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# Appendix A

**Appendix A. Search Strategy**

## Ovid MEDLINE Search Strategy

1 urolith*.mp. or exp Urolithiasis/
2 (urinary calcul* or kidney calcul* or ureteral calcul* or renal calcul* or kidney stone*).mp.
3 renal colic.mp. or exp Renal Colic/
4 hypercalciuria.mp. or exp Hypercalciuria/
5 exp Hyperoxaluria, Primary/ or exp Hyperoxaluria/ or hyperoxaluria.mp.
6 hyperuricemia.mp. or exp Hyperuricemia/
7 cystinuria.mp. or exp Cystinuria/
8 (hyperuricosuria or hypercitraturia or nephrolith*).mp.
9 (calcium stone* or calcium phosphate stone* or calcium oxalate stone* or uric acid stone* or urate stone* or cystine stone* or struvite stone*).mp.
10 or/1-9
11 limit 10 to (controlled clinical trial or meta analysis or randomized controlled trial)
12 limit 10 to systematic reviews
13 11 or 12
14 exp meta-analysis/
15 exp randomized controlled trials/ or systematic review.mp.
16 exp controlled clinical trial/
17 or/14-16
18 10 and 17
19 13 or 18
20 limit 19 to English language

## Cochrane Central Register of Controlled Trials (CENTRAL) Search Strategy

1 (urolith$ or urolithiasis):ti,ab,kw in Clinical Trials
2 urinary calcul* or kidney calcul* or ureteral calcul* or renal calcul* or kidney stone* in Clinical Trials
3 renal colic in Clinical Trials
4 hypercalciuria in Clinical Trials
5 hyperoxaluria in Clinical Trials
6 hyperuricemia in Clinical Trials
7 cystinuria in Clinical Trials
8 hyperuricosuria or hypercitraturia or nephrolith* in Clinical Trials
9 calcium stone* or calcium phosphate stone* or calcium oxalate stone* or uric acid stone* or urate stone* or cystine stone* or struvite stone* in Clinical Trials
10 urolith* or Urolithiasis in Clinical Trials
11 (1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10)

# Appendix B

## Appendix B. Excluded Studies

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# Appendix C

**Appendix C. Table 1. Evidence Table: Diet trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| Dussol 2008[1]<br><br>Location: France<br><br>Funding Source: none stated | Inclusion Criteria:<br>• idiopathic calcium stone formers, regardless of the number of stone-forming episodes they had experienced<br>• over age 18 and under 70<br><br>Exclusion Criteria:<br>• systemic disease (including primary hyperparathyroidism, sarcoidosis,vitamin D excess, bowel disease of any kind, renal tubular acidosis, primary hyperoxaluria or urinary tract infections).<br>• hereditary or acquired anatomical disorders of the kidney or the urinary drainage system, except medullary sponge kidney | N=175<br>Age (yr): 44<br>Gender (Male %): 65<br>Race/Ethnicity (%): NR<br>BMI, weight, or percent with obesity: BMI 24, weight 152 lbs<br>Previous bariatric surgery: NR<br>Chronic kidney disease: NR<br>Serum creatinine (mg/dL): 1 mg/dL<br>Estimated GFR (ml/min/1.73m$^2$): NR but creatinine clearance was 88 ml/min/1.73m$^2$<br>Solitary kidney: NR<br>History of renal transplant: NR<br>Urinary tract anatomic abnormality: NR<br><br>Pregnancy: NR<br>History of CAD: NR<br>History of DM: NR<br>History of HTN: NR | <u>Stone characteristics:</u><br>Stone type: calcium oxalate or a mixture of calcium phosphate and oxalate<br>Number of past stone episodes: NR but included patients regardless of number of past stone episodes.<br>Residual stones/ fragments: NR<br><br>Urine analysis: Hypercalciuria 38%; Hypocitraturia NR; Hyperuricosuria NR; Hyperoxaluria 0%; Mixed NR; No metabolic disorder; NR<br><br>Blood analysis: abnormalities were not stated | 1. Low animal protein diet, decrease intake of animal protein by limiting consumption of meat and fish to 3 servings per week and to not exceed 100 g/day of milk products. The target was to obtain a daily contribution of protein to energy of <13% (n=55).<br>2. High fiber diet, increase intake of fruits and vegetables and to substitute their usual cereals with whole grain dietary products in order to limit the increase in energy. The target was to obtain a 25-g/day increase in fiber intake.<br>Subjects were not instructed to exclude fruits and vegetables particularly rich in oxalate (n=60).<br>3. Controls (usual diet) (n=60)<br><br>Study dietician | 1. Allocation Concealment: adequate<br>2. Blinding: assessor<br>3. Intention to Treat Analysis: no<br>4. Withdrawals/Dropouts adequately described: yes<br><br>*Quality of harms reporting:*<br>No adverse events reported<br><br>: |

**Appendix C. Table 1. Evidence Table: Diet trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| | | | | reinforced assigned dietary recommendations during every 4 month participant phone calls.<br><br>Followup period: 48 mos<br><br>Study withdrawals (%): 58 (n=102) at month 48<br><br>Assessment of compliance and adherence to treatment: 23.3% of high fiber group, 29.1% of low animal protein group, and 15% of controls withdrew because of the assigned diet (p=NS). In high fiber group, mean fiber intake increased from 17 g/day at baseline to 27 g/day at 1 year (p<0.01 vs baseline) and 23 g/day at 4 years (p<0.01 vs baseline). Mean fiber intake in control diet group did not | |

