	29.3 ± 17.3	38.6 ± 26.4	<0.0001	<0.0001
AI	10.4 ± 13.9	15.3 ± 20.3	<0.0001	<0.0001
AHI	25.7 ± 20.5	33.5 ± 26.5	<0.0001	<0.0001
Awake saO2	95.6 ± 2.1	95.5 ± 2.1	0.106	
min saO2 REm	82.0 ± 11.2	78.4 ± 14.7	<0.0001	<0.0001
min saO2 NREm	86.0 ± 7.0	84.5 ± 8.8	<0.0001	<0.0001

Table 3:
Prevalence of patients Tanvahtiyim according to different categories of BMI, AHI and age

Variable	Number of patients	Positional Patients (PP) (%)
AHI		
10 - 19.9	628	390 (62.1)
20 - 29.9	348	200 (57.5)
30 - 39.9	189	112 (59.3)
≥40	534	214 (40.1)
BMI		
20 - 24.9	192	125 (65.1)
25 - 29.9	886	520 (58.7)
30 - 34.9	647	317 (49.0)
35 - 39.9	228	103 (45.2)
≥40	90	37 (41.1)
AGE		
20 - 39.9	255	143 (56.1)
40 - 59.9	1,256	688 (54.8)
≥60	563	285 (50.6)

Effect of AHI, BMI and Age on the prevalence of Positional Patients (PP). The number and percentage for each group category are presented. The prevalence of PP significantly decreased as the AHI increased ($\chi^2 = 62.06$, $df = 4$, $p < 0.0001$). Similarly, the prevalence of PP significantly decreased as the BMI increased ($\chi^2 = 37.1$, $df = 5$, $p < 0.0001$).

Table 4:
Independent contribution of AHI, BMI and age to hang position

Variable	β	SE	Wald	df	OR (95% CI)	p value
AHI ≥ 40	-0.662	0.106	38.92	1	0.69 (0.57 - 0.83)	< 0.0001
BMI ≥ 30	-0.372	0.093	16.10	1	0.52 (0.42 - 0.64)	< 0.0001
AGE ≥ 60	-0.153	0.102	2.24	1	1.16 (0.95 - 1.42)	0.13

Although the prevalence of PP decreased as the Age increased, this change has not reached significance ($\chi^2 = 3.5$, $df = 3$, $p = 0.320$). Multivariate logistic regression analysis. The variable that most significantly explains the positional dependency in OSA patients was AHI followed by BMI. Age was not an independent significant factor for positional dependency.

Hebrew. Example 4

? ?????? And pharyngitis in children: a comparison between the attitude of family doctors to access of pediatricians

[Authors]

Background: pharyngitis Straftokoakit is common in children and adolescents. There is a difference approach to diagnosis and treatment of this issue of Family Physicians Pediatrics.

Goals: to characterize the diagnostic and treatment approach pharyngitis Straftokoakit among family doctors pediatricians in the south, and find possible differences between these populations.

Methods: The convenience sample of family physicians pediatricians general health workers in the Negev. Self-administered anonymous questionnaires were filled by family physicians during clinic meetings or when attending courses. Included pediatricians Soroka University Medical Center community clinics in the Negev.

Results: The study included 52 family physicians and 48 pediatricians. Most participants could evaluate the criteria pharyngitis Straftokoakit) 93 (. Is a statistically significant difference), $P < 0.01$ (therapeutic approach of the two groups of doctors. Twenty-seven) 51.9 (family physicians begin empiric antibiotic treatment in cases where it is very likely pharyngitis Straftokoakit, compared to nine) 18.8 (paediatricians only. Most pediatricians prefer this case to complete laboratory tests. is a noticeable difference on the therapeutic approach. all family physicians) 100 (recommended for treatment Berpapne. In contrast, only twenty-seven) 57.4 (Pediatrics recommended this treatment), $P < 0.0001$ (.

Conclusions: Planning and implementation should be a broader national study, to formulate uniform guidelines for this common phenomenon of pharyngitis Vsterptokoak against infection.

Introduction pharyngitis is common in children and adolescents, and is

About 6% of the primary reasons for a doctor [1]. Causing the infection is generally

Usually viral, such as Raynaud virus) rhino virus (HIV mastery) Adeno virus (

% 2 [30% -60 [, and only at 30% of the generator is strep infections

Beta hemolytic group β -hemolytic Streptococcus type A) A) d [3].

The main complaints when pharyngitis include body temperature above 38.5

MP, sore throat, difficulty swallowing, headaches and stomach, nausea and decreased

Appetite] 6-4, 2 [. Physical examination shows pharyngeal redness, swelling

Ahskedeime, Atplet on - the Ahskedeime, sensitivity extension lymph

The front triangle of the neck lymph nodes] 7-5, 2 [. Pharyngitis in light pollution

Streptococcus is not accompanied by cough and development snot] 3.2 [. Age

Typical development pharyngitis Straftokoakit is 15-3 years [3].

Pharyngitis Straftokoakit is spontaneous disease in the past 4-3

Days even without treatment, and usually not life-threatening [7]. Objective

Primary treatment with antibiotics is to prevent rheumatic fever.

There are also a number of targets for secondary prevention of complications including

Sores, such as an abscess adjacent Lskedeime, preventing infection and shortening

Duration of illness] 7,2 [.

Pharyngitis against infection Straftokoaki There are also aspects

Social and economic, such as an average absence of 1.9 days of children

School adolescents, and 1.8 days of parental

Work [6]. Accuracy of clinical diagnosis based on patient complaints,

Physical examination, epidemiological and demographic data. Trained physician can

Precise diagnosis to a rate of 3% [75 [. Execution or notice crater surface

Quick presence of streptococcus ability to help in establishing diagnosis

Reduce unnecessary treatment with antibiotics] 5,4,2 [. The common background

High background of the phenomenon and the non-treatment with antibiotics is justified

In many patients, for many years made attempts to consolidate access

Best) optimal (diagnosis and treatment of pharyngitis Straftokoakit.

Clinically suspected case of pharyngitis Straftokoakit Epidemiology

Are two main recommendations by bodies recognized medicine

Children. The first recommendation is making a quick notice. If you notice

Interpreted as positive, there is to recommend antibiotics. If you notice

Interpreted as negative, and has completed investigation of crater surface performance, and recommend

The antibiotic treatment if there is growth in the surface. The second recommendation,

Crater surface and making a recommendation on antibiotic therapy, is given only if There is positive growth in the surface] 4,3 [. Family medicine adopt a more practical approach based on Clinical data. The data include an increase in body temperature over 38 degrees Celsius,

Extension lymph nodes in the front triangle of the neck, increasing the Ahskedeime Utplet. Each receives clinical data of weight One point. Kids ages 14-3 years and add another point, Adults aged over 45 deducted one point. If the information given Pharyngitis Straftokoakit risk from one low, not recommended Make no laboratory test or antibiotic treatment. Patients with risk Medium - high) Total 3-2 points (recommend that you fast or notice Crater surface and begin antibiotic treatment after receiving an answer Positive. High risk patients) total score 4 or higher (recommended to Antibiotic therapy without further clarification. Also, in patients with rheumatoid Rheumatic fever in the crater, it is recommended to treat with antibiotics without performing Additional tests [5].

Different approach to diagnosis and treatment of physicians and family physicians Children emphasized previously [4]. Work published in Israel] 8 [, Not Found Difference in the diagnostic ability of family physicians compared with pediatricians Community regarding pharyngitis Straftokoakit. However, is lack of Uniformity regarding dose antibiotic treatment. The aim of this study was to characterize the diagnostic and treatment approach Pharyngitis Straftokoakit family physicians pediatricians South of the country and find possible differences between the two populations These physicians.

Research Methods

- research population: convenience sample consisted of family doctors physicians Children's general health workers in the Negev. Physicians included Family who participated in meetings of family physicians in clinics Community or graduate courses. Center were included pediatricians Soroka University Medical community clinics in the Negev.
- Research tools: self-administered anonymous questionnaire that included socioeconomic data - Demographics, questions of knowledge, attitudes regarding access pharyngitis Straftokoakit.
- Data collection period: between the months of October 2007 - June 2008.
- Data Analysis: The questionnaires were entered Excel software, data analysis Statistical software was SpSS. Aktegorime variables were Frequencies, you'll notice that - square) chi Square (was used to compare Variables Aktegorime. $p > 0.05$ was considered statistically significant.

Results

Of 60 family physicians to contact members of this article, 55 agreed Fill out the questionnaire. Three questionnaires were filled only partially so Not included in the results. Total collected 52 questionnaires filled in Full.

Of 52 pediatricians to this article the authors contacted, 50 agreed Fill out the questionnaire. Two questionnaires were filled only partially. Total Collected 48 questionnaires filled out completely.

The data summarized in Table 1 socio - demographic of the population Research. Rate specializing in both groups was similar, reaching about % 50. Even more data socio - demographic, such as age and the state in which Studied medicine, there was no statistical difference between the groups. Table 2 detailed approaches for diagnosis and treatment of pharyngitis Family physicians pediatrician. Most doctors in the study

)% 93 (could appreciate the typical criteria pharyngitis Straftokoakit. In addition, no statistically significant difference was found between Family physicians pediatricians in assessing the likely age Pharyngitis Straftokoakit. Statistically significant difference), $p > 0.01$ (

Therapeutic approach in two groups of doctors: twenty - seven)% 51.9 (family physicians reported that they tend to give treatment Empirical antibiotics according to emerge when there is reasonable clinical Infection Straftokoaki high, compared to nine)% 18.8 (doctors Children. Most pediatricians reported that they prefer in this case Complete laboratory tests. Emerge regarding the less obvious clinical Streptococcus infection, Select two teams to make a surface crater and start antibiotic treatment only After receiving a positive response, with no statistical difference. In addition, No statistically significant difference was found between the groups, the probability Streptococcus infection was lower by clinical emerge. Most physicians chose not to perform laboratory tests and to give treatment Antibiotic. Noticeable difference was statistically about accessing Straftokoakit pharyngitis therapy. All family physicians)% 100 (Recommended the treatment Berfapne) phenoxymethylpenicillin (. In contrast, only Twenty - seven)% 57.4 (Pediatrics recommended this treatment.

Discussion

Most doctors familiar with the current sample criteria Raising clinical pharyngitis Straftokoakit reasonable. Differences Diagnostic approach between family physicians pediatricians found In this work are similar to previous findings in the medical literature worldwide [3]. According to this work, most pediatricians refer laboratory tests To verify pharyngitis Straftokoakit, contrast, doctors take Clinical approach to family. In addition, there is a difference in choosing treatment The recommended antibiotic pharyngitis patients Straftokoakit] 9,4 [. It seems that these differences arising from the compliance of some doctors Guidelines. Thus, the Association of American Pediatrics Center Infectious Disease Control and Prevention [4] advocate that the criteria K to N. Y. Y. Y. F from a D from S. F. J. R. C. K. S. J. and S. Y. D and C to D to Y. A's in H and N D to K and Z to A. Straftokoakit among children, and reliance on them may cause For other antibiotics. Consequently, these two bodies believe that there Place to complete the clinical diagnostic laboratory tests. Association of family physicians in the United States adopted the position of center Infectious Disease Control and Prevention [4] The U.S. and Infectious Diseases Society of America, and [2], and recommends to refer any patient diagnosed Check with pharyngitis crater surface act on the results] 10 [. There is a recommendation relating to adult, which provides treatment Empirical antibiotic clearly emerge pharyngitis Straftokoakit] 13, 12 [. However, there is a position that calls for antibiotics Without additional testing, and clinical criteria likely High Straftokoakit pharyngitis among children] 12,11 [. Position This is not supported by scientific or professional body some, and is a position The only private investigators. This suggests that some family physicians Throw the recommendations for adults on child care. About the difference in choosing a drug to treat pharyngitis Straftokoakit, Even in previous studies [3] found that physicians prefer to give Rafapne) phenoxymethylpenicillin (drugs of choice, compared to physicians Children often prefer to give other medications. Study tested That taking antibiotics in children, significant differences were found Statistical type of antibiotics administered, depending on the taste of medicine] 14 [. Pediatricians may consider, on behalf of drug Muxipne Preferred by children over that of Rafapne, while family doctors - Often prescribed tablets - do not take into account the aftertaste Of suspensions. Add this research questions about the drugs taste Was to add knowledge, but these questions were not included in the study objectives. The current study had several limitations: 1 (since it was impossible to calculate the sample size workmanship, It was decided that each group) Pediatricians family doctors (will About 50 doctors. As a result, still remains the possibility that the lack of differences Statistical significant result smaller than the number of participants

Research.

2 (This is a convenience sample. Most family doctors answered the questionnaire during the study Of Family Medicine. It is very possible that access is slightly different from that of Doctors who come to school, and that could tilt the Results of the study.

3 (as every study examined attitudes, the study does not reflect Necessarily normal clinical practice of physicians. The best way Is to check diagnosis and treatment patterns of doctors direct view. But this way requires many resources, that were not available Authors of this article.

4 (the questionnaire had a number of methodological problems: For example, did not ask The authors very interesting question as to the cause of choice Or other antibiotics.

Conclusion

We recommend a national research plan with a larger sample more representative, To find differences in access to diagnosis and treatment among physicians Family Pediatricians. These data can assist in understanding formulation Uniform guidelines for this common phenomenon of pharyngitis in light pollution Streptococcus. •

Author author: Yann Award
Department of Family Medicine
Ben Gurion University

A. D 653, Beer Sheva, Zip

Table 1:
Socioeconomic data - demographics of the study population

Doctors Children **Doctors Family P-**
value

Age (years)

<44

Over 44

Medicine graduation Country:

Israel, U.S., Western Europe, Canada, South America

Russian and East European

Work Place:

Only community

Only hospital

Community hospital

Expertise

Specialize

Experts

טבלה 1: נתונים סוציודמוגרפיים של אוכלוסיית המחקר				
	רופאי ילדים (N=48)		רופאי משפחה (N=52)	P-value
	N	%	N	%
גיל (שנים):				NS
<44	40	83.3	38	73.1
44 ומעלה	8	16.7	14	26.9
ארץ סיום לימודי רפואה:				NS
ישראל, ארה"ב, מערב אירופה, קנדה, דרום אמריקה	22	45.8	20	38.5
רוסיה ומזרח אירופה	26	52.4	32	61.5
מקום עבודה:				NS
קהילה בלבד	37	71.1	14	29.2
בית חולים בלבד	3	5.8	27	56.2
קהילה ובית חולים	12	23.1	7	14.6
מומחיות:				NS
מתמחים	25	52	27	52
מומחים	23	48	25	48

עבלה 2: השוואה בין רופאי משפחה ורופאי ילדים בגישת האבחונות והטיפולית בדלקת לוע סטרפטוקוקית						
		רופאי ילדים (N=48)		רופאי משפחה (N=52)		p-value
		N	%	N	%	
3.	מהי גישתך למקרה בו על סמך הסתמנות קלינית אתה בטוח שמדובר בדלקת לוע סטרפטוקוקית?					
4.	לתת טיפול ללא שום תבחין נוסף	9	18.8	27	51.9	0.01
5.	גישה אחרת	39	81.2	25	48.1	
6.	מהי גישתך למקרה בו על סמך הסתמנות קלינית קיים ספק לדלקת לוע סטרפטוקוקית?					
7.	לשלוח משטח לוע ולתת טיפול אם יש צמיחה	32	66.7	28	53.8	NS
8.	גישה אחרת	16	33.3	24	46.2	
9.	מהי גישתך למקרה בו על סמך הסתמנות קלינית אתה בטוח שלא מדובר בדלקת לוע סטרפטוקוקית?					
10.	לא לבצע תבחנים, לא לטפל	33	68.8	41	78.8	NS
11.	גישה אחרת	15	31.3	11	21.2	
12.	באיזו אנטיביוטיקה אתה בוחר בחולה עם דלקת לוע סטרפטוקוקית ולא ידוע על רגישות לפני ציליין?					
13.	רפאפן	*27	57.4	52	100	0.0001
14.	מוקסיפן	20	34.2	0	0	
15.	באיזה גיל (ובשנים) לדעתך עולה הסבירות שמדובר בדלקת לוע סטרפטוקוקית?					
16.	14-3	45	94	50	96	NS
17.	גיל אחר	3	6	2	4	
18.					 *נתון חסר

1. Table 2:

Comparison of Family Physicians Pediatricians approach diagnosis and treatment of pharyngitis Straftokoakit

2. Doctors Children Doctors Family P-value

3. What is your approach to signify that emerge based on clinical you sure that pharyngitis Straftokoakit?

4. Provide treatment without any further notice

5. Another approach

6. What is your approach to signify that emerge based on existing clinical pharyngitis Straftokoakit provider?

7. Send surface crater and give treatment if there is growth

8. Another approach

9. What is your approach to signify that emerge based on clinical you sure that this is not pharyngitis Straftokoakit?

10. Did not make criteria, no deal

11. Another approach

12. Which antibiotic you choose a patient with pharyngitis Straftokoakit no known sensitivity Penicillin?

13. Rafapne

14. Muxipne

15. At what age) in (do you think the more likely it is pharyngitis Straftokoakit?

16.14-3

17. Other age

18. * Missing data

Italian. Example 1 (html)

Ropivacaine 0.2% or less in association sufentanil in epidural analgesia in patients undergoing reconstruction anterior cruciate ligament

L limitation in mobility following interventions reconstruction of the anterior cruciate ligament is a well-known and troublesome complication of surgical intervention. The use of anesthetic techniques regional anesthesia during the postoperative period has been shown to produce positive effects on outcomes surgery and functional rehabilitation after inter-winds of major knee surgery, reducing the length of the rehabilitation period. 2

Among the techniques of loco-regional analgesia peridurale analgesia is widely used for control of the postoperative pain in orthopedic patients. Although widely used solutions as well of local anesthetic, they are not always sufficient and in fact have been suggested anesthetic mixtures local and opioids with positive clinical results. 5 Despite what the side effects of opioids often concerned with anesthesiologists, especially peridurale do analgesia is maintained outside the recovery room. While the clinical efficacy of mixtures of local anesthetic and opioids has been questioned by some authors. 7-9

It was shown that lipophilic opioids, such as fentanyl and sufentanil, improve the control of lower abdominal pain after surgery. 10 Chithoracic surgery. And despite what little is known the utility of adding small amounts of opioids solutions of local anesthetic intervention for reconstruction of the anterior cruciate.

We therefore conducted a prospective, randomized, double-blind trial to assess the effect of the addition of small doses of sufentanil to Ropivacaine 0.2% for the control of postoperative pain in patients undergoing inter-Wind cruciate ligament reconstruction antethan.

Materials and methods

After obtaining the approval of the ethics committee and written informed consent of patients, 20 patients were enrolled ASA Physiological status I-II candidate for reconstruction surgery anterior cruciate ligament. Were excluded patients with contraindications to the placement epidural catheter, with the age of 18 years and more than 65 years, carriers of allergy-solutions of local anesthetic or opioid, as well as pregnant patients and all patients who can not breathe running a patient-controlled epidural analgesia.

Prior to surgery, during the preoperative visit it was explained to patients the operation has patient controlled epidural analgesia and VAS (Visual analogic scale). Patients were premedicated with oral diazepam (0.1 mg kg⁻¹) 1 hour before surgery and the infusion was started 10 ml kg⁻¹ Ringer lactate solution. The patient you were then placed in lateral recumbency with the side to operate at the bottom. After individual with the epidural space in the gaps or L3-L4 L4-L5 with a 18 gauge Tuohy needle, was performed spinal anesthesia with bupivacaine 10 mg of hyperbaric 0.5% (Marciana, Astrazeneca, Sweden) via I know 27 gauge Whitacre needle, using a technique without needle-through-needle (Durasafe, Becton-Dickinson, New Jersey), and finally a catheter-peridural 20-gauge Tuohy needle was inserted through a 4 cm and fixed to the skin.

The distribution of the sensory level (pinprick test) and motor block (modified Bromage scale: 1 = locked hip, hip, and 2 = knee blocked, 3 = hip, knee and ankle-block ed) were recorded by a blinded observer every 5 min up to the loss of sensibility to the pinprick test at T10 with a Bromage ≥ 2 (First patient in). If it was not recorded layer an adequate surgical block within 20 min parachnoid injection of local anesthetic, further boluses were injected with 2 ml of ropivacaine 0.75% in the epidural catheter. Sedation with propofol was administered to the patient if necessary (25-75 μ g kg⁻¹ min⁻¹).

At the end of surgery, patients veni-compartment placed randomly to receive Ropivacaine 0.2% (group Ropivacaine, n = 10) or ropivacaine 0.2% / 0.5 μ g ml⁻¹ sufentanil (group Sufentanil-ropivacaine, n = 10). Analgesia peridural-the patient-controlled analgesia (PCEA) was carried out by using a standard PCA pump. The mixtures of local anesthetic were prepared Double-blind in one of the authors who did not take part in the subsequent data collection and management of the patient. The PCEA infusion was initially set to 4 ml h⁻¹ solution of study, with incremental doses of 2 ml and a lockout time of 20 min. If pain control was inadequate (VAS > 30 mm), were administered 100 mg intravenous ketoprofene (maximum dose 300 mg / day).

The degree of pain was assessed at 1, 8, 16, 24 hours after surgery, the same times the motor block was assessed, the level of sedation and the saturation device. The level of sedation was assessed using a scale with 4-pun

of local anesthetic is in agreement with previous of Lorenzini *et al.* reported that the addition of 1 mg / ml of sufentanil to ropivacaine 0.2% in the postoperative analgesia when compared with the 1 only ropivacaine 0.2% after surgery May greater knee, however, this also led with a higher incidence of side effects such as itching, nausea and vomiting.

In comparing combinations of 0.5 mg / ml sufentanil or 0.02 mg / ml of morphine with ropivacaine 0.2% for major abdominal surgery Gianferri *et al.* have shown that the use of sufentanil was associated with a lower level of pain at rest 16, 20, 24 hours after surgery with a lower level of pain on movement at 24 hours. In addition, the group of patients who received morphine showed a higher incidence of nausea, vomiting, itching than those who had received sufentanil with a longer time than necessary to the duct, while Palm *et al.* have showed that 0.75 μ g / ml sufentanil decreased by almost 30% as the lowest concentration of anesthetic necessary for a local delivery of effective analgesia in 50% of pregnant women. Debono *et al.* the addition of 5, 10 and 15 mg of sufentanil in 12 ml of ropivacaine 0.2% and sufentanil showed that the improvement significantly the quality of analgesia, while three Brodner *et al.* suggested that 0.75 μ g / ml sufentanil may be regarded as the best compromise between the analgesic efficacy and the side effects when compared with the concentrations of 0.5 μ g / ml and 1 μ g / ml.

According to the study of Brodner *et al.* The lack of difference in efficacy that analgesic we observed during the mobilization step-it could be explained by the low dose of sufentanil used. Brodner *et al.* Showed a better pain control when they use to 0.75 μ g / ml or 1 mg / ml with sufentanil-ropivacaine 0.2%, but not when they used 0.5 μ g / ml. The addition of doses of 0.5 μ g / ml sufentanil could well be sufficient for improving the control of pain at rest but not during movement.

In this study we have demonstrated no difference in the incidence of side effects related to the addition of 0.5 mg / ml sufentanil. Nevertheless, the small sample size does not allow us to reach any conclusion definitive about the incidence of side effects. Lorenzini *et al.* have shown an increased incidence of pruritus, nausea and vomiting due all the addition of 1 μ g / ml sufentanil to ropivacaine 0.2%. Snijders *et al.* have reported the safety of epidural administration up to 6 μ g / h-sufentanil while in another study of 614 patients were reported 3 cases of respiratory depression with 10 μ g / h of sufentanil.

However, these doses are significantly higher than those used in our study, in which the maximum dose of sufentanil was 5 μ g / h.

In conclusion, this prospective, randomized, double-blind study demonstrated that the addition of 0.5 μ g / ml sufentanil to ropivacaine 0.2% holder to a better pain control at rest, but not during passive motion after intervention to the reconstruction of the anterior cruciate ligament.

Summary

Objective: The aim of this prospective study, randomized, double-blind trial was to evaluate the effects of adding 0.5 μ g / ml ropivacaine 0.2% for epidural analgesia by patient-controlled analgesia (PCEA) on the quality of postoperative pain in patients undergoing chronic ligament reconstruction of the anterior cruciate ligament.

Methods: We enrolled 20 patients ASA physical status I and II are candidates for surgery to rebuild the anterior cruciate ligament. It was a self-made combined spinal-epidural anesthesia at the level of interspaces L3-L4 or L4-L5 using a technique need-through-the-needle. Spinal anesthesia was induced with 10 mg of hyperbaric bupivacaine 0.5%. The postoperative epidural analgesia was initiated with a continuous epidural ropivacaine 0.2% (n = 10) or ropivacaine 0.2% / 0.5 μ g / ml sufentanil (n = 10). The level of pain was assessed at 1, 8, 16, 24 and 48 hours after the completion of surgery, the same intervals were recorded also the degree of motor block, the level of sedation, oxygen saturation device, the total consumption of anesthetic solution and the number of doses delivered to the patient.

Results: There were no differences in intraoperative quality of anesthesia and in no patient had to resort to general anesthesia for complete the surgery. Patients who had not received the combination of ropivacaine and sufentanil showed levels of pain at 16 hours after surgery lower than those of surgery patients who received ropivacaine group (P = 0.02). There were no differences in pain levels between 2 groups during passive motion.

Conclusions: The addition of 0.5 μ g / ml ropivacaine 0.2% for epidural analgesia controlled by the patient improves the patient's pain control at rest, but does not make a significant improvement in the A-Pain during mobilization passive.

Keywords: postoperative analgesia peridurale - patient-controlled - anesthetics, local - Ropivacaine - anesthetics, opioids - Sufentanil.

Italian. Example 2 (html)

Comparison of combined spinal-epidural anesthesia sequential and spinal anesthesia for cesarean section

It is well known that to be able to have adequate anesthesia with that obtained with only the cord in patients undergoing elective Cesarean section, it is necessary to obtain a sensory block of spinal segment-re T4-S5. Used alone for epidural technique for obtain-
tain an extensive sensory block as exhibits in an high incidence of hypotension and the risk of toxicity by local anesthetics for the need to use high doses.

The epidural block may be inadequate in most 25% of patients, mainly due to the difficulties to block the sacral nerve roots. It is believed that the epidural space has a medial fold ridge that would lead to a partitioning the same, and this anatomical explanation would be the difficulty of the epidural anesthesia alone to reach the sacral roots, which manifests itself visceral pain in the manipulation of the bladder.

Spinal anesthesia (*spinal anesthesia*, AS) is the technique used in most regional Cesarean sections, for ease of implementation for the rapid onset of action and predictability of the effects, but the higher-level than the block can be very variable and the technique can become very dangerous for the fetus, if you uncontrolled maternal hypotension develops. From Because the subarachnoid block is usually technique in a single administration is not possible to improve intraoperative block inappropriate or to provide postoperative analgesia if the patient not adding morphine to the local anesthetic, device on which not everyone agrees.

The technique combined spinal-epidural (CSE) seems to overcome the limitations of previous techniques because it combines the predictability of the spinal flexibility of epidural with a lower demand of drugs than the same techniques used singly.

Starting from this premise, we wanted to compare anesthesia with the CSE sequence

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Materials and methods

It was performed a prospective, randomized study.

One hundred patients with healthy full-term pregnancy by undergo elective Cesarean section were consecutively allocated randomly in 2 groups of 50: the patient SA group you have been treated with SA, those of CSE group sequential CSE technique. In all patients was performed with a preload of 500 ml plasma expanders and intravenous 5 mg of ephedrine.

The CSE was performed in patients with position with single puncture (spinal cord first, then epidural) conducted in the same area L1-L2, somministrating in the cord, with a needle Whitacre 25G Levobupivacaine 5 mg + 5 µg of sufentanil, and 18G Tuohy epidural anesthesia with a needle, 10 or 12 ml levobupivacaine 0.25% (depending on the height of patients: 10 ml: <162 cm, 12 ml: > 162 cm), lamination, after extraction, followed by positioning of the catheter for postoperative analgesia (Not more than 3-4 cm into the epidural space).

In the group receiving only HS-to-patient sedation, were administered via the L1-L2 through August Whitacre 25G, 7.5 mg or 8 mg levobupivacaine 0.5% based on the height of the patients (7.5 mg: <162 cm, 8 mg: > 162 cm) plus 5 µg of sufentanil.

In both groups, after the execution of the reports of the techniques, patients were placed supine with a pillow under your right hip.

They evaluated the following side effects: hypotension (a reduction of blood pressure 20% compared with the previous anesthesia or

systolic blood pressure below 100 mmHg), which is quickly treated with 5 mg of ephedrine endo-vein; bradycardia (defined as a reduction in the heart rate below 60 b / m)-treated atropine 0.4 mg intravenously, vomiting (treated with setron 4 mg intravenously), motor block, assessed through the *straight leg raise* (the ability to lift legs extended) at 50 min from the execution of A-anesthesia, intraoperative discomfort (especially in maneuvers externalization and subsequent rest-operation of the uterus).

The statistical analysis was carried out by means of the z comparison of two proportions with large samples and independent.

Results

The comparison between the two groups shows CSE group, there is an incidence of motor block 4%, 4% of discomfort, vomiting, 6% of bradycardia edipotensione 12% 18% (Figure 1), whereas in the SA group, the incidence of block motor is 86%, 34% of discomfort, vomiting of- to 12%, bradycardia 24% edipotensione 36% (Figure 2).

Given an error probability of the first species to maximum of 5% (P = 0.05), one may conclude that the incidence of motor block, the discomfort edipotensione was larger in the SA group compared with CSE, whereas for other adverse effects under study, the difference in incidence is not statistically significant cannot.

The actual significance levels were respectively for motor block P <0.001; for the discomfort P <0.001, P = 0.021 for hypertension; for vomiting P = 0.147 and P = 0.067 for bradycardia (Table I).

Discussion

The CSE was used for the first time as a midwife in 1979 by Brownridge purposes anesthetic for a cut Caesarean. But in the last decade has earned popularity analgesic purposes, especially in countries Anglo-Saxon.

This popularity is due, in part, all'immissione on the market that atraumatic spinal needles have significantly reduced the incidence of headache postpuntura dural (<1%), in part, to better knowledge of the mechanisms and practices of opple of intrathecal.

Before 1974 the action had not been demonstrated on the spinal cord of opiates. In that year, In fact, Kitaharà showed that morphine adminis-trata in the space directly depressed the spinal transmission of pain by acting in the laminar in I, II, V of Rexed of the dorsal horn.

Opioids, in fact, act on specific receptors There, in the spinal cord and brainstem, which are responsible for both the positive effects (analgesia) and adverse effects (respiratory depression, vomiting,

Receptors in the spinal cord are so representative I: 10% δ, μ 40%, 50% κ.

The mechanism of action of spinal opioids pre- sees action at presynaptic (A and C fibers delta) that is expressed by inhibiting the release of substance P, a mediator involved in the transmission of nociceptive impulse in the bone marrow. At the postsynaptic level, however, opioid-ways Figs (inhibition / modulation) currents neural ion channels (calcium and potassium), pro- vocando in iperpolarizzazione membranes and decreasing, therefore, the frequency and amplitude of action potentials of cells of laminae I, II, V the dorsal horn with a break or slow down the stimuli.

The effects are obtained following the admin- Directors receptor affinity and capacity opioid to achieve it. This ability is fun- tion of molecular weight, degree of lipid solubility and protein binding.

Opioids in obstetrics are the most ideal lipo- soluble (fentanyl - sufentanyl), since, because of this feature easily enter the spinal cord with the immediate onset of action than opioids water-soluble, accumulate rapidly in substantial za gelatinosa of the posterior horn, rapid escape heating from the marrow and accumulate in the plasma. It leads to the permanence of low- opioid in the CSF, therefore, a lack of both- the effect of deposit (depot) and diffusion-rostra the (typical hydrophilic opioid), which cause controlled analgesia little over time and effects of con- unpleasant side (respiratory depression and alter- tion of consciousness) long-term.

The effects of neuraxial opioid-dependent also the route of administration. The adminis- epidural administration, in fact, provides indubbiamen- you cross the harsh and, therefore, a mechanical spinal mechanism of action, and it suffered the absorption tion by adipose tissue, and the conse- You vascular absorption. The consequence of this is that only a peak- often unpredictable and the amount of opioid enters CSF.

So probably the ideal way in which the sum- heter lipophilic opioids is the way to the spinal predictability of the dosages and greater con- plability of the effects.

The fat-soluble opioid, the liquor, where it is coming- to quickly and where he pursued his action analgesic, walks quickly to the movement systemic and this is possible because CSF suffers no protein binding, also stay is not affected either by changes in temperature or pH.

The fat-soluble opioid administered spinal can therefore accumulate in plasma but not in CSF.

We must also consider that the administration of lipophilic opioids in the epidural space is conditioned by the absorption of the venous sinusoids, for better comfort of the patient, the amount of blood flow in the plexus and peridural epidural fat, all are very variable from patient to patient and influence the passage of the opioid.⁹

The sites of action of local anesthetics administered in the spinal space are the spinal nerve roots and bone marrow.¹⁰

Local anesthetics, in fact, act in both the dorsal and ventral horns of the spinal cord, blocking sodium channels and inhibiting calcium and, therefore, the generation and propagation of the pain-stimulus.^{11, 12}

In addition, local anesthetics inhibit in a non-competitive binding of substance P with its receptor neuronal¹³ and the re-uptake of inhibitory neurotransmitters (GABA).¹⁴

It makes sense to give at the same time temporarily in space and spinal opioid anesthetic there local, since it seems that opioids facilitate the entry of the latter in-neu cells.¹⁵ Opening the channels of the slow Na^+ (Ronald¹⁶) and hyperpolarized the cell to open-channel them of K^+ .

Therefore, combining local anesthetics and opioids may reduce the dosage, resulting in improved stabilization of analgesia with fewer side effects.¹⁶

To explain the extension of subarachnoid block which is obtained after the sequential CSE in-chef administration of small doses of local anesthetics in epidural, different assumptions were made: 1) the existence of subclinical analgesia to a higher level, that would be supported and would become evident to the patient or perineural local anesthetic-transdural administered in the epidural¹⁷; 2) the passage of local anesthetic in the epidural space subarachnoid through the hole in the hard¹⁸⁻²¹; 3) the exchange of epidural pressure, which becomes atmospheric which would lead to a better diffusion of anesthetic through a local effect on the volume and the circulation of CSF^{22,4}; 4) compression of the spine by the volume of the solution of anesthetic; 5) the shrink by the volume of the solution of anesthetic; 6) the squeezing of liquor and a greater spread local anesthetic in the subarachnoid.²³⁻²⁷

Conclusions

In this study, the sequential CSE anesthesia showed a lower incidence of vomiting and brady-

cardia (though not statistically significant) and a lower incidence of hypotension, of discomfort intraoperative motor blockade and statistically significant compared to the single cord technique.

Emphasis must be placed in the last two points, for better comfort of the patient, to make the technique more accepted by patients and improves the working conditions of the gynecologist, but, more importantly, reduced motor block allows you a faster mobilization of the patient reducing the risks associated with immobilization postoperative hospital stay less than one-border. Another important aspect is that patients are completely self-sufficient from the point of view with movements, so much so that by the end of the intervention they move independently from the operating floor of the laboratory to the stretcher, thus reducing the physical effort paramedical staff.

One criticism that can be made against this work is that the incidence of intra-discomfort postoperative SA was lower in the group increased and the dose of levobupivacaine to 9-10 mg overlooked, however, a greater incidence of other adverse effects studied.

The objective of this study was to show how, even reducing the dose of levobupivacaine in spinal to the minimum compatible with a degree of anesthesia allows the execution of a caesarean section, the incidence of hypotension and motor block is significantly greater in mind than the SA group.

For these reasons, it is reasonable to think that the CSE sequence represents a step forward in regional anesthetic techniques used in elective Caesarean section.

Summary

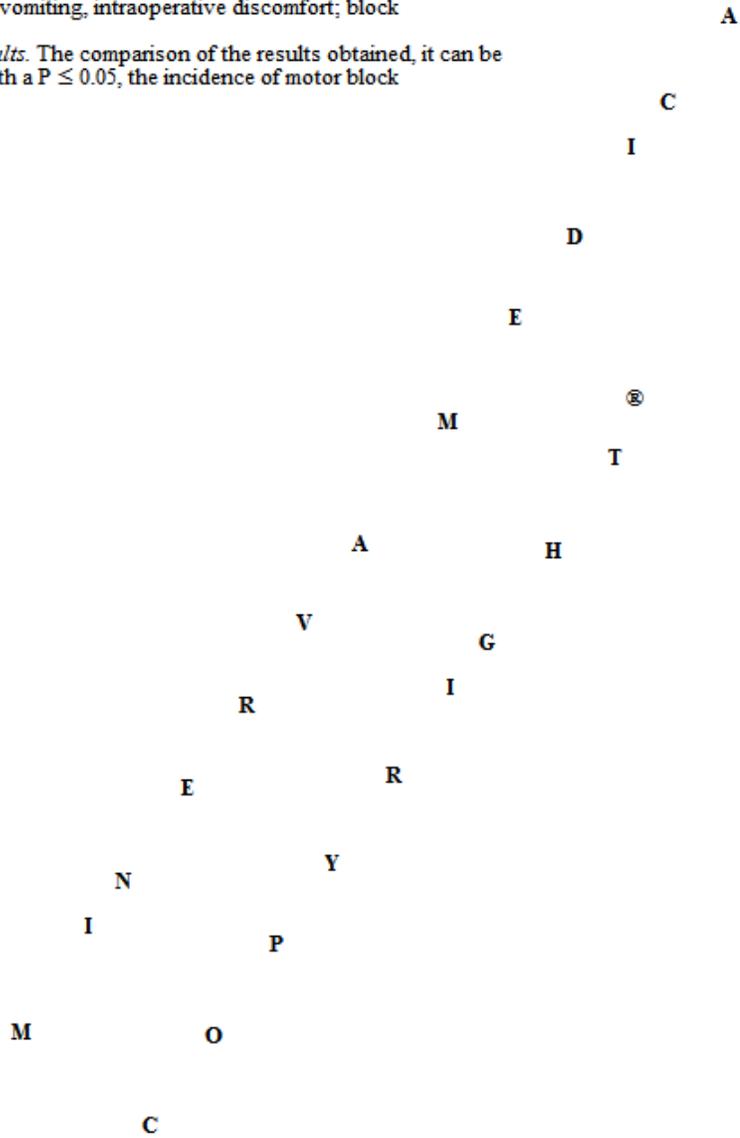
Objective. The purpose of this study was demonstrated. The King, who, with the combined spinal-epidural technique (CSE) sequence, you can exceed the league, you use one of the spinal anesthesia (spinal-Anesth and SA) in elective caesarean section.

Methods. Were examined 100 patients undergoing cesarean section: 50 underwent SA and 50 in CSE. Each 500 patients were infused ml of plasma expander and administration Prior to 5 mg of ephedrine. The CSE was carried-out low pricking at L1-L2-administered spinal 5 mg of levobupivacaine plus 5 μ g of sufentanil, and epidural 10-12 ml, depending on the height of patients, followed by 0.25% levobupivacaine placement of an epidural catheter for in-postoperative analgesia; in the group given SA has only ever point to L1-L2 and were administered 7.5 to 8 mg of levobupivacaine, depending on the height of the patients, most of sufenta-5 μ g nil. All patients were evaluated fol-

COMPARISON OF SEQUENTIAL COMBINED SPINAL-EPIDURAL AND SPINAL Anesthesia with Epidural Anesthesia

you intraoperative adverse effects: hypotension, bradycardia, vomiting, intraoperative discomfort; block motor.

Results. The comparison of the results obtained, it can be say, with a $P \leq 0.05$, the incidence of motor block



Italian. Example 3 (html)

I INTRODUCTION

L Acute otitis media (AOM) is a process inflammation of the middle ear infectious origin, characterized by pay-tion in exudative tympanic cavity.

The clinical presentation, rapid onset, the manifestation is with signs and symptoms of inflammation associated with obvious changes of the tympanic membrane with or without otorrhea [1].

L OMA is one of the most frequent pathologies pediatric age: within three years of age-ol three 90% of children had suffered at least one episode and one third of these in the years suc- following presented more relapses [2-3].

Despite the widespread use of antibiotics OMA to treat pediatric

in the last 40 years has led to a so- permanent decline of its most serious and dangerous infectious complications such as mastoiditis and meningitis, in recent years has opened a intense debate on the need for always and early antibiotic therapy for all episodes of acute otitis media age pediatric or rather restrict the treatment selected cases [4-6].

Even on what the most appropriate term

treatment there are quite a few controversial

sie. Numerous studies, though different in As regards methodology, show that the therapeutic pia in the short term for 5 days with penicillin and oral cephalosporins is as effective as

Conventional treatment for 10 days, limit- OMA to treatment with membrane complement, not

complicated, non-recurring in children over 2-3 years, while in small children coli in the presence of episodes of otorrhea or appli- ent treatment effectiveness is a short cli- only one that the lower microbiological [7-11].

The purpose of this study was to be- lutare the clinical effectiveness of cefaclor, cefalospo- rina second generation is characterized by high antibacterial activity against all the major causative agents responsible for OMA, according to two different regimens to dosage and duration of treatment.

I PATIENTS AND METHODS

The study involved 22 pediatric fa- milies that do business in City of Rome, who helped both the elastic- collaboration of diagnostic and therapeutic protocol

tico, that the selection of the patient, the prescription of therapy and evaluation of results- results.

In the period between November 2001 and March 2002, 410 patients were selected Outpatients of both sexes, with OMA non-recurring, aged between 2 and 6 years. The children were assigned according to a list randomization of previously developed to two different regimens: *Group A-Cephax* 50mg/kg/die chlorine for 5 days in two administrations daily, 204 children; *Group B* cefaclor 40mg/kg/die for 10 days in two-som trations day, 206 children.

The diagnosis of AOM was placed according to following clinical signs and symptoms: fever (> 38 °C), otalgia and / or irritability associated with under-otoscopic hyperemia of the tympanic membrane with evidence of payment entotympanic (alterations of translucency, extroversion or perforation of the tympanic membrane), with or without otorrhea. Children were included in the study only if the symptoms had started from no more 36 hours.

They represented a reason for exclusion The hypersensitivity to the β-lactam taking antibiotics in the 72 hours preceding teeth start of treatment provided by pro-Protocol of study, the presence of concurrent renal, hepatic, hematological neoplastics, immune system disorders, immunosuppressive therapy. The evaluation of clinical efficacy and tolerance ity was performed in four controls all arruolamento following:

The control: visit to the 3rd-4th day from the beginning of therapy;

The control II: visit at the end of therapy (5 ° day for Group A and 10 ° day for Group B);

Control III: first follow-up after 15-20 days after the treatment, reserved only in those patients healed after treatment

IV control: A second follow-up after two months after the end of therapy.

Pediatricians have assessed adherence to prescription therapy, the disease course and the possible occurrence of side effects, not only during monitoring visits, as protocol, but also by telephone during therapy.

Healing was defined by the disappearance dell'otalgia, irritability, fever and improving the otoscopic (reduction tion hyperaemia, decreased dell'estroflexion and opacity).

The failure was defined as persistence symptoms and otoscopic picture one, with possible perforation, otorrhea and / or development of complications.

The results were evaluated in terms of Statistical data obtained by applying the test calculating (With Yates correction).

I RESULTS

Total, 410 were enrolled patients 369 patients with acute otitis media monolaterale and 41 bilateral. 145 of them present-otorrhea compartment, in particular, in Group A, 184 OMA patients had unilateral and 20 bilaterally with otorrhea in 71 cases and in Group B, 185 patients had unilateral AOM and 21 with bilateral otorrhea in 74 cases. In ten children, belonging to Group B, all with unilateral AOM, treatment is been suspended earlier and were then excluded from the comparative assessment of efficacia.

Over 98% of patients complained to visiting Enrollment otalgia and irritability, fever was present in more than three quarters of cases and complaints nonspecific respiratory in less than half of cases.

The tympanic membrane was hyperemic in all patients, everted and opaque in the May-most cases, perforated with otorrhea in 11%. There were no differences be- cally significant of these values among children included in the two treatment protocols (Table 1).

The healing at the end of therapy was achieved in 95.5% of the cases dealt with 50mg/kg/die for five days and in 94.8% of those treated with 40mg/kg/die for 10 days no statistically significant differences (Table 2).

The failures at the end of therapy were re- encountered in 9 patients undergoing treatment short and in 10 of those treated pro- trafficking. In these patients do not fully gauge- rites, was observed within 15 days after the rice- lution of the process in all cases, except the persistence of a small perforation in 2 patients (in brief therapy) and 1 (in therapy long), which resolved thereafter (Table 3).

Table 1 - Clinical and initial otoscopy.

	<i>Group A</i> <i>No patients</i>	<i>Group B</i> <i>No patients</i>	<i>Total</i> <i>No patients</i>
OMA	204	206	410
Unilateral AOM	184	185	369 (90%)
Bilateral AOM	20	21	41 (10%)
Fever	155	163	318 (77.5%)
Otalgia and / or irritability	201	203	405 (98.7%)
Respiratory disorders associated	100	96	196 (47.8%)
Tympanic membrane			
hyperemic	204	206	410 (100%)
everted	175	180	355 (86.5%)
changes in translucency	111	113	224 (54.6%)
perforation and otorrhea	71	74	145 (35.3%)

Table 2 - Evaluation of clinical efficacy at the end of therapy.

- *Healing*:
- Group A: 195 on 204 children (95.5%)
- Group B: 186 out of 196 children (94.8%)
- *Failures* *
- Group A: All 9 children with otorrhea (4 with bilateral form)
- Group B: all 10 children with otorrhea (6 with bilaterally)

* Persistent fever and / or otalgia and / or onset of otorrhea.

Table 3 - Evaluation of the effectiveness of the follow-up.

- *Healing*:
- Group A
- 202 children out of 204, small perforation in 2 cases persisted. Follow-up: relapse in 19 of 204 (9.3%)
- Group B:
- 195 children in 196. If persisted in a small perforation. Follow-up: relapse in 17 cases out of 196 (8.6%)

In the follow-up period of two months: 36 on 400 children (8.9%) had a new episode of AOM in 19 (9.3%) in brief therapy and 17 (8.6%) in prolonged therapy (Table 3). Under no circumstances are real-ified hearing loss, mastoiditis or complications serious.

The episodes of recurrence were treated with al-three antibiotics (amoxicillin / clavulanate or macrolides).

Side effects were observed in 30 pa-patients (7.3%): 13 (6.4%) in group A and 17 (8.7%) in Group B. It was always minor episodes (vomiting, diarrhea, pain abdominal and skin rashes), which have never required discontinuation of therapy. In particular, intestinal disorders appeared after 4-5 days of treatment tion (Table 4).

I DISCUSSION

Acute otitis media is one of the most frequently af-fections to bacterial etiology, and one of the main leading cause of medical consultation and prescription antibiotics in children [12].

In Italy, in the absence of a registry of disease providing precise figures, an estimated 3 million of cases per year in the population under the age to six years.

Such a high incidence in children is to be placed mainly in relation to its pathogenesis. In fact, the reduced diameter and me-nore slope of the Eustachian tube (10%) in children, facilitate the invasion middle ear by micro-smi colonizing the nasopharynx. An earlier viral infection, leading to edema, blocking muco-ciliary transport, stagnation of secre-

Table 4 - Side Effects

	Group A (N = 204)	Group B (N = 196)	Total (N = 400)
Vomiting	1	1	2
Diarrhea	4	5	9
Abdominal pains	3	5	8
Rash	5	6	11
Total	13 (6.4%)	17 (8.7%)	30 (7.3%)

tions and poor ventilation, facilitates engraftment of bacteria [13].

The OMA is bacterial etiology in 75-80% of cases and the organisms isolated most frequently in children aged 2 months to school age are: *Streptococcus pneumoniae* 20-40%, *Haemophilus influenzae* 10-30% (in the majority of cases non-typable strains), *Moraxella catarrhalis*, and *Staphylococcus aureus* 1-3% (14-16). In particular, in Italy *Streptococcus pyogenes* is the etiologic agent responsible in about 10% of cases and *Moraxella catarrhalis* only 2-3% (1, 17).

The OMA is age-related symptoms: in the infant and young child-Prevalence of nonspecific symptoms (fever, irritability, crying, malaise, poor appetite, vomiting and diarrhea) in later life otalgia spontaneous and is the dominant symptom. Nausea. Fever in some cases can not be present. The occurrence of otorrhea is habitually mild, followed by resolution of the symptomatology painful.

The clinical diagnosis should always be confirmed by otoscopic examination. The initial finding is characterized by hyperemia of the membrane, with slight evagination in the posterior-upper-quadrant. Subsequently, the hyperemia-efestofles becomes more evident, the membrane becomes opaque and can be associated with a gradient yellow-brown. The only hyperemia is not whether the membrane is GNO of otitis, but can be also linked to prolonged crying. Microbiological diagnosis should be carried out in the middle ear taken by means of tympanocentesis, as pathogens isolated from the nasopharynx does not match those of the tympanic cavity. The exudate culture drawn (in the case of Otorrea) over the membrane within the first day, may have some significance [4, 18].

The AOM usually resolves without hesitation or

Complications, however, when present, are slight: the tympanic perforation, which heals usually in 2-3 weeks, leaving a small atrophic area, the second-hearing loss, which slowly fades until it disappears with the resolution of the payment, the outpouring of endo-tympanic that may persist for some weeks, but has little clinical significance. Serious complications (mastoiditis, meningitis, brain abscess, facial paralysis, blood clots in lateral sinus) are rare and occur with more frequency in developing countries [19, 20].

Currently, as much from the AU-tion of the spread of bacterial resistance and secondary to the excessive use of antibiotics is that acute otitis media of the child usually undergoes spontaneous resolution, the indiscriminate use of antibiotic therapy. Early policy has been questioned [21-24]. In this regard, a broad-letter study which provides data and results in part-contradictory: two and a meta-study conducted by a large number of pediatricians-English, reported that antibiotic therapy determines the reduction of pain (even after the second day), a modest benefit on the symptomatology general and a lower incidence of contralateral commitment, but no advantages on the risk of perforation, duration of hearing loss and relapse [24-26]. Other authors, however, stressed that the early use of antibiotics reduces pain, fever, frequency

of OMA contralateral and the risk of complications. In the evolution of the process and that healing in more than half of the cases not associated with bacterial [27-29].

The American guidelines, although the numerous evidence of a nonsignificant May greater efficacy of antibiotic therapy compared to controls, suggesting a constant use of antibiotics in all cases of AOM.

In Italy and Europe with more behavior-split is instead to use antibiotics in all cases of AOM, as long as the diagnosis is were taken with a high degree of certainty (With or without positive otoscopic examination of the ear), especially in children under 2 years of age and when risk factors are present: was toxic, reduced immunity, patient who can not be re-evaluated [1, 30]. Ultimately, the attitude of most part of Italian paediatricians is to begin still symptomatic treatment only in cases after 48-72 hours [24, 30]. The choice of antibiotic used for treating OMA treatment must take into account tion with its microbiological activity in-fronts of the main etiologic agents, its penetration into the cavity and persistent existence at that place in concentrations adequate for sterilization and then the problem of resistance. In Italy the situation relative antibiotic resistance of the main respiratory pathogens may be summarized as-reached: the resistance of *S. pneumoniae* to penicillin is equal to about 10%, and macrolide-up exceed 30% of the strains of *H. influenzae* and *M. catarrhalis* producing beta-lactamases, are 5-10% and 80% respectively, while the macrolide resistance of these pathogens is insignificant [31, 32]. In the case of a single episode of AOM without stories of anniversaries, in geographic areas with low prevalence of bacteria and producers betalactamase with low incidence of *S. pneumoniae* resistant to penicillin (as in Italy) or amoxicillin in some alternative oral cephalosporin 2nd generation (eg, cefaclor, cefuroxime-axetil and cefpodoxime-Proxetil) may be used as drugs of choice. In suspected intermediate resistance in pneumococcal strains these antibiotics can be used at doses higher.

In the case of treatment failure with persistence of symptoms after 3-4 days of therapy or a new episode in the course of therapy, in areas High prevalence of bacterial β -lactamase producers or suspected pneumococcal High-strength assistance is appropriate to use another antibiotic. You can use the amoxicillin / acid clavulanate, which is less tolerated by the possibility of intestinal disorders or, in the most challenging to cephalosporin 3rd generation IDUs [33, 34].

The new macrolides (clarithromycin and azitromycin), although effective on *H. influenzae*,

M. catarrhalis and intracellular pathogens and achievable reach high concentrations in the cavity tympanic, due to the strength of pneumococcus remain propose an alternative- only in subjects allergic to β -lactams.

The cefaclor is active against all strains of *S. pneumoniae*, to over 85% of the strains *S. pneumoniae* (including strains of returns-intermediate resistance) to the most strains of *H. influenzae* and to *M. catarrhalis* [31, 32] and also has a high level of penetration cellular and periplasmic concentration, a good bond with the PBP target, a high bioavailability, a post-antibiotic effect and interfere a positive function on the immunomodulatory industry [35].

In conclusion, amoxicillin and cephalosporin 2nd generation (cefaclor and cefuroxime-axetil) are the drugs of first choice for doctors may exceed the highest risk of strains of *S. pneumoniae* with intermediate resistance. In this study, the healing of the IMO, non-recurring in children aged two and six years was achieved as early as 3-4 days treatment with cefaclor in more than 95% of cases treated, with no significant differences between the patients treated with short-term therapy or prolonged.

The few cases have been resolved not healed in two weeks with no results, except the persistence of a small perforation Only in three cases.

The treatment dosage slightly higher than shorter duration and involve fewer side effects side and above all more grip to therapy.

In the follow-up to 2 months for about 9% of the cases presented new episodes without differences-significant between the two treatment groups. In addition, it is conceivable that the increase in the dosage-Thurs could help, as well as amoxicillin and some 2nd generation cephalosporins, the control of some strains of *S. pneumoniae* in resistant-intermediate resistance.

In conclusion, cefaclor for its characteristics that drug, for its spectrum of activity reported the epidemiology of the species most frequent and frequently to their strengths, can be considered a viable alternative to amoxicillin OMA therapy in non-recurring.

The short-term therapy is indicated in children so-practical for the age group between 2 and 6 years with AOM without perforation and tympanic otorrhea in the absence of or deficit was Toxic immune and non-recurring forms. A

more prolonged treatment for 10 days is probably recommended in children under 2 years, case of perforation of the tympanic membrane or in case of a toxic or immune deficiency.

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Key words: cefaclor, acute otitis media, short treatment

ABSTRACT

We evaluated the clinical efficacy and tolerancability of *cefaclor* in the treatment of otitis acute otitis media (AOM), a non-recurring, in children aged between 2 and 6 years, with-comparing two different treatment protocols. Within five months were enrolled 410 patients divided on the basis of a list randomization into two groups: *Group A*, 204 patients treated with cefaclor, 50mg/kg/die for 5 days (short-term therapy); *Group B*, 206 patients treated with cefaclor, 40mg/kg/die for 10 days (conventional therapy). The diagnosis of AOM was made on the basis of the symptoms of inflammation of the middle ear associated with alterations in TIMP-membrane Nica and, sometimes, in the presence of otorrhea. At the end of therapy were cured 195 out of 204 children (95.5%) under the compliance short of 196 and 186 (94.8%) of those under-places to conventional therapy. The lack of improvement to the first control

covered a total of 19 patients: respectively 9 of 10 *Group A* and *Group B*. In the two months following discontinuation of treatment relapse occurred and / or re-cidive in 36 children (9%) of which 19 patients subjected to brief therapy and 17 therapy pro-long. Side effects were minor (Vomiting, diarrhea, abdominal pain and rash cu-TANEO), and are seen in 7.7% of cases (6.4% and 8.7% in the two groups). Adherence to therapy was higher in Children in brief therapy 100% as against 95.1% the other group. This study shows that therapy IMO, not the applicant, with cefaclor in children 2 to 6 years is effective and well tolerated installment, with no significant differences in rap-ports to the duration of treatment. The com-pliance and the incidence of side effects result-Tano decidedly favorable to the short-term treatment.

SUMMARY

Clinical efficacy and tolerability of two different regimens of cefaclor Were Studied in 410-PAED atrice Patients affected by non-recurrent acute otitis media (AOM). 204 Patients Were Randomly Treated with cefaclor given at the dosage of 50mg/kg/die in Two Doses for 5 days; 206 Patients with 40 mg / kg / day in two Doses for 10 days. At the end of the treatment 95.5% of Patients Were cured after the interruption of treatment) 19 and 17 patients respectively Had a recurrence. Side effects Were Observed in 6.4% and 8.7% of Patients re-spectively (not statistically significant); They Were never requiring interruption of the treat-ment. Cefaclor therapy is very effective for treat-ment duration. Short-course treatments ap-pear in terms of better compliance and tolerability.

Italian. Example 4 (html)

SUMMARY

Objective: This Study Was Designed to Assess the effect of intra-articular injection of sodium hyaluronate (SH) on clinical Findings of temporomandibular osteoarthritis (OA) and on synovial fluid (SF) levels of nitric oxide (NO).
Methods: Twenty seven Patients (7 men, 20 women, mean (SD) age 53.9 (11.8) years) with OA of the temporomandibular joint Were Allocated randomly to receive an injection of SH Either (2ml, Hyalgan ®, Fidia SpA, Abano T., PM 500-700000, 20mg/2ml; ounces a week for 5 weeks) or in Ringer's lactate solution (once a week for 5 weeks).
Clinical evaluation procedures Each Was done before, and at 1 week, 1, 3 and 6 months post-injection. Intensity of temporomandibular joint pain, jaw function, maximal mouth opening and lateral jaw Movements Were recorded at Each visit. NO Was Measured on SF Collected by rinsing the joint with saline 1 ml before the treatment.
Results: Injection of SH Caused Significant improvement in the main clinical Symptoms until the last follow-up Which Was Carried out 6 months after last injection. Among Patients Who Received SH injection, Those Who Reached in good outcome Showed the lowest basal levels of NO.
Conclusions: The results of this study Showed That intra-articular injections of SH lead to a lasting improvement in the Clinical Symptoms of temporomandibular OA. Furthermore, Our Findings Suggest That low NO levels in SF are relatively and to a better outcome of temporomandibular OA Among Patients Treated with intra-articular injection SH.

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INTRODUCTION

Temporomandibular joint (TMJ) arthritis or osteoarthritis (OA) is the arthropatia most common joint time-ro-mandibular joint (TMJ) (1). As with other localization, but recognizes a TMJ OA multifactorial pathogenesis, characterized by progressive grading of articular cartilage and alterations of the subchondral bone. A differential

in other joints, the degenerative events are found mainly in charge of the ATM-mind in females (2). Symptoms is frequently characterized by tenderness, palpation, joint noise, particularly crepitii, reduced motility and painful jaw re in the execution of normal movements. The treatment of OA of the TMJ is still controversial, especially when the severity of the disease is not sufficient to justify aggressive actions. Among the most effective therapies, especially when there is a monoarticular involvement, there are the infiltration intra-articular. The drugs most commonly actually used for this purpose are the steroids that however, are not always effective and, according to some (3), may be condrolesivi over time. The

Address for correspondences:

Watch Dr. Luca Nardini
Chair and Division of Oral and Maxillofacial Surgery
University of Padova
Via Giustiniani 2, 35128 Padova
E-mail: luca.guarda@unipd.it

intra-articular treatment with hyaluronic acid (IA) has aroused considerable interest in recent years in OA of the knee (4). The AI, which is the main component of synovial fluid (LS) has an important role in the homeostasis-articular, is important for the visco-elastic that which gives the LS, both for its effect analgesic and anti-inflammatory (5-7). The AI, in fact, is able to reduce the production of substances pro-inflammatory (8) and vascular permeability (9), of inhibit the migration of inflammatory cells and protect against cell damage mediated by free radicals (10). LS in patients with pathologic degenerative joint there is a decrease concentration and molecular weight of the IA which leads to a reduced viscosity of the same liquid (11). It has been suggested that this decrease may be due to reduced expression of hyaluronan synthase-1 and 2 in the synovial membrane of patients with OA and rheumatoid arthritis, together with increased expression of hyaluronidase-2, enzymes involved in regulating the volume of the IA (12). Recently the use of AI has been proposed for the treatment of diseases of head articular other than the knee, among them the ATM. Non- because there is no general agreement on the value of this therapy for diseases of the TMJ, other Studies have demonstrated the effectiveness of the improvement of symptoms and clinical parameters (13). Few authors have instead evaluated the effect of the IA in OA temporomandibular (14). We therefore decided to investigate the effectiveness of injections of AI on the main symptoms and clinical of patients with TMJ-OA. It also tested the effectiveness of treatment in reducing the inflammatory component LS collected in the wash during arthrocentesis. In particular, have been investigated such as nitrite stable metabolites of nitric oxide (ON), substance associated with the presence of inflammatory mediators with increased activity of proteolytic enzymes and depolymerization of the macromolecules cartilage matrix (16).

PATIENTS AND METHODS

27 patients with OA of the TMJ (7 males and 20 females, mean age 53.9 ± 14.6) were randomized to receive a series of infiltration TO 5

(2 ml, Hyalgan®, Fidia SpA, Abano T., PM 500 - 700,000, 20mg/2ml) (19 patients, group A) or Cycle 3 washes with Ringer's lactate (8 patients, group B) on a weekly basis.

The diagnosis of OA of the TMJ was performed by means clinical examination and magnetic resonance nuclear as described by Emshoff et al. (17). The arthritic changes were detected: flattening of the condyle, subchondral sclerosis, surface irregular erosions of the condyle or presence of deformed condylar lesions osteophytic disasters. The criteria inclusion were: presence of unilateral pain-bilateral or the ATM especially during the palpation of joints, articular noises, and limitation of mandibular movements. Before treatment, Patients underwent a conscious-sedation by the administration of clordimetildiazepam (1 mg) and oral diazepam (2 mg) intravenously. Infiltration and washing-articular have been performed on the joint space-higher education after anesthesia in the subcutaneous region preauricular and after detection of the line tragus-hand side according to the method proposed by Holmlund (18). Before each treatment, the clinical picture of the patient was evaluated using following parameters: pain at rest, but pain-activity, pain speech, chewing ability er, detected in VAS 0-10; limiting function of the normal activities of the joint speech and mastication, according to a punscorecard from 0 to 4 (0 = none, 4 = severe); assessment of effectiveness of the treatment and trial of the tolerability assessed by patients using a punscorecard from 0 to 4 (0 = poor, 4 = excellent). In addition to this TSI was assessed for spontaneous and open-mouth, with a gauge measuring the distance between the incisal edge of the upper incisors and that of the lower incisors, and the movements laterality, measuring the amount of movement of the mandible compared to the midline higher than. The follow up of patients included the reevaluation of all measurements to a week, one month, three months and six months since the last infiltration or washing. Patients in both groups were then divided into improved, stationary and worse, depending on the evolution of the framework 6-month clinical onset of treatment. Have treated patients who improved an improvement of at least five parameters, those who had worsened worsening at least five parameters, the other stationary. To obtain the LS 1 ml of saline was injected into the joint cavity. The solution is sta-

Table I - Evolution of clinical parameters of the group of patients treated with hyaluronic acid.

	Treatment					Follow-Up		
	BASE	The week	Second Week	Third Week	Fourth Week	1 month	3 months	6 months
DAR	4.63 ± 2.93	3.00 ± 2.88	2.87 * 3.11 ± 3.16	3.03	2.89 ± 2.32	2.63 ± 2.32	2.53 ± 2.88	2.1 ± 3.39
DAM	4.68 ± 2.43	3.28 ± 2.74	3.05 ± 2.76	2.76	2.05 ± 2.53	1.11 ± 2.73	0.80 ± 3.03	3.03 * 3.05 ± 3.39 **
DAF	3.32 ± 3.48	2.57 ± 2.92	2.84 ± 2.99	2.57 ± 2.92	2.79 ± 2.92	2.05 ± 2.48	1.16 ± 2.54	2.42 ± 2.78
CM	6.26 ± 2.02	5.84 ± 2.56	5.00 ± 2.56	3.32 ± 2.38	2.57 ± 2.45	2.84 ± 2.27	2.42 ± 2.04	2.44 ** 7.21 ** 7.11 ± 2.81 *
LF	2.16 ± 0.76	0.95 ± 0.92	1.00 ± 1.05	0.74 ± 0.73	0.79 ± 0.85	0.47 ± 0.77	0.84 ** 1.53 ** 1.47 **	1.47 ± 0.96 ± 1.17 *
AS	34.26 ± 11.9	34.40 ± 10.60	36.10 ± 8.03	36.73 ± 7.33	37.00 ± 7.33	42 ± 5.19	47 ± 5.38	47 ± 6.79 38.58 ± 6.53
GE	-	1.05 ± 1.08	1.32 ± 1.16	1.89 ± 2.00	1.10 ** 1.00 ** 2.37 **	2.32 ± 1.21	1.11 2.32 ± 1.06	** ** 2.32 ± 1.20 **

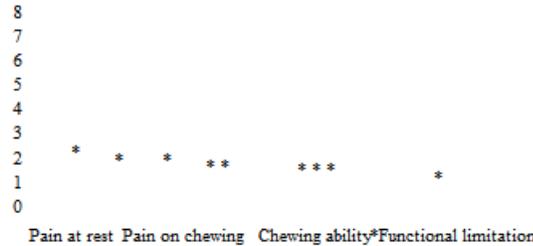
* P <0.05, ** p <0.01 vs baseline. Analysis of variance for repeated measures and post hoc Dunnet test.
 DAR: pain at rest, DAM: pain on chewing, DAF: pain in the speech, CM: chewing ability, LF: functional limitation, AS: opening spontaneously of the mouth, GE: assessment of effectiveness

ta then aspirated and re-injected repeatedly (5 volumes). The average LS diluted so recoverable to was 0.80 ml (range 0.4 to 1 ml). Samples were then centrifuged to remove cells immediately and stored at -20 ° C. The level of them were determined by the reaction-colorimetric Griess (19) before treatment (baseline), after the first and second infiltration or washing.
 At harvest the LS was followed by washing with 20 ml Ringer's lactate followed, only for the group A bit, the injection of 1 ml of AI. For the analysis is statistical variance test was used to im-repeated measures to assess the effect of treatment on various clinical indices over time. The Mann-Whitney was used to compare the levels of On the 2 groups, while the Spearman test for the correlation analysis.

RESULTS

After the full course of treatment (5 weeks mane) patients in group A presented a significant improvement in most considered part of the clinical indices, in particular particular with regard to pain-chewing (p <0.05), chewing ability (P <0.01), the functional limitation (p <0.01) and pain at rest (p <0.05) (Table I, Fig 1). Latter was significantly reduced after the first infiltration with AI (p <0.05) while for the other parameters the significance is been highlighted from the week successive last infiltration. In group B no clinical index showed an improvement cally significant. The effectiveness of therapy expressed by patients in group A increased

Figure 1 - Improvement of the main clinical indices in the group of patients treated with hyaluronic acid



after the initial invasion and remained an- that controls subsequent benefit that the group- some of the controls did not express. The improve- tion indices in group A, persisted in Control 6 months. As far as the dosage is not the NAO was no evidence of significant difference between the two groups either at baseline or after the second treatment. However, in group A, basal levels of ON patients improved (2.44 ± 1.10 μM) were dimostarti lowest re- patients compared to those of stationary (5.21 ± 3.99 μM) (p <0.05) (Table II). The correla- its concentration between baseline and the NAO pa- rameters clinical baseline and 6 months were found to be statistically significant (r = 0.602, P <0.01) only for "joint pain at rest (DAR) on the gene- bit A (Fig. 2), noting that concentrations ON correspond to more pain than high- VATO. In group B there were no cor- significant relationships between the levels of ON and Clinical say.

Table II - Comparison between the concentrations of evolution in the group of patients treated with hyaluronic acid.

Classes evolution	ON (im) Group A	ON (im) Group B
IMPROVED	2.44 ± 1.10 *	8.44 ± 7.50
STATIONARY	5.21 ± 3.99	1.36 ± 1.03

* P <0.05 vs stationary (Mann-Whitney test)

DISCUSSION

The main purpose of our study was that- to observe the effects of intra-articular infiltration of AI in OA of the TMJ. For a more complete evaluation we used a number of in- about clinical and bio-humoral substance of particles particularly important to the joint inflammation such as ON. Secondary objective was the observation of eventual relationships between the NAO and the clinical indices. The results of our study demonstrate efficacy of infiltration of AI on most indicators clinical chosen by us. In particular in the treatment group- ed with AI, but not in the control group, there is- a significant reduction in pain-but sticazione a week after the end of the cycle of infiltration and the ability to do the chewing- bit a month after the end of infiltration. Instead much more rapid were the effects on the limited- tion functional, observable as early as the third infiltration and, in general, the effectiveness expressed by the patient. It is very interesting finding that Most of the best indicators remain this improvement to the control six months. This has been demonstrated for the pain to chewing- ability to chewing, for the limited- tion functional and, more generally, the effectiveness media. This type of reaction in long-term little has been reported in other studies with AI and reflexes probably the capacity of all substantive ze therapeutic potential to act on the structure, so-called drug "structure modifying drugs "or also known as Chondroprotection or an- Cora, "slow-acting drugs in osteoarthritis," by virtue of their action demonstrated symptomatic slow but

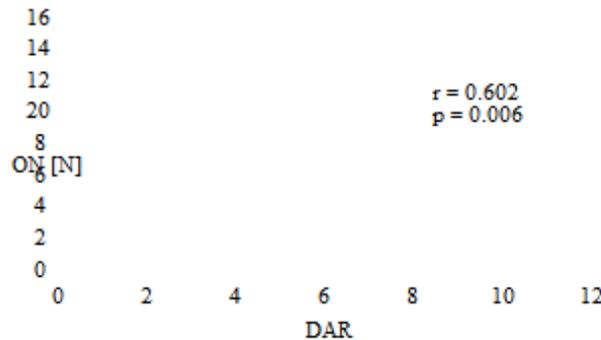


Figure 2 - Correlation between oxidative-nitric (ON) and baseline pain at rest (DAR) at 6 months in the group of patients treated with hyaluronic acid.

ral course that, at the cartilage-artrosica, metabolism characterized by a very slow, seem justified. However, the effect more rapidly observed in some patients, may be correlated with the influence on inflammation and pain that the AI could have. In-made in some studies has been shown that AI can reduce the levels of certain substances involved syno-

Sometimes joint inflammation, such as prostaglandine and metalloproteases (21, 22). For quantification could be important to the correlation observed at 6 months between the levels of basal ON and a particular clinical trial as DAR, pro-

most probably reflects inflammatory activity. On the other hand, this correlation reevaluation in its volta the clinical significance of this index is five-

carefully analyzed in the evaluation of TA-activity of disease. Therefore we can assume that patients who have higher levels of basal ON therapeutic intervention is required more energy

opment.