**Appendix C. Table 1. Evidence Table: Diet trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| | | | | change during follow-up. In low protein group, mean total protein intake increased from 84 g/day at baseline (57 g/day animal protein) to 68 g/day at 1 year (38 g/day animal protein), a level that was maintained at 4 years (p<0.001 versus baseline for both total protein and animal protein). By comparison, mean total protein intake in the control diet group was 84 g/day at baseline (55 g/day animal protein) and did not change during follow-up.<br><br>Setting (e.g. medicine, urology): Nephrology clinic<br><br>Follow up biochemical measures collected: (y/n): yes | |

**Appendix C. Table 1. Evidence Table: Diet trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| Sarica 2006[2]<br><br>Location: Turkey<br><br>Funding Source: none stated | Inclusion Criteria:<br>• renal stone subjects who underwent shock wave lithotripsy 3 months prior<br>• calcium oxalate stones located in the renal pelvis without any urinary tract infection<br><br>Exclusion Criteria:<br>• other types of calculi<br>• patient with previous stone disease history with stone passage<br>• no metabolic abnormality (including hyperoxaluria, hypercalciuria, hyperuricosuria, and hyperparathyroidism) could be demonstrated, and no prior intervention | N=21 (of 45 total) stone free patients<br>Age (yr): 32(mean reported as 32 yrs)<br>Gender (Male %): 64<br>Race/Ethnicity (%): NR<br>BMI, weight, or percent with obesity: NR<br>Previous bariatric surgery: NR<br>Chronic kidney disease: NR<br>Serum creatinine (mg/dL): NR<br>Estimated GFR (ml/min/1.73m$^2$): NR<br>Solitary kidney: NR<br>History of renal transplant: NR<br>Urinary tract anatomic abnormality: NR<br><br>Pregnancy: NR<br>History of CAD: NR<br>History of DM: NR<br>History of HTN: NR | <u>Stone characteristics:</u><br>Stone type: calcium oxalate 100%<br>Number of past stone episodes: single 100%, multiple 0%<br>Residual stones/ fragments: 53% by plain abdominal X-ray (including renal tomography) and kidney sonography (n=24)<br><br>Urine analysis: Hypercalciuria 0%; Hypocitraturia NR; Hyperuricosuria 0%; Hyperoxaluria 0%; Mixed NR; No metabolic disorder 100%<br><br>Blood analysis: no metabolic disorder 100% | 1. Forced fluid to achieve urinary output of >2.5 liters (n=12 (of 25) that were stone free)<br>2. No treatment (n=9/20 that were stone free)<br><br>Followup period: 24-36 mos<br><br>Study withdrawals (%): 0<br><br>Assessment of compliance and adherence to treatment: Reported 'good compliance' in majority of participants in the intervention group<br><br>Setting (e.g. medicine, urology): none stated, authors noted to be affiliated with department of urology<br><br>Follow up biochemical measures collected: (y/n): no | 1. Allocation Concealment: unclear, not specified<br>2. Blinding: none stated<br>3. Intention to Treat Analysis: yes<br>4. Withdrawals/Dropouts adequately described: none reported<br><br>*Quality of harms reporting:*<br>No adverse events reported |

**Appendix C. Table 1. Evidence Table: Diet trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| Borghi 2002[3]<br><br>Location: Italy<br><br>Funding Source: non-industry | Inclusion Criteria:<br>• idiopathic hypercalciuria (urinary calcium excretion, >300 mg per day on an unrestricted diet<br>• recurrent formation of calcium oxalate stones (≥ 2 documented events colic episodes with expulsion of stones or radiographic evidence of retained stones)<br><br>Exclusion Criteria:<br>• presence of condition commonly associated with calcium nephro-lithiasis (e.g., primary hyperparathyroidism, primary hyperoxaluria, enteric hyperoxaluria, bowel resection, inflammatory bowel disease, renal tubular acidosis, sarcoidosis, or sponge kidney)<br>• previous visit to a stone disease center<br>• current treatment for the prevention of recurrent stones except for the advice | N=120<br>Age (yr): 45<br>Gender (Male %): 100<br>Race/Ethnicity (%): NR<br>BMI, weight, or percent with obesity: 171 lbs<br>Previous bariatric surgery: NR<br>Chronic kidney disease: NR<br>Serum creatinine (mg/dL): 1.1<br>Estimated GFR (ml/min/1.73m$^2$) NR but creatinine clearance was 126 ml/min<br>Solitary kidney: NR<br>History of renal transplant: NR<br>Urinary tract anatomic abnormality: 0%<br><br>Pregnancy: NA<br>History of CAD: NR<br>History of DM: NR<br>History of HTN: NR | <u>Stone characteristics:</u><br>Stone type: calcium oxalate 100%<br>Number of past stone episodes: Single 0%; Multiple 100%<br>Residual stones/ fragments: 27% by ultrasound and radiography<br><br>Urine analysis: Hypercalciuria100 %; Hypocitraturia NR; Hyperuricosuria NR; Hyperoxaluria 18% with “mild hyperoxaluria”; Mixed NR; No metabolic disorder 0%<br>Blood analysis: no metabolic disorder 0% | 1. Low calcium diet (<10 mmol) (n= 60)<br>2. Low protein (<93 g) and low sodium (50 mmol) diet (n=60)<br><br>Both diets included daily increases in water intake to 2-3 liters.<br><br>Followup period: 60 mos<br><br>Study withdrawals (%): 14 (n=17)<br><br>Assessment of compliance and adherence to treatment: Mean urine volume increased from 1.1 L/d at 1 year to > 2.5L/d in intervention group compared to a maximum of 1.3L/d at 1 year in the control group<br><br>Setting (e.g. medicine, urology): not stated; authors affiliated with | 1. Allocation Concealment: adequate<br>2. Blinding: none stated<br>3. Intention to Treat Analysis: yes<br>4. Withdrawals/Dropouts adequately described: none reported<br><br>*Quality of harms reporting:*<br>1. Adverse events predefined: no<br>2. Adverse events reported for all participants: yes<br>3. Number of participants with adverse events reported for each study group: yes<br>4. Number of participants with each type of adverse event reported for each study group: yes<br>5. Number of participants that withdrew/lost to followup adequately described: yes |

**Appendix C. Table 1. Evidence Table: Diet trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| | to increase water intake | | | departments of clinical sciences and internal medicine and nephrology<br><br>Follow up biochemical measures collected: (y/n): yes | |
| Di Silverio 2000[4]<br><br>Location: Italy<br><br>Funding Source: none stated | Inclusion Criteria:<br>• received ESWL for idiopathic calcium kidney stone.<br>• episodes of recurrence (3 recurrences within the last 4 years or 2 recurrences within the last 3 years).<br>• free from clinically evident residual stones or fragments<br><br>Exclusion Criteria:<br>• patients with severe diabetes, gout or urinary infections. | N=384<br>Age (yr): 39<br>Gender (Male %): 60<br>Race/Ethnicity (%): NR<br>BMI, weight, or percent with obesity: NR<br>Previous bariatric surgery: NR<br>Chronic kidney disease: NR<br>Serum creatinine (mg/dL): NR<br>Estimated GFR (ml/min/1.73m$^2$): NR<br>Solitary kidney: NR<br>History of renal transplant: NR<br>Urinary tract anatomic abnormality: NR<br><br>Pregnancy: NR<br>History of CAD: NR<br>History of DM: NR ("severe" diabetes excluded)<br>History of HTN: NR<br><br>*No data provided regarding what proportion | <u>Stone characteristics:</u><br>Stone type: calcium 100%<br>Number of past stone episodes: Single 0%; Multiple 100%<br>Residual stones/ fragments: 0% by X-ray and abdominal echographic studies<br><br>Urine analysis: Hypercalciuria NR but mean baseline calcium levels were above the thresholds defined for hypercalciuria; Hypocitraturia NR; Hyperuricosuria NR; Hyperoxaluria NR; Mixed NR; No metabolic disorder; NR | 1. "Fiuggi water'" oligo-mineral water with a calcium content of 15 mg/l, 2 liters within a 24-hour period (n=192)<br>2. tap water with a calcium content between 55 and 130 mg/l, 2 liters within a 24-hour period (n=192)<br><br>A varied diet with a mean calcium content of 600 mg/day was prescribed for all patients.<br><br>Followup period: 19 mos<br><br>Study withdrawals (%): 0<br><br>Assessment of | 1. Allocation Concealment: unclear, not specified<br>2. Blinding: none stated<br>3. Intention to Treat Analysis: yes<br>4. Withdrawals/Dropouts adequately described: none reported<br><br>*Quality of harms reporting:* No adverse events reported |

**Appendix C. Table 1. Evidence Table: Diet trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| | | of participants underwent ESWL in the prior 90 days versus more than 90 days before baseline. | Blood analysis: none stated | compliance and adherence to treatment: NR<br><br>Setting (e.g. medicine, urology): stone centers<br><br>Follow up biochemical measures collected: (y/n): yes | |
| Kocvara 1999[5]<br><br>Location: Czech Republic<br><br>Funding Source: non-industry | Inclusion Criteria:<br>• first idiopathic calcium kidney stone.<br><br>Exclusion Criteria:<br>• primary hyperpara-thyroidism<br>• primary hyperoxaluria<br>• renal tubular acidosis, with struvite, uric acid and cystine stones<br>• medullary sponge disease | N=242 (number randomized per arm unclear)<br>Age (yr): range 18-72<br>Gender (Male %): 46 (those completing trial)<br>Race/Ethnicity (%): NR<br>BMI, weight, or percent with obesity: NR<br>Previous bariatric surgery: NR<br>Chronic kidney disease: NR<br>Serum creatinine (mg/dL): NR<br>Estimated GFR (ml/min/1.73m$^2$): NR<br>Solitary kidney: NR<br>History of renal transplant: NR<br>Urinary tract anatomic abnormality: NR<br><br>Pregnancy: NR<br>History of CAD: NR | <u>Stone characteristics:</u><br>Stone type: calcium 100% (primarily oxalate and some mixed with phosphate)<br>Number of past stone episodes: single 100%, multiple 0%<br>Residual stones/ fragments: 21% by ultrasound and radiography (n=43)<br><br>Urine analysis: (Tailored diet only): Hypercalciuria 67% ; Hypocitraturia 19%; Hyperuricosuria 27%; Hyperoxaluria 18%; | Tailored diet:<br>1. Hypercalciuria: Restriction of animal proteins. Regular intake of calcium-rich food (0.75-1.0 g Ca) divided into small doses during the day<br>2. Hyperuricosuria/ hyperuricemia: Restriction of meat products to 80 g/day; 1-2 meatless days per week<br>3. Mild hyperoxaluria (up to 0.8 mmol/day): Firm restriction of oxalate-rich diet. Regular dairy intake in main meal. Lemons, increased fiber intake. | 1. Allocation Concealment: unclear, not specified<br>2. Blinding: none stated<br>3. Intention to Treat Analysis: no<br>4. Withdrawals/Dropouts adequately described: no<br><br>*Quality of harms reporting:* No adverse events reported |