As many variables can influence the assay in serum (23).

NB is a substance which is newly defined believed to play a central role in the pathogenesis of degenerative arthritis including very as OA (24). We therefore thought that could be useful to investigate the possible value predictive of this drug on the type of evolution tion of OA of the TMJ. We focused on the determination in the LS, which is a liquid organic lends itself well to reflect what is happening in major articular tissues such as cartilage or synovial membrane. In fact the results of our study were reassuring in this regard because

those who had low baseline levels of most-ON yes. It is not possible in the light of current knowledge establish the exact reasons for this increase- ta production of ON in patients who have age-

worst solution. One of the possible interpretations Bili is that these high levels to be determined by a provided that local inflammation is considered to be at-

arthritis. In agreement with this type of inter-

tion observed at 6 months between the levels of basal ON

and a particular clinical trial as DAR, pro-

most probably reflects inflammatory activity. On the other hand, this correlation reevaluation in its volta the clinical significance of this index is five-

carefully analyzed in the evaluation of TA-activity of disease. Therefore we can assume that patients who have higher levels of basal ON therapeutic intervention is required more energy

opment.

In conclusion, our study shows effi- cia IA intra-articular arthritis in long-romandibolari that endures over time. This ef- therapeutic effect was seen in group control, thus excluding the possibility that these ef- fects were attributable to the placebo. The assay NAO does not allow us to adequately assess- you effective clinical observations. Therefore, can be assumed that patients in the basal ab- Bianco ON highest levels is needed inter- therapeutic stronger wind.

Perhaps a truer assessment of the com-

ABSTRACT

This study evaluated the effectiveness of intra-articular infiltration of hyaluronic acid (AI) in the treatment of patients with osteoarthritis (OA) of the temporomandibular joint. 27 subjects were randomized to receive a cycle of five infiltration of AI (PM 500-700000) or a cycle of three washes with Ringer's lactate in every seven-

Manali. Before each treatment were assessed pain, chewing ability and joint function.

The synovial fluid obtained by washing the joint space was used for the determination of nitric oxide (ON), so-

room pro-phlogogenic involved in the degradation of the IA.

Patients with AI presented with respect to the control group, a significant improvement in the May- day of the clinical parameters considered, the improvement that has persisted to the control of 6 months. In the group of pa- AI-treated patients, baseline levels of ON in patients have shown improved rates compared to those of pa- stationary patients. Our study showed that the effectiveness of the IA for intra-articular temporomandibular joint in OA- system for at least 6 months after treatment. In addition, he highlighted the possible predictive value in the NAO against the therapeutic response to treatment with intra-articular AI.

Keywords - temporomandibular joint, hyaluronic acid, osteoarthritis, nitric oxide.

Key words - *Temporomandibular joint, hyaluronic acid, osteoarthritis, nitric oxide.*

Japanese. Example 1

Randomized Controlled Trial Evaluation of duration of treatment with adjuvant chemotherapy of colon cancer

Colorectal Cancer Chemotherapy Study Group Kitakyuusyu (ACT one: KK Kiwamu Ken
[Authors]

First Department of Surgery, Occupational and Environmental Health
Kitakyushu Municipal Medical Center
Tobata Kyoritsu Hospital 共愛会
門司労災病院 Surgery
Mihagino Hospital
Mitsubishi Chemical Corporation (Corporation) Kurosaki Plant Hospital
Kyushu Rosai Hospital
新日鐵八幡記念病院 Surgery
Central Hospital Nougata
Kokura Memorial Hospital
National Kokura Hospital
Mozi Hospital, Kitakyushu City
Shin Kokura Hospital. - Surgery
Kazuki Central Hospital
Hazama Naka Municipal Hospital
福岡大学筑紫病院 Pathology
Oita Medical Clinical Pharmacology
Carer representatives
Caretaker
Case Review Board
Controllers

Contact hill = 〒 807-8555 1-1 months of life physician-ku, Kitakyushu Yahatanishi 治 Hirata Takashi Occupational and Environmental Health School of Medicine First Department of Surgery

Summary (Purpose) as adjuvant therapy for patients with oral cancer resection for colorectal doxifluridine (5 'one DFUR) on the optimal duration of treatment were compared by randomized controlled trial. (Method) - December 1994 curative resection of colorectal cancer cases were integrated by March 1997. (Stage I ~ plate b, curability A · B patients), and 5 to 10 months after surgery as planned 'one DFUR was administered to 239 patients targeted, and colon After stratification before the rectum, the most: minimization method (stratification factors: progress, curability age, histology, presence of vascular invasion), the treatment group a year or three years The assignment to treatment groups. 5 'DFUR is a, 1, 200 mg / body / day was administered on an intermittent dosing regimen is repeated two days off the medication was administered for 5 days. Entire cases Were followed over 5 years after surgery. (Results) Registration: 239 cases recorded in patients analyzed (full analysis set = FAS) 113 patients treated in group 1, 108 in treatment group 3 Cases, 221 cases in total. Treatment groups in a 5-year survival rate of 92.0%, 91.4% three years and treated groups were both good prognosis (log-rank test: p = O. 734.) Incidence of side effects in a treatment group 14.8%, 19.5% in the treated group three years, grade 3 cases of patients over a two year treatment group, five cases in three treatment groups Both small and both groups. (Conclusion) because it was much better results than expected survival 5-year survival rate in both groups, no Itaru of 5 DFUR Could not clarify the appropriate treatment period, the study: From S "one DFUR likely be obtained with good prognosis, long-term safety and It was suggested that may be administered.

Introduction

The standard adjuvant therapy for curative resection of colorectal cancer in Japan is thought to have anti-drug I Rofutsu pyrimidine series of after than before, recently, meta-analysis 1 has been reported but its usefulness .) However, it did not become clear from the period of optimal adjuvant treatment of cancer drugs after Rofutsu disciple of Jin Pirimi test was conducted comparing three dose was administered in one year. In considering the

anti-cancer drugs is one of Russia after fluoropyrimidine doxifluridine (5-fluorouracil) was used. 5-fluorouracil is of advanced and recurrent colon cancer Phase II trial is 467 days and median survival time, that the relatively long survival prognosis was obtained by 23), a variety of other basic experiments and compared with fluoropyrimidine anti-cancer drugs, immune function 4) and bone marrow function 5) have been reported such as the small impact. The No 5 DFUR treatment modality, the five they Yoshikawa 'one DFUR by law rest two throw five repeated washout for 2 days was administered for 5 days, 5-fluorouracil of dose limiting factor to the expression of diarrhea in Since 6 can be reported at least), this regimen was adopted.

1. Materials and methods

Joint research facility (Table 1) in December 1994 to March 1997 between the eyes, it was agreed to participate in this study, cases were cases of temporary registration of the following conditions are met. Histological ①, was diagnosed with colon cancer in clinical treat preoperative (neo adjuvant, such as Poribekutomi) has not been the case, the clinical stage ② Stage I (mp potential cancer cases) II, a plate or dish in case b, gross curability A or B patients, and patients younger than age 76 today ③, ④ PS 0 before surgery is between three cases, no serious complication ⑤ case, simultaneous double cancer of metachronous ⑥, may precede (12 months) in patients with advanced colorectal cancer-free, cases include a clear genetic component ⑦ (which determines your doctor) before surgery ⑧ The laboratory values of WBC $\geq 3,000 / \text{Mm}^3$, $i \geq$ platelets Number $10 \times 10^4 / \text{mm}^3$, $6 \geq$ total protein. Og / dL ($A / G \geq 1.0$), AST, ALT $100 \leq$, \leq serum creatinine $1.5 \text{ mg} / \text{d}$ Shino patients meet the criteria. Registration of cases, after the eligibility check at the Central Registration System to the intestines or rectum before forming another layer, were provisionally registered. Submitted 10 months after surgery - 12 "10 months a progress report on the treatment" to exclude based on the following cases, the remaining cases were registered for this. Exclude cases: pathological findings in ① stage O, stage I (sm cancer), stage IV, histological curability C patients, some patients relapse after temporary registration ②, other anti-cancer drugs ③ (BRM, including) patients were treated, 80 will be administered during the treatment period until the patient is less than 10 months after surgery ④%.

Method of minimizing the probability assignment for patients judged eligible for this stratification factor (: stage (1, II t dish a, plate b); histological curability (A, B); age (30 years old, 30 to 49 years, 50 to 69 years over 70 years); histology (well differentiated, moderately differentiated, poorly differentiated, etc.); the presence of phosphorus invasion path; i made in the presence of venous invasion, Zelen facility law correction is performed in 7), treatment group was determined.

5-fluorouracil administration was carried out on a dosing schedule shown in Figure 1. 2 weeks after surgery - no more 5-fluorouracil $1,200 \text{ mg} / \text{body} / \text{day}$ (40 years old or body weight below 70 kg patient $800 \text{ mg} / \text{body} / \text{day}$) 2 days off the drug orally for five consecutive days (two 5 investments rest) repeated administration, a year after one year treatment group, treatment group were given three years to three years after surgery. During this period, the following items "on the treatment of attention," he said. Unless you were an obvious progression of the disease and can not be administered ① and other anti-cancer drugs, mild adverse reactions ②, and her general condition worsened or complications, the doctor was reduced after withdrawal If you think that it is better to lose weight, adverse reactions of moderate to ③, complications or worsening of his condition, in the absence of side effects improved with rapid weight loss Tomari Hashi rest, medication Once it possible to resume the medication, serious adverse events ④, or a worsening of his condition serious complication, patients should be discontinued if the desired dose, total dose prescribed period of 80 or more ⑤% doing therapy.

1. Review and analysis of study results

Point end primary question of this study was survival, point end secondary is disease-free survival (DFS), and adverse events.

All Aggregate Analysis, Statistical Analysis System Software (SAS ver 6. 12) were used.

Integrated goal setting conditions for setting the number of cases (group 1 dosing in 8 70.0% 5-year survival rate > 80 in treatment group 3. 0%, $\alpha = 0.05$, $1 - \beta = 0.8$. Hazard $H_i = 1.3$ to 1.4 , an integrated two-year period of patients, 5-year follow-up period) using these Schoenfeld 9) is calculated by the method of 150 cases of fish, with a total of 300 cases.

Patients, decision analysis, recurrence and relapse Sun, site of recurrence date of death, cause of death and determination of all cases of Case Report Form was determined objectively based on case studies committee.

Patients, the analysis at the start of the study intention-to-treat (ITT) in accordance with the principles, was planned to target all cases were registered after the start of the study, in the year 1998 ICH clinical guidelines. Statistical Principles lo) was shown for in accordance with the guidelines, full analysis set (FAS), cases of all patients were ineligible for that, untreated cases, the patients with no data after randomisation excluded from the analysis, the study population and analyzed the remaining cases.

The DFS and overall survival, Kaplan-Meier method li) estimation in the curve was calculated. Events survival curve, with death Regardless of the date of death. DFS event was the date of death and recurrence Arui Sun. The evaluation of the safety criteria for solid tumors increased efficacy of chemotherapy Japan Society for Cancer Therapy: loading style, the side effects recorded.

Deviation of background factors X2 test questions in both groups, Wilcoxon test, comparing incidences of side effects X2 test, Fisher's exact test for. : Kaplan-Meier curve comparison test between treatments were calculated by the method, log-rank test, generalized Wilcoxon for inspection.

Dish. Results

1. Treatment of patients

Of 239 patients registered, 18 cases of analysis excluded patients (3 patients withdrew consent, seven cases there is no data after assignment cases, eight cases of Q less than 10 months during dosing) and, FAS (cases analyzed), 221 cases [1 year 108 cases treated group (61 cases of colon cancer, 47 cases of rectal cancer), three cases in 113 treatment group (62 cases of colon cancer, 51 cases of rectal cancer), respectively.

2. Case Background

Table 2 shows the patient background. Stratification before the colon or rectum, histological main factor behind the subsequent two and Masaru Masaru stage, histological curability, age, histological type, lymphatic invasion, venous invasion Rarenakatsu observed bias in or.

3. Medication status

Medication results are shown in Table 3 were aggregated by treatment duration.

4. Prognosis

All cases analyzed (FAS) of over 11 survival curve shown in Figure 2. In the treated group 1 year, 3 year survival rate 96.1%; 5-year survival rate of 92.0 percent in the three treatment groups in the 3-year survival rate of 96.3%; 5-year survival rate of 91.4% in both groups and both high survival rate was obtained, significant differences were observed in both groups Q (log-rank test: $p = 0.734$, Wilcoxon test: $p = 0.919$). DFS tended to be similar to the results of the survival curves shown in Figure 3.

5. Adverse event

5' DFUR Table 4 shows the status of an adverse event and the causal relationship could not be denied.

One year in the group treated 16 patients (14.8%) and adverse reactions, and organ system failure was found in two cases of grade 3 consumption. The three treatment groups in 22 cases (19.5%) and adverse reactions to bone marrow dysfunction in 1 patient each grade 3,4, and digestive disorders were found in 3 patients grade 3.

Significant difference in the incidence of side effects of the two groups showed no problems, other side effects in the treated group was significantly higher in the skin lesions three years, was expressed in all patients treated within one year. The lightness or consumption by the reduction or discontinuation 失Shita side effects have shifted.

Dish. Thought police

Study of the treatment period optimal adjuvant chemotherapy for colon cancer Engineering ntergroup-12 Test 0089), Intergroup-0089-46-5113) are 討 search trial, five as a result-FU ten: Leucovorin (: LV) administration is 12 months and 6 months of treatment has proven to be equivalent, in the subsequent trial of ten 5-FU and LV was 6 months. However, this result is that if 5-FU intravenously, as a study of the optimal duration of treatment with adjuvant anti-cancer drugs Ru Oke Rofutsu pyrimidine series of after the current trial in progress Although there is still no report has been.

This study, five of adjuvant to curative resection for colorectal cancer 'DFUR was an aim to clarify the optimal treatment period, the results of our study revealed the optimal treatment period could not. The cause of the treatment groups at 1 year study, 90 five-year survival rate in treated group and 3% with the largest Wareru think that the patients were significantly higher than predicted prognosis more. Although this study has excluded a recurrence within 10 months following a surgery, sample size they used to calculate about 5-year survival rate, did not sufficiently take into account the respect of recent surgery 14 were considered to affect colorectal cancer prognosis has improved and advances in law.) Therefore, the accumulated number of cases to analyze this result was not enough.

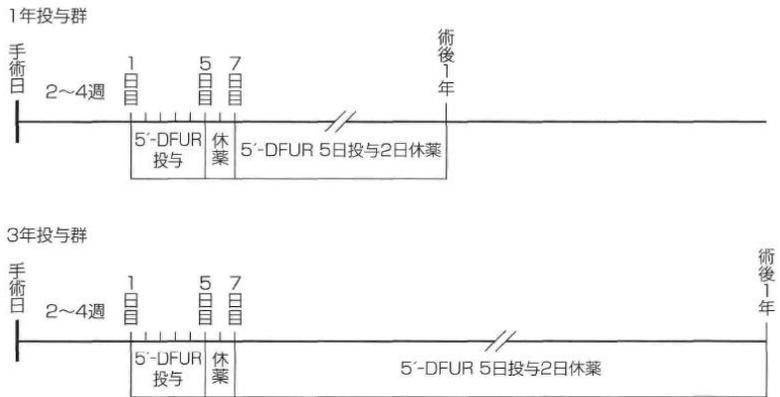
On the other hand, there are also variations in the treated group during treatment, the treated group one year, in particular, and suggestions from patients, 25 patients were treated by more than 14 percent over the months, the quality of test The point was a negative factor. Adverse reactions rate of patients in this study was more common in patients treated group three years, but significant differences between treatment groups was 1 year (X^2 test: $p = 0.359$) o

Recently ,5-FU +: LV compared with the first Phase dish: the study on the usefulness of adjuvant therapy, the results in this study used 5' DFUR a cancer of the ear vertical Rofutsu through the generation of pyrimidine agent capecitabine has been in effect at least equal or higher t5). To that capecitabine is at 16 NCCN guideline is recommended as standard therapy in the adjuvant chemotherapy of colorectal cancer}, and becomes easier for the home treatment of pyrimidine-based anti-cancer drugs in Western economics Rofutsu considered the benefits of increased colorectal cancer patients.

Or, in this study 5' DFUR an optimal duration of treatment with adjuvant therapy, but not significantly, 5' DFUR one is likely to be obtained in good prognosis in safety and long-term administration It was suggested that possible.

Table 1 North 九州大腸癌化学療法研究会参加施設

First Department of Surgery, Occupational and Environmental Health	Kitakyushu Municipal Medical Center
Kazuki Central Hospital	Kyushu Rosai Hospital
Fukuoka Prefectural Kaho Hospital	Kokura Memorial Hospital
National Kokura Hospital	Mozi Hospital, Kitakyushu City
Shin Kokura Hospital	新日鐵八幡記念病院 Surgery
Tobata Kyoritsu Hospital 共愛会	Hazama Naka Municipal Hospital
Central Hospital Nougata	Mitsubishi Chemical Corporation (Corporation) Kurosaki Plant Hospital
Mihagino Hospital	門司労災病院 Surgery



5'-DFUR (経口) : 1,200mg/日×5日間/週
800mg/日×5日間/週 (70歳以上, または体重40kg以下の症例)

図 1 投与スケジュール

Dosing schedule in Figure 1

Treated group 1 year

日
日

Day

5'-DFUR 5日投与2日休薬 2 days 5 days administration of FUR Shino

術
後
1
年

1 year after surgery

Three treatment groups in

5'-DFUR

投与

5 'DFUR administration of a

休
薬

Withdrawal

S 'one DFUR (po): 1200mg / Sun × 5 days / week

800mg / Sun × 5 days / week (patients over the age of 70 t weight 40kg or less)

Table 2 Background factors

	Colon cancer			Rectal cancer			Colon cancer		
	A law	Method B	Test	A law	Method B	Test	A law	Method B	Test
	(n=61)	(n=62)	p-value	(n =47)	(n=51)	p-value	(n= 108)	(n= 113)	p-value
- histological stage;									
I									
II									
III A									
III B									
[Histological curability;									
A									
B									
- histology;									
Differentiated adenocarcinoma									
Offer differentiated adenocarcinoma									
Poorly differentiated adenocarcinoma									
Other (mucinous carcinoma)									
- lymphatic invasion;									
ly0									
ly1									
ly2									
ly3									
- venous invasion;									
v0									
v1									
v2									
v3									
*: Wilcoxon test, **: X2; test									

	結腸癌			直腸癌			大腸癌		
	A 法 (n=61)	B 法 (n=62)	検定 p 値	A 法 (n=47)	B 法 (n=51)	検定 p 値	A 法 (n=108)	B 法 (n=113)	検定 p 値
【組織学的 stage】									
I	8	7	0.515*	6	7	0.906*	14	14	0.573*
II	29	28		22	23		51	51	
III a	20	20		15	15		35	35	
III b	4	7		4	6		8	13	
【組織学的根治度】									
A	60	60	0.568**	47	50	0.335**	107	110	0.335**
B	1	2		1	1		1	3	
【組織型】									
高分化腺癌	27	30	0.715**	24	23	0.755**	51	53	0.557**
中分化腺癌	30	28		22	26		52	54	
低分化腺癌		1			1			2	
その他（粘液癌）	4	3		1	1		5	4	
【リンパ管侵襲】									
ly0	22	18	0.088*	21	21	0.882*	43	39	0.193*
ly1	30	25		15	19		45	44	
ly2	9	17		11	11		20	28	
ly3		2						2	
【静脈侵襲】									
v0	42	40	0.547*	32	34	0.907*	74	74	0.595*
v1	18	19		12	14		30	33	
v2		2		3	3		3	5	
v3	1	1					1	1	

*: Wilcoxon 検定, **: χ^2 検定

Medication status in Table 3

Actual duration of treatment	Treated group 1 year (n=108)	Three treatment groups in (n=113)
Less than 10 months		
10 to 12 months		
12 to 14 months		
14 - 18 months		
18 to 24 months		
24 to 30 months		
30 to 36 months		
36 months or more		
Approximately 80% to 120%		

表 3 投薬状況

実投与期間	1年投与群 (n=108)	3年投与群 (n=113)
10か月未満	1 (0.9%)	
10～12か月	46 (42.6%)	
12～14か月	34 (31.5%)	33 (29.2%)
14～18か月		
18～24か月		
24～30か月	27 (25.0%)	
30～36か月		27 (23.9%)
36か月以上		53 (46.9%)
約80～120%	80 (74.1%)	80 (70.8%)

Survival curve in Figure 2 (FAS cases)

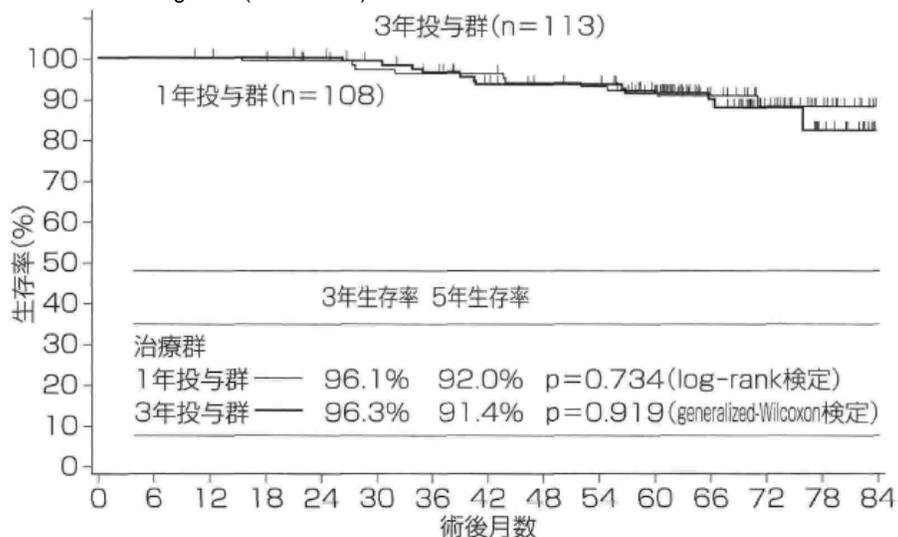


図 2 生存曲線 (FAS 症例)

1年投与群(n=108)

... Administered in group P (n = 108) II

Treatment group	3-year survival rate of	5-year survival rate	
In one treatment group D 1	96.196	92.096	p 0.734 (log-rank test)
In one treatment group D 3	96.3%	91.4%	p 0.919 (generalize Wilcoxon test)

x-axis: Months after surgery

Figure 3 DFS curve (FAS cases)

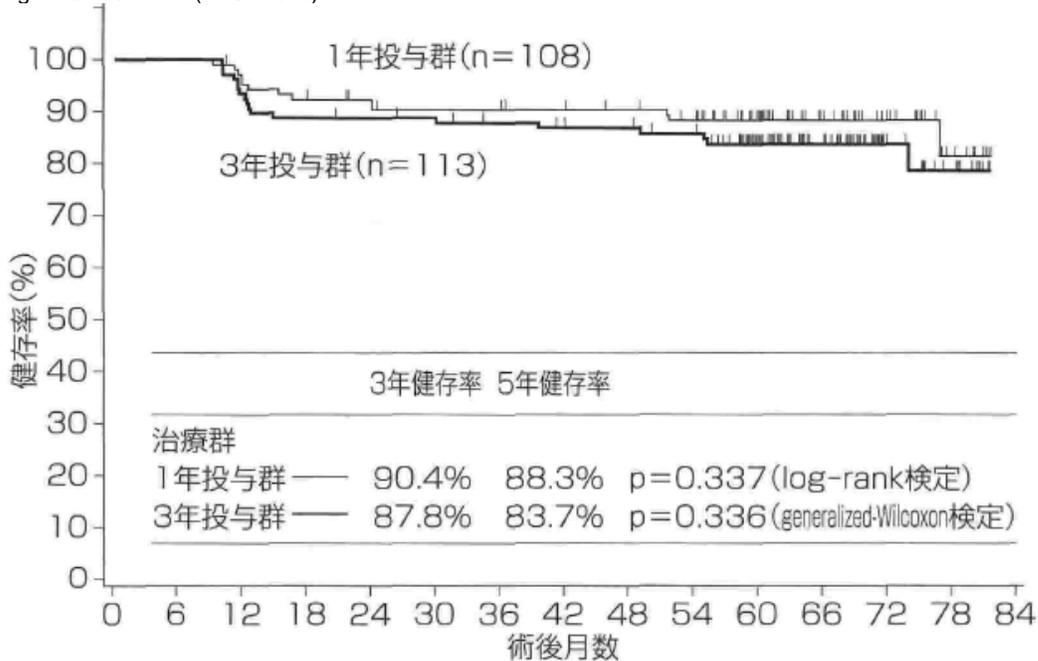


図 3 DFS 曲線 (FAS 症例)

表 4 副作用発現状況

	1年投与群 (n=108)					3年投与群 (n=113)					p 値
副作用発現症例数 (発現率)	16例 (14.8%)					22例 (19.5%)					0.359*
grade	1	2	3	4	発現率	1	2	3	4	発現率	
骨髓機能障害	2	4			5.6%	7	3	1	1	10.6%	0.477*
肝機能障害	4				3.7%	2				1.8%	0.360**
腎機能障害						2				1.8%	1.000**
消化器系障害	3	2	2		6.5%	2	3	3		7.1%	0.840*
中枢神経系障害	5				4.6%	3	3			5.3%	0.722**
皮膚障害						4	2			5.3%	0.029**

*: χ^2 検定, **: Fisher's 検定

Table 4 shows the incidences of side effects

	In treatment group 1 (n = 108)					In treatment group 3 (n = 113)						
Number of cases adverse drug reactions (incidence)	16 cases (14.8%)					22 cases (19.5%)						
grade		1	2	3	4	Incidence		1	2	3	4	Inc
Bone marrow dysfunction												
Liver dysfunction												
Renal dysfunction												
Digestive disorders												
Central nervous system disorders												
Impaired skin												
*: test κ^2 , **: Fische Tobago s test												

Japanese. Example 2

Original

Comparison of the coating is applied one week and 4 weeks for tinea pedis hydrochloride Terubinafinkurimu

[Authors]

Summary

Intended for tinea pedis with 1% hydrochloric acid Terubinafinkurimu (Ramishiru (R) cream) applied a simple week 1 (II group), the usefulness of applying simple safety 4 weeks (I group) as the control of four more examined by a double-blind clinical trial. Of the 43 cases registered, 39 cases of patients valid for analysis, safety cases were analyzed 42 cases. serviceability ratio, the group 1 63.2%, II group was 60.0%, significant differences among groups were observed. Terubinafinkurimu more than 1% hydrochloric acid (Ramishiru (R) Cream) is expected to be comparable to the effect can be expected simply applying a short-term treatment for 4 weeks in a week a simple application, easy to obtain a useful therapy to patient compliance was considered.

Key words: terbinafine hydrochloride (terbinafine), athlete's foot (tinea pedis), short-term treatment (short term treatment), double-blind trial (double-blind study)

Introduction

Terbinafine hydrochloride Sandofama companies (companies Nobaruti Sufama now) has been developed in which a new type of antifungal allylamine having skeletal system. Terbinafine hydrochloride cream 1% (Ramishiru (R) cream) is a dermatophyte as well as Candida, Pityrosporum omle is said to be effective for 1-3), its excellent penetration into the skin rather than into the reservoir of the horny layer 4-6), in particular, use a mild form of ringworm week We have enough Toi 7-9). this time on the basis of these results, 1% for tinea pedis in the group applied a simple utility application group and four weeks to one week the possibility of a simple short-term treatment of hydrochloric acid Terubinafinkurimu In this report, was examined by comparing the safety.

Test method

1. Target

慶應義塾大学 period from March 1997 until August 1996, Kyorin University, Tokyo Women's Medical Hospital, came second, while enrolled students and staff at each facility, Shimizu City Hospital life or the type of clinical interdigital 庖型 urine was diagnosed with tinea pedis were patients with confirmed bacterial elements by direct microscopy.

2. Exclusion criteria

That falls under any of the following items were excluded from the target.

- 1) of hyperkeratotic type tinea pedis
- 2) Contact dermatitis test site, or if they merged or pyogenic infection
- 3) Those using topical steroid medication
- 4) Patients with severe systemic disease.
- 5), an antifungal agent within one week before the start of the study (including topical medication), what was used to
- 6), pregnant women and women suspected of being pregnant
- 7) was considered unsuitable for incorporation of doctor exam

3. Agree

Aimed at what was a voluntary oral consent to participate in the study.

4. How to test drug administration

1) Drug Testing

Terubinafinkurimu hydrochloride (A): 1g of terbinafine hydrochloride cream containing 10mg. Cream base (B): cream base only brewed.

2) the method of administration

Method of administration Fig. 1 shows.

Group I: Terubinafinkurimu hydrochloride (A) applying a simple four weeks

Group II: one week before Terubinafinkurimu hydrochloride (A) is applied to a simple one week, then three weeks base (B) only a simple application

Drug use Unidentified 10g with the guidance to be used one at a time each week to patients filled in tube, it was decided to collect the drugs used each week during the visit. Once daily, the affected area before bedtime or after bath including the whole foot (interdigital and plantar) were applied. assigned to each group was performed randomly by the envelope method.

5. Concomitant drug

During the study period of monotherapy with this drug as a rule, oral and topical antifungal agents, especially other, oral and

topical steroids are banned in combination.

6. See observation day and observe

1) Sun observation

Hazime Higai administration was required to observe the day and 4 weeks after 2 weeks.

2) cutaneous manifestations

Established observation sites in one place the site of drug administration, clinical symptoms of each observation day, cancer itching, redness, pimples, 痂膿 痂 water, maceration, 爛 demons, infiltration, scaling, crusting For each item, 3: high, 2: moderate, 1: mild, 0: No symptoms were determined in four stages.

3) Bacteria test

Direct microscopic examination of the body search conducted at the site observations were obtained each day before the start of each observation and testing positive for the presence of bacteria (+), negative (-) was determined by. Isolation and identification of pathogens before starting the test carried out using a Sabouraud dextrose agar.

4) side effects

They have symptoms other self can not deny the relevance of drugs is a side effect abnormal changes in laboratory values generally confirmed as much detail as possible, including a minor. The questionnaire as well as determination of side effects, side effects "Yes" in the case of the symptoms, location, severity, date expression, treatment, and be completed in detail and the relationship between outcome and drug.

7. Therapy evaluation

1) skin findings Genotoxicity

Compared with pretreatment findings observed daily skin weekly, determine the following five stages, five stages were determined following the final general consideration of the change skin findings at the end of therapy.

1. Markedly improved: most of those disappeared completely or skin symptoms

2. Improvement: light skin symptoms were

3. Improved slightly: a little light skin symptoms were

4. Invariance: What lasting skin symptoms

5. Worse: skin symptoms became worse

2) evaluate the effects of mycology

Direct microscopic examination was evaluated in two stages: positive-negative bacteria and fungi.

3) determine overall effect

Test results for all skin conditions and bacteria were determined in the following five steps as compared to the investigation start date for each day the total effect of each observation.

1. Remarkable effects: negative for bacteria, skin symptoms were markedly improved

2. Valid: negative for bacteria, were improved or somewhat improved skin symptoms

3. Minor response: positive bacteria, a slight improvement of symptoms were markedly improved the skin -

4. Disabled: positive bacteria, regardless of the negative skin symptoms invariable

5. Worsened: positive bacteria, regardless of the negative skin symptoms became worse

4) determine the safety

Side effects and clinical laboratory findings were determined by taking into account the following four stages accidental disease further complications. "Secure", "almost safe" is a particular treatment can continue without requiring Kiwamu Ken about "a little suspect safety," continued the extent possible Kiwamu Ken took some action, "Safety Problems" was about the research must be aborted.

5) determine the usefulness

Consider the effectiveness and safety of its entire course study end date "very useful," "useful," "somewhat helpful", "for free", "harmful" was determined in five stages. However, during the study period cure or side effects, and discontinuation due to worsening when the Sun was determined at that time.

8. Stop loss criteria

After the research, decided cases and handling of cases of contract violations dropped out at case conference.

9. Statistical Analysis

Patient background factors Willcoxon-sample test also establishes a direct calculation method Fisher 2, t-test was to test the homogeneity between the two groups. For the evaluation criteria, Willcoxon-sample test or establish a direct calculation of 2 Fisher Law, Mann-Whitney-U test were analyzed. bilateral significance level of 5 percent. On the Changes of clinical symptoms and sample Willcoxon-test for a significance level of 5% was unilateral.

Results

1. Be patient handling and analysis

The cases of patients with 43 (I group 21 cases, II 22 patients) in patients after an initial examination did not visit them (I group) were excluded for analysis. In addition, three cases of less than four week study period (I case group, II group 2 cases) were evaluated for safety only, the cases analyzed is from 39 (I group: cases 19, II group: 20 cases), respectively. The background is shown in Table 1 in 18 male cases (I = 9 group, II = 9 group), 21 female cases (I 10 patients, II group 11 cases), mean age (I group 58.9 ± 14.8 years, II group 52.6 ± 20.3 years) respectively. In another case of severe severity (II group), 28 cases of moderate (I = 13 group, II group 15 patients), 10 cases of mild (I 6 cases, II in 4 groups), the causative Trubrum cases are 20 (I 10 patients, II 10 patients), T. mentagrophytes cases of 12 (I 4 cases of group, II group of eight cases) were isolated, cultured unsuccessful cases 7 (I 5 cases of group, II group two cases), respectively. The average period of investigation (I group 4.0 ± 0.3 weeks, II group 4.0 ± 0.2 weeks), respectively.

Bias between the groups for each item analyzed background factors showed no efficacy.