**Appendix C. Table 1. Evidence Table: Diet trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| | | History of DM: NR<br>History of HTN: NR | Hypomagnesuria 9%;<br><br>Blood analysis (Tailored diet only): Hyperuricemia 10%; Hypomagnesemia 12% | 4. Magnesium deficiency: Increased fiber intake, especially bran. Regular intake of dairy products. High magnesium mineral water.<br>5. Hypocitraturia: Animal protein restriction. 1-2 lemons/day (orange juice in normal oxaluria). Increase fruit & vegetables (depending on oxaluria)<br><br><u>General diet recommendations</u> moderate intake (100–120 g) of animal proteins, restriction of oxalate-rich foods, an adequate calcium intake (0.75–1.0 g), increased fibre intake, and a moderate sodium intake.<br>(n= 94 completers)<br><br>Followup period: 36 mos | |

**Appendix C. Table 1. Evidence Table: Diet trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| | | | | Study withdrawals (%):<br>14 (n=35)<br><br>Assessment of compliance and adherence to treatment: NR<br><br>Setting (e.g. medicine, urology): department of urology<br><br>Follow up biochemical measures collected: (y/n): yes | |
| Borghi 1996[6]<br><br>Location: Italy<br><br>Funding Source: none stated | Inclusion Criteria:<br>• treatment for first idiopathic calcium kidney stone<br>• absence of other retained calculi<br>• absence of arterial hypertension or other metabolic pathology that requires regular dietary measures or drug therapy<br><br>Exclusion Criteria: none provided | N=220<br>Age (yr): 41<br>Gender (Male %): 67 (those completing trial)<br>Race/Ethnicity (%): NR<br>BMI, weight, or percent with obesity: 154 lbs<br>BMI, weight, or percent with obesity: NR<br>Previous bariatric surgery: NR<br>Chronic kidney disease: NR<br>Serum creatinine (mg/dL): NR<br>Estimated GFR (ml/min/1.73m$^2$): NR<br>Solitary kidney: NR<br>History of renal transplant: | <u>Stone characteristics:</u><br>Stone type: calcium oxalate 100%<br>Past stone episodes: single 100%, multiple 0%<br>Residual stones/ fragments: 0% by plain abdominal x-ray, renal echography, and infusion excretory urography<br><br>Urine analysis: Hypercalciuria NR; Hypocitraturia NR; | 1. Achieve urine volume >2 liters/day. Urine volume to be measured every 2 months to ensure high volume (n=110)<br>2. No treatment (n=110)<br><br>Followup period: 60 mos<br><br>Study withdrawals (%): 10 (n=21)<br><br>Assessment of compliance and adherence to | 1. Allocation Concealment: unclear, not specified<br>2. Blinding: none stated<br>3. Intention to Treat Analysis: no<br>4. Withdrawals/Dropouts adequately described: no<br><br>*Quality of harms reporting:*<br>No adverse events reported |

**Appendix C. Table 1. Evidence Table: Diet trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| | | NR<br>Urinary tract anatomic abnormality: NR<br><br>Pregnancy: NR<br>History of CAD: NR<br>History of DM: NR<br>History of HTN: NR | Hyperuricosuria NR; Hyperoxaluria NR; Mixed NR; No metabolic disorder; NR<br><br>Blood analysis: none stated | treatment: Reported that 3 participants withdrew as they did not want to comply with the diet. Also reported no difference in dietary compliance but did not give specific information<br><br>Setting (e.g. medicine, urology): stone center<br><br>Follow up biochemical measures collected: (y/n): yes | |
| Hiatt 1996[7]<br><br>Location: United States<br><br>Funding Source: non-industry | Inclusion Criteria:<br>• documented single calcium oxalate kidney stone analyzed as ≥ 65 percent calcium oxalate<br>• aged between 20-60 years<br>• abdominal radiograph (x-ray film) with negative results within the previous 6 months.<br><br>Exclusion Criteria:<br>• known metabolic | N=99<br>Age (yr): 43<br>Gender (Male %): 79<br>Race/Ethnicity (%): 77 white, 13 Asian, 5 Hispanic, 4 black<br>BMI, weight, or percent with obesity: BMI 25.5<br>Previous bariatric surgery: NR<br>Chronic kidney disease: NR<br>Serum creatinine (mg/dL): NR<br>Estimated GFR (ml/min/1.73m$^2$): NR<br>Solitary kidney: NR<br>History of renal transplant: | <u>Stone characteristics:</u><br>Stone type: calcium oxalate 100%<br>Number of past stone episodes: single 100%<br>Residual stones/ fragments: 0% by radiography<br><br>Urine analysis: Hypercalciuria 18%; Hypocitraturia NR; Hyperuricosuria NR; Hyperoxaluria | 1. Low animal protein and high fiber diet: Decrease intake of animal protein (56 to 64 gm/day) and purine containing foods (75 mg/day); increase fruits, vegetables, and whole grains; and add 1/4 cup bran/day (n= 51, 50 included in study, 1 excluded post randomization)<br>2. Standard advice | 1. Allocation Concealment: unclear, not specified<br>2. Blinding: assesor<br>3. Intention to Treat Analysis: yes<br>4. Withdrawals/Dropouts adequately described: no<br><br>*Quality of harms reporting:* No adverse events reported |