2. Therapy

1) skin findings Genotoxicity

Overall determination of the date the last observation skin findings in Table 2. Improvement rate of more than one group of cases 13/19 (68.4%), II group 13/20 patients (65.0%) and no significant difference between groups observed.

The overall verdict of the weekly changes of skin findings Fig. The two shows. Improvement, that is, the skin of patients with symptoms who visited during the week or more "improved" the percentage of patients showing the week Later the group I 4 / Example 16 (25.0%), II 4 groups / 13 cases (30.8%) in group 2 I 9 weeks / cases 17 (52.9%), II 8 groups / 20 cases (40.0%) three weeks later a group of 10/14 cases (71.4%), II 9 groups / 13 cases (69.2%) groups at week 4 I 12/18 cases (66.7%), II group 12/19 patients (63.2%) and increased with time. scores of skin symptoms in the survey at the end of the "scales" were not all zeros.

2) The rate of negative bacteria

Rate at the date of final determination is negative bacteria in the streets of Table 3, I group 12/19 cases (63.2%), II group 13/20 (65.0%), respectively. I somewhat negative rate in those bacteria was low, up 少 Naita target, statistically significant difference was found between the two groups. negative bacteria depends on the day of the change in each observation Fig. 3 shown. I 7 weeks after the start of the survey group 1 / Example 16 (43.8%), II 5 groups / 13 cases (38.5%), 10/17 cases in weeks 2 I group (58.8%), II group 13/20 patients (65.0%) at week 3 I Group 7 / Example 14 (50.0%), II 9 groups / 13 cases (69.2%) groups at week 4 I 12/18 cases (66.7%), II group 12/19 (63.2%) skin findings in generally increased with time similarly in both groups.

3) The effect of the final general

Table 4 shows the final overall effect. The effective rate of more than 12/19 cases of group I (63.2%), II group 12/20 (60.0%), respectively. I slightly higher rate than those with valid statistically higher in the two groups showed no significant difference in question.

3. Safety

II irritation side effects were observed on the second day of initiation of topical application of cream and one case of group Terubinafinku hydrochloride. The loss of the coating was continued without treatment. Terubina fin hydrochloride cream was applied after the test, as well as The irritation was observed, suggesting we could be caused by hydrochloric acid Terubinafinkurimu.

4. Usefulness

Usefulness of the date the final determination shown in Table 5. Rate over the useful useful not useful, I group 12/19 cases (63.2%), II group 12/20 (60.0%), respectively. More useful The percentage was higher and statistically I group and showed no significant differences between the two groups.

Thought

Allylamine antifungal agent terbinafine hydrochloride is based, in vitro fungicidal activity against a dermatophyte 1-3). In addition, Hill 6 et al) applying a seven-day back Terubinafinkurimu of hydrochloric acid by the dermatophyte, even after 7 days after stopping application MIC ensure that there is a concentration of terbinafine in stratum corneum than enough, and announced the good of retention in the horny layer of this medication. a feature of terbinafine hydrochloride these Because of the storativity of the horny layer and acts fungicidal that, as mentioned earlier, the International has been studied treatments in the short term than the cream fin Terubina hydrochloride. Bergstresser 8 et al), this was applied twice daily for one week simply tinea pedis 趾間 type agent to achieve cure of both the symptoms and fungi, showed no recurrence reported in most patients until 12 weeks that. In addition, Evans7) et a case applying a simple once-daily drug intended for tinea pedis, 3, 5, and compare divided into four groups of rats given seven days mycology be clinically and reported no significant difference in each group and also, to suggest the possibility of short-term therapy with this drug. In addition, Watanabe et al 10 in Japan) simply applied once a day for three weeks this drug is have confirmed the usefulness of short-term treatment for.

We report on the reports of more than 1% in tinea pedis simple coating fabric group once daily for 4 weeks and 1 week groups simply applied once a day for Me 探 Ruta the possibility of short-term treatment of hydrochloric acid Terubinafinkurimu usefulness, I consider that to compare the safety. As a result, this drug showed no statistically significant differences in their usefulness when applied to four weeks in a simple straightforward application of only one week, four has shown that this effect is comparable to the coating can be expected simply weeks.

The comparison of these trials Bihonazoru Nakajima, the rate of four weeks simply applied negative bacteria Terubinafinkurimu group 73.8% and 72.5% response rate reported was a 11.) Additionally, Okabe et al Terubina also negative for any bacterial efficacy rate and the rate of six weeks with a simple cream coated fabric fins and reported that 84.6% and was 12). In this trial the response rate is somewhat lower than those previously reported is shown as the reason, this higher rate of detection elements fungus from the lesion because it was involved in a lot of doctors skilled in microscopy directly, lower rate of negative fungal Accordingly, the results have be considered lower in efficiency. Thus, not only will the presence of bacterial factors, such as using neutral red method, by evaluating the viability of the bacteria, confirmed the usefulness of the drug is more accurate Considered Rubeki 13.) reinfection rate in this comparison of long-term recurrence rate will never consider you, what treatment you need to consider short-HCl Terubinafinkurimu has obtained the patient's compliance with ease, has the advantage of reducing the burden can be reduced to honor a patient by the total dose, suggesting that this therapy results more useful.

The meeting summary of this paper is the 44th Japanese Society for Medical Mycology (November 2000, Nagasaki) was reported in.

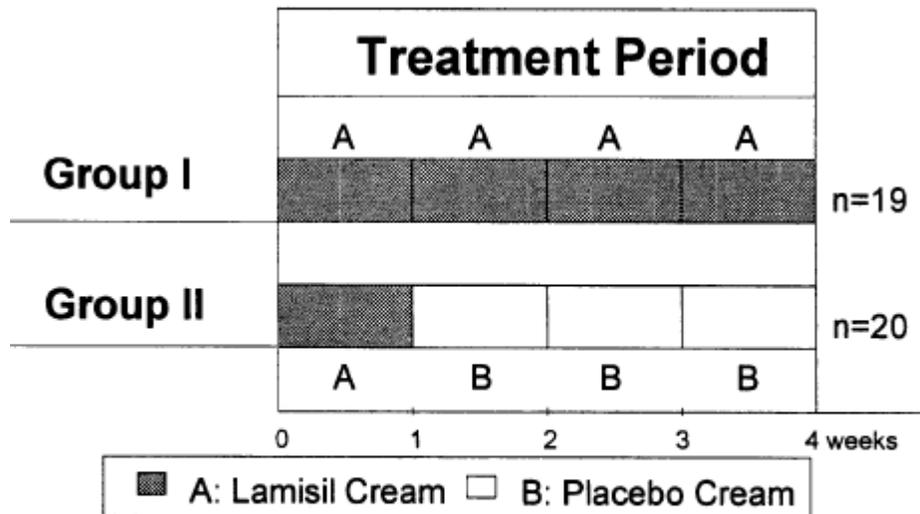


Fig. 1. Treatment groups and drugs administered.

Table 1. Patient demographics

Category	Stratum	Number of patients		
		Group I	Group II	Total
Sex	Male	9 (47.4)	9 (45.0)	18 (46.2)
	Female	10 (52.6)	11 (55.0)	21 (53.8)
Age	<19	0 (0.0)	1 (5.0)	1 (2.6)
	20-29	1 (5.3)	2 (10.0)	3 (7.8)
	30-39	1 (5.3)	4 (20.0)	5 (12.7)
	40-49	2 (10.5)	2 (10.0)	4 (10.3)
	50-59	4 (21.1)	3 (15.0)	7 (17.8)
	60-69	6 (31.6)	4 (20.0)	10 (25.6)
	70-79	4 (21.1)	2 (10.0)	6 (15.4)
	80-	1 (5.3)	2 (10.0)	3 (7.8)
	Average ± SD	58.9 ± 14.8	52.6 ± 20.3	
Min. ~ Max.	28 ~ 83	19 ~ 85		
Median	63	55.5		
Hospitalization	In-patients	2 (10.5)	2 (10.0)	4 (10.3)
	Out-patients	13 (68.4)	17 (85.0)	30 (76.9)
	In/Out-patients	4 (21.1)	1 (5.0)	5 (12.8)
Type of disease	Interdigital type	15 (78.9)	11 (55.0)	26 (66.7)
	Vesicular type	4 (21.1)	9 (45.0)	13 (33.3)
Causative organ	<i>T. rubrum</i>	10 (52.6)	10 (50.0)	20 (51.3)
	<i>T. mentagrophytes</i>	4 (21.1)	8 (40.0)	12 (30.7)
	Culture negative	5 (26.3)	1 (5.0)	6 (15.4)
	Not able to identify	0 (0.0)	1 (5.0)	1 (2.6)
Duration of current episode	Unknown	3 (15.8)	0 (0.0)	3 (7.8)
	Less than 1 month	7 (36.8)	6 (30.0)	13 (33.3)
	Less than 3 months	2 (10.5)	3 (15.0)	5 (12.8)
	Less than 6 months	1 (5.3)	0 (0.0)	1 (2.6)
	Less than 1 year	1 (5.3)	1 (5.0)	2 (5.1)
	Less than 2 years	3 (15.8)	4 (20.0)	7 (17.9)
	10 years or more	2 (10.5)	6 (30.0)	8 (20.5)
	Average ± SD	1.5 years ± 3.3 years	4.8 years ± 7.4 years	
Min. ~ Max.	7 days ~ 10 years	1 day ~ 20 years		
Median	1.5 months	10 months		
Severity	Severe	0 (0.0)	1 (5.0)	1 (2.6)
	Moderate	13 (68.4)	15 (75.0)	28 (71.8)
	Mild	6 (31.6)	4 (20.0)	10 (25.6)

Table 2. Final evaluation of clinical findings

Treatment Group	Markedly improved (%)	Moderately improved (%)	Slightly improved (%)	Unchanged (%)	Aggravated (%)	Total	U-test	Moderately to markedly improved (%)	Slightly to markedly improved (%)
Group I	3 (15.8)	10 (52.6)	4 (21.1)	1 (5.3)	1 (5.3)	19	P=0.5848	(58.4)	(89.5)
Group II	7 (35.0)	6 (30.0)	4 (20.0)	3 (15.0)	0 (0.0)	20	Z=0.564	(55.0)	(85.0)

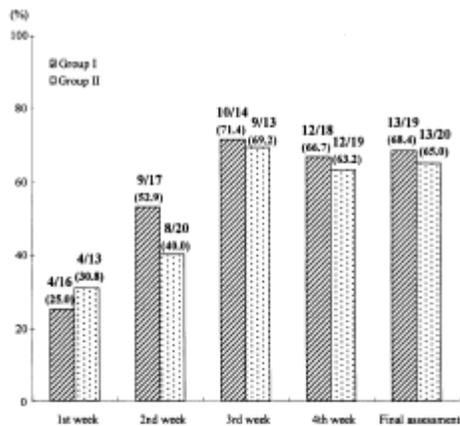


Fig. 2. Trend of final evaluation of clinical findings (Improvement rate).

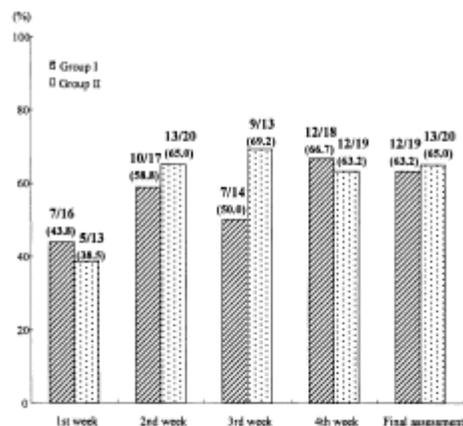


Fig. 3. Trend of mycological findings.

Table 3. Mycological findings

Treatment Group	Total	Negative microscopy (%)	Positive microscopy (%)	Fisher's Exact Test (2-tail)
Group I	19	12 (62.3)	7 (36.8)	—
Group II	20	13 (65.0)	7 (35.0)	1.00000
	39	25 (64.1)	14 (35.9)	

Table 4. Final evaluation of global improvement

Treatment Group	Markedly effective (%)	Moderately effective (%)	Slightly effective (%)	Unchanged (%)	Aggravated (%)	Total	U-test	Moderately to markedly effective (%)	Slightly to markedly effective (%)
Group I	3 (15.8)	9 (47.4)	5 (26.3)	1 (5.3)	1 (5.3)	19	P=0.6288	(63.2)	(89.5) P=1.0000
Group II	7 (35.0)	5 (25.0)	5 (25.0)	3 (15.0)	0 (0.0)	20	Z=0.4835	(60.0)	(85.0)

Table 5. Final evaluation of usefulness

Treatment Group	Extremely useful (%)	Moderately useful (%)	Fairly useful (%)	Useless (%)	Undesirable (%)	Total	U-test	Moderately to extremely useful (%)	Fairly to extremely useful (%)
Group I	3 (15.8)	9 (47.4)	5 (26.3)	2 (10.5)	0 (0.0)	19	P=0.6601	(63.2)	(89.5) P=1.0000
Group II	7 (35.0)	5 (25.0)	5 (25.0)	3 (15.0)	0 (0.0)	20	Z=0.4890	(60.0)	(85.0)

Japanese. Example 3 (html)

Antifungal "internal use of itraconazole solution" is to be administered for the prevention of fungal infections in patients with hematological malignancies and that its usefulness is known. On the other hand, has a bitter taste in specific 同薬 low medication adherence becomes difficult. Sporadic cases have been linked below. So this time we will be taking pills with orange juice to 同薬 Method (s orange juice) to devise a drug absorption (plasma concentration), and ease of consumption (taste evaluation 5) impact Were investigated. Consequently, if the medication with water (control group) compared with no group differences in blood levels of orange juice, Showed improvement in ease of drinking. This method can be performed easily and safely in the clinical stage, to improve medication adherence Was considered to be expected. (Clinical Hematology 51 (5): 315 - 319,2010).

Key words: Itraconazole, Adherence, Orange beverage

<p>Concord Word</p> <p>In a severe infection during chemotherapy complication time, it is difficult to take medicine. Thus, agents and Zella commercial agar The frequency of disease is high, if the disease once treated, it is difficult to continue for agents, improve adherence. And there are many cases hinder chemotherapy. Listen. The study was made by effective control of anti-bitter jelly. Early diagnosis of fungal infections because it is difficult for the preparation is required for each dose. Stem cell grafts and 50% neutropenia 10 days or more of this. For a simpler method, ITCZ in To continue in these cases, the prophylactic use of antifungal drug method for the liquid medication with orange juice at the same time Have been conducted.</p> <p>Itraconazole (ITCZ) is a diagnosis of deep mycosis. And ease of consumption (five taste evaluation) and quality improvement of Treatment Guidelines (2007) "Candida genus and Aspergillus" are reported.</p> <p>Both species may prevent the virus "was proposed internal use. Materials and methods Than in a conventional capsule formulation, a stable absorption can be obtained.</p> <p>Useful for 2) As a preliminary test, ITCZ 20 m l solution internal use and commercial beverages (wheat Juice, orange juice or 100%) 20 m l</p> <p>ITCZ internal use solution, the solubilizing agent is Hydroxypropyl-beta-cyclodextrin (HP-beta-CD) by adding Juice, orange juice or 100%) 20 m l</p> <p>The high lipid solubility solubilize the ITCZ, and the improved immediate absorption for patients committing at the mouth this in five medical staff Stability is obtained, unaffected by gastric pH values more came out, the taste was evaluated at five. In this case 3.8 of 5 Does not decrease the absorption features even when used based on the result of the taste evaluation. (2 Points), "Ri drink without worrying about touching the tongue and bitterness" (3 points), "Beauty Shiku drinking taste "(4 points), "very delicious drink "(5 points) And 5)</p> <p>Reception: July 22, 2009 Accepted: 01 April 2010 Social Insurance Central Hospital Koube Hematology Oncology Shinkou Himezi Red Cross Hospital, Department of Hematology and Oncology</p>	<p>Be.</p> <p>Adherence decreased when oral medication but because of bitterness. Thus, agents and Zella commercial agar. The frequency of disease is high, if the disease once treated, it is difficult to continue for agents, improve adherence. And there are many cases hinder chemotherapy. Listen. The study was made by effective control of anti-bitter jelly. Early diagnosis of fungal infections because it is difficult for the preparation is required for each dose. Stem cell grafts and 50% neutropenia 10 days or more of this. For a simpler method, ITCZ in To continue in these cases, the prophylactic use of antifungal drug method for the liquid medication with orange juice at the same time Have been conducted.</p> <p>Or. This time, drug absorption and water samples (blood levels) impact on And ease of consumption (five taste evaluation) and quality improvement of Treatment Guidelines (2007) "Candida genus and Aspergillus" are reported.</p> <p>Materials and methods As a preliminary test, ITCZ 20 m l solution internal use and commercial beverages (wheat Juice, orange juice or 100%) 20 m l</p> <p>Improved immediate absorption for patients committing at the mouth this in five medical staff came out, the taste was evaluated at five. In this case 3.8 of 5 based on the result of the taste evaluation. (2 Points), "Ri drink without worrying about touching the tongue and bitterness" (3 points), "Beauty Shiku drinking taste "(4 points), "very delicious drink "(5 points) And 5)</p> <p>Then, after seven days or more Grade4 chemotherapy neutropenia of Patients with hematological malignancies are expected to continue (4, 2008 and 2009) targeted, ITCZ 20% solution used internally and m l 100</p>
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Orange juice (Morinaga Milk Industry (Inc.) Sankisutoorenji 100%) 20 m l when mixed with the medication for the "orange Zhu Source group "and 20 m l commercial water mixed with the medication for a time versus	Table 1 Preliminary results	Average score
Control group, "provided, that the administration was randomized. In order to prevent fungal infections in both groups, first to 7 days	Another species Original solution	1.8 points
Remains undiluted solution for internal use medication, 8 to 14 oranges	Barley tea	1.0 points
Medication made by mixing equal amounts of juice or water. Soshi	Green Tea	2.0 points
To, day on day 14 and 7 HPLC method (hypersil ODS column,	Yakult	2.8 points
Mobile phase 40% acetonitrile, 254 fluorescence wavelength nm, 10 the detection limit	Yogurt drink	2.8 points
ng / m l) in blood trough concentration of itraconazole in	100% Grape Juice	3.6 points
, And also a subjective evaluation of five patients and ease	100% Orange Juice	4.6 points
Or. However, ITCZ concentration in the blood there and the active	Barley: (Co) Kagome Article barley, green tea: (Co) Yakult Headquarters default, yogurt drink: Akira Dairy Division (Inc.) Bulgaria drink Yoguru Meizi Default, 100% grape juice: Coca-Cola Japan Minute Maid fruit "healthy breakfast Real cassis and grape, orange 100%	
Hidorokishitotakonazoru Ru (OH-ITCZ) totaling		
Were compared.		
Bitter taste sensitivity and the patient problem or with the chem		
Because chemotherapy can not be denied the same patients could		
The first two courses in the Act, taking away mixing equal amount		
After performing crossover study carried out, evaluation of ease of drinking		
The only makeup prices.		
Statistically significant difference, t test (blood levels)	Example, one case of adult T cell leukemia, multiple myeloma and one	
Mann-Whitney U test (ease of consumption) and evaluation	Patient Orange juice and control groups in these	
Was. However, our test facility at the participating hospital	Patients committed only assigned to each one.	
Approved, subject to the patient sufficient informed consent	ITCZ concentration in the blood of the control group on day 7 of 1,394.6 ± 462.6	
Written informed consent was obtained later made default	ng / m l on day 14 1,924.5 ± 668.6 ng / m l was measured,	
ResultsFruit	Showing a significant increase in blood levels of treatment as extended periods	
Preliminary results ①	Or (p = 0.012; this phenomenon as well as during trial.) On the other hand, orange	
An average score of five staff, and evaluate barley 1.0	7 day juice group 1,307.1 ± 789.2 ng / m l, in 14 days	
Is, when the juice as it was taking 1.8 points worse than,	Women 1,859.2 ± 1,076.9 ng / m l was measured, as well as target group	
Was shown to be amplified taste. In addition, when using	There average blood level was about extending the duration of treatment increased	
Rating is 2.0 points also to improve the taste and they will	From there there was no significant increase (p = 0.099).	
Did.	There was a variation was considered. However, over the same period	
Meanwhile, Yakult ((Co) Yakult Yakult Honsha), you	Significant difference between groups was not observed in, you'll gastrointestinal absorption of drugs	
And drinking yoghurt (Meiji Dairies (Inc.) Drinking Meiji	Yakult showed no effect of orange juice (Table 2).	
Yogurt) with 2.8 points in 100% Grape Juice	In the evaluation of the ease of drinking, the control group (mixing equal amounts water) stock solutions	
(Coca-Cola (Inc.) Minute Maid fruit "health of the morn	By mixing equal amounts taken during the period and taking no significant difference,	
"Real cassis and grape) obtained in the 3.6-point improv	In the groups of orange juice, undiluted dose of 2.4 ± 0.6 during	
The additional 100 percent of orange juice is the best rat	Higher than in the equivalent period a mixed dose 3.0 ± 0.7 points and significantly improved	
Point and was confirmed to be able to taste the medication	(Table 0.023; 3 tables.)	
1.) This allows the patients in this study, 100% orange	The purpose of mixing the drink has a strong sense of bitterness in the juice	
Decided to consider using Jijusu.	Jiru patients, by preventing a decrease adherence	
The study results ②	From there, orange juice group and control group (equivalent Wed	
Total of 36 cases 10 cases 26 cases of men and women	Mixed) phase at one point taking stock solution (to drink bad), or	
Value of 60.3 years) were included in the study. Breakdo	Of 29 to 80 years old patients (n = 15)	
Myelogenous leukemia in 17 cases, 10 cases of non-Hodg	None of disease satisfied analysis. As a result, the target group,	
Three cases of adult syndrome, two cases of acute lymph	for lymphoma, but no cases in both groups than when taking orange juice concentrate	
	Specific leukemia, Hodgkin's disease, and other hematologic diseases (target group: p = 0.046, I	

Table 2 shows the blood concentration of itraconazole

	Blood concentration (ng / ml)		
	Taking stock soft (Week 1)	Water mixing (2 weeks)	p-value
Target group (N = 17)	1,394.6 ± 462.6	1,924.5 ± 668.6	0.012
Orange juice group (N = 17)	1,307.1 ± 789.2	1,859.2 ± 1,076.9	0.099
p-value	0.697	0.833	

a) blood levels: itraconazole (unchanged) + Hidorokishiitorakonazoru (Active metabolite)
b) t test

Ease of consumption in the present study in Table 3 (taste evaluation) Comparison

	Taste evaluation (points)		
	Taking stock soft (Week 1)	Water mixing (2 weeks)	p-value
Target group (N = 17)	2.7 ± 0.6	2.8 ± 0.7	0.474
Orange juice group (N = 17)	2.4 ± 0.6	3.0 ± 0.7	0.023
p-value	0.213	0.636	

*Mann-Whitney U test

Njijusu group: p = 0.010), with mixed drinks adhere Juice (or water), mixing equal amounts "(Sun 1 - 7) →" juice "

Suggesting the possibility of improving balance (Table 4) to 14) will replace the order of taking, (Miyasu

A rash of cases by both groups as a common side effect were evaluated by.

(Grade1) also showed, only a group of 18 orange juice Tested in 36 cases of the two courses at the same regimen

Diarrhea in 2 cases (grade2; cases 1, grade1; one case) repeated therapy was repeated among patients, evaluate the ease of drinking

Is, and any minor side effects not Mitomezu grade3 The 14 cases were performed (control group n = 7, Orange

And what can be recovered easily by this method increased side effects = 7). Results by changing the order of the

Was considered negative. Undiluted by time period after chemotherapy dose, take it when you drink mix

Significant differences were seen each taste evaluation (Table 5).

③ crossover test results

In the previous study after chemotherapy, ITCZ internal use solution, "the original

Solution "(Sun 1 - 7) →" orange juice (or water) equivalent Recently, ITCZ medication compliance and reduce the liquid bitter internal use

Mix "(8 to 14) will be taken in the order of their drinking To improve the device attempts to sweet-tasting beverage for Medication

And evaluated the ease. Meanwhile, crossover study Have been made, 7) However, mixing with the beverage or

, The first two courses of chemotherapy in patients of the medicine is there an impact on gastrointestinal drug absorption and pharmacokinetics

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Patients feel a strong bitter taste in Table 4 (a rating point or two flavors) Effect of mixed drinks

	Taste evaluation (points)		
	Taking stock solution (Week 1)	Mixing equal amounts (2 weeks)	p-value
Target group (N = 6)	2.0 ± 0.0	2.8 ± 0.8	0.010
Orange juice group (N = 9)	1.9 ± 0.3	2.7 ± 0.5	0.046

*Mann-Whitney U test

飲Miyasu crossover study with the study of Table 5
The (taste evaluation) Comparison

	Taste evaluation (points)		p-value	Mann-Whitney U test
	Taking stock solution	Mixing equal amounts		
Cool 1 (N = 14)	2.6 ± 0.8	3.0 ± 0.8	0.55	0.82
2 Cool (N = 14)	2.4 ± 0.5	2.9 ± 0.8		

*Mann-Whitney U test

Pufurutsu cytochrome P450 (CYP3A4, etc.), metabolic
Includes a large number of isohit related to metabolism
The drug, even a small amount of grapefruit juice
And prolonged blood levels, there are side effects could lead to an increase
When this study is to take orange juice
Consider the possibility of similar effects due to prior literature
Examined. Takanaga et al, each with cane juice
Consider the impact on drug metabolism, orange juice
CYP3A4 has no effect on the reported 10) The group
Detect inhibition of drug metabolism by Repufurutsujusu
諸家 reported that the issue further, having no inhibitory effect of metabolic control
Orange juice is a generic 11, 1) The results
Fruit, orange juice and discussion about the issues as no
Was.

It is necessary to deny in advance.

Coca-Cola ITCZ capsules formulation (pH3 back and forth) For the major components of cell membrane lipids
By the time the medication has been reported with increased drug inhibition in the hypothesis of Le Chitoku mammalian
That. ITCZ 100 mg capsules in healthy volunteers and P450 in Rome has also been reported less impact13)
Coca-Cola 325 m l were taken at the same time Jarurata in addition, the major active metabolite of the OH-ITCZ, ITCZ and almost unchanged
In their study, the blood levels of medication than when it was reported to exhibit antifungal activity comparable com
C. Approximately 2.2-fold, AUC increased approximately 1.8-fold
The protective coating is dissolved under acidic drugs From one study to be conducted to combine them
Ru that are involved. Or. Based on these results, we used internally ITCZ amber liquid

In this regard, 100% orange juice with high acidity The same drug devised Jijusu時服, the impact on the actual blood concentration
(Typically around pH4) for internal use liquid medication. Do not use that there is no Symphony.

In it, the idea is expected to increase blood levels of Results from the literature or this study, the present method (ITCZ
Or. However, this study found that results from such Equal volume of 100% solution for internal use when mixed with orange juice for
Did. Solubilizer (HP-b-CD) were added in the ITCZ How to medication) does not affect the intestinal absorption, a reduction in bitterness
For the solution, because it is already solubilized, is affected by the resulting expected increase in medication adherence
Shall not be suggested. Were considered to be Kiru.

Meanwhile, citrus (especially grapefruit) and the correlation between drug
Interactions also should be noted. Recent studies, gray Results of the present study, the Japanese Society of Hematology meeting in Japan 2008

Korean. Example 1

Ulcers after variceal band ligation on the healing effects of proton pump inhibitors

Chosun University College of Medicine

[Authors]

INTRODUCTION

Endoscopic band ligation for treatment of a hemorrhoid develop doeoteu I, 1,2 1986 Stiegmann and Goff Politics is a Sample with bleeding esophageal varices after the first three being the most preferred in recent years is to treat esophageal varices. Varicose veins with a rubber band, which attempt to capture some of the machines end up shutting down due to a clot of blood vessels are varicose necrosis is a lost cause.

Band ligation of esophageal varices (esophageal variceal ligation, EVL) have been used for a long time in the past endoscopic variceal sclerotherapy (esophageal variceal sclerotherapy, EVS) compares the efficacy of treatment of acute bleeding and fewer complications due to similar or superior to first Treatment is recommended, and even more effectively and safely delivered for example, a room with a small number of treatments for varicose veins is known to be lost from 0.4 to 7, but EVL performed three days after being eliminated from the necrotic blood vessels in almost all cases, the toughness of Cause of ulcers, and in two weeks to three weeks the ulcer is healed. 7,8 Most ulcers that occur after the EVL and deep confined mainly to the mucosa and submucosa, so this is a complication occurs mostly minor, but Anterior wall of the esophagus over a rare case of death of patients due to necrosis, 9-11 treatment was also due to ulcers and bleeding occurs in about 2-5% .5,6,12

Acid exposure of the disorder itself is an important etiology biu in gastritis, duodenitis, gastric ulcer, duodenal ulcer, and esophageal reflux, but in recent years yeome seoppun manyi wijeommakjeol polyps removal and salvage procedures such as gastric acid suppression and ulcer healing righteous .13,14 actively being performed after the procedure, which caused the exposure of acid expression can slow down the healing dogweyangeseodo concept and know the foreign literature, and EVL performed in the EVS and to inhibit gastric acid values need PARTNERS 12,15-26 The study claims that there were four objections to the current controversy is about dragons. However, in our country also underwent endoscopic convincing evidence that many doctors, but after EVL performed several gastric acid suppression therapy has been. In our country, yet after EVL treatment of ulcers caused by whether or not the research. This study has the strongest inhibitory effect on gastric acid secretion inhibitors, proton pump (proton pump inhibitor, PPI) over the use of ulcer healing after EVL performed to evaluate the effect on this patient and for seven days and 14 days after surgery Endoscopic examinations were performed to measure the size of the ulcer Now heretofore whether the symptoms assessed by questionnaire and leave it to PPI and control treatment groups were compared.

Materials and methods

1. Target

March 2005-June 2006 Wheat bran, Chosun University Hospital, bleeding from the equation is confirmed by two of the 47 patients who underwent EVL were enrolled. The definition of esophageal variceal bleeding include hematemesis or black mutation presenting with an upper gastrointestinal bleeding among patients who underwent endoscopy, esophageal varices, causing it to bleed from the confirmation of the activity, or the presence of esophageal varices, while certain In other areas there is no evidence of upper gastrointestinal bleeding from March 2005 to June 2006, Chosun University Hospital with variceal bleeding in the expression of Milling been diagnosed with a total of 47 patients who underwent EVL were enrolled. The definition of esophageal variceal bleeding include hematemesis or black mutation presenting with an upper gastrointestinal bleeding among patients who underwent endoscopy, esophageal varices, causing it to bleed from the confirmation of the activity, or the presence of esophageal varices, while certain In other areas there is no evidence of upper gastrointestinal bleeding

2. How to

All of the patients and practitioners, double-blind tests by non-drug group and control group were randomly chosen, and to reduce bias Child-Turcotte-Pugh classification A, B, C 3 minutes ryuhaeseo grades were asked to share. After the EVL group underwent positive PPI Mac pantoprazole (Pantoloc, Altana Pharma AG., Konstanz, Germany) 40 mg once a day, three days after injection with oral pantoprazole 40 mg in the morning, before the 11 days that were to be taken in the control group Saline placebo intravenously for 3 days after the 11 days were to take placebo before breakfast. To eliminate variables other antacids, histamine H2 receptor antagonists, gastric adjuvant therapy, etc. are banned medication during the study period performed. After surgery all patients terlipressin intravenously for 3 days after injection without contraindications propranolol and nitrate were administered continuously

Olympus endoscope's GIF-H260 (Olympus Optical Co., Ltd., Tokyo, Japan) was used, EVL rubber band ligation of the Pneumo-activated mechanism (Pneumo-activated EVL device, Sumitomo Bakelite, Co., Ltd., Tokyo, Japan) and four with a flexible over-tube was yongha. EVL performed at 7 days and 14 days respectively after the two Endoscopic examinations were performed to measure the size of ulcers caused transverse diameter 7 mm at the open biopsy forceps (oval type, MTW endoscopy, Wesel, Germany), the vertical length the retrograde catheter damgwanjoyoungsulyong (tapered type, MTW endoscopy, Wesel, Germany) was a four yongha, transverse diameter and vertical length by multiplying the area of seeking more than the sum of the area in multiple ulcers were measured and averaged out (Fig. 1). The definition of ulcers after EVL EVL previously part of the lower esophagus or proximal wibunmunbueseoo Dunn sihaenghaet endoscope that can be seen as sufficiently deep lesions, or with a notch to define a distinct point maksonsangeuro transverse diameter and vertical length of the longest were measured. After photos were taken endoscopy to improve the accuracy of the information is not shared with other endoscopic ulcer size measured again was so green. Ulcers the size of the Child-Turcotte-Pugh classification A, the Olympus Corporation Endoscope GIF-H260 (Olympus Optical Co., Ltd., Tokyo, Japan) was used, EVL a Pneumo-activated rubber band ligation Organization (Pneumo-activated EVL device, Sumitomo Bakelite, Co., Ltd., Tokyo, Japan) and four with a flexible over-tube was yongha. EVL performed at 7 days and 14 days respectively after the two Endoscopic examinations were performed to measure the size of ulcers caused transverse diameter 7 mm at the open biopsy forceps (oval type, MTW endoscopy, Wesel, Germany), the vertical length the retrograde catheter damgwanjoyoungsulyong (tapered type, MTW endoscopy, Wesel, Germany) was a four yongha, transverse diameter and vertical length by multiplying the area of seeking more than the sum of the area in multiple ulcers were measured and averaged out (Fig. 1). The definition of ulcers after EVL EVL previously part of the lower esophagus or proximal wibunmunbueseoo

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EVL performed at 7 days and 14 days after the endoscopy sihaengha track on the daythe patient felt uncomfortable symptoms through a questionnaire whether the barrelchest, hyunggolha heartburn, dysphagia, and assessment of symptoms and medication side effects of medication compliance assessment Was. Of questionnaire about symptoms of GERD is mainly used in health-related quality of life (HRQOL), applied the tool was to use simplified sikyeoseo chest pain, burning hyunggolhadysphagia, and about three kinds of symptoms in each severity 5 point score of 0 represents the share (15-point scale) were evaluated by the sum of .27,28 EVL bleeding and vital signs to determine whether the serum hemoglobin levels every 3 days after surgery, and 7 days And 14 days after the measure was bleeding from ulcers after EVL include the definition of the serum hemoglobin 3 g / dL or more is reduced or hematemesis occurred during this time done by endoscopy, esophageal ulcers, hemorrhage, or when you see causing bleeding from other sites With the exclusion of blood in the stomach as if you were standing.

3. Statistical analysis

SPSS (version 12.0, SPSS inc., Chicago, IL, USA) statistical programs by using sex, cause of cirrhosis, Child-Turcotte-Pugh classification, type classified according to endoscopic findings of varices, EVL performed past medical history, and above Whether or not accompanied by varicose veins, cancer, and recent alcohol consumption, whether accompanying or as a discrete variable, age, ulcer size and symptom score, defined as a continuous variable, and χ^2 -test and univariate analysis of the PPI group compared with the control group, all statistical analysis The significance level was defined as a p-value less than 0.05.