**Appendix C. Table 1. Evidence Table: Diet trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| | explanation for stone formation (e.g., renal tubular acidosis, hyperparathyroidism, acromegaly, Cushing's syndrome)<br>• chronic urosepsis, creatinine ≥1.8 mg/dl (137 unol/liter)<br>• chronic small or large bowel disease | NR<br>Urinary tract anatomic abnormality: NR<br><br>Pregnancy: NR<br>History of CAD: NR<br>History of DM: NR<br>History of HTN: NR | NR; Mixed NR; No metabolic disorder; NR<br><br>Blood analysis: none stated | instructed on fluid intake and calcium intake (n=51, 49 included in study 2 excluded post randomization)<br><br>Subjects advised to consume 2 servings of dairy products or 500 mg of calcium carbonate daily.<br><br>Followup period: 48 mos<br><br>Study withdrawals (%): 24 (n=24)<br><br>Assessment of compliance and adherence to treatment: Self reported reduction in dietary protein and purine at 6 mos in intervention group<br><br>Setting (medicine, urology): NR<br><br>Followup biochemical measures collected: (y/n): y | |

**Appendix C. Table 1. Evidence Table: Diet trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| Shuster 1992[8]<br><br>Location: United States<br><br>Funding Source: non-industry | Inclusion Criteria:<br>• male<br>• aged 18-75 years<br>• physician-confirmed urinary stone episode.<br><br>Exclusion Criteria:<br>• Soft drink consumption <160 mL daily | N=1009<br>Age (yr): 43<br>Gender (Male %): 100<br>Race/Ethnicity (%): NR<br>BMI, weight, or percent with obesity: NR<br>Previous bariatric surgery: NR<br>Chronic kidney disease: NR<br>Serum creatinine (mg/dL): NR<br>Estimated GFR (ml/min/1.73m$^2$): NR<br>Solitary kidney: NR<br>History of renal transplant: NR<br>Urinary tract anatomic abnormality: NR<br><br>Pregnancy: NR<br>History of CAD: NR<br>History of DM: NR<br>History of HTN: NR | <u>Stone characteristics:</u><br>Stone type: All stone types<br>Number of past stone episodes: single 37% ;multiple 63%<br>Residual stones/ fragments: NR<br><br>Urine analysis: Hypercalciuria NR; Hypocitraturia NR; Hyperuricosuria NR; Hyperoxaluria NR; Mixed NR; No metabolic disorder; NR<br><br>Blood analysis: none stated | 1. Intervention group: Asked to refrain from soft drinks, educated about the link between soft drink consumption and stone formation (n= 504)<br>2. No intervention (n=505)<br><br>Followup period: 36 mos<br><br>Study withdrawals (%): 7 (n=72)<br><br>Assessment of compliance and adherence to treatment: 43.1% at 6 months: defined as self reported consumption of < 680mL soda/week<br><br>Setting (e.g. medicine, urology): urology clinics<br><br>Follow up biochemical measures: (y/n): n | 1. Allocation Concealment: unclear, not specified<br>2. Blinding: controls were blinded and telephone contact was masked for the treatment group<br>3. Intention to Treat Analysis: yes<br>4. Withdrawals/Dropouts adequately described: yes<br>*Quality of harms reporting:*<br>No adverse events reported |

CAD = coronary artery disease; DM = diabetes mellitus; ESWL = extracorporeal shock wave lithotripsy; HTN = hypertension; NR = not reported; UTI = urinary tract infection

**Appendix C. Table 2. Evidence Table: Thiazide trials for recurrent nephrolithiasis**

| Study/Region / Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics/ Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| Fernández-Rodriguez, 2006[9]<br><br>Location: Spain<br><br>Funding Source: none stated | Inclusion Criteria:<br>• aged 18-65 years (male and female);<br>• more than one prior episode of calcium stones in the past 36 months, resolved after stone passage, ESWL, or surgery (endoscopic and/or open);<br>• normal renal function and morphology;<br>• absence of endocrine disease.<br><br>Exclusion Criteria: NR | N=150<br>Age (yr): NR, range 18-65<br>Gender (Male %): NR<br>Race/Ethnicity (%): NR<br>BMI: NR<br>Previous bariatric surgery (%): NR<br>Chronic kidney disease (%): 0<br>Serum creatinine (mg/dL): NR<br>Estimated GFR (ml/min/1.73m$^2$): NR<br>Solitary kidney (%): 0<br>History of renal transplant (%): 0<br>Urinary tract anatomic abnormality (%): 0<br><br>Pregnancy: NR<br>History of CAD: NR<br>History of DM: NR<br>History of HTN: NR<br><br>*No data provided regarding how many participants previously underwent ESWL and how many, if any, underwent ESWL in the prior 90 days. | Stone type: calcium oxalate 100%<br>Past stone episodes: single 0%, multiple 100%<br>Residual stones/ fragments: NR<br><br>Urine analysis:<br>Hypercalciuria 35%; hypocitraturia 15%; hyperuricosuria 4%; hyperoxaluria 2%; mixed 16%;<br>no metabolic disorder 29%<br><br>Blood analysis: NR<br><br>Diet characteristics: NR | 1. Hydrochlorothiazide 50 mg/d (n=50)<br>2. Potassium citrate 20 mEq/d + hydrochlorothiazide 50 mg/d + (n=50)<br>3. No treatment (n= 50)<br><br>Followup period: 36 months<br><br>Study withdrawals (%):<br>• Overall: 0<br>• due to adverse events: 0<br>• due to loss to follow-up: 0<br><br>Assessment of compliance and adherence to treatment: NR<br><br>Setting (e.g. medicine, urology): NR<br><br>Follow up biochemical measures collected: (y/n): yes | 1. Allocation Concealment: unclear, not specified<br>2. Blinding: not specified<br>3. Intention to Treat Analysis: yes<br>4. Withdrawals/Dropouts adequately described: none reported<br><br>*Quality of harms reporting:*<br>[No adverse event data reported]<br>1. Adverse events predefined: no<br>2. Adverse events reported for all participants:no<br>3. Number of participants with adverse events reported for each study group: no<br>4. Number of participants with each type of adverse event reported for each study group: no<br>5. Number of participants that withdrew/lost to followup adequately described: none |
| Ahlstrand, | Inclusion Criteria: | N=41 | Stone type: calcium | 1. Hydrochlorothiazide | 1. Allocation Concealment: |

**Appendix C. Table 2. Evidence Table: Thiazide trials for recurrent nephrolithiasis**

| Study/Region / Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics/ Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| 1996[10]<br><br>Location: Sweden<br><br>Funding Source: none stated | • calcium oxalate stone formers with hypercalicuria or hypomagnesium<br><br>Exclusion Criteria:<br>• none stated | Age (yr): 35<br>Gender (Male %): 83<br>Race/Ethnicity (%): NR<br>BMI: NR<br>Previous bariatric surgery (%): NR<br>Chronic kidney disease (%): NR<br>Estimated GFR (ml/min/1.73m$^2$): NR<br>Solitary kidney (%): NR<br>History of renal transplant (%): NR<br>Urinary tract anatomic abnormality (%): NR<br><br>Pregnancy: NR<br>History of CAD: NR<br>History of DM: NR<br>History of HTN: NR | oxalate 100%<br>Past stone episodes: multiple 100%<br>Residual stones/ fragments: NR<br><br>Urine analysis: Hypercalciuria 90%; hypocitraturia 0%; hyperuricosuria 0%; hyperoxaluria 0%; mixed 0%; hypomagnesuria 10%;<br>no metabolic disorder 0%<br><br>Blood analysis: NR<br><br>Diet characteristics: NR | 25 twice daily (n=17)<br>2. No treatment (n= 24)<br>(An additional 16 subjects randomized to combined hydrochloro-thiazide + Mg aspartate HCl, which isn't included in analyses since Mg aspartate HCL is ineligible treatment)<br>All patients to increase fluids and decrease oxalate intake<br><br>Followup period: mean 47 mos (up to 60)<br>• Study withdrawals (%) overall: 19 (46)<br>• due to adverse events: Thiazode, 5 (12), none in control<br>• loss to follow-up: NR<br><br>Assessment of compliance/ adherence to treatment: NR<br><br>Setting (e.g. medicine, urology): NR, authors affiliated with department of urology<br><br>Follow up biochemical measures collected: (y/n): yes | unclear, not specified<br>2. Blinding: open-label<br>3. Intention to Treat Analysis: yes<br>4. Withdrawals/Dropouts adequately described: yes<br><br>*Quality of harms reporting:*<br>1. Adverse events predefined: no<br>2. Adverse events reported for all participants: no<br>3. Number of participants with adverse events reported for each study group: no<br>4. Number of participants with each type of adverse event reported for each study group: no<br>5. Number of participants that withdrew/lost to followup adequately described: yes |
| Borghi, 1993[11] | Inclusion Criteria: | N=75 | Stone type: calcium | 1. Indapamide 2.5 mg/d | 1. Allocation Concealment: |