Results

1. Characteristics of patients and 2 patients in Endoscopic examinations Wed

There were a total of 47 patients with Child-Turcotte-Pugh grade over high-ryeoha PPI group and control group were distributed randomly. The number of patients the PPI group, 25 patients were 22 patients in the control group this average age of four the two groups, there was no significant difference in gender ratio. And the cause of cirrhosis, Child-Turcotte-Pugh grade, morphological classification of esophageal varices on endoscopy, the presence of gastric varices, who underwent EVL previous history, whether unaccompanied or accompanied by liver cancer, clinical features, such as drinking in the last two groups There was no significant difference (Table 1). 7 days after EVL Endoscopic examinations performed in the average duration of Inspection PPI group 7.16 ± 1.13 days, control group was 7.29 ± 1.21 일 patients in both groups 47 members of the PPI-to-army without loss in 25 patients, 22 patients underwent control . Additional 14 days after EVL ever performed endoscopic examination, the mean duration of PPI group 14.26 ± 1.53 days, control group 14.31 ± 1.42 days and PPI total of 26 patients treated in 16 patients, 10 controls not prosper in the PPI group was performed in 9 patients, and 2nd in the control group of 10 patients refused examination, group 2 patients with complications were not enforcing. In this study, not to test 14 days after 7 days also underwent

tests for Endoscopic comparison between the two groups to be judged in the full meaning anateu not excluded from the study said, 47 people a jujjaeneun (PPI group, 25 patients control group, n = 22) compared with pathological and two jujjaeneun 26 people (PPI group, 16 patients, control group n = 10) were compared with those targets. This study showed a picture of the overall flow (Fig. 2). EVL of medication compliance in both groups 7 days and 14 days after the procedure was good all the side effects of PPI was not found. The mean serum hemoglobin of the two groups at admission cow PPI group 7.8 ± 2.5 g / dL, control group 7.9 ± 2.1 g / dL was the nine year period, the amount of red cell transfusion during the dose PPI therapy were charging an average 2.9 ± 1.2 pints, 3.1 in the control group was ± 0.9 pints.

2. After the PPI group and the control group underwent EVL-sized comparison of esophageal ulcers

EVL ulcers at day 7 of the procedure on the size of the army-to-PPI, respectively 98.7 mm², controls 119.4 mm², respectively, in the PPI group 14 days after the procedure 32.3 mm², 43.8 mm² in the control group in two meetings Endoscopy in trace levels in both groups ($p < 0.001$) in the PPI group were lower than the size of ulcers (Table 2). In other words, in the treatment group compared with the control group at 7 days after surgery 83.7%, 73.7% at 14 days after the procedure was further reduced by Child-Turcotte-Pugh class, depending on the hierarchical system, each the size of the ulcer 7 days after surgery when compared ratings from the PPI group A 95.5 mm², grade B 95.8 mm², grade C 100.4 mm², to control the grade A 111.9 mm², grade B 120.3 mm², grade C 130.2 mm², and 14 days after surgery in the PPI group grade A 31.8 mm², EVL performed 7 days after ulcer surgery in the size of the army-to-PPI, respectively 98.7 mm², controls 119.4 mm², respectively, in the PPI group 14 days after surgery 32.3 mm², 43.8 mm² in the control group in two meetings Endoscopy in trace levels in both groups ($p < 0.001$) in the PPI group were lower than the size of the ulcer (Table 2). In other words, in the treatment group compared with the control group at 7 days after surgery 83.7%, 73.7% at 14 days after the procedure was further reduced by Child-Turcotte-Pugh class, depending on the hierarchical system, each the size of the ulcer 7 days after surgery when compared ratings from the PPI group A 95.5 mm², grade B 95.8 mm², grade C 100.4 mm², to control the grade A 111.9 mm², grade B 120.3 mm², grade C 130.2 mm², and 14 days after surgery in the PPI group grade A 31.8 mm², grade B 31.6 mm², grade C 34.4 mm², ratings in the control group A 41.8 mm², grade B 46.7 mm², the two groups in grade C 47.3 mm². Most of the severity rating for all the ulcers were also all the results and bigger. However, when analyzed by univariate dualistic in the two groups were significant ($p < 0.001$), Child-Turcotte-Pugh class, each such A, B, C, between PPI therapy and Child-Turcotte-Pugh, such as whether the sudden death of this interaction There was a significant effect ($p > 0.05$) (Fig. 3). Depending on the type of esophageal varices on endoscopy hierarchical system, each the size of the ark positive 7 days after surgery when compared PPI in group F1 95.7 mm², F2 94.9 mm², F3 101.8 mm², in the control group F1 113.1 mm², F2 121.0 mm², F3 119.9 mm², and 14 days after surgery in the PPI group F1 37.5 mm², F2 31.9 mm², F3 30.0 mm², from control F1 42.3 mm², F2 44.0 mm², F3 44.7 mm² was found in

3. PPI group and control group comparison between the total symptom score

Symptoms through a questionnaire combined score of 15 out of an average of 0.7 points PPI group, there was no significant difference between groups was 0.4 points ($p > 0.05$) (Table 2). Very uncomfortable symptoms of the patients had chest pain when the percentage of patient groups in the PPI 5.25 (20%), controls 22.9 (9.1%), burning sensation in the sternum in the PPI group 3.25 (12%), control group 1.22 (4.5%), younger soils: 5 / 25 (20%), controls 22.9 (9.1%) (Table 2). PPI group rather than in the control group, slightly higher symptom scores of patients

experiencing symptoms that were more results. However, in both groups after surgery, chest pain, burning sensation in the sternum, dysphagia and a high frequency of symptoms did not appeal the loan was minimal minutes.

4. Bleeding and other complications

Significant bleeding during the study period is one in the control group were raised for the first 10 days after EVL was performed emergency endoscopic band ligation was performed to confirm that the bleeding at the site of EVL were performed again the next day with signs of sepsis with massive hemorrhage were killed. The other one from controls Child-Turcotte-Pugh Class C corresponding to 11 days after the patient underwent a second hepatic EVL were killed.

High kicks

Last EVL for acute bleeding caused by rupture of esophageal varices bleeding, as well as in the primary and the secondary has been performed widely for the prevention of rebleeding. EVS in the literature compared with numerous success rates and loss rates are similar in varicose veins or even better the local, systemic complications, the conclusion that it makes much less a treatment method was the most widely performed EVL .4-7,29-31 but also After treatment, most ulcers are made in the case of degrees less empty after the procedure due to ulcer rebleeding has been reported, dysphagia, chest pain, heartburn and other symptoms can occur hyunggolha very rare but fatal hemorrhage leading to death, and esophagus Perforation, esophageal stricture is reported a case of .8-11,32,33 For these reasons, underwent endoscopy in clinical practice that many doctors thought that gastric acid suppression therapy and to support that, but the use of these materials is still Some do not have enough foreign literature in the past to the EVS and EVL ulcer healing after the procedure than the needs of the wealth of research has been reported .13,15-26

EVS on the need for research and treatment of ulcers, many studies have shown that using wisaneok formulation. Research into using Sucralfate Roark15 and after two other studies 16,17 EVS sucralfate in the treatment of ulcer bleeding in the standing hayeoteu treatment is effective or, in the other three studies that there is no meaningful opposition was the result of the lesson. With 18-20 Ranitidine study had two EVS21,22 and the results were contradictory to each other in the treatment of ulcers all. Of gastric acid secretion inhibitors, omeprazole, one of the most powerful PPI formulation of three research with histamine H2 receptor antagonists and sucralfate in 23-25 within amounts to the ineffective after EVS reported that omeprazole is effective, but other research Garg And 26 to demonstrate the effectiveness of the study was unsuccessful. After EVL for the treatment of ulcers, one kind of study, including ten thousand and two was 12 Shaheen ulcers after EVL for the PPI pantoprazole formulation of the therapeutic effect compared with placebo in treatment of the ulcers were smaller in size by about half reported Was. Ulcers after EVL like this: A study on whether the treatment is very scarce, especially in domestic wholly lacking is a state.

In this study, pantoprazole group to leave 1 or 2 weeks compared to the size of the ulcer with no significant sujuneu PPI group than in the control group after EVL ulcer the size of 83.7% on day one week, two weeks jjaee 73.7 % Of all found to be reduced further. Child-Turcotte-Pugh classification and hierarchical system based on the size of the ark amount compared with the degree of A to C is usually larger than the size of the ulcer was able to determine that there was no statistical significance. However, up to 50% from the previous foreign literature that showed

a clear decrease compared to 12 who do not meet expectations in both groups was the result of 14 days does not cure ulcers, came completely.

Chest pain, hyunggolha burning, dysphagia symptoms after the procedure and the ratio of EVL goeseoneun no significant differences between the two groups rather than the slightly higher scores of PPI treated group complained of symptoms that many patients, but the results came back, the symptoms were The total incidence of 47 patients with patients in 9 patients (19%) and not the lower level of daily life most severe when the total of 15 points between two point four points clear difference between the two groups deulyeoseo mild symptoms I think that the writer must have been tough.

Complications of EVL Inhibitor gastric ulcers in the ultimate goal of the occurrence of bleeding complications during the study period in comparison with the control group one patient died from massive bleeding and sepsis, increased vertical and there was bleeding in the PPI group. In this study, the incidence of bleeding complications from ulcers after EVL is one person in all patients, 47 patients (2.1%) too low to be statistically significant between the two groups showed no difference in results of previous literature deuleseoui 2-5% 5,6,12 This is enough to prove that if you see a lot more in patients with a multi-institution research is needed.

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In this study, the PPI group eventually after EVL ulcer size decreased significantly more, but during the study period of two weeks bin complete loss amounts yeobunableeding complications, onset of symptoms, whether by questionnaire did not differ in comparison. However, in previous studies of gastric and duodenal ulcers are large and severity of ulcer bleeding, the incidence of severe complications, 34,35 the results of the authors to see a reduction in ulcer size, reduction of bleeding complications indirectly preview Is thought to be bin yangeseoui bleeding after EVL in PPI group was in control but the result is that PPI treatment can preview the effect seems to be.

7-day study period, 47 people in all patients, but the next two weeks to check progresstests nine people in the PPI group, rejection control group, 11 patients were tested. This is one kind of limitation in this study during the first test to measure the size of ulcers in the process takes a long time the test done most of the ranking of EVL to observe in detail the lower esophagus in several patients taking a deep breath to be tough Requires the cooperation of the points many patients are thought to be led to reject the test.

Finally, the limitations of this study, first, as mentioned above, after EVL ulcer bleeding in the lower incidence of complications as a result of Arthur, it could not get the ultimate research on behalf of it's worth indirectly by measuring the size of the ulcer for four PPI. The effect could be obtained. Second, EVL symptoms and whether arising by the ulcer to compare the results of the questionnaire was found, survey tools used in this study of gastroesophageal reflux disease has been used in previous studies the authors applied the tool to the product used After EVL ulcers yongdoeetneunji ever appropriate to use a point to review the need for and frequency of these symptoms, so a comparison could not have been sufficient to slightly lower the possibility can not be ruled out. Third, EVL and after treatment with PPI in Suginami City Office this year using pantoprazole 40 mg once a day, three days and 11 days of intravenous 40 mg once daily oral administration of the treatment period was two weeks and the dose and route of administration ever

The question can be depreciated promised goodies. In conclusion, randomized, double-blind study, and then publishes the EVL procedure on the healing of the ulcers, the effectiveness of PPI with placebo twice. Lessons learned from the pursuit of endoscopy, PPI treated group compared to placebo in ulcer size. The results were significantly reduced. Therefore, on the basis of these results after EVL performed PPI treatment for ulcer healing and is thought to be helpful.

ABSTRACT

(esophageal band ligation, EVL) and low incidence of complications due to recent treatment is the most widely performed. After the procedure, but most of EVL ulcers in the esophagus of the righteous, because balsaengha bleeding, pain, burning hyunggolha, is associated with complications such as dysphagia. In this study, proton pump inhibitors (Proton pump inhibitor, PPI) pantoprazole using a type of drug to suppress rain wisanbun EVL ulcers healing was conducted to evaluate the effects. Materials and Methods: A total of 47 patients with liver cirrhosis patients with esophageal varices a PPI group and control group was divided into non-random. EVL performed in PPI group and 40 mg of pantoprazole 3 일간 were administered intravenously once a day, 11 days later to 40 mg were administered. In the placebo group in the same period, copper was administered intravenously and orally. Company EVL EVL endoscopic examination 2 after 7 days and 14 days respectively, were performed. Results of the study to measure the size of ulcers gwamulro and the number of points obtained by questionnaire and symptoms were compared between the two groups. Results: All patients with 47 people (PPI group, 25 patients, control group 22 patients) and 7 days after the EVL endoscopic path tracking tests were performed, 26 patients (PPI group, 16 patients, control group n = 10) Endoscopic examinations in 14 days was performed. 19 people (PPI group 9, group 10) of the patients were men they're tested at 14 days, control of the complications occurred in 2 patients is examined did the improvement with one of them, the other one after EVL died of sepsis with bleeding ulcers were at all. In both groups there were no differences between the patient characteristics, EVL and the size of ulcers compared with 7 days from 14 days a level of significance in both the control group was smaller than in the PPI group (7 days; 98.7 mm²: 119.4 mm², 14 days; 32.3 mm²: 42.8 mm², p < 0.001). Through questionnaires, chest pain, burning hyunggolha, in comparison with symptom scores of younger soils did not differ between the two groups. Conclusion: EVL ulcers occurred after the procedure compared the size of 7 days and 14 days after the procedure in the PPI group than the control group both significantly smaller size of the ulcer. Thus, PPI treatment after EVL performed on ulcer healing is thought to be helpful.

Index words: ligation of esophageal varices, ulcers, proton pump inhibitor, symptoms scores

For Tables and Figures (in English) see G:\META\Methods_Translation\Korean RCTs\Original\Boo GB 2008 18516002 Korean J Gastroenterol.pdf

Korean. Example 2

Lani T Dean rabepeurajolgwa for treatment of reflux esophagitis prospective multicenter comparative study

Chungnam National University College of Medicine, Department of Preventive Medicine *, Chungbuk National University, †, Soonchunhyang University College of Medicine ‡, Dankook University College of Medicine §, Catholic University of Korea, Daejeon St. Mary's Hospital, //, University of Medicine, Internal Medicine, ¶, ** Department of Internal Medicine, Daejeon Sun General Hospital

[Authors]

INTRODUCTION

Gastroesophageal reflux disease, a common digestive disease in the world of American country of about 10% complained of daily heartburn, and 40% of adult patients with gastroesophageal reflux disease to evaluate that, but more often than actually .1,2 Korea The prevalence of gastroesophageal reflux disease on general health screening been done, but in one study with a 2.4 to 5.8%, of patients with upper gastrointestinal symptoms in daesangeu was reported as 1.3 to 7.2% in one study, 0.3 to 5, these lower frequency compared to the West, recently been increasing incidence of GERD is clear that the trend .3,6

Gastroesophageal reflux disease degrades the quality of life of patients, reflux esophagitis and its complications cause, and after successful initial treatment by 80-90% relapse within 1 year of initial treatment of a chronic disease is difficult to treat and prevent recurrence. 7,8 Treatment goal to eliminate the symptoms, heal esophagitis, and for them to prevent complications that inhibit gastric acid secretion and therapeutic lifestyle changes are needed. Expression doyeomui reflux treatment and prevention of recurrence compared with the H2-receptor antagonists peu Lawton pump inhibitors are superior to all known to be cost-effective 0.9-11 proton pump inhibitors in the treatment of reflux esophagitis within 4-6 weeks in 75% of esophageal mucosa Check for damage and healing, improvement of symptoms in nearly 100% .12,13 seems safe endoscopic healing of reflux esophagitis, but the effect of domestic H2-receptors in the road compared to the Act and the analysis of proton pump inhibitors, not all reports .

We War. Chungcheong Province with symptoms in patients with reflux esophagitis and proton pump inhibitors, H2-receptor antagonist rabepeurajolgwa Rani esophagitis healing effects of tea with Dean was to evaluate the degree of improvement in their symptoms.

Materials and methods

Multicenter study, prospective, single-blind, randomized clinical study comparing the War. Chungchong University and the seven were in hospital. Each clinical trial review committee (institutional review board, IRB) at the W cuts the patient's clinical evaluation and endoscopic examination was performed by a gastroenterologist physicians. All patients evaluated each institution approved by the Commission in the prescribed consent form was signed and registered in this study. The study started on 17 April 2003 on 2 June 2004 was terminated.

1. Target

Patients in this study, a description of the process and accept the one under the age of 18 years and over 75 were female patients. Gastrofiberscopy according to the LA classification grade A or more patients with reflux esophagitis and heartburn of at least 3 months, gastric reverse flow, chest or throat irritation symptoms were included only if it is. Reflux esophagitis and no other serious disease, a blood test, production, chemical tests and yogeomsaeseo yimyeonseo normal, the possibility for women in pregnancy or during the trial piimhal the women were enrolled. Reflux esophagitis, gastrointestinal diseases other than the temperamental or if you have a history of serious disease, irritable bowel symptoms County, gastrointestinal bleeding, upper gastrointestinal surgery, if there is power, and gastroesophageal varices, yumunryun stenosis, esophageal stricture or Barrett's esophagus, esophageal clear hiatal hernia, pregnant or lactating women were excluded from the patients. In addition, within 2 weeks of the start of the study H2-receptor antagonist peu Jenna Lawton pump inhibitors were also excluded if ingested.

2. Treatment and Management

Enrolled patients who visited the subjects in each institution according to the order predetermined by a random code rabepeurajol 10 mg two times a day, or ranitidine 300 mg 2 times medication dosage, and dosing period of 8 weeks. Doctors could not find the prescription drugs, but both groups of patients can see a difference in a single-blind study was conducted. Patients visited the hospital a total of four times, during the first visit for research purposes, a description of methods and procedures, symptoms, physical examination and active power measurements, including clinical symptoms, medical history, laboratory tests, endoscopic examination, Helicobacter pylori (H. pylori) infection was examined. During the second visit, patients evaluated the symptoms of gastroesophageal disease and medications u49884. Jakha respectively. Used to evaluate drugs that can affect study antacids, motility drugs, such as promoter forbade four dragons. The severity of symptoms of heartburn, acid reflux, esophageal irritation, respectively, for chest pain and no symptoms, asymptomatic (scale 0), mild symptoms, but can tolerate (scale 1), or to disrupt daily life of a moderate degree (scale 2), daily life, or even face to lead a reasonably severe (scale 3), patients were divided into two as 0.14 hayeogeum

symptoms were reviewed journal to record daily for 1 week. 4 weeks after the third visit were evaluated for signs of improvement, drug adverse reactions and of other related matters were identified. By the fourth visit after 8 weeks of study was terminated. The laboratory test, symptom assessment, endoscopic examination, an assessment and synthesis of drug administration were evaluated.

3. Statistical analysis

The statistical analysis of preventive medicine at the start of the study on the doors and the target's size, randomization of treatment groups, data cleanup and analysis was carried out. Statistics used for statistical analysis program for the Window SPSS 11.0 (SPSS Inc. Chicago, IL, USA) was used.

Rabepeurajol ranitidine treatment group and comparison of treatment differences in the composition of the categorical variables, Pearson chi-square examination of the information, or Fisher's exact probability test was performed, the difference between continuous variables Student's t-test (independent samples t - test) were performed. P-value less than 0.05 level of significance in the sense that were evaluated.

Results

1. Clinical characteristics of patients

Rabepeurajol entire group of 69 registered patients eg, ranitidine treatment in 79 148 patients, for example, screening out of 5 people my oedoeoteumyeo ITT (intention to treat) analysis, 66 cases subjects rabepeura Sol group, ranitidine group, 77 respectively. Endoscopic examination during the course of tracking sihaengchi study did not randomly abandoned or if the patient, if no symptoms such as journal entries, except two patients rabepeurajol group quit the study 53 patients, for example 110 examples 57 ranitidine group, on the clinical characteristics of these PP (per protocol) analysis for each age group and sex, weight, height, blood pressure, smoking, alcohol consumption and H. pylori positivity was not significantly different in (Table 1).

2. Endoscopy chiyuyul

By LA grade at diagnosis of reflux esophagitis degree of esophagitis and ranitidine treatment group difference in rabepeurajol said eopeoteu (Table 2), 8 주간 medication follow-up endoscopic examination confirmed the healing rate of esophagitis group and two rabepeurajol Dean raniti to 86.8% compared with 57.9% of placebo group was significantly higher (Fig. 1).

3. Symptom Improvement rate of RE

Of the patients who complained of heartburn rabepeurajol 8 weeks after treatment showed improvement in their symptoms and 91.2% cases (31/34), and ranitidine Politics ryoguneun 76.2% (32/42) showed improvement in the rate of treatment rabepeurajol Improvement rate of RE There was no significant difference was higher ($p = 0.085$, Table 3). Rate of improvement of reflux symptoms, 35 cases before the cause of rabepeurajol group was 100%, 83% of the ranitidine group (39/47) was significantly higher in group rabepeura Sol ($p = 0.009$). ABBE peurajol treatment of chest pain and improved rate of 89.7% (26/29), ranitidine group was 86.8% (33/38) showed no significant difference in. Globus rabepeurajol treatment rate of 77.4% improvement (25/30), ranitidine group were 80.3% (24/31) there was no difference (Table 3). Especially within 7 days of treatment the symptoms disappeared completely different loss rate increased heartburn treatment rabepeurajol 76.7% of the ranitidine group was significantly higher than 45.2%, reflux 65.7% in the ranitidine group rabepeurajol group than 27.7% of higher chest pain rabepeurajol ranitidine treatment group two 72.4% higher than 42.1% of pharyngeal foreign bodies with closed 33.3% and 25.8% showed no significant difference (Table 4).

4. Safety

Symptoms of adverse reactions due to drugs dosed rabepeurajoleul 4 of 69 patients (6.1%) occurred in the face of a fever, abdominal distension, both through the ocular pain, respectively, complained, complained of ocular pain medication cases was discontinued. Ranitidine treatment group, 3 cases of 79 patients (3.9%), bowel obstruction in 1 case was saengha feet, heartburn an example, headache and nausea was 1 yeyeot, heartburn, headache and nausea was the major factor to discontinue the medication. Examples from laboratory abnormalities were observed in each group.

High kicks

The incidence of reflux esophagitis and economically prosperous region standing on the western high and low in developing countries. This difference between the health and nutritional status of the country's richest countries and the related H. pylori infection is low, high fat high calorie diet with this and other yugwanha .15,16 However, it still occurs for reflux esophagitis H. pylori infection in relation to the role of the controversy continues. Multicenter study performed in Korea in the asymptomatic H. pylori infection and the overall prevalence rate is 46.6%, 17.2% in children and adults is 66.9% .17 In this study, average age 46 years in patients with reflux esophagitis and H. pylori infection rates to 28.0 percent, significantly lower than the 66.9 percent reported was yubyeongryulin H. pylori were tested for the 109 cases diagnosed by rapid urease test alone, because the 65 yeyeot wiumseongeuro all appeared to have included a number of examples. The comparison by age, gender, lifestyle, and for consideration of such a group, not more, fewer patients would have the greater significance is lost. However, the incidence of reflux esophagitis in Korea, and H. pylori infection on the relationship between the necessity of large-scale epidemiological studies may indeed be the result.

In the treatment of reflux esophagitis, gastric acid secretion than 24 hours it is important to control the river ryeokhage. Rabepeurajol 10 mg per day if two doses of 20 mg once daily dose and a inhibitory effect on gastric acid secretion in the few studies about the treatment and it will not. In a dynamic force rabepeurajol 20 mg medication once a day administration of 3.5 hours to reach peak plasma concentration and plasma half-life of about one hour, and excretion rate

3.8 mL / min / kg in the capacity of 10-40 mg rabeprazole. There is a difference. In fact, rabeprazole 10 mg 2 times a day to 20 mg once daily dose group and two groups ranked in the 24 hours, according to data on gastric acidity, LA beprazole administration of 10 mg 2 times a day to 20 mg once daily more excellent inhibitory effect on gastric acid secretion and, CYP2C19 no difference depending on the other, especially at night with low incidence of gastric acid breakthrough. Thus, failure to treat 10 mg rabeprazole. LA beprazole beonbodaneun 10 mg per day to 20 mg administered 2 times longer than that can expect a strong effect on gastric acid secretion in this study, all 0.18 possible endoscopic reflux esophagitis rabeprazole ways to improve cure rates of 10 mg 2 times a day-to-yeoha was 300 mg ranitidine as a control for the same reason was administered 2 times. Rabeprazole typically 10 mg once a day to respond to medication, Dean Lani Tea 150 mg 2 times the capacity of the treatment followed by medication, rabeprazole 10 mg 2 times in response to ranitidine 300 mg were administered.

Proton pump inhibitors in the treatment of gastroesophageal reflux disease, initial treatment and maintenance therapy is superior to the H₂-receptor antagonist, is well known that already at 0.19, especially with early treatment the healing rate of reflux disease expression and type of proton pump inhibitor drugs depends on the capacity and rabeprazole 20 mg once a day for four weeks after treatment a cure rate of 71-81% were reported to 0.14 after 8 weeks treatment with cure rates of 76-92% reported in the same capacity rabeprazole treated with 20 mg of 86.8% in this study were similar. In this study, the healing rate of 57.9 percent during ranitidine treatment showed minimal change esophagitis healed by the state, except for example, if much less to 45.6 percent. Depending on the degree of reflux esophagitis Group Playing of Melodic difference in value is expected to be particularly proton pump inhibitors, H₂-receptor antagonist, compared to the later reaction times tend to get slow about 2 0.20 2 weeks, 4 weeks, 6 weeks, 8 weeks and 12 weeks After treatment of each other healing rate when compared to proton pump inhibitors entire chiyuyul 83.6% and H₂-receptor antagonists 51.9% was 0.21 motility promoting agent cisapride and 37.9% healing rate of mucosal protective agent sucralfate's 39.2 percent lower than .22,23 proton pump inhibitors the first 2 weeks the healing rate of 31.7% per week, 4 weeks per week are 17.0% and 15.0% a week until 6 weeks, 8 weeks and 12 weeks are 10.6 percent share to 7.6% per week over time higher cure rate decreases. Thus, a 91.2 percent cure rate 12 weeks after treatment to 8 weeks after treatment, but significantly higher than 84.8% chiyuyul large because the drug as a result of eight weeks after treatment to compare the treatment outcomes that would not be a problem all .20,21 ranitidine capacity, 300 mg four times a day, ie If you are using Wu and 67.9% at 8 weeks and 12 weeks has risen to 77.3% in proportion to the degree of inhibition gastric acid secretion rate was increased 0.24 The Palace ranitidine 300 mg 2 times this year when administered 57.9 % of the reflux esophagitis was no significant difference chiyulgwa completed. National reporting mild - moderate reflux esophagitis and the standard dose in the low-dose omega Pradesh Rani Sol Tee Dean compared the therapeutic effect of omeprazole 10 mg, 1 week therapy with ranitidine 150 mg, 2 times a cure rate of reflux esophagitis treated with 8 weeks of therapy, respectively between 55% and 43% were treated with 0.25 this capacity could vary materially from this study. Reflux esophagitis and proton pump in the formulation of one hundred million rabeprazole in endoscopic cure rates, ransopeprazole, etc. pantoprazole tidinbodaneun Rani was similar to the existing omeprazole was superior to 0.13 for the 38 papers survey of eight weeks through MEDLINE After treatment, esophagitis, cure rates for my PD ransopeprazole 30 mg 75-93%, rabeprazole 20 mg 76-92%, pantoprazole 40 mg 80%, omeprazole 20 mg 76-84% .13 There was no difference in

Reflux esophagitis healing rates and pain relief treatment before the reflux that differed in expression level doyeom but in this study on the LA grade A esophagitis, 87.5% rabeprazole group, Lani tidin group 59.4%, B esophagitis and 84.2 in the group rabeprazole %, ranitidine group 54.5%, C esophagitis rabeprazole group at 100%, 66.7% ranitidine treatment must be made according to the degree of esophagitis was similar chiyuyul 0.19

In this study, rabeprazole 8 weeks after treatment of heartburn improvement rate of 91.2%, 76.2% higher than the mean, T, Dean showed. Treatment within a week, especially if the disappearance of symptoms of heartburn and 76.7% of the Labeprazole ranitidine treatment group came to 45.2% higher than that. In foreign literature ransopeprazole symptoms one week after treatment with bovine silryulyi 65.2% 53.5% higher than that of omeprazole. In addition, eight weeks after treatment with omeprazole ransopeprazole 85.9% 72.5% protection of all other reported symptoms, the rate was 0.26 rabeprazole 8 weeks after treatment was 64 percent overall symptom improvement rate, mean, T Dean 27 European and 53% .12 countries studied in the joint report of the administration of the rabeprazole 20 mg once daily after 4 weeks of reflux esophagitis healing rates at 81%, 92% after 8 weeks, heartburn symptom relief rates after 8 weeks of daytime 87% to 78% and two times during the night of the study was similar. Symptoms of heartburn after 4 weeks of the loss rate to 62%, respectively, were like night and day, and 8 weeks after treatment was 68% and 64% .27

Rate of improvement of reflux symptoms after treatment for 8 weeks with 100% rabeprazole Rani tea was better than 83% of Dean, one week after the treatment of symptoms, the rate to 65.7% and 27.7% were excellent rabeprazole.

Gastroesophageal reflux symptoms without the use of gastrointestinal motility promoter ABBE prazole have improved 100% after radiotherapy alone is related to acid reflux disease, suggest that the precedence. Globus symptoms of chest pain and improved rate rabeprazole treatment group 8 weeks after treatment 89.7%, 86.8% in ranitidine group equaled one week after the treatment of chest pain of loss rate to 72.4 percent two rabeprazole ranitidine treatment group was higher than 42.1% of . Globus in the loss rate of symptomatic improvement rates were similar. For gastroesophageal reflux disease 'PPI test' is a clinically useful way, but two colors, such as chest pain and throat symptoms are nonspecific symptoms of GERD is difficult to determine about whether, after proton pump inhibitor therapy, and so on Improvement rate of RE Not a bit of data to compare with this study, the de ryeopda 0.28

The study on the safety of drugs in the treatment rabeprazole drug adverse reactions occurred in 6.1% and a lighter that much, but complained of eye and head pain medication were discontinued cases. From 3.9% in LA nitidin group had adverse reactions, two cases of reflux esophagitis Being about the medication to stop the occurrence of adverse reactions during treatment will be necessary to pay attention.

In the treatment of reflux esophagitis according to the results of this study used proton pump inhibitors and ranitidine cost - to analyze the effect, rabeprazole 1422 won the 1st two 10 mg doses at two and 2,844 won 1,012 won ranitidine 150 mg 2

Tablets won the day when two doses are required. To compare a single drug prices only cost more to rabeprazole therapy of esophagitis at endoscopy This remarkable high cure rate, that so superior symptom improvement also effectively improved symptoms and endoscopic therapy rabeprazole treatment ranitidine used to induce economic value should be considered. Therefore, the treatment of reflux esophagitis and proton pump inhibitors, such as drug selection for the rabeprazole H₂-receptor antagonist that is more efficient than the first dose.

ABSTRACT

Purpose: Proton pump inhibitors in the treatment of reflux esophagitis. H₂-antagonist, the choice of coverage depending on the patient's condition and jeongdoenda Results. Confirmed by endoscopic proton pump inhibitor in the treatment of erosive esophagitis rabeprazole H₂-receptor antagonist ranitidine treatment of reflux esophagitis and to evaluate the degree of symptom relief. **Materials and Methods:** War and the Chungcheong area with symptoms of reflux esophagitis patients who in 110 patients a multicenter, prospective, single-blind, randomized clinical study was performed. Rabeprazole 10 mg in the morning and before dinner, the mean, 300 mg of T-Din in the same way two times a day, a total of 8 weeks after treatment by endoscopic inspection station to investigate the flow rate of esophagitis healing and pain relief assess the safety was. **Results:** A total of 8 weeks after medication the patient underwent endoscopic examination rabeprazole 53 cases, mean, Dean's T-57 in each group, for example gender, age, weight, height, blood pressure, drinking, smoking, there was no significant difference. H. pylori infection in 23 of the 92 cases were positive in both groups at 28% yes, 28.2% (11 cases), 27.9% (12 cases) with no differences. At diagnosis, severity of esophagitis at endoscopy, significant rabeprazole 32 patients with LA grade A (60.3%), ranitidine group 32 cases (56.1%), LA B and 19 patients in each group (35.9%), 22 (37.1%), LA C and 2 patients in each group (3.8%) and 3 (5.3%) showed no significant difference in. Esophagitis at endoscopy after 8 weeks treatment the rabeprazole 86.8% cure rate, 57.9% were Dean T rabeprazole Rani was significantly higher (p = 0.001). 8 weeks after the treatment of heartburn and rabeprazole 91.2% improvement (31/34), 76.2% were mean, Dean T (32/42) was higher than the rabeprazole (p = 0.085). Especially within the first 7 days showed improvement in 76.7% cases rabeprazole ranitidine group was significantly higher than 45.3% (p = 0.008). Acid reflux symptom relief rates rabeprazole 100% (35/35), Lani Dean's Tea 83% (39 of 47) were significantly higher in the rabeprazole (p = 0.009). Improvement of chest pain and discomfort is rabeprazole Lani two groups did not differ between T-Din. Drug-related adverse events were mild in both rabeprazole tidingun Rani, laboratory findings showed the award was an example. **Conclusion:** War and the aftermath of the Chungcheong region doyeom expression rate of healing of erosive esophagitis in patients rabeprazole symptom improvement was greater than the mean, T, Dean was a relatively safe-to-weak.

Index words: reflux esophagitis, ranitidine, rabeprazole

Table 1. Patients Demographics and Baseline Characteristics (%)

Characteristic	Rabeprazole (n=53)	Ranitidine (n=57)	Total (n=110)	p-value*
Age	46.6±13.3	45.0±12.7	45.8±13.0	0.619
Sex (male/female)	43/10	45/12	88/22	0.775
Weight (Kg)	61.4±11.1	62.5±10.1	61.5±11.0	0.146
Height (cm)	163.5±8.7	165.5±8.3	164.6±7.9	0.158
Systolic BP (mmHg)	124.0±14.7	124.4±17.0	124.3±15.7	0.899
Diastolic BP (mmHg)	76.8±10.8	75.8±11.3	76.3±11.0	0.664
Smoking (yes)	18 (34.0)	25 (43.9)	43 (39.1)	0.288
Alcohol (yes)	33 (62.3)	37 (64.9)	70 (63.6)	0.773
<i>H. pylori</i> (+)	11 (28.2)	12 (27.9)	23 (28.0)	0.976

BP, blood pressure; *H. pylori*, *Helicobacter pylori*.

Mean±SD.

* Student's t-test (or independent samples t-test).

Table 2. Baseline Endoscopic Findings: Rabeprazole versus Ranitidine (%)

Grade*	Rabeprazole	Ranitidine	Total	p-value†
A	32 (60.4)	32 (56.1)	64 (58.2)	0.872
B	19 (35.8)	22 (38.6)	41 (37.3)	
C	2 (3.8)	3 (5.3)	5 (4.5)	
Total	53 (100)	57 (100)	110 (100)	

* LA classification of reflux esophagitis.

† Chi-square test.

서 병주형 변수의 구성비 차이는 Pearson의 카이스퀘어 검정, 또는 Fisher의 정확확률 검정을 실시하였고, 연속 변수의 차이는 Student's t-test (독립표본 t-검정)를 실시하였다. 유의수준은 p값이 0.05 미만에서 의미가 있다고 평가하였다.

Table 3. Symptom Improvement Rates after Treatment for 8 Weeks (%)

Symptom	Rabeprazole	Ranitidine	Total	p-value*
Heartburn	31/34 (91.2)	32/42 (76.2)	63/76 (82.9)	0.085
Regurgitation	35/35 (100)	39/47 (83.0)	74/82 (90.2)	0.009
Chest pain	26/29 (89.7)	33/38 (86.8)	59/67 (88.1)	1.000
Globus sensation	25/30 (83.3)	24/31 (77.4)	49/61 (80.3)	0.561

* Chi-square test (estimated by each symptom).

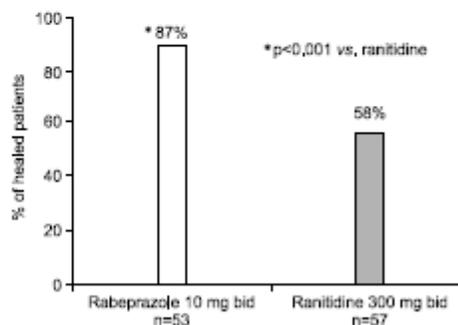


Fig. 1. Healing rates of reflux esophagitis after treatment for 8 weeks. The rabeprazole-treated patients achieved 87% healing compared to 58% in the ranitidine group. Healing rates were significantly higher in the rabeprazole group than in the ranitidine group at 8 weeks ($p < 0.001$).

Table 4. Symptom Resolution Rates within 7 Days after Treatment (%)

Symptom	Rabeprazole	Ranitidine	Total	p-value*
Heartburn	26/34 (76.7)	19/42 (45.3)	45/76 (59.2)	0.008
Regurgitation	23/35 (65.7)	13/47 (27.7)	36/82 (43.9)	0.001
Chest pain	21/29 (72.4)	16/38 (42.1)	37/67 (55.2)	0.035
Globus sensation	10/30 (33.3)	8/31 (25.8)	18/61 (29.5)	0.561

* Chi-square test (estimated by each symptom).

Portuguese. Example 1

USE OF CORTICOSTEROIDS AFTER DILATION IN PATIENTS WITH ESOPHAGEAL STENOSIS BY CORROSIVE SUBSTANCES -

A prospective, randomized E DUPLOCEGO

[Authors]

Trabalho realizado no Departamento de Moléstias do Aparelho Digestivo Gastrocentro - Faculdade de Ciências Médicas, Universidade Estadual de Campinas - SP.

ABSTRACT - PURPOSE. Determine through a randomized double-blind study, the effect of intralesional injections of triamcinolone associated with esophageal dilatation in corrosive stenosis cases. **METHODS.** Fourteen adult patients (six men and eight women) with severe esophageal corrosive strictures were randomized into two groups: Group A: treated with esophageal dilatation and subsequent intralesional injection of triamcinolone 10 mg / ml, Group B: treated with esophageal dilatation and subsequent injection of 0.9% saline (placebo). Applications were made based on patient symptomatology. We examined the frequency of dilations, dysphagia and diameters obtained before and after searching for 12 months. **RESULTS.** In our study, eleven patients had ingested caustic soda, ammonia and ate two took acetic acid. There was no statistically significant difference ($p > 0.05$) in dilation frequency and dysphagia between the groups. However, improvement was observed in the diameter obtained in the group receiving steroids, compared to the control group ($p < 0.05$). Comparing before and after steroids, the outcome was very favorable ($p < 0.01$) in group A. **CONCLUSIONS.** The use of multiple injections of intralesional triamcinolone hexacetonide 10 mg / ml in association with esophageal dilatation is effective in increasing the diameter obtained in subsequent sessions.

KEYWORDS: esophagus. Caustic strictures. Corticosteroids. Endoscopy.

INTRODUCTION

The esophageal stenosis is a complication of various disease processes such as ingestion of corrosive esophageal surgery, gastroesophageal reflux, variceal sclerosis esofágicas¹. We will highlight the lesions caused by ingestion of caustic strong. Caustic soda (sodium hydroxide) is the agent most frequent^{1, 2}, with 50% risk of causing 67% narrowing esofágicos^{1, 3}, followed by acid intake with risk of about 25%³. Alkali ingestion results in corrosion of the pharynx and esophagus. The lesion is deep, due to necrosis of type liquefied or saponification of the superficial layers of the wall esofágica²⁻⁹. In contrast, the necrosis produced by acid intake is of type coagulative and more superficial³ and tends to spare the esophagus. The most important factor predicting response to therapy is the depth of the lesion. There are three degrees of injury:

Grade I - Penetration surface - superficial mucosal injury. There will be estenoses^{7, 8}.

Grade II - Penetration mean - beyond mucosal injury exposing the submucosa and muscular layer^{7, 8}.

Grade III - Deep Penetration - results in transmural injury of the esophagus or stomach wall. There may be perforation^{7, 8}.

Between 20% and 40% of patients with grade II and III lesions will develop estenose⁷. This is a situation without a definitive cure and treatment time is undetermined.

Within one week after injury, there is formation of granulation tissue with proliferation of new vessels and fibroblasts. The latter form new collagen fibers, stiff and inflexible, while the second and third weeks following ingestion. In grade II and III lesions damage occurs to the muscle layer and muscle fibers do not regenerate injured and replaced by fibrous tissue. The contraction of these collagen fibers (cross-link ") results in progressive decrease in length and reduction of the esophageal lumen, after the third semana². After six weeks, epithelialization is complete and the lesion is covered by a dense layer of fibrosis that can form multiple channels or even completely block the light from esôfago⁷. Can be displaced in the cranial direction of the esophagogastric junction, determining the onset of esophageal hernia and gastroesophageal reflux symptoms. Reflux, in turn, leads to more aggression to esôfago¹⁰.

Treatment aims to relieve symptoms and is done through periodic esophageal dilatations.

The corticosteroids reduce the inflammatory response, interfere with the synthesis of collagen, fibrosis and chronic wound healing, inhibiting the formation of restenosis after dilatações^{4, 5}. After the excellent

results observed in the treatment of dermatologic scars (keloids, burns, etc.). Corticoesteróides^{11 to-13}, it was believed that his job could be very useful in the treatment of esophageal stricture. Among the corticosteroids available in the market, triamcinolone is noteworthy since it is believed that interfere with crosslink of collagen, which results in scar contraction. Several studies have demonstrated its usefulness in the treatment of stenosis esofágicas^{6, 14,15,16}.

OBJECTIVE V

HECK efficacy of intralesional injections of corticosteroids associated with the usual treatment of mechanical dilation in esophageal strictures resulting from injuries caused by corrosive substances. It was expected to get after applying the method: increase in the average diameter obtained in the expansion, increasing the time interval between treatments, ie, lower frequency of dilations by time and the symptoms improved in the group who received the drug.

METHODS

Among a population of 38 patients with esophageal stenosis consequent to ingestion of corrosive substances, currently in the program esophageal dilatations Gastrocentro - Unicamp, we selected 14 patients with grade II and III injuries that required dilatation up to four months and with a diameter up to 15 mm made in recent dilation procedures.

After presentation of the Term of Consent, in accordance with the rules of the Ethics Committee of FCM - Unicamp, we obtained consent from all patients, except one. Any new cases, fulfilling the above requirements, would be included in the study aimed to evaluate the use of corticosteroids in the initial phase of treatment with dilation. There was only one new case included. The study lasted 12 months.

The 14 patients were randomized into two groups:

Group A: patients undergoing dilation and injections of corticosteroid (triamcinolone) in place of the narrowest stenosis.

Group B (control): patients undergoing dilation and injections of saline (placebo) at the site of the narrowest stenosis.

The study was double-blind, for patients and researchers did not hold information about the groups, only the endoscopist had them, to make possible the application of the method.

At the first application of each patient, there was particularly an intercept survey to obtain a detailed history, the reasons for the ingestion of a corrosive substance, the actual degree of dysphagia and diet of the patient at that time.

The preparation of patients for endoscopy and dilation procedure was performed using 3 ml of dimethicone orally, an ampoule of N-butyl bromide (20 mg) intravenously and local anesthesia with lidocaine spray 10% by orally. For sedation, the patient received an injection of 1 ml diazepam (5 mg) and 1 ml meperidine (50 mg) diluted in 8 ml of saline intravenously in small fractions until you submit an adequate level of sedation .

Endoscopy was performed using video endoscopes or flexible fiber endoscope (Olympus®). The dilation technique employed in all patients was through the passage of guide wire under direct vision by endoscopy and use of the Savary-Gilliard dilator, believe this to be the most effective expansion difficult, narrow and winding as the corrosive lesions, and offer lower risks of complications, for example, drilling esófago^{1, 4,6,17,18}.

The corticosteroid used was hexacetonide triamcinolone 20 mg / ml diluted in 0.9% saline, obtaining a concentration of 10 mg / ml. We used the catheter for sclerotherapy for esophageal varices with injection immediately after dilation. We applied 4 ml of the dilution of corticosteroids (or placebo, in the case of the control group) per session, divided into four quadrants (1 ml in each quadrant) in the area of greatest stenosis of the esophagus. One patient (B2) had more than one area of severe stenosis (20 and 25 cm respectively from the upper dental arch) and we decided to make this application also another area.

At each visit, based on the symptoms the patient, this new application received corticosteroid or placebo and were questioned about symptoms and changes in their diet, to assess their degree of dysphagia. Sometimes, at the discretion of the physician endoscopist, no injection was administered because the patient was clinically well and 15 mm dilator passed through the stenosis without difficulty on the first try.

The degree of dysphagia was obtained through the patient's swallow function according to Table I.

RESULTS

Table 2 shows the main characteristics of the groups:

To perform the statistical analysis was necessary to exclude a patient from each group, since they both

returned only once after the study began, making it impossible to analyze the evolution of these. There were no significant differences between the two groups in relation to sex, age and substance intake ($p > 0.05$).

Table 3 shows the number of dilations performed before and during the survey, the number of sessions of application of steroids or placebo and follow up of patients examined. It was observed that the group has the largest number of patients with dilated before the survey, which we attribute to chance, because all patients were randomized.

Disregard the first expansion of research, because this day the patient received the first injection and its effects were analyzed only from the return follows:

We analyzed the following parameters (considering p -value < 0.05):

Table 4 contains the values of key data analyzed:

1. Frequency of dilations (IDP): The frequency of dilatations was standardized through a periodic dilation index (PDI) calculated as:

Number of dilations

Time (months)

Figure 1 outlines the analysis of the frequency of dilations:

Statistical analysis was performed using the Student t test (two samples assuming equal variances).

Initially, we compared the total number of sessions held previously by the patient (Total IDP) with the number of sessions during the research (After PDI). There was no significant difference between groups ($p > 0.05$). However, it is known that early in the treatment of caustic stenosis of the severity of injury is greater, therefore, the expansion tends to be more difficult (smaller diameter) and more frequently. Thus, the total IDP includes the initial phase (most severe) and changes over time.

To decrease the influence of the initial expansion in the workplace, comparing "IDP 2 versus IDP After" (covering the same number of sessions before and after). Again there was no significant difference between groups ($p > 0.05$).

2. Diameter:

To study this variable was used Student's t test (two samples assuming equal variances).

It is observed in Figures 1 and 2 patients who received corticosteroids in their largest diameter reached dilations (the majority had a diameter greater than or equal to 13mm) and remained more stable than the control group:

We compared the difference between the average diameter less After the Before the study (same number of sessions before and after). There was a significant difference between groups ($p < 0.05$), showing that the use of injections of corticosteroids - coesteróides determined an improvement in the average diameter of patients.

In Figure 3, positive values indicate improvement, while negative values indicate worsening:

We also analyzed the average diameter in each group separately before and after treatment. We obtained highly significant for group A ($p < 0.01$) and no difference in group B ($p > 0.05$).

3. Dysphagia:

We compared the value of the patient's dysphagia at baseline with the value at the last visit. Improvement was defined as an increase of at least one point on the scale of dysphagia (Table 1). Statistical analysis (chi-square test) showed no difference between groups ($p > 0.05$).

Charts 4 and 5 show the evolution of dysphagia the patient during the study:

DISCUSSION

In children, accidental ingestion of chemicals is the main cause of stenosis. It is estimated that 50% to 80% of cases are accidental and that about 89% of these children are under five years of idade³. In sober adult, the intake is closely related to suicide attempts, but also occurs during states of intoxication.

Despite the cases of ingestion of corrosive substances are more common in children, 8 adults account for the more severe cases that require more intensive treatment. Hawkins, Demeter & Barnett¹⁹ report that only 8% of children in need of treatment compared with 81% in adults. In our study, intentional ingestion, primarily by suicide attempts, accounted for 64% of all cases and accidental ingestion of 36%. In female patients, the ingestion was intentional and accidental in five cases in three other cases. In males, four patients had ingested intentionally.

Ingestion of strong alkali, especially caustic soda, is known to be harmful to the esophagus, leading to more extensive lesions and profundas^{1, 3,8,12,17,19,20}. It is estimated that 35% to 45% of these cases will develop estenoses^{6, 19}. Secondly there are the injuries acids. Among our cases 93% were due to

alkali (n = 11, ingestion of caustic ammonia and n = 2) and 7% due to acid (n = 1 muriatic acid) Regarding the use of steroids and other substances in the acute phase of caustic ingestion, there is still considerable contro versy. The effectiveness of corticosteroids used alone or combined with early expansion is criticized for alguns^{2, 3,10,21}, but defended by others^{1, 8,19}. However, each article makes reference to types and dosages of various steroids and other associated methods (antibiotics, swelling early, nasogastric tube, etc.).

Just as the prevention of stenosis, the treatment of stenotic lesions already established is also home to much discussion. The treatment of choice is endoscópica¹⁷ dilation, but the caustic stenosis are often narrow, tortuous and protracted, and therefore more difficult to dilatar^{4, 5,17,20}. Broor et al.⁵ demonstrated that in such cases, the number of sessions required for adequate dilation was significantly higher and the recurrence of dysphagia compared to patients with peptic strictures. In an analysis of 500 cases of benign esophageal stricture in our department, it was concluded that the caustic strictures to achieve the highest failure rate for conservative therapy, ie only with dilation, compared with other etiologies of benign stenosis of esôfago²⁰.

The application of corticosteroids when the esophageal stricture is already established has been highlighted in recent years^{4, 8,10,14,15,16,21}. There were no randomized studies in the literature with the use of corticosteroids. This encouraged us to undertake this research to prove the effectiveness of the method.

Each dilation procedure performed, involves a new lesion site of stenosis, which leads to a local inflammatory reaction with proliferation of fibroblasts and deposition of colágeno¹⁰. A variable period, the stenosis is restored, returning the patient's discomfort and dysphagia. In cases where the stricture recurrence is frequent and rapid (less than three months) we believe the use of corticosteroids may be beneficial in slowing this process.

In recent years, the corticosteroid triamcinolone acetonide has been the choice for stenotic lesions in cases of caustic ingestion. References found in the acetonide was used triancinolona^{6, 14,15,16}. In our study we used the hexacetonide triamcinolone, a corticosteroid with a potent anti-inflammatory effect and is absorbed more slowly from the site of injeção²².

We apply the injections every patient's return because we believe that repeated injections carry the sum of long-term results, as reported by Lee et al.¹⁴. As the dose of steroids was small, do not expect a significant immunosuppressive effect. Therefore, we find unnecessary use of antibiotic prophylaxis after application. Kocchar et al. ⁶ had very satisfactory results in 17 patients with intralesional use of 10 mg / ml triamcinolone, applied in a maximum of three sessions, but the authors argue that increasing the number of applications could get even better results. These authors used ketoconazole for one week after injection due to fear of inducing intramural infection, but stressed the need for more studies to substantiate this risk.

Zein et al.¹⁴ and Lee et al.¹⁵ used triamcinolone acetonide 10 mg / ml in seven and 31 patients respectively. Gandhi et al.¹⁶ used triamcinolone acetate 1%, 0.1 ml in 12 patients. These three studies have shown quite impressive results with the intralesional use in esophageal strictures of various etiologies, including póscáusticas. However, the number of sessions per patient was small. In our study were on average 6.7 (range 3 to 12) applications of steroids per patient.

In our series, there were no cases of complications with dilators candle using guidewire or with sedation or with multiple applications of corticosteroids. This result almost matches the one found in the literature that estimates the risk of perforation, bleeding and death in 0.2%, 0.07% and 0.01% respectively⁴. Other studies estimate the rate of perforations between 0.3% to 8% by using velas^{1, 17,23,20}.

The analysis of the total IDP reflected all sessions of dilation experienced by the patient before the study. It is known that early in the treatment of caustic stenosis of the severity of injury is greater, therefore, the expansion tends to be more difficult (smaller diameter) and more frequently. In the outcome, patients with recurrent strictures set a standard in terms of diameter reached, time to relapse and worsening of symptoms. We also observe that there are periods of improvement or worsening over time. Thus, the total IDP includes the initial phase (most severe) and changes over time. However, we believe this is not the only variable suitable for analysis. Just look at the evolution of patient B1 (control), followed by us since the first session of dilatation (new case), in Figures 2 and 5. Its diameter and dysphagia improved significantly over the months, receiving applications placebo.

Therefore, we also calculated the IDP² that, in our opinion, best reflects any change in the evolution of patients after the use of injections since it compares the same number of dilations before and after the search. However, Kochhar et al.⁶ analyzed only the total IDP, achieving significant results.

On the analysis of the diameter obtained also used the same number of sessions before and after calculating the averages, it is even more evident progress of the patients passed the initial stage, ie after stabilization of the lesion.

For analysis of dysphagia we could not compare it with the expansion before the survey. Therefore, we defined criteria for improvement and we applied the chi-square test, which showed no significant difference. Because it is an abstract variable, it was not possible to assess the progression of dysphagia in each return.

FINAL

Although there was no statistically significant improvement for variables and total IDP IDP2, the results suggest an improvement in group A. We believe the factors that hampered the analysis of these variables were: the small number of patients followed, the fact that subsequent queries are marked by the physician, and finally, the deflection caused by the patient B1 (new case - see discussion) and the patient B2 .The latter had, in our view, an unusual development, since it had great relief of symptoms without reaching diameters compatible with such progress (Figures 2 and 5). Therefore, both provided a mistaken impression of improvement in the control group.

A larger number of patients and follow through voluntary return could bring significant results in this analysis. Nevertheless, our analysis of the mean diameters was statistically significant, demonstrating the effectiveness of the method. Therefore, we emphasize the importance of making it more controlled studies and even a multicenter study to analyze the issue, since the existing studies have a small sampling.

In the opinion of the researchers, after the monitoring of patients were satisfied with the progress made by the group that received intraoperative steroids - injury. We can cite as an example of this patient group (A2) had no indication for surgical replacement of the esophagus due to their symptoms, although approximately 1.5 years of dilations (total of 36 sessions). This patient started an amazing recovery after the initiation of applications, the point for the first time, we can overcome your stricture with the endoscope before we do the dilation. His dysphagia, he said, also improved significantly. Surgical indication in this case was suspended.

CONCLUSIONS

We conclude that the use of multiple injections of intralesional triamcinolone hexacetonide 10 mg / ml associated with esophageal dilatation is effective in increasing the diameter obtained in subsequent sessions. We also observed an improvement in symptoms of patients and increasing the interval between sessions of dilation, although no statistical evidence.

It is a safe, relatively simple, providing a decrease in spending on common procedures and their complications.

THANKS TO Apsen Pharmaceuticals SA for their collaboration and provision of medication (Triancil ® 20 mg / ml) and CNPq / PIBIC-UNICAMP.

Table 1 - Classification of dysphagia - second Saeed et al.18

Scale Score of Swallowing Ability

- 0 Unable to swallow
- 1 Ingestion of a liquid with difficulty, not sound inge
- 2 Ingestion of liquid without difficulty, can not eat solid
- 3 occasional difficulty with only solid
- 4 Difficulty rare, with only solid
- 5 Normal swallowing

Table 2 - Characteristics of the groups regarding sex, age, race, cause and reason for ingestion

Features	Group A	Group B
Masc Sex: Fem	3:4	3:4
Average age	39 (23-64)	46.4 (22-65)
Color	White 5 (72%)	3 (43%)
Parda	1 (14%)	3 (43%)
Black	1 (14%)	1 (14%)
Caustic Soda Cause	5 (72%)	6 (86%)
Ammonia	1 (7%)	1 (7%)
Acid	1 (7%)	0
Reason Intentional	6 (86%)	3 (43%)
Accidental	1 (14%)	4 (57%)

Table 3 - Number of dilations (before and after the research), and tracking applications each patient in each group

Patients	In search of dilations before	In dilations during search	In sessions Steroid / Placebo	Follow-up Follow-up (months)
A1	15	4	5	8,8
A2	37	13	12	9,2
A3	29	2	3	6,2
A4	66	7	8	8,8
A5	82	6	7	8,3
A6	51	4	5	7,2
B1	0*	10	8	6,5
B2	16	16	8	9,9
B3	17	3	4	6,7
B4	11	5	5	9,5
B5	10	2	2	6,5
B6	12	2	3	5,3

* New case

Table 4 - Periodic dilatation index, diameter and dysphagia before and after the research

Group	periodic dilatation index			average diameter		Dysphagia	
	Total	IDP 2	Após	Antes	Após	Entrada	Final
A1	1,17	1,10	0,46	13	14	2	5
A2	2,03	2,36	1,41	12,73	14,23	4	5
A3	0,66	1,09	0,32	12	13,5	5	5
A4	1,27	1,12	0,80	14	14,29	2	3
A5	2,10	1,65	0,72	12,83	13,5	4	4
A6	1,24	0,98	0,56	14,13	14,75	4	4
B1*	-	-	1,55	-	-	2	5
B2	3,33	3,33	1,62	9,07	9,81	2	2
B3	0,28	0,65	0,45	12,33	12,5	5	5
B4	1,14	1,09	0,53	13,1	13,5	2	3
B5	0,69	0,67	0,31	13,5	13	3	4
B6	0,82	0,67	0,38	13	13,5	5	5

Figura I - Plano do cálculo de IDP

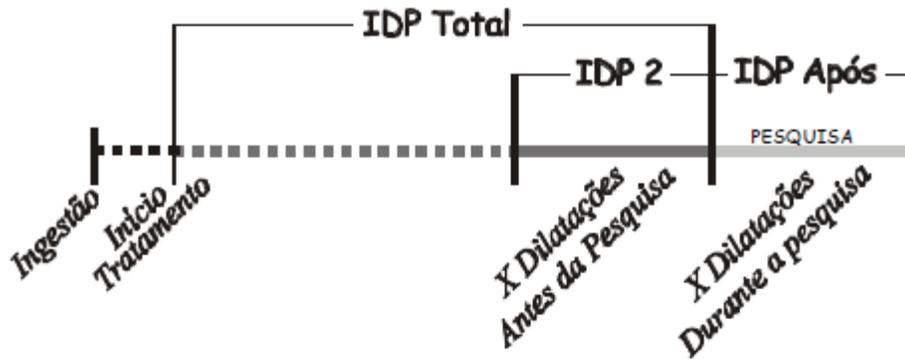


Gráfico I - Diâmetro em cada retorno grupo A

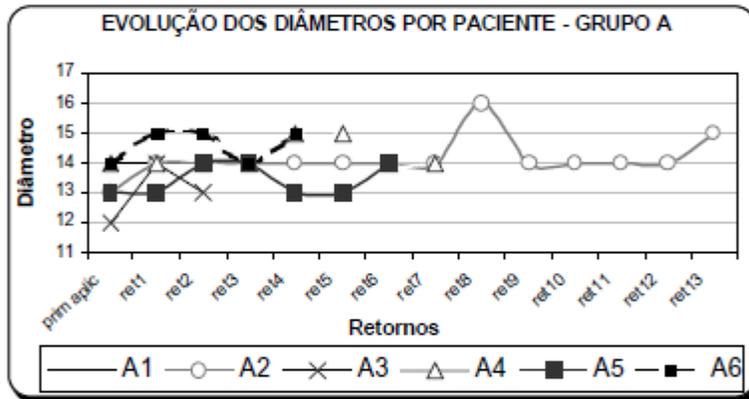


Gráfico 2 - Diâmetro em cada retorno grupo B

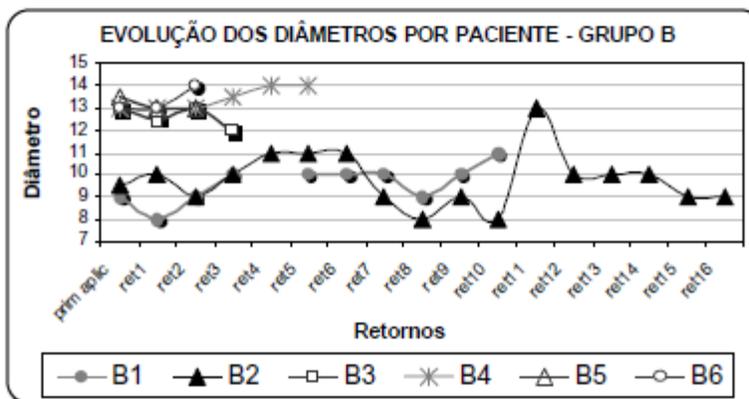


Gráfico 3 – Comparação entre média dos diâmetros (Diâmetro após-antes da)

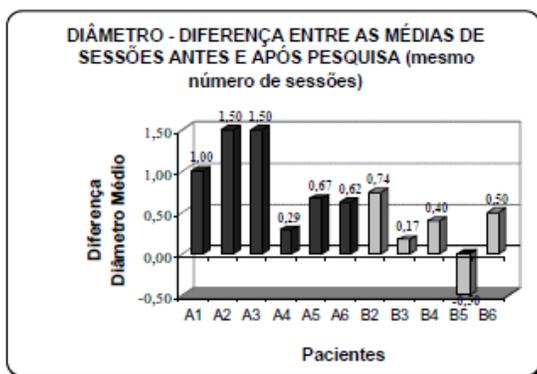


Gráfico 4 – Disfagia em cada retorno - grupo A

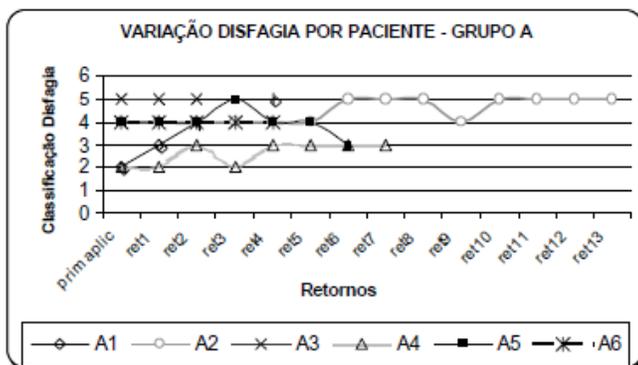
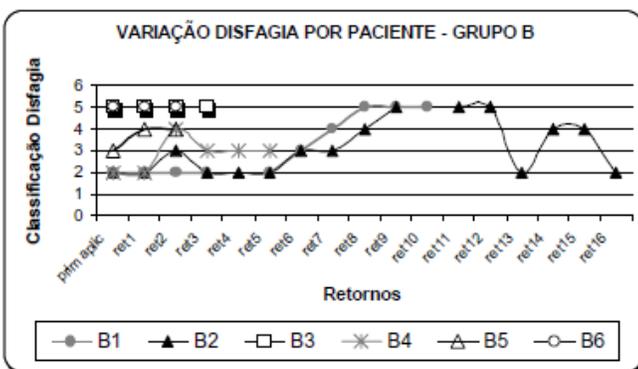


Gráfico 5 – Disfagia em cada retorno - grupo B



Portuguese. Example 2 (html)

Summary: **FUNDAMENTAL** The ABCD rule is used to guide physicians, health professionals and patients quant to the recognition of the key characteristics of suspicious skin lesions from melanoma. There, in Brazil, studies that validate the use of the ABCD rule by patients after advice given by dermatologists.

OBJECTIVES: To evaluate the learning of the ABCD rule for patients treated at the center of dermatological reference in southern Brazil.

METHODS: Randomized study of 80 outpatients of both sexes, aged 12 years or more. Were evaluated: level of education, income and access to the media. The intervention group received, received the employment guidelines of the ABCD rule, while the control group did not. Both groups were tested for their responses on three occasions (baseline, outside the office and the office, 15 days) in a panel of photographs. The level of significance was $p < 0.05$ and power 0.80.

RESULTS: The group that received the information answered correctly, more often, as the diagnosis of melanoma when compared with the control group ($p < 0.01$). Except for access to radio, which positively influenced the results ($p < 0.05$), the other variables not affected them.

CONCLUSIONS: The ABCD rule can be used to empower patients over 17 years to identify alterations suggestive of melanoma. This learning is independent of sex, educational level, monthly income and access to the media except radio.

Keywords: Diagnosis; Melanoma; Patients

Abstract: **BACKGROUND:** **FUNDAMENTAL** The ABCD rule is used to guide medical professionals health and patients regarding the recognition of the key characteristics of suspicious skin lesions of melanoma. There, in Brazil, studies that validate the use of the ABCD rule by patients after orientation guidelines on how performed by dermatologists.

OBJECTIVES: To evaluate the learning of the ABCD rule for patients treated at the center of dermatological reference in southern Brazil.

METHODS: Randomized study of 80 outpatients of both sexes, aged 12 years or more. Were evaluated: level of education, income and access to the media. The intervention group received, received the employment guidelines of the ABCD rule, while the control group did not. Both groups were tested for their responses on three occasions (baseline, outside the office and the office, 15 days) in a panel of photographs. The level of significance was $p < 0.05$ and power 0.80.

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CONCLUSIONS: The ABCD rule can be used to empower patients over 17 years to identify changes suggestive of melanoma. This learning is independent of sex, educational level, monthly income and access to the media except radio.

Keywords: Diagnosis; Melanoma; Patients

INTRODUCTION

Melanoma represents between 3% and 5% of neocutaneous neoplasias, however, its mortality rate is more vada that of basal cell carcinomas and squamous cell home skin. Furthermore, their incidence is increasing-State in several countries in recent years, including Brazil, where the state with more occurrences is Santa Catarina, with 8.61 cases per 100,000 men and Secondly, Rio Grande do Sul, with a incidence of 8.2 cases per 100,000 men. 1,2

Estimates of cancer incidence Brazil, 2010, 2960 new cases are expected melanoma in men and 2970 new cases women. 2 Efforts to reverse this trend have been focused on primary prevention through orientation programs to the population.

Cutaneous melanoma is located on the surface skin and thus can be detected, or at least suspected by medical and nonmedical. 4,5 In a Brazilian study, 75% of a sample of cases melanoma were initially discovered the injury by lay people (the patient himself, his spouse, another member ber of the family or friend).

Early detection of melanoma can be facilitada by the application of the ABCD rule, in which color responds to asymmetry, irregular borders B, C various colors and a diameter D greater than 6mm. 5,7

In Brazil, no studies on the process of Learning the ABCD rule by patients after medical information. He is likely to be influenced by the socioeconomic and educational reality.

This study aims to evaluate the ability of patients for diagnosis of suspected melanoma after receiving information about the ABCD rule in a Public Health Service in southern Brazil, where population is exposed to significant risk of a cancer of the skin.

METHODOLOGY

The Ethics Committee and University Research Federal Health Science of Porto Alegre (CFUPA) has approved the ethical and methodological study. This consisted of a cohort study, prospective-vo, randomized trial that included patients 12 and older, literate, and which were excluded patients with skin cancer at the time query or a previous history of cancer skin. The following variables were recorded: age, sex, family income, education, access to television, radio, Internet and / or newspapers. Primary end-cho was the correct identification of melanomas in parent 63.3% of patients were female. The average age was 46.7 years (SD = 15.5), and age minimum 17 and maximum 80 years. Regarding income, predominated the range of income over \$ 1,000.00, reported by 53.8%. With respect to

appropriate for the study by professors of dermatology that institution.

Were selected and randomly assigned 80 patients outpatients, of whom 40 received information and explanatory material on the ABCD rule (Intervention group or group A) and 40 did not receive any information or material on the rule ABCD (control group or group B).

Before the initial intervention (time 1 or baseline), 80 patients received a sheet with eight color pictures and captions containing no injuries melanoma, benign melanocytic lesions and lesions non-melanocytic, assess and respond to what would be the type of skin cancer melanoma.

The second time was carried out with the answers for a new group of pictures (other than above but with the same degree of difficulty) in environment outside the clinic (patients led Can the material), which were discarded in return to the clinic after 15 days.

The third time, after 15 days, was carried out with the answers to a third group of photographs (Different from previous, but with the same degree of difficulty), again in the clinic.

At every moment, among the eight photos submitted, three were from melanoma. All patients in the control group also received the information and explanatory material, but after the conclusion of three moments.

Besides assessing the ability of patients to suspected diagnosis of melanoma, after receiving information on the ABCD rule, the remaining vari-BATCH described were analyzed in relation to the outcome.

The calculations for determining the size of sample were based on a probable rate-responses tas correct 60% of the intervention group and 20% the control group, with significance level $p < 0.05$ and a power of 80%.

Statistical analysis, according to the requirements, and simple description of frequency-related tions, standard deviation, median, mean estimators, chi-square test, Fisher exact test, Mann-Whitney.

The data received statistical treatment with software SPSS 13.0 (Statistical Package to Social Sciences for Windows).

RESULTS

Considering the total sample (n = 80); 63.3% of patients were female. The average age was 46.7 years (SD = 15.5), and age minimum 17 and maximum 80 years. Regarding income, predominated the range of income over \$ 1,000.00, reported by 53.8%. With respect to

schooling, incomplete primary education complete was the most important, with 26.3%, followed by Elementary and middle grades complete (22.5% of patients in each). The two groups did not significant difference regarding the vari-

Based on the results observed in Table 3, obtained by chi-square test, a significant that, when the first (test 1, before the intervention tion), there was no statistically significant association ($P > 0.05$), indicating that the number of hits in two groups showed a similar distribution.

In the second test results, it was detected associated ing statistically significant ($p < 0.01$), so the intervention group was significant- mind associated with three hits, while in control group, the association was with the numbers ments zero, 1 and 2.