**Appendix C. Table 2. Evidence Table: Thiazide trials for recurrent nephrolithiasis**

| Study/Region / Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics/ Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| Location: Italy<br><br>Funding Source: non-industry (University of Parma) | • Idiopathic recurrent stone formers (pure CaOx or with less than 20% of CaP);<br>• hypercalciuric (urine Ca > 300 mg/d in men >250 mg/d in women or >4 mg/kg or Ca/creatinine >0.20 mg/dL for both);<br>• formed at least 1 stone in the previous 3 years;<br>• calculi free before treatment.<br><br>Exclusion Criteria: NR | Age (yr): 45<br>Gender (Male %): 79<br>Race/Ethnicity (%): NR<br>BMI: NR<br>Previous bariatric surgery (%): NR<br>Chronic kidney disease (%): NR<br>Serum creatinine (mg/dL): 1.0<br>Estimated GFR (ml/min/1.73m$^2$):<br>Solitary kidney (%): NR<br>History of renal transplant (%): NR<br>Urinary tract anatomic abnormality (%): NR<br><br>Pregnancy: NR<br>History of CAD: NR<br>History of DM: NR<br>History of HTN: 26.6% | oxalate 100% (stones could be all CaOx or mix of CaOx + CaP)<br>Past stone episodes: multiple 100%<br>Residual stones/ fragments: 0% on intravenous pyelography and renal echography)<br><br>Urine analysis: Hypercalciuria 100%; hypocitraturia NR ; hyperuricosuria NR; hyperoxaluria NR; mixed NR;<br>no metabolic disorder 0%<br><br>Blood analysis: Hyperuricemia NR<br><br>Diet characteristics: NR | (n=25).<br>2. Allopurinol 300 mg/d + Indapamide 2.5 mg/d (n=25).<br>3. Control (diet/increased fluid treatment) (n=25)<br><br>All groups to increase fluid intake; limit sodium, calcium, oxalate and purine intake.<br><br>Followup period: 36 mos<br>Study withdrawals (%):<br>• overall: 11 (15)<br>• due to adverse events:2(3) 0<br>• due to loss to follow-up: 0<br><br>Assessment of compliance and adherence to treatment: NR<br><br>Setting (e.g. medicine, urology): NR<br><br>Follow up biochemical measures collected: (y/n): yes | unclear, not specified<br>2. Blinding: open-label<br>3. Intention to Treat Analysis: no<br>4. Withdrawals/Dropouts adequately described: yes<br><br>*Quality of harms reporting:*<br>1. Harms predefined: no<br>2. Harms specified as ALL events collected: no<br>3. Number of participants that withdrew/lost to follow up adequately described: yes<br>4. Total number of participants affected by harms specified for each study group: yes<br>5. Number for each type of harm event specified for each study group: yes |
| Ettinger, | Inclusion Criteria: | N=124 | Stone type: calcium | 1. Chlorthalidone 25 | 1. Allocation Concealment: |

**Appendix C. Table 2. Evidence Table: Thiazide trials for recurrent nephrolithiasis**

| Study/Region / Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics/ Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| 1988[12]<br><br>Location: US<br><br>Funding Source: Industry and non-industry | • recurrent calculous disease;<br>• calculous composition exceeding 79% calcium oxalate;<br>• 2 or more calculi within the previous 5 years and at least 1 calculus within the previous 2 years.<br><br>Exclusion Criteria:<br>• secondary causes for nephrolithiasis. | Age (yr): 47<br>Gender (Male %): 88<br>Race/Ethnicity (%): white 94<br>BMI: NR<br>Previous bariatric surgery (%): NR<br>Chronic kidney disease (%): NR<br>Serum creatinine (mg/dL):<br>Estimated GFR (ml/min/1.73m$^2$): NR<br>Solitary kidney (%): NR<br>History of renal transplant (%): NR<br>Urinary tract anatomic abnormality (%): NR<br><br>Pregnancy: NR<br>History of CAD: NR<br>History of DM: NR<br>History of HTN: NR | oxalate 100% (stones could be all CaOx or mix of CaOx + CaP)<br>Past stone episodes: single 0%, multiple 100%<br>Residual stones/ fragments:47% on X-ray<br><br>Urine analysis: Hypercalciuria 36%; hypocitraturia %; NR hyperuricosuria 37%; hyperoxaluria NR; mixed <u>hypercalciuria and hyperuricosuria</u> 23%;<br><br>Blood analysis: NR<br><br>Diet characteristics: NR | mg/d (n=19)<br>2. Chlorthalidone 50 mg/d (n=23)<br>3. Magnesium hydroxide 650 mg/d (n=30)<br>4. Magnesium hydroxide 1300 mg/d (n=21)<br>5. Placebo (n=31)<br><br>All groups to drink fluid for urine output of 2L/day; restrict salt, animal protein, and high oxalate foods; increase cereal fiber; avoid vitamin C; consume ≤2 dairy servings/day.<br><br>Followup period: 36 mos<br><br>Study withdrawals (%):<br>• overall: ~32* (possibly 26)<br>• due to adverse events: unclear, range was 3.2% (placebo) to 22.6% (Chlorthalidone 25 mg). None reported for Magnesium hydroxide 650 mg<br>• due to loss to follow-up: 0<br>Setting (e.g. medicine, urology): NR<br><br>Assessment of | inadequate (medical record number)<br>2. Blinding: double, outcomes assessor<br>3. Intention to Treat Analysis: no<br>4. Withdrawals/Dropouts adequately described: yes<br><br>*Quality of harms reporting:*<br>1. Adverse events predefined: no<br>2. Adverse events reported for all participants: yes<br>3. Number of participants with adverse events reported for each study group: no<br>4. Number of participants with each type of adverse event reported for each study group: no<br>5. Number of participants that withdrew/lost to followup adequately described: yes |

**Appendix C. Table 2. Evidence Table: Thiazide trials for recurrent nephrolithiasis**

| Study/Region / Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics/ Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| | | | | compliance and adherence to treatment: Pill counts, no results reported. Approximated 13-18% of the study population dropped out due to loss of interest<br><br>Follow up biochemical measures collected: (y/n): yes<br><br>* Approximate estimate based on the percentages provided in the text by each treatment arm. Actual number of subjects not reported (and it was difficult to calculate the number of patients withdrawing due to the discrepancies between the reported percentages and the numbers in each arm that were reported). | |
| Ala-Opas, 1987[13]<br><br>Location: Finland<br><br>Funding Source: none stated | Inclusion Criteria:<br>• recurrent urinary calcium stones.<br><br>Exclusion Criteria: NR | N=73<br>Age (yr): 48<br>Gender (Male %): 82<br>Race/Ethnicity (%): NR<br>BMI: NR<br>Previous bariatric surgery (%): NR<br>Chronic kidney disease (%): NR | Stone type: calcium 100%<br>Past stone episodes: single 0%, multiple 100%<br>Residual stones/ fragments: NR<br><br>Urine analysis: | 1. Hydrochlorothiazide 50 mg twice daily for first 5 months (+ bran) (n=28)<br>2. Control (bran) (n=45)<br><br>Both groups to drink ≥2.5 L/day fluid; diet of 40 gm/d bran, low | 1. Allocation Concealment: unclear, not specified<br>2. Blinding: open-label<br>3. Intention to Treat Analysis: yes<br>4. Withdrawals/Dropouts adequately described: none reported |