In evaluating the third test, the intervention group significantly associated with three hits, while in the control group, the association has with numbers of hits zero and 1 ($p < 0.001$).

Targeting the analysis, we compared the variability between the time 1 and time 3, between cases and controls concerning the number of hits (3). Comparing the difference in the number of patients who had three hits between tests 1 and 3, between the two groups, we observed differ- ça statistically significant by chi-square for comparisons of proportions ($\chi^2_{calc} = 8.548$, $p = 0.0035$), so that the intervention group submit- sat a significantly greater number of patients who had three hits, when com- ered to the control group.

It was found that in the intervention group, the variability was 75.6% ($n = 31$), ie the test 1, five patients had three hits, while in to that in test 3, 36 patients had three hits. In the control group, in turn, the variability oc- rida between the number of hits between the three tests and a 3 was 37.9% ($n = 11$), ie in a test, nine patients had three hits and, in test 3, 20 patients answered correctly.

TABLE 1: Sociodemographic

Variables	Groups		Total
	Intervention (n = 40)	Control (n = 40)	
Gender *	p = 0.344		
Male	16 (40,0)	11 (27,5)	27 (33,8)
Female	24 (60,0)	29 (72,5)	53 (66,2)
Age **	p = 0.653		
Mean ± SD	47.5 ± 14.3	45.9 ± 16.8	46.7 ± 15.5
Minimum - Maximum	23-73	17-80	17-80
Income *	p = 1.000		
<1000	18 (45,0)	19 (47,5)	37 (46,3)
> 1000	22 (55,0)	21 (52,5)	43 (53,8)
Education ***	0,644		
EFI	13 (32,5)	8 (20,0)	21 (26,3)
EFC	7 (17,5)	11 (27,5)	18 (22,5)
EMI	8 (20,0)	6 (15,0)	14 (17,5)
EMC	9 (22,5)	9 (22,5)	18 (22,5)
ESI	1 (2,5)	2 (5,0)	3 (3,8)
ESC	2 (5,0)	4 (10,0)	6 (7,5)

* N (absolute and%)

** Mean ± standard deviation

*** EFI: Elementary School, RT: Primary complete; EMI: Incomplete High School; EMC: Complete high school; ESI: Higher incomplete; ESC: Complete College Education

Chi-square test with continuity correction

Student t test for independent groups assuming equal variances

Chi-square test

TABLE2: Characteristics relating to access to information

Variables	Groups		Total
	Intervention (n = 40)	Control (n = 40)	
* TV	p = 1.000		
Yes	39 (97,5)	38 (95,0)	77 (96,3)
No	1 (2,5)	2 (5,0)	3 (3,8)
Radio *	p = 0.5167		
Yes	36 (90,0)	33 (82,5)	69 (86,3)
No	4 (10,0)	7 (17,5)	11 (13,8)
Internet *	p = 1.000		
Yes	12 (30,0)	13 (32,5)	25 (31,3)
No	28 (70,0)	27 (67,5)	55 (68,8)
Newspapers *	p = 0.543		
Yes	30 (75,0)	31 (77,5)	61 (76,3)
No	10 (25,0)	9 (22,5)	19 (23,8)

* N (absolute and%)
 Chi-square test with continuity correction
 Fisher Exact Test

TABLE3: Number of hits per group in each test

Variables	Groups		Total
	Intervention (n = 40)	Control (n = 40)	
Test 1 *	p = 0.352		
0	2 (5,0)	5 (12,5)	7 (8,8)
1	16 (40,0)	13 (32,5)	29 (36,3)
2	17 (42,5)	13 (32,5)	30 (37,5)
3	5 (12,5)	9 (22,5)	14 (17,5)
Test 2 *	p = 0.006		
0	1 (2,5)	4 (10,0)	5 (6,3)
1	2 (5,0)	9 (22,5)	11 (13,8)
2	6 (15,0)	11 (27,5)	17 (21,3)
3	31 (77,5)	16 (40,0)	47 (58,8)
Test 3 *	p < 0.0001		
0	0 (0,0)	6 (15,0)	6 (7,5)
1	0 (0,0)	9 (22,5)	9 (11,3)
2	4 (10,0)	5 (12,5)	9 (11,3)
3	36 (90,0)	20 (50,0)	56 (70,0)

* N (absolute and%)
 Chi-square test

Differences in the number of patients at five to 36 in the intervention group and nine to 20 in control group were statistically significant. The percentage difference observed was 37.7% (95% CI - 14.25, 56.24).

Except for the variable access to radio, no the others showed no statistically significant differences on the number of correct answers between the groups, quantified by means of mean, median and standard deviation.

Regarding access to information via radio there was a significant difference in the number of hits in the intervention group ($p < 0.05$). The Patients who reported having had access significantly higher numbers of correct answers to group of patients who reported not having such access (Mann-Whitney test, $p = 0.032$).

DISCUSSION

Although Brazil indicate incidence rates progressively larger cutaneous melanoma in last two decades, studies relating to employment of self-examination for early detection of disease are from other countries. Particularly as to the ABCD rule, although its use consecrated to secular and academic education, little is aware of their potential in employment between Brazilians.

This randomized, held in Porto Alegre (RS), Brazil, aimed to establish three moments: the first baseline to ascertain the state of prior knowledge of the intervention was similar the intervention groups and control.

Tried to demonstrate in the second month, as with the work performed on one of components, what remained of learning to prove influence of the level of each patient, because the test was answered in the home or other locations to the doctor. The have third time aimed to measure the ability of respond properly after the redemption of informations received 15 days before the initial intervention.

With this background, the cohort found that use of the ABCD rule for diagnosing melanoma skin can be well spent per patient TES literate, over 17 years, regardless mind sex, income, education level and access to media like television, news-printed and online.

Access to information via radio seems to be an independent factor that increases the capacity of properly use the rule ($p < 0.05$), perhaps it is a medium that fosters a closer contact

Extended day and where information are more recurrently repeated throughout the day.

It is interesting that the group of intervention, and hit more often diagnosis of melanoma, showed a great variation ability before and after intervention ($p < 0.05$).

The present study examined a cohort of follow soon. Thus, it is a limitation of the study's failure even in predicting long-stay learning term. Central to the growing expansion of number of Brazilians who know the rule ABCD and maintain this learning, the inclusion of theme in health for the general population in schools, workplaces and institutions vary-of, and for transmitting the information by through different media, particularly radio.

CONCLUSION

The study demonstrates, in a population sample tion in southern Brazil, the applicability of the rule ABCD for proper identification of changes suggestive of melanoma. The learning rule depend on the sex of the patient, occurs in different levels of education and income and appears to be easier for those who have access to radio as vehi-communication.

Portuguese. Example 3 (html)

Summary **FUNDAMENTAL** Many patients report improvement of acne with exposure to sunlight, and various studies show that blue light is effective in treating acne.

OBJECTIVE To assess the safety and efficacy of blue light (electromagnetic spectrum from 407 to 420 nm) in the treatment of acne grade II and III, compared to topical therapy with benzoyl peroxide 5%.

METHOD The study evaluated 60 patients at five visits: a screening, with a 7, 14 and 28 days treatment and a final follow-up, 14 days after the treatment. Thirty were randomly assigned to blue light (eight sessions twice a week), and another 30 to benzoyl peroxide 5% twice a day, everyday. The assessment was by counting the number of lesions and photographs.

RESULTS The reduction in the average number of lesions was similar with both treatments, regardless of the type of lesion ($p > 0.05$), but treatment with blue light showed fewer side effects.

CONCLUSION Blue light was a treatment as effective as benzoyl peroxide 5% for the treatment of acne grades II and III, but with fewer adverse effects.

Keywords: Acne vulgaris; Phototherapy; benzoyl peroxide

Abstract: **BACKGROUND** Many patients improve acne after exposure to sunlight and there are many reports about the efficacy of blue light phototherapy on acne lesions.

OBJECTIVE The purpose of this study was to evaluate efficacy and safety of blue light treatment versus topical 5% benzoyl peroxide formulation in patients with acne grades II and III.

METHOD Sixty volunteers with facial acne were evaluated in May and included visits: the first one for screening, another third held on days 7, 14 and 28 of treatment, and the last one after 14 days of the end of treatment. Thirty of them were irradiated with blue light (8 times, twice a week) and the other thirty were treated with topical benzoyl peroxide 5% formulation, self-applied twice a day, every day. We assessed the severity of acne by counting the lesions and analyzing the photographs.

RESULTS The improvement achieved by the blue light was the same with the benzoyl peroxide, regardless of the type of lesion ($p > 0.05$). Otherwise, the side effects less frequent were in the group treated with blue light.

CONCLUSION Blue light irradiation was effective to the benzoyl peroxide in acne treatment grades II and III but there were fewer side effects.

Keywords: acne vulgaris, benzoyl peroxide; Phototherapy

INTRODUCTION

Acne is a chronic inflammatory disease of pilosebaceous unit and affects approximately 80% of young people. Changes in training and cell differentiation in the pilosebaceous follicle result in hyperkeratinization duct with consequent hot cell accumulation in the lumen, which, associated the retention of sebaceous secretion, so the comedons, which are the initial lesions of acne. This means propitious to the development of bacteria, predominantly *Propionibacterium acnes* (*P. acnes*), which alters the lipid composition of sebum. Besides addition, the immune response to *P. acnes* and pulblotted with their pro-inflammatory lipids seem be involved in the formation of the inflammatory process that causes papules, pustules and nodules. 1,2

The classical treatments recommended for acne aim correct one or more factors involved the genesis of the process. The choice will depend on the and the extent of disease. Little clinical presentations inflammatory and non-extensive are treated in general with topical medication: benzoyl peroxide (CP), retinoids or azelaic acid. For more severe cases and extensive, we use systemic drugs: antibiotics, ticos, antiandrogens or isotretinoin. 3-7 All these arrangements are well known, indications are precise in the inhibition and regulation of sebum production, but occasionally may trigger adverse effects not tolerable, such as severe dryness of mucous and skin, increased levels of triglycerides and cholesterol and teratogenesis induced by isotretinoin. Other important aspect is the emergence of resistance antibacterial properties in the presence of erythromycin and fortazolidonam and least 15 days. We distribute of randomly into two groups: 30 patients used the light blue, and 30, benzoyl peroxide 5%. Individuals in the group GL (light blue) underwent cardiac of the eight sessions of exposure to light for 15 minutes each, twice a week with a minimum interval of 48 hours for four weeks. Individuals in GP group (benzoyl peroxide) applied to essential tion daily, twice daily for four weeks, in. All patients in both groups used facial hygiene soap and sunscreen SPF 15 equal, daily throughout the study period.

Many, regardless of treatment, describe clear improvement of acne when exposed to sunlight. 9,10 Accordingly, studies have shown that visible light is an alternative mode and effective treatment of acne. 11-13 This result can be explained by the production of porphyrins, especially uroporphyrins, and protoporphyrin IX coproporphyrins by *P. acnes*. The protoporphyrin have the ability to absorb light and thereby promote a photo-reaction dynamic that leads to bacterial destruction. In this context, the blue light, which has long range wavelength from 407 to 420 nm, may also be able to activate these porphyrins to produce the same reaction and dynamics. 17 Therefore, the light treatment can be effective in acne, because it causes selective damage to the and destruction of the pilosebaceous *P. acnes*, without producing visible damage to your surroundings. Recently, demonstrated that irradiation of *P. acnes* with UVA and Blue light can modify the influx of protons transmembrane of the bacteria and induce cell damage by

alterations of intracellular pH. An important aspect of blue light is that, unlike the spectrum of radiation ultraviolet sun, is not carcinogenic.

In relation to topical agents, the peroxides of 5% benzoyl is a classical formulation for treatment of inflammatory acne. Can be used in monotherapy or as combination therapy with other medications, both topical and systemic, in concentrations ranging from 5% to 10%. The concentrated 5% produces less local irritation and can be applied twice each day. At these concentrations the peroxides of benzoyl has anti-inflammatory and antibacterial and, therefore, is recommended for the treatment of acne grade II or III. 3-6

Given this knowledge, the authors put studies with the aim of verifying safety and efficacy of blue light as a modality of treatment of acne grade II or III, comparing it to treatment with the peroxide Benzoyl 5%.

MATERIAL AND METHODS

The study was a prospective, open, randomized, comparative and included, in order of attendance at November/2006 september/2007 the period. 60 patients with inflammatory lesions of acne grade II or III, according to the classification of the Brazilian Acne Group. The protocol was approved by the Ethics Clinical Research PUC Campinas (No. 491/06).

The 60 individuals selected to start study were not using any medication-specific and fortazolidonam and least 15 days. We distribute of randomly into two groups: 30 patients used the light blue, and 30, benzoyl peroxide 5%. Individuals in the group GL (light blue) underwent cardiac of the eight sessions of exposure to light for 15 minutes each, twice a week with a minimum interval of 48 hours for four weeks. Individuals in GP group (benzoyl peroxide) applied to essential tion daily, twice daily for four weeks, in. All patients in both groups used facial hygiene soap and sunscreen SPF 15 equal, daily throughout the study period.

The emission of blue light was obtained through a light source that illuminates a specific area Circular 55 mm in diameter, which is protected optically by a spherical globe, non-transparent you, made for this specific purpose. This apparatus is called Blue Light and was developed by the Evttech Komlux Fibres. Outputs a high-intensity light, ranging from 407 to 420 nm, with average power in the region illuminated 40 mW/cm². This wavelength of light is efficient for the photostimulation of porphyrins, accord-

in vitro and *in vivo*. The penetration of light is approximately 1 mm into the skin, and therefore reaches *P. acnes* which lies on the surface and the ducts. Patients received protection with eye goggles for dark lenses Speedo during the sessions. The benzoyl peroxide 5% was prepared in the form of vehicle cream topical and provided in vials with 20 g per laboratory reference the Department of Dermatology.

The monitoring of patients occurred in five visits as follows: (V0) - visit funding, guidance and case selection, there will be of one week before the start of treatment, (V1) - visit to randomization and inclusion of patients able and early treatment, (V2) - first visit for evaluation with two weeks of treatment, (V3) - Second visit in four weeks for evaluation of treatment, (V4) - the third assessment visit carried out two weeks after the treatment.

Quantification of clinical improvement of acne was performed by counting the total number of inflammatory (papules and nodules) and noninflammatory (Comedoneas) observed between the initial visit and V0 visit V3, present on the face and documented by photographic exhibitions. The photographs were performed with the HP Photosmart camera digital 3.3 megapixels and 3x optical magnification.

Regarding safety and tolerability was questioned patients the occurrence of erythema, dryness, flaking and burning during the treatment at all visits.

To meet the objectives of the study, were calculated descriptive measures of each type of lesion - high (mean and standard deviation) and constructed charts means with their standard errors to illustrate the results.

Performed tests of non-Kolmogorov-Smirnov normality for lesions, grouped in inflammatory and noninflammatory and inflammatory, and was accepted normality of data distribution. To compare the two treatments with regard to injuries, were compiled the quantities of lesions detected on visits V0 and V3, observed for each patient, which demonstrated variation between beginning and end of treatment. The visits in the interval between visits V0 and V3 were control to verify patient adherence to treatment and to adverse effects. Comparisons were made with the Student t test unpaired.

The tests were performed at the level of significance of 5%.

For the analysis of side effects, was utilized chi-square.

RESULTS

After signing the consent form free and informed consent, 60 patients were grouped

randomly into two groups: 30 underwent treatment with benzoyl peroxide (GP) and the other 30 applications were submitted to blue light (GL). These 60 patients were included, 1 completed the study and nine did not finish (three belonged to the GP, and six to GL). No tests were performed in sensitivity adversity or treatments. All feature-VAM healthy with no other comorbidities and unused drugs that could interfere with the development or adherence.

A total of 60 patients enrolled, 26 were females and 34 males, and in GP There were 12 men and 18 for women, in GL, 14 women to 16 men. Eleven and 47 were mulattos were white, for two patients had no refer-ecy to the color chart. The mean age at start of study was 17.3 years. Of the 60 patients, 39 already had undergone some form of treatment in the past, from topical products up to systemic use, including oral isotretinoin. As the severity of acne, three were classified as acne grade III and 57 as grade II acne.

GP patients' average number of non-inflammatory lesions at V0 was 128.67 and the visit V3, of 93.50, representing a reduction of 27.3%.

As for the inflammatory, the average number of lesions was 35.37 to 19.14 in the V0 V3 (reduction 45.8%). Adding to the inflammatory lesions and not inflammatory (total injuries), there was a reduction of 31.32% after treatment (from 164.03 in V0 112.64 for the V3).

In the GL group the mean number of lesions not inflammatory in V0 was seen at 111.60 and V3 of 85.92 (23% reduction), while for the inflammatory was from 27.87 to 23.33 in the V0 V3 (down 16.28%).

Analyzing the average of total injuries, there was a reduction of 21.66% after the use of benzoyl peroxide (from 139.47 to 109.25 in the V0 V3) (Table 1).

Statistical analysis of the results of this study was performed by comparing the number of V0 lesions present at the visit with the number observed after 30 days of treatment (V3) by t test unpaired. The last visit (V4) was performed only for patient follow-up after completion of treatment, not being used to analyze the efficacy by counting the number of injuries. Visits V1 V2 and served as a control to verify the compliance of patient and adverse effects.

The adverse effects, it was observed that 28 patients using benzoyl peroxide, or 93.3% had some symptoms related to product use, and only two patients did not complained. Signs and symptoms reported have some degree of erythema, scaling, resected tion or burning. In some patients being

TABLE1: Description of the measurements for each type of treatment

Type of injury	Treatment	Visit 0			Visit 3		
		Average	DP	N.	Average	DP	N.
Noninflammatory	PB	128,67	90,81	30	93,50	69,74	28
	LA	111,60	45,03	30	85,92	57,78	24
	Total	120,13	71,59	60	90,00	63,99	52
Inflammatory	PB	35,37	22,16	30	19,14	17,95	28
	LA	27,87	18,08	30	23,33	15,10	24
	Total	31,62	20,40	60	21,08	16,67	52
Total	PB	164,03	97,31	30	112,64	77,70	28
	LA	139,47	45,25	30	109,25	58,49	24
	Total	151,75	76,25	60	111,08	68,86	52

benzoyl peroxide - PB and light blue - LA

need to reduce the frequency of use of the product to once a day, which led to improved symptoms. Moreover, among patients who used zàram blue light, only 23.3% complained of some unwanted effect, characterized by scaling and / or dryness, but it was mild. In this group, but did not require discontinuation of treatment in any patient due to such effects. Thus, by result of the chi-square, the percentage of elements is statistically higher in the group using benzoyl peroxide ($p < 0.001$).

DISCUSSION

Despite reports of clinical improvement acne to sun exposure in low intensity, in the medical literature there are no rigorous studies that explain and demonstrate this improvement using the sunlight throughout its visible spectrum or only weak-tions of the spectrum, like light blue or light-worm ðe. Tzung,¹⁴ in a study of 31 patients, reported improvement in acne grade II in 52% when treated one side of the face with light blue and the other side as control. In this work, based on par-tion of porphyrins, the author related the intensity pre-and post-treatment with fluorescent lamp Wood and found no difference in the effectiveness of treatment with the change in intensity of fluorescence. Shalita,¹³ in a study involving 35 patients, showed an average decrease of 60% of the car-quantity of inflammatory lesions and improvement of the clinical in 80% of patients with light applications blue for a month. The study, however, was not controlled with the other treatment for acne.

Papageorgiou¹⁵ compared in 107 patients, Four groups of acne treatment: exposure to light blue alone, the combination of exposure to red light blue and white light exposure and treatment with peroxides benzoyl oxide 5%. Noted improvement in 76% of

inflammatory lesions and comedones in 58% of the treated pre- with the combination of blue light over red light, which was significantly higher than in the groups of light blue and benzoyl peroxide alone. Results the groups treated with blue light alone and peroxides benzoyl oxide were similar. The average improvement in the group of blue light was 45% for comedones and 63% for inflammatory lesions with a hand-It is of a cumulative dose of 320 J / cm². Thus, Papageorgiou¹⁵ found that the combination of the two types of radiation, light blue and red light, gave better results than other treatments alone.

Our study showed an improvement im-you frame of acne with both treatments, both the LA and with the CP (Figures 1 and 2).

Analyzing only the number of isolated noninflammatory and inflammatory lesions, weeks V0 and V3, the reduction of inflammatory lesions not stop it ce similar in both groups (GP and GL) (Chart 1), while there seems to be a trend-cia the best results in lesion counts inflammatory group of benzoyl peroxide quan-compared to the group of blue light (Figure 2). In However, analysis of total lesions (inflammatory-inflammatory cytokines and non-inflammatory) (Chart 3), the reduction average number of lesions is the same for both treatments, regardless of the type of injury, there of the value of p in the analysis of the inflammatory lesions ($P = 0.500$) and noninflammatory ($P = 0.177$). This ap-cannot inconsistency was due to large variation results in reducing the amount of injuries between a patient and another, within groups, evident-enced by the values of standard deviation (Table 1).

Thus, when analyzing all patients together, using the test of com-tion (Student's t test), results showed that both treatments have the same reduc-tion in the number of injuries, both in total injury

FIGURE Patient female before treatment with blue light

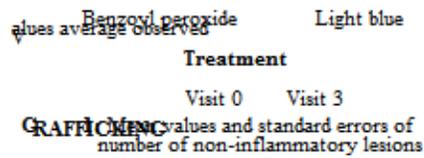
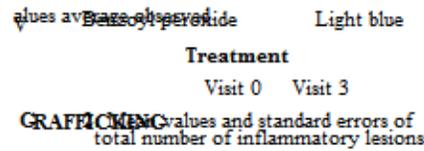
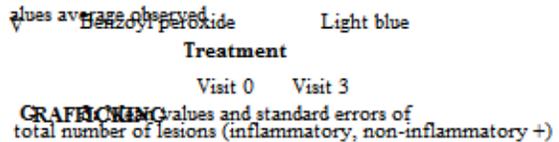


FIGURE Result after eight sessions light blue



as in isolated analysis of each type of lesion, inflation
pect or noninflammatory ($p > 0.05$).

In this study, as observed by Papageorgiou,¹² the outcome of treatment with blue light was similar to the treatment with peroxide benzoyl. Thus, the reduction of lesions after four weeks of treatment was similar between the two groups. However, unlike our findings, of the study by Shalita¹³ found that blue light improved inflammatory lesions in a more wave-tuada. We note that although the two treatments have demonstrated similar efficacy, light blue was better tolerated, because there were fewer complaints irritation of the skin during treatment, in contrast to River of benzoyl peroxide, which with two applications daily demonstrated greater discomfort from a mild erythema or dry desquamation and burning up in moderate. This has raised the need for inter-



tion in the initial proposal of two applications, such as reducing the frequency of use or discontinuation of medication for a few days. You should consider these side effects could be minimized since the beginning with the application of CP only once a day. However, it should be noted that the application in two often aimed to improve results and may was so used to be alone. In addition, the PB was not formulated in cream and gel, which produces an emollient effect of higher and could well minimize the adverse effects of the application twice daily. Despite the necessity of stopping it ment, the authors felt that there was no interference in the results since the interruption occurred at a very short period of time.

With respect to LA, the authors observed that there was less compliance with treatment when compared with the CP. This was interpreted as a consequence of the need for the patient to move to the center

treatment twice a week to perform LA applications.

CONCLUSION

The authors concluded that treatment with blue light was as effective as a method with peroxides of benzoyl in reducing the number of lesions acne grades II and III and with fewer adverse effects compared with the CP alone. This fact confirms LA to be a real option for treatment, mainly for patients with contraindications to other treatment methods. Further studies with combination of light blue and other treatments should be performed in order to maximize results by combination therapy. The introduction of blue light in clinical practice, combined with the methods of this study, may bring a new breath, with better results and more an option to acnéic patients.

Spanish. Example 1 (html)

ABSTRACT

Objectives: We present a study of 56 patients who underwent extraction of mandibular third molars with Akinosi technique as an alternative to direct mandibular block. In order to assess the effectiveness of the technique Akinosi.

Study design: A group of 28 patients was anesthetized by a lock jaw and other direct of 28 cases with Akinosi technique. Parameters evaluated were pain at the puncture, suction rate positive perception, latency time, pain during intervention and complications.

Results: Pain at the puncture was of less intensity and percentage time of the Akinosi technique. Hematic aspiration was positive in 4% of block queos jaw and 46.4% according to the technique Akinosi. The latency period was lower in cases anesthetized using conventional technique - 2.9 minutes - that technique Akinosi - 3.8 minutes. The pain during surgery and anesthesia, duration of effect Tescic were similar for both techniques. The groups-po of patients anesthetized with Akinosi technique greater number of reinforcements received buccal nerve to perform the operation. 10.7% failed direct mandibular blocks and 17.8% of procedures

procedures with the technique of Akinosi.

Conclusions: Although the technique can be used Akinosi Zarse for mandibular third molar extraction, re-consultation more effective and safe anesthesia by blocking mandibular direct.

Keywords: Third molars, blocking mandibular Akinosi technique.

INTRODUCTION

Most professionals prefer to lock direct or conventional mandibular as the most effective interventions mandible (1-7). In this technique, the anesthetic is deposited in pterygomandibular space near the foramen of Spix taking into account a number of references intraoral as the retromolar trigone, ligament pterygomandibular and the occlusal plane. Not always achieved total success, according Yücel (8) and Bremer (9) the percentage of failures anesthesia technique differs from conventional or direct 5% to 15%. There are other techniques that can be used in the jaw, such as the Gow-Gates (10) and Akinosi (11).

In 1977, Akinosi (11) developed a procedure for when the patient can not open your mouth, making impossible conventional mandibular block. The patient's mouth should be partially closed without coming to occlusal contact, this allows the relaxation of cheek muscles to separate them and get better visualization of the area, and decreases the perflute trauma of needle insertion. The area of insertion of the needle is placed between the ascending branch of the jaw in medial tuberosity and the maxillary, near the junction adjacent to the second Mucogingival maxillary molar or the third molar, if present (3). The patient should be seated with semirreclinado head, neck and shoulders supported. With the index finger separate thumb cheek laterally to allow better visualization of the area, placing the syringe occlusal plane parallel to the upper jaw. In this composition, the needle penetrates the soft tissue to a depth of 25 mm from the tuberosity maxilla, the anesthetic is deposited in the mesial pterygomandibular space near the main Palestine inferior nerve branches (5). It is shown that the aspiration is negative and deposited 1.8 ml. solution anesthetic, in about 60 seconds to des- then remove the needle. If the technique is well realized the patient begins to feel tingling in the area the lower lip and tongue in 40-90 seconds and can start working in the area in 5 minutes (3,4,11,12).

The direct mandibular block is commonly used, with known results. However, occasions may be required other techniques, such as Akinosi. Performed a study on 56 patients who underwent extraction of mandibular third molars with In order to assess the effectiveness of the technique as Akinosi alternative to conventional mandibular block.

MATERIAL AND METHODS

The study included 56 patients who were informed consent and asked to be part of same. Of the 56 patients, 22 were men and 34 women. The mean age was 23.3 years (range 14 to 38). It randomly established two groups of 28 patients each requiring removal of lower third molar previous and were anesthetized by blocking direct to mandibular - control group - and the other technique Akinosi - study group -. In all patients used the same anesthetic solution, a cartridge of 1.8 ml articaine 4% with epinephrine 1:100,000, and for to clarify buccal or lingual reinforcement used 1 ml each point reinforced. All procedures were

made by the same professional.

The puncture pain was assessed by reference Mc Gill scale: 0 = absent, 1 = mild, 2 = moderate, 3 = fairly, 4 = much, 5 = excruciating. The aspiration assessed as 1 = negative, 2 = positive, when it was hematic. The latency is the elapsed des anesthetic injection until the patient noticed the first symptoms of numbness, expressing this interval in minutes. If the patients reported sensitivity true during maneuvers needle is reform Zaba anesthesia of the buccal or lingual nerve. Du pain during the intervention was assessed as 1 = no pain, 2 = yes pain. The duration of anesthesia was expressly do in minutes.

In the study of significance for comparison of quantitative means used the "t" Student test and for qualitative variables, Chi-Square. We conducted a descriptive analysis for each of the variables. The comparisons between different groups, once verified for statistical assumptions are performed using analysis of variance, when variation came dependent variable in the scale interval and by Test Chi-Square (X 2) For categorical variables cas.

RESULTS

The direct mandibular block was performed in 28 patients, 12 men and 16 women, mean age 24.1 years. The group anesthetized with the technique of Akinosi was 10 men and 18 women, mean age 22.5 years, in 2 patients after waiting 10 minutes after anesthetic infiltration was not possible consequir no effect, considering them as failures, compared to patients anesthetized with conventional technique in which there was no failure whatsoever. The initial manifestation of the anesthetic effect with the technique conventional lower lip was numb. With Akinosi technique in 4 patients the onset was in perioral area and another 4 in the genial area and angle mandible.

The sensation of pain during the puncture (Fig. 1) was higher in the group of patients anesthetized with the technical ca conventional, showing 73% mild pain and moderated 27% of these cases. Of patients anesthetized with Akinosi technique, 19% no reference laugh pain, 65% mild discomfort and pain 16% moderate. The differences were statistically significant cannot (ANOVA, $p < 0.05$).

Hematic aspiration showed 13 of the 28 positive infiltration (46.4%) were performed with conventional technique and 4% of those made with the technique of Akinosi

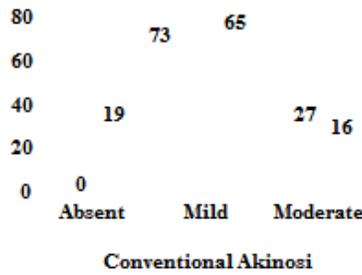


Fig 1. Percentage of pain at the puncture. Percentage pain in response to needle puncture. Absent: Absent, Mild: Mild, Moderate: Moderate. Conventional: Conventional

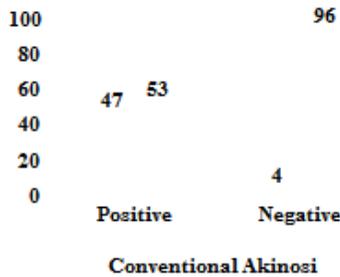


Fig 2. Percentage of hematic aspiration. Percentage blood aspiration. Positive: Positive, Negative: Negative

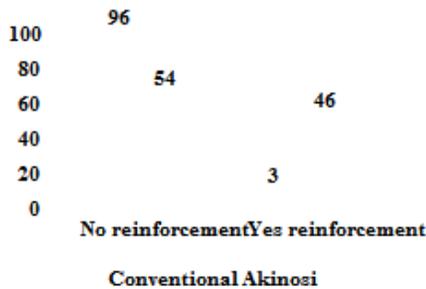


Fig 3. Percentage of reinforcement buccal nerve. Percentage reinforcement anesthetic buccal nerve. Reinforcement: Reinforcement

(Figure 2), the differences were statistically significant (Chi-square, $p < 0.05$). With respect to the latency period of patients treated two with the conventional technique provided the first symptoms of numbness of the lower lip form earlier, with an average of 2.9 minutes compared to the groups-Akinosi po that had an average of 3.8 minutes, the differences were statistically significant (t , $p < 0.05$).

With regard to reinforcements in the lingual and buccal nerves (Figure 3) in one patient technique Akinosi was necessary to strengthen the lingual nerve, while while in patients anesthetized with technical-conventional reinforcement was not necessary nerve.

When considering the strengthening of the buccal nerve-found themselves significant differences sections, 12 of 26 patients anesthetized with Akinosi technique - 46% - need-infiltration were buccal nerve, while only one of 28 cases - 3% - anesthetized with conventional technique tion or direct this reinforcement was made (Chi-square $p < 0.05$).

With regard to pain during surgery, no significant differences. With the technical-conventional 10% expressed mild pain and the patient TES anesthetized Akinosi technique, 12% had mild pain. If we consider the existence of pain failure during surgery or the inability to obtain anesthesia, mandibular block group 3, 28 failed (10.7%) and the technique of Akinosi 5 of 28 (17.8%).

The mean duration of anesthesia with the technical conventional AC was $267.7 + 11.5$ min., the average duration of anesthesia technique was Akinosi $233.9 + 13.1$ min. The differences were not statistically significant, although the duration of me-day of anesthesia was greater with the conventional technique. The complications that we observed in both groups post have been the typical triad of pain, swelling, and trismo feature surgical extractions of third cer molar, listed in most ca-resources to the surgical and anesthetic technique with no used. One patient of the 26 anesthetized with technical AC said Akinosi subjective feeling of not being able to close the eye but it was rapidly decreasing.

DISCUSSION

Anesthesia was achieved using the technique con-ventional in 100% of cases, and the technique Akinosi in 92%, two of the 28 patients anesthetized with this technique after waiting 10 minutes after the in-

filtration for anesthesia and anesthetic effects were considered as failures. 19% of patients anesthetized with technique Akinosi felt no pain during the puncture, by In contrast none of the patients anesthetized with conventional technique showed the absence of dolor, referring most of them (73%) mild pain. Two authors consulted similar results and claim that the puncture technique is Akinosi less painful than conventional due to the greater laxity of the tissues at the puncture site, although not present data on this parameter me- by means of which we can draw a comparison (2,10,11,13-15).

In 4% of patients anesthetized with technique Akinosi aspiration was positive, compared to 47% of cases of the conventional technique. Akinosi technique has a lower percentage of positive aspirations and this is due to the small number of blood vessels localization two at the injection site, thus, the complications due to the injection of anesthetic in the blood decreases significantly or not occur (8.11 to 14). The latency period Akinosi technique was higher previous (3.8 minutes) the direct locking group (2.9 minutes). These times away enough of the exposed cough for Akinosi (11) and Gustainis and Peterson (12), who argue that the lower lip numbness pre- leads to the 40 seconds after the injection, intervention can begin to ninety seconds two. Sisk (13) found an onset of anesthesia more fast technique Akinosi (90%) than with technical conventional (85%), although the percentage of patients who had symptoms of anesthesia at 10 minutes was the same in both techniques (90%). By contrast, Yücel and colleagues (8), Todorovic and colleagues (14) and Donkor and Colak (15) found a faster start with the technical- than with the conventional Akinosi. According to Yücel and colleagues.

(8). 88% of patients anesthetized with technology conventional beginning to feel the numbness lower lip in the first 5 minutes, and only 51% of anesthetized patients Akinosi technique sen- tian, numbness at the same time.

One of the most significant parameters in our study given was the need for reinforcements buccal nerve 47% of patients anesthetized with technique Akinosi, compared to 3% of the technical anesthetized conventional. Akinosi (11), and Gustainis and Peterson (12) claim that technology is only necessary Akinosi an injection to get the maxi-nerve anesthesia lar less, our results show that they have been numerous instances in which required two in- injections to achieve full anesthesia.

The pain during the procedure has been another parameters analyzed, yielding virtually same results with both techniques. Three patients each group showed only mild pain during the intervention, apparently achieved the depth of anesthesia with both techniques is similar. However, it taken into account in assessing the effectiveness, especially the Akinosi technique reinforcing the need for nerve mouth. Results similar to ours are those of Sisk (13), in contrast Todorovic and colleagues (14) had higher number of patients expressing pain during intervention when anesthesia is done according to Akinosi technique. If we consider the existence failure pain during surgery or the inability to achieve anesthesia, block group 10.7% failed mandibular and technical Akinosi 17.8% of procedures. Figures similar to Malamed (3) who estimated the success after making anesthetized sia with the technique of Akinosi by 80% and 85-90% for technical conventional. Donkor and Col. (15) find- have showed a number of unexpected effects after completion from anesthesia following the technique of Akinosi. 8% patients reported "tingling" of the upper lip- previous, 2% infraorbital nerve anesthesia, 2% anesthesia posterior alveolar nerve in an area 1% was observed ischemia on the infraorbital region. In our es- study, a patient of the 26 anesthetized technique Akinosi said subjective feeling of being unable to close the eye but it was falling rapidly, possibly was due to paresis of the extraocular muscles eye, by spreading the anesthetic into the orbit (16). It follows from our experience that the technique Akinosi is a technique for interventions lower lip mandibular region, which although useful is not as effective as conventional (15) although a higher embodiment habit in their tion could make it a safer technique.

Spanish. Example 2 (html)

Background: Zinc is important for insulin synthesis, storage and secretion. When zinc concentration DECREASES, There Is a Reduction in insulin secretion concomitant and peripheral insulin sensitivity. *Aim:* To Assess the effects of zinc sulfate on insulin sensitivity, leptin and androgens in obese individuals. *Material and methods:* A randomized, double-blind, placebo-controlled clinical trial in 14 obese WAS Volunteers Performed Between 21 and 30 years old, with body mass index (BMI) ≥ 27 kg/m². DURING one month, seven Subjects Received 100 mg / day of Orally zinc sulfate (ZNG) and The Other seven Received placebo as control group (CG). At baseline and after the intervention, insulin sensitivity using a Measured WAS-hyperinsulinemic euglycemic clamp technique. Blood glucose, serum lipids, zinc, androgens and leptin Were Also Measured in a fasting blood sample. *Results:* After the intervention, a rise in zinc Concentrations from 11.8 to 16.9 $\mu\text{mol} / \text{L}$, $P = 0.001$ and in leptin Levels from 15.2 to 27.7 ng / mL, $p = 0.029$, WAS observed in the ZNG. No Were Changes observed in the CG. There Were no significant Changes in insulin sensitivity and androgens after the intervention with zinc sulfate. *Conclusions:* Zinc INCREASED the leptin Concentrations in Obese Individuals, But Did not modify insulin sensitivity and androgens (Rev Méd Chile 2006, 134: 279-84).

(Key words: hyperinsulinism; Insulin, Leptin.

L a relationship between insulin and zinc is known decades. Zinc is important important for the synthesis, storage and secretion of insulin concentrations decreased Zinc is associated with a reduction in insulin secretion, with a tissue resistance action of this hormone 1-3 and consequentemia, with an increase in circulating glucose 4. *In vitro* studies show that at low concentration There zinc concentrations of glucose-stimulation neogenesis and inhibition of glycolysis 5. The literature shows controversy over the concentration zinc concentrations in subjects with obesity Dad, as some studies have reported decreased 6,7 and other increases 8,9 of this element.

Obesity in humans is associated with a large number of metabolic abnormalities include insulin resistance, hyperinsulinemia, mia, dyslipidemia, hyperleptinemia resistance to leptin, decreased concentrations of sex hormone binding globulin (SHBG), total testosterone (TT) and testosterone free (TL) 10-14. Subjects with obesity occur with increasing concentrations of leptin, show a decrease in SHBG and the TT 15. There is no known involvement of zinc on the action of insulin and its relation to SHBG TT, TL and leptin. The aim of this study was to identify the effect of an intervention Pharmacological zinc sulfate on the sensitivity to insulin, leptin and androgens in obese men.

MATERIAL AND METHODS

It conducted a randomized clinical trial, double blind, placebo-controlled study in 14 men between 21 and 30 years of age, with obesity [index mass index (BMI) $\geq 27 \text{ kg} / \text{m}^2$]. The voluntary Lilly Co., Mexico) was infused continuously, with the goal of reaching levels of insulin blood of $100 \mu \text{U} / \text{mL}$, so the rate Insulin infusion was fixed at $40 \mu \text{U} / \text{m}^2 \text{ Min}$. The Blood glucose concentration remained constant (approximately $90 \text{ mg} / \text{dL}$, with a coefficient of variation $<5\%$) throughout the study (120 min) by infusing 10% glucose variable rate, according to determinations blood glucose performed at intervals 5 min. At the end of the 120 min test

The randomization of participants to receiving zinc sulfate or placebo was by simple chance, with the selection of a sealed envelope containing the option A or B. Neither investigator nor the participants knew du the study during the intervention. End the study were divided into 2 groups: one group of 7 volunteers who orally ingested a capsule 100 mg of zinc sulfate (Mallinckrodt Backer, Inc. Paris), every 24 h for a period 30 days (GZn) and a group of 7 individuals ingested a capsule containing 100 mg daily placebo, similar features to supplement and last-you the same time, he served as group control (GC). Adherence to treatment oversaw the accounting for the capsules surplus each week.

Each patient was obtained at the beginning and end of pharmacological intervention on fasting of 12 h euglycemic-hyperinsulinemic clip for estimate insulin sensitivity, the quantification of serum zinc, leptin, insulin, TT, TL, SHBG and a biochemical profile [glucose, total cholesterol, triglycerides, high density lipoprotein (HDL) uric acid and creatinine].

The insulin sensitivity corresponded to value of overall glucose metabolism (M) obtained by the method of the clamp-euglycemic-hyperinsulinemic, previously described by De Fronza et al 16. To carry out this test placed two venous access, the first to form in any vein retrograde hand, through a catheter 23 G, for sampling throughout the test hand wrapped in a thermal mattress to local temperature is raised above 40°C for arterialized blood. The second venous access installed in the contralateral arm with a catheter 23 G as a means of infusion. Insulin (Humulin R, Eli Lilly Co., Mexico) was infused continuously, with the goal of reaching levels of insulin blood of $100 \mu \text{U} / \text{mL}$, so the rate Insulin infusion was fixed at $40 \mu \text{U} / \text{m}^2 \text{ Min}$. The Blood glucose concentration remained constant (approximately $90 \text{ mg} / \text{dL}$, with a coefficient of variation $<5\%$) throughout the study (120 min) by infusing 10% glucose variable rate, according to determinations blood glucose performed at intervals 5 min. At the end of the 120 min test

clamp was maintained infusion of 10% glucose for 30 min more, as a precaution against hypoglycemia in the volunteer.

The serum zinc was measured by spectrometry atomic absorption. Glucose was determined by the technique of glucose oxidase and lipid (cholesterol, HDL cholesterol and triglycerides) by colorimetric methods in automated equipment (Dimension Chemistry System, Dade Behring). Cholesterol low density lipoprotein (LDL) was estimated using the Friedewald formula (LDL cholesterol = Total cholesterol - HDL cholesterol - TG / 5) and very low density lipoprotein (VLDL) is calculated as triglycerides / 5. Insulin, TT, TL and SHBG were measured by radioimmunoassay and leptin by IRMA (Diagnostic Products Corporation, Los Angeles, California, USA). Each study group before surgery determination coefficients of variation intra- and inter-assay less than 3 and 5% respectively.

The sample size was calculated with a formula for clinical trials¹⁷ with a level of 95% confidence, a power test 80%, a standard deviation of the clamp M euglycemic-hyperinsulinemic of 0.8 mg / kg.min and an expected difference of at least twice standard deviation (1.6 mg / kg.min), which obtained a score of 6 patients per group.

We included 7 patients per group for the possibility of being lost to follow up. Test Wilcoxon was used for analysis between before and after pharmacological intervention. The Mann-Whitney U was used to compare changes between both groups. A level of significance at a p value <0.05.

To have a reference value serum concentrations of zinc in individuals without obesity (BMI <27) kg/m². For comparison, the determination was made 15 men from 21 to 30 years old, who denied family history of diabetes in first-degree mellitus type 2 and hypertension and which did not undergo the rest of determinations covered by the study laboratory for the obese.

Participants signed a consent-sheet consent under information, the study met requirements for human research and was approved by the Committee for Research Hospital Ethics.

RESULTS

The age of volunteers was 21.8 ± 2.8 and 25.1 ± 4.5 years for the GZn and GC, respectively (p = 0.318). Both groups had a BMI similar (30.7 ± 2.6 vs. 30.5 ± 3.0 kg/m² for GZn and GC, respectively).

There was a lower concentration of zinc serum in both groups [11.8 (8.3 to 13.7) for GZn and 12.9 (7.7 to 17.4) μmol / L for GC], in compared with the value of 21.8 (15.9 to 26.7) μmol / L we obtained in the male population and obese (BMI 23.1 ± 1.2 kg/m²).

The sensitivity to insulin, estimated by the M value obtained by euglycemic-clamp technique and hyperinsulinemic was similar in both groups study groups before surgery pharmacological as well as leptin, the androgen and the rest of the biochemical profile (Table 1).

After administering a supplement zinc sulphate, found an increase in Serum zinc (Figure 1) and leptin (Figure 2). LT showed a trend increase after pharmacological intervention with zinc sulfate (9.8 ± 2.3 vs 12.3 ± 4.7 nmol / L; p = 0.082). Insulin sensitivity and profile chemistry did not change with the administration of zinc sulfate (see values in Table 1).

The placebo did not alter the sensitivity to insulin, leptin, androgens, or the profile biochemical volunteers (see values in the Table 1). BMI was not different between the two groups at the end of the intervention (31.3 ± 2.6 vs 30.3 ± 4.3 kg/m² for GZn and GC, respectively; p = 0.535).

Adherence to both the supplement as for placebo, was greater than 95%. Sulfate zinc and placebo were well tolerated and volunteers had no undesirable effects to throughout the study.

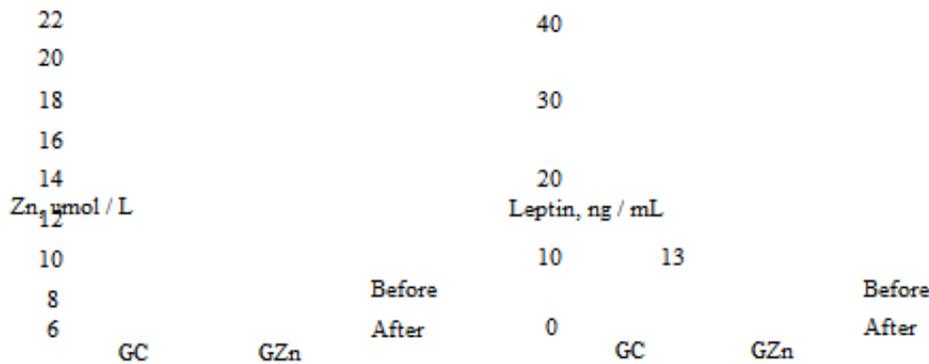
DISCUSSION

Obesity is associated with a number of abnormalities include metabolic and hormonal insulin resistance, dyslipidemia, decreased concentrations of TT, FT and SHBG. There is also evidence in animal models

Table 1. Sensitivity to insulin, leptin, androgens and biochemical profile of study groups

	Before Intervention			After Intervention		
	GZn n = 7	GC n = 7	p	GZn n = 7	GC n = 7	p
Insulin (μ U / mL)	13.0 \pm 11.0	6.7 \pm 2.8	0,091	10.5 \pm 4.9	10.1 \pm 5.5	0,805
M _i (mg / kg.min)	3.6 \pm 0.9	4.0 \pm 2.0	0,902	3.6 \pm 1.0	3.8 \pm 1.5	0,902
Glucose (mg / dL)	94.6 \pm 4.6	80.8 \pm 9.0	0,128	91.5 \pm 7.5	90.0 \pm 9.14	0,165
Total cholesterol (mg / dL)	158.8 \pm 15.4	163.9 \pm 31.7	0,165	151.4 \pm 16.7	163.2 \pm 33.1	0,128
HDL (mg / dL)	35.1 \pm 4.6	37.8 \pm 7.7	0,152	35.1 \pm 6.4	42.8 \pm 8.8	0,097
LDL (mg / dL)	91.2 \pm 13.1	109.0 \pm 43.3	0,165	91.6 \pm 16.9	99.8 \pm 41.6	0,383
Triglycerides (mg / dL)	145.5 \pm 32.2	131.7 \pm 41.2	0,710	123.4 \pm 30.2	132.5 \pm 32.1	0,620
VLDL (mg / dL)	29.1 \pm 6.4	33.4 \pm 22.2	0,902	24.6 \pm 6.0	31.4 \pm 11.1	0,259
Creatinine (mg / dL)	0.9 \pm 0.1	0.9 \pm 0.1	0,915	0.8 \pm 0.1	0.9 \pm 0.1	0,805
Uric acid (mg / dL)	6.3 \pm 0.7	6.9 \pm 1.7	0,456	6.0 \pm 0.8	6.4 \pm 0.7	0,535
Leptin (ng / mL)	16.4 \pm 7.1	17.7 \pm 6.3	0,817	20.2 \pm 7.9	18.1 \pm 5.5	0,537
TT (ng / mL)	5.2 \pm 1.5	5.1 \pm 2.5	0,620	6.0 \pm 2.1	4.5 \pm 2.6	0,128
TL (ng / mL)	9.8 \pm 2.3	6.3 \pm 2.4	0,535	12.3 \pm 4.7	5.7 \pm 2.8	0,011
SHBG (ng / mL)	23.4 \pm 11.1	37.4 \pm 6.9	0,710	26.8 \pm 12.2	33.8 \pm 11.1	0,259

M = total metabolism of glucose estimated insulin sensitivity. HDL = high density lipoprotein. LDL = Low density lipoprotein. VLDL = very low density lipoproteins. TT = total testosterone. TL = free testosterone. SHBG = sex hormone binding globulin.



other obesity-related disorders such as a decrease in concentrations of zinc. Zinc is one of the most important in nutrition and health humans, it plays an important role in a series of metabolic processes such as synthesis, storage and secretion of insulin- also plays an important role in action of leptin and androgens. Our study showed that young subjects obesity had low concentrations zinc, a finding similar to what occurs in rats induced obesity is genetic or diet. The decrease in any element trace may be due to a reduction in intake, to increased needs body or to changes in the absorption element in the presence of an adequate intake given in the diet. However, in our study, although there was a reduction of zinc obese individuals, this was not associated with changes in insulin, or the sensitivity to it.

It is known that zinc plays an important role important in the regulation of appetite and expenditure energy, such regulation could be mediated through hunger hormone called leptin. In the present study showed that after pharmacological intervention with zinc in obese, leptin increased significantly its circulating levels without have documented a change in BMI.

Further studies are required to elucidate pathophysiological pathways by which the zinc could regulate appetite and energy expenditure through of leptin.

Obesity is often present with concentrations low TT and FT and the actions of zinc modulation of androgen in man. In our study only found a trend the increase of TL with the administration of zinc, without modification of the TT. This lack of Androgens increase may be because the suppressive effect of leptin on the TT and TT^{4,23} and decreased the stimulating effect of insulin on these hormones.¹³

It should be noted that the failure to find significant changes to the administration of zinc in some of the laboratory variables studied, could be due to the size of the sample was calculated only to see results insulin sensitivity estimated with the M euglycemic-hyperinsulinemic clamp, so this should be taken as limiting the study.

In conclusion, our study showed a low serum zinc in patients young people with obesity and management zinc sulfate for one month, increased the leptin concentrations in these patients, without changing the sensitivity to insulin, nor androgens. Further studies are needed *in vitro* and *in vivo* to identify possible mechanisms of zinc to explain these findings.

Spanish. Example 3 (html)

Topical antifungal treatment

patients with chronic candidosis

mouth. Comparative Study

AUTHORS

Silvia Adriana López de Blanc (1), Nelly Salati of Mugnai (2), Fabián Libero Femopase (3), Monica Beatriz Benitez (4), Rosana Andrea Morsicato (5), Lucia Astrada of Green (6), Diana Masih (7).

- (1) Professor of Clinical Stomatology I and II B. Faculty Dentistry, National University of Cordoba. Argentina.
- (2) Professor of Pharmacology A. Faculty of Dentistry, Universidad Nacional de Córdoba.
- (3) Assistant Professor Dental Clinic I and II B. Faculty Dentistry, National University of Cordoba.
- (4) Teaching Dental Clinic I and II B. Faculty Dentistry National University of Córdoba.
- (5) Teaching Dental Clinic I and II B. Faculty Dentistry. Universidad Nacional de Córdoba.
- (6) Associate Professor, Pharmacology A. Faculty of Dentistry Universidad Nacional de Córdoba.
- (7) Professor Mycology. Biochemistry Department Clinic. Faculty of Chemistry. National University of Cordoba.

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ABSTRACT

The aim of this study was to evaluate the effect of Fenticonazole in the topical treatment of chronic candidiasis in the mouth and compare it with that of ketoconazole and nystatin.

We included eighty patients with chronic candidosis erythema, which ended the fifty-one test. Were divided into four groups to which they administered: Fenticonazole 3% 2% Fenticonazole, nistatina 100000 IU and ketoconazole 2%, respectively in orabase form. They were monitored at 7, 15, 30 and 45 days. Data were analyzed statistically with ANOVA and

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the Kruskal Wallis and Wilcoxon. There was a decrease of the injuries was highly significant in all patient groups ($p \leq 0.0001$). We analyzed the degree of remission as the location of the lesions found in all patients located in buccal mucosa commissure and reached complete remission, while tongue and palate lesions showed a significant decrease of intensity of them ($p \leq 0.00001$) with all treatments. The Fenticonazole proved so effective as nystatin and ketoconazole in the treatment to the topic of oral candidiasis.

Key words: oral candidiasis, topical treatment, fenticonazole, ketoconazole, nystatin, an antifungal effect.

INTRODUCTION

The species of the genus *Candida* are microorganisms common saprophytes in the oral cavity. *Candida albicans* is the most common pathogen of the group, the transition from commensal to pathogen, depends on changes in the ecology local microbiological, the virulence of the fungus, as well as a decrease in host resistance (1-5). The clinical features have led to numerous classifications currently the most used is an infection-related HIV which divides them into: pseudomembranous candidiasis or thrush, which is seen as plaques or yellowish cream colorish arising scraping, can settle in any surface mucosa, erythematous candidiasis, which appears as red patches on any mucosal surface-even that are more frequent in back of the tongue and palate, the lesions may occur in the mouth as opposed to injury back of the tongue where it makes contact with the palate. Angular cheilitis, which manifests itself as cracks and enrojecimiento at the corners. Two or three types of candidiasis have may appear together (6-8). Candidiasis is more frequent in the buccal mucosa (9).

Laboratory diagnosis of oral candidiasis is based in the microscopic observation of the clinical sample and cultivation and subsequent identification of the isolated yeast. 1996 Pontoon Quindós-relate the different methods can be used for identification (colorimetric enzyme matic, etc.) explaining more than 13 different types of studies ent (10).

In the last two decades there has been a substantial increase in the number of patients with oral candidiasis due special especially the indiscriminate use of antibiotics, steroids and the emergence of new diseases such as infection HIV virus (3, 8, 11). Simultaneously with this increase, have developed a wide variety of antifungal topical and / or systemic. The most frequently used agents two topically are derived polyene (nystatin and amphotericin B), imidazole (miconazole, ketoconazole, and clotrimazol) and triazole (fluconazole and itraconazole). The treatment initial treatment of choice for a first episode of candidates oral dose is a topical agent such as nonabsorbable-nis

Tatrina or clotrimazole. When this treatment failure is used zan systemic agents such as fluconazole and itraconazole, which are widely used especially in the candidate dose associated with HIV (12-15). Allylamines are a new class of fungicides, currently under study, being the third binafina an agent that can be applied topically and systemic (16-20).

In recent years the Fenticonazole, a derivative of imidazole lic synthetic has been used successfully as an agent topic (21-27). Like other azoles this inhibitory agent acts do the synthesis of ergosterol, thereby causing changes changes in the permeability of the membrane. It has also shown that destroys important cell organelles fungi such as mitochondria, lysosomes, peroxisomes, and endoplasmic reticulum, leading to cell destruction.

When analyzing the dependence of the activity azoles with pH is shown that these compounds are effective near neutral pH than acidic. This effect has been explained considering that azoles not must be protonated to be active. However Fenticonazole found that produces more inhibition to decreases the pH suggesting that there are differences in the pH / activity of azoles depending on the species or strain *candida* (3). This drug has been used in the treatment superficial mycoses such as vaginal candidiasis, dermatomycosis, seborrheic dermatitis, etc., proving to be high therapeutic efficacy and safety (21-27).

Despite the wide range of therapeutic possibilities cas, there are still difficulties in the treatment of candid- oral system due to any of the following reasons: a) the topical application requires a lengthy application with disadvantage that some drugs are unpleasant, not to- followed the acceptance and / or assistance needed from patient (28), b) systemic medication can not be used of repeated or prolonged over time, due to undesirable side effects that may occur (nausea, hepatotoxicity, etc.) (16, 17, 29), c) drug-resistance antifungal gas particularly the new oral agents as fluconazole in patients with advanced HIV infection HIV (12, 20, 30-38).

The increase in the incidence of oral candidiasis, the fungus resistance and current therapeutic limitations, us to continue to pursue the ideal medication. With this objective in this work, a clinical study to evaluate the therapeutic effect and safety of topical Fenticonazole, besides its effect was compared with that of nazol and nystatin in the treatment of chronic candidiasis cas mouth.

MATERIALS AND METHODS

In the present study included 80 patients, of which only 51 completed the trial, constitute our group study. Of these patients 26 were male and 25 female, which had two or more injuries chronic erythematous candidiasis, some also cheilitis

angle. The clinical evidence was confirmed by tests mycology: direct, cultivation and characterization of colonies.

All patients expressed their consent written, free to make abandonment of the test. The study protocol was reviewed and approved by the UNC School of Dentistry. The study was double blind at random, with the participation of four parallel groups patients. The medications used included Fenticonazole, ketoconazole and nystatin in oral adhesive for administered topically.

We excluded children, pregnant or are breastfeeding breastfeeding, diabetics, immunosuppressed patients with disabilities renal function and / or liver and those treated with medication xerostomising or antibiotics or steroids for at least two weeks prior to their inclusion, were also discarded individuals with hypersensitivity to Groups polyene or azole.

Test design:

1) Preparation of a unique history, which recorded traron the general and local predisposing factors.

2) Oral exam: The first stage was recorded following parameters to evaluate the lesions:

a-Values of erythema of the mucosa: 0: absent, 1: mild, 2: moderate and 3: severe (13, 19, 39).

b-values of atrophy of filiform papillae on the back lingual: 0: absent, 1 mild, 2 = moderate and 3: severe.

In the case of angular cheilitis is considered cracked erythema track the bottom and edges of the crack, since it is always accompanied by the same and once healed the rift, decrease- / or disappearance of erythema.

In a second step, using the above mentioned values shall be calculated on indices to standardize and achieve better control of the injuries:

- Injury Lingual Index (ILL), determined as the sum of the values of erythema and atrophy (a + b).

- Oral Lesion Index (ILO) for each patient, calculated side as the sum of the values of all injuries all locations: tongue (ILL), palate, buccal mucosa and corners.

The clinical evaluators were previously standardized two, each patient was examined by two observers, If differences in the estimation of indices was taken average.

The lesions were documented photographically before and after treatment were also diagrams to record the size and location of injuries.

3) Analysis mycological, clinical evidence was confirmation given in all cases by mycological examination. Were taken samples of the lesions of different locations with Sterile metal spatulas, to carry out extended and subsequent staining with Gram and Giemsa stains (Direct examination). For crops the material was obtained a cotton swab moistened with sterile saline.

The smears were analyzed by optical microscope identify the presence of pseudohyphae and hyphae. Tests

TABLE 1

Evolution of lesions of the palate

Group	Day 0		Day 7		Day 15		Day 30		* Day 45	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
1	1,67	0,58	0,91	0,38	0,67	0,29	0,50	0,50	0,50	0,50
2	1,25	0,76	1,08	0,49	0,67	0,26	0,46	0,78	0,50	0,77
3	3,00	0,00	2,33	0,58	1,67	1,53	0,67	0,58	1,00	1,00
4	1,50	0,50	1,40	0,55	1,10	0,55	0,50	0,50	0,40	0,42

Analysis of variance. * P < 0.00001 after 45 days of treatment in all groups. Sd: standard deviation.

were confirmed by direct crops that were made in Petri dishes containing dextrose agar, Sabouraud and chloramphenicol and incubated at 35-37 ° C for 5 days at least (40, 41). *C. albicans* was identified by testing training of germ tubes and chlamydozoospores. The other species *Candida* were typed by carbohydrate assimilation (Candifast, International Mycoplasma, France).

Patients were considered positive when observed yeast, hyphae or colonies developed at any any location. Excluding those with clinical symptoms Nicos but negative mycological examination.

4) Patients were divided randomly into four groups according to the composition of the cream used:

- Group 1 (10 patients) Fenticonazole to 3% in orabase
- Group 2 (20 patients) Fenticonazole 2% in orabase
- Group 3 (10 patients) 100000 IU nystatin in orabase
- Group 4 (11 patients), ketoconazole 2% in orabase

* INE Squib.

5) Instruction to patients so that after each food made oral hygiene techniques and implement the cream in the lesioned areas three times a day is advised patients should not eat or drink for one hour after application of medication.

6) Clinical examination of patients 0-7-15-30 and 45 days. At each visit, evaluated each of the signs and symptoms oral candidiasis registering the ILO for each patient. It controlled the acceptance and compliance with instructions observing the amount of medication remaining.

7) Suspension of medication when clinically resolved mind injuries or completed 45 days of treatment. Four days after the second test was performed mycological.

The absence of clinical lesion and mycological studies negative, determined the criteria of cure in each patient. Those who discontinued treatment was not- were considered. Adverse effects such as irritation, tion, nausea, heartburn, edema of the mucosa, etc. were che- Blocked at every visit through the interview and exam- medical men.

8) The statistical analysis was applied to the analysis of the za for repeated measures (ANOVA), nonparametric test Kruskal Wallis and Wilcoxon test for paired samples, adas. Statistical significance was set at 0.05.

RESULTS

Candida species that developed on 139 cul- positive incentives were as follows: 88% *C. albicans*, 5% *T. glabrata*, 2% *C. tropicalis*, 2% *C. guilliermondii*, 1% *C. bei- Gelli*, *C. s. sudotropicalis* 1% and 1% *C. s / p*. There were no species changes after treatment.

Statistical analysis (Kruskal Wallis test) showed that no significant differences between the injury rate of different groups at baseline ($p \leq 0.85$). It determine the degree of remission of the lesions by the local lización and analyzed the evolution of the ILO.

Evolution of lesions of the palate: Table 1 shows significant reduction in injury rate on the palate after 45 days of treatment in all groups ($p \leq 0.00001$). It was noted that there was a difference between the degree initial lesion group but not significantly. The nystatin group showed a faster decline injury rate during the first 30 days, probably because it began with an injury rate higher than the other groups.

Evolution of tongue lesions: analysis allowed determine a significant difference over time ILL in all groups ($p \leq 0.00001$) (Table 2). As in the palate, there were no significant differences between groups ($p < 0.79$). These results indicate that all workers treatments had the same effect on reducing index over time.

Evolution of buccal mucosa lesions and cheilitis: All these lesions resolved completely, you, why only compared the time required sary with the different treatments. Importantly, that only included groups 1, 2 and 4 because no All patients had lesions in these locations. It used the nonparametric test of Kruskal Wallis for analysis of variance of these data. In the buccal mucosa not significant differences between groups ($p \leq 0.12$) (Table 3). However, it is possible to observe as timed- po means to achieve complete resolution was higher in the group and the corner lesions (angular cheilitis) the Comparative analysis indicated no differences between groups ($p \leq 0.53$), however the average time for the group 1 was lower than for the others (Table 4).

TABLE 2

Evolution of lingual injury rate

Group	Day 0		Day 7		Day 15		Day 30		* Day 45	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
1	2,44	1,05	1,44	1,03	1,53	1,17	1,00	1,68	1,25	1,55
2	3,02	1,06	2,15	0,82	1,98	1,14	1,77	1,29	1,75	1,28
3	2,88	0,78	2,19	0,55	1,50	1,22	1,31	1,07	1,13	1,65
4	2,83	1,07	2,17	1,09	1,60	1,06	1,15	1,30	1,13	1,34

Analysis of Variance. * P < 0.00001. Sd: standard deviation.

TABLE 3

Time to resolution of injuries buccal mucosa

Group	* Days	
	Mean	SD
1	11,60	10,29
2	22,43	0 9,81
4	11,00	0 5,66

Kruskall Wallis method. * P < 0.12. Sd: standard deviation.

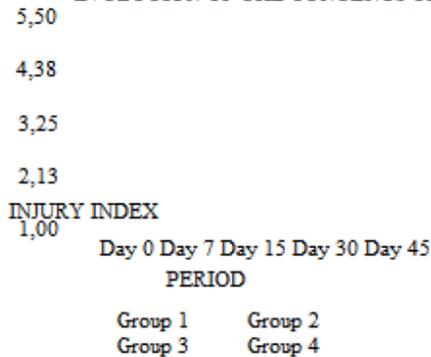
TABLE 4

Evolution of lesions commissure (time to complete resolution)

Group	* Days	
	Mean	SD
1	0 7,00	0 0,00
2	10,20	0 4,38
4	17,86	18,54

Kruskall Wallis method. * P < 0.53. Sd: standard deviation.

EVOLUTION OF THE CONTENTS OF INJURY



Evolution of the ILO: Figure 1 shows a significant decrease of the ILO with time in all groups (p ≤ 0.0001).

There were no significant differences between treatments after 45 days (p ≤ 0.85). We report the values of ILO standards IDMT curves, since not all patients had the same

index at the start of the test. The analysis showed that only 7 there was an influence of the ILO's initial value (Table 5). These indices allowed us to quantify in some way

Clinical observations on each test, which is usually useful for statistical analysis. The size of the lesion is not was used to calculate these indices, as it was considered that an injury must go to achieve healing.

We believe this method offers advantages over those used by other authors such as "improved and cured" (13, 14, 19, 45) or "0 = no lesion, 1 = localized lesions, 2 = extensive lesions (13, 19)."

DISCUSSION

By comparing the results with those of other authors-Tuvia We consider the location of the lesions. As observed is in Tables 3 and 4 to 100% of the injuries and corner buccal mucosa healed, these data are consistent with found by Budtz Jorgensen and Bertram (46) and Martin MV and et al. (45), who managed the healing of lesions commissure in patients treated locally with nystatin for fourteen days. On the other hand, Nairn (47) conducted double-blind study with nystatin, amphotericin B and plabait, in patients with angular cheilitis and deep fissures achieved complete cure in a month in ninety-three

The results of this study indicate that special *Candida* species isolated from the lesions were similar to those previously published, the most common *C. albicans* and *C. glabrata* (28, 42-44).

The clinical appearance of lesions was evaluated in each location separately using the methodology and rates

TABLE 5

Evolution of oral injury rate

Group	Day 0		Day 7		Day 15		Day 30		* Day 45	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
1	4,19	0,80	1,94	0,94	2,30	1,42	1,37	2,14	1,62	1,97
2	4,44	1,56	2,89	0,70	2,42	1,10	2,44	1,05	2,08	1,68
3	5,25	1,06	3,87	0,95	2,25	2,33	1,37	1,70	1,87	2,59
4	4,08	1,29	3,33	1,48	2,52	1,07	1,56	1,44	1,46	1,60

Analysis of Variance. * P < 0.0001. Sd: standard deviation.

percent (93%) of patients treated with active drug. Lamey PJ et al. solved a case of chronic candidiasis hyperplastic (leukoplakia and *candidiasis-candida-retrocom* (oral), treating systemically with 50 mg of fluconazole daily for eleven days (40). These authors obtained resolution of clinical and pathological lesions.

With respect to tongue lesions and palate a significant decrease over time without regardless of the antifungal employed. In addition, results of our study indicated that only 22% of patients achieved complete resolution of all lesions. Despite the significant decrease in the time of the ILO all groups ($p \leq 0.0001$). It is important to emphasize that this value is good enough considering the strict cure criterion used: studies and clinical resolution negative mycology, having taken the samples mycological analysis four days after completion of the work treatment to avoid false negatives (39).

The Fenticonazole applied locally has been well tolerated its therapeutic effect was comparable with that of other drugs widely available as nystatin and ketoconazole. While Fenticonazole has been used successfully in the treatment of vaginal mycoses and dermatomycoses (20, 21, 26), not found in the literature works that use this medication in the oral mucosa.

The comparison of our results with those of other authors have been very difficult, given the various criteria healing in the literature. We have tried to summarize them as follows:

- Resolution clinic (28, 32, 48, 49).
- Disappearance or marked improvement of erythema or of the lesions (13, 19, 41).
- Improved clinical and mycological cure (13, 19).
- clinical and mycological resolution (14).

Not only are there marked differences in the criteria healing taken, but the correlation between Clinical and mycological findings. Thus, the persistence of positive mycological studies after injury clinically cured, can be interpreted as:

- Colonization and carriage of yeasts (13, 14, 49).
- Failure to eradicate *Candida* treatment.
- microbiological relapse (14, 48, 50).

For example, Phillips et al. (19) considered response complete as disappearance of all symptoms and signs except erythema "using this criterion were the 90% complete response or marked improvement, with 53 and 60% of negative mycological studies. However, all groups they studied showed between 34 and 37% of early relapses. In 1996, Silverman et al. (28) observed that 81% of the cultures remained positive after antifungal treatment with oral ketoconazole for seven days. Also about half of patients treated by Graybill et al. (13) relapsed in 1 month after completion of treatment. The greatest therapeutic response was observed until day 15, yielding no significant differences in the values of ILO later, this leads us to ask how long ideal treatment.

Finally, we must give special consideration increasing use of azoles for systemic treatment oral candidiasis, the most common opportunistic infection of HIV positive patients. Fluconazole has been shown to greater clinical efficacy than topical agents in the treatment of oropharyngeal candidiasis and time of recurrence after the treatment (14). However, it is worrying the increase in cases resistant to fluconazole in patients who received prolonged treatment. These data suggest that the development of resistance could be prevented or delayed by treating oral candidiasis with topical agents and reserving systemic azoles for the treatment of refractory patients with oral candidiasis (20, 51).

This paper shows that when used topically Fenticonazole mind, it is able to significantly reduce ILO mind from the beginning to the day 15 of treatment, most demonstrating then a slow and gradual decrease in injuries until the end of it. It is therefore possible to conclude that this drug is as effective as nystatin and ketoconazole and that can be used in the topical treatment of the candidates oral dose.

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