**Appendix C. Table 2. Evidence Table: Thiazide trials for recurrent nephrolithiasis**

| Study/Region / Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics/ Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| | | Serum creatinine (mg/dL): NR<br>Estimated GFR (ml/min/1.73m2): NR<br>Solitary kidney (%): NR<br>History of renal transplant (%): NR<br>Urinary tract anatomic abnormality (%): NR<br><br>Pregnancy: NR<br>History of CAD: NR<br>History of DM: NR<br>History of HTN: NR | Hypercalciuria 44%; hypocitraturia 0%; hyperuricosuria 0%; hyperoxaluria 0%; mixed 0%;<br>no metabolic disorder 56%<br><br>Blood analysis: NR<br><br>Diet characteristics: NR | calcium, low oxalate.<br><br>Followup period: 24 mos<br><br>Study withdrawals (%):<br>• overall: 0<br>• due to adverse events: 0<br>• due to loss to follow-up: 0<br><br>Assessment of compliance and adherence to treatment: Self reported questionnaire on calcium intake. Results report no discontinuation of therapy<br><br>Setting (e.g. medicine, urology): NR<br><br>Follow up biochemical measures collected: (y/n): yes | *Quality of harms reporting:*<br>1. Adverse events predefined: no<br>2. Adverse events reported for all participants: no<br>3. Number of participants with adverse events reported for each study group: no<br>4. Number of participants with each type of adverse event reported for each study group: no<br>5. Number of participants that withdrew/lost to followup adequately described: none, no withdrawals |
| Laerum, 1984[14]<br><br>Location: Norway<br><br>Funding Source: Industry | Inclusion Criteria:<br>• at least 15 years of age with or without hypercalciuria (> 6 mmol/24 hr) and/or hyperuricosuria (> 3.5 mmol/24 hr); | N=50<br>Age (yr): 44<br>Gender (Male %): 76<br>Race/Ethnicity (%): NR<br>BMI: NR<br>Previous bariatric surgery (%): NR<br>Chronic kidney disease (%): NR<br>Serum creatinine | Stone type: calcium stones 100%<br>Past stone episodes: single 0%, multiple 100%<br>Residual stones/ fragments: NR<br><br>Urine analysis: Hypercalciuria 26%; | 1. Hydrochlorothiazide 25 mg twice daily + potassium chloride 1.2 gm/d (n=25)<br>2. Placebo (n=25)<br><br>Both groups to drink fluid for urine output ≥2L/day; restrict salt, calcium, oxalate and purine-rich | 1. Allocation Concealment: unclear, not specified<br>2. Blinding: double<br>3. Intention to Treat Analysis: yes<br>4. Withdrawals/Dropouts adequately described: yes<br><br>*Quality of harms reporting:*<br>1. Adverse events |

**Appendix C. Table 2. Evidence Table: Thiazide trials for recurrent nephrolithiasis**

| Study/Region / Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics/ Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| | • two or more stones totally formed if the most recent stone, associated with renal colic, had occurred during the last 2 years and was verified by X-ray examination, surgery, or stone passage.<br>Exclusion Criteria:<br>• chronic and/or active UTI;<br>• pyelographically verified urinary obstruction;<br>• uric acid and triple phosphate stones;<br>• chronic diseases such as heart congestion, cancer and sarcoidosis. | (mg/dL): NR<br>Estimated GFR (ml/min/1.73m2): NR<br>Solitary kidney (%): NR<br>History of renal transplant (%): NR<br>Urinary tract anatomic abnormality (%): NR<br><br>Pregnancy: NR<br>History of CAD: NR<br>History of DM: NR<br>History of HTN: NR | hypocitraturia NR%;<br>hyperuricosuria 24%;<br>hyperoxaluria NR%;<br>mixed NR%;<br>no metabolic disorder NR%<br><br>Blood analysis: NR<br><br>Diet characteristics: NR | foods.<br><br>Followup period: 40 mos<br><br>Study withdrawals (%):<br>• overall: 2 (4)<br>• due to adverse events: 0<br>• due to loss to follow-up: 0<br><br>Assessment of compliance and adherence to treatment: NR<br><br>Setting (e.g. medicine, urology): "general practice"<br><br>Follow up biochemical measures collected: (y/n): yes | predefined: no<br>2. Adverse events reported for all participants: yes<br>3. Number of participants with adverse events reported for each study group: yes<br>4. Number of participants with each type of adverse event reported for each study group: yes<br>5. Number of participants that withdrew/lost to followup adequately described: yes |
| Scholz, 1982[15]<br><br>Location: Germany<br><br>Funding Source: none stated (industry | Inclusion Criteria:<br>• metabolically active calcium stone formation.<br><br>Exclusion Criteria:<br>• primary hyperparathyroidi | N=51<br>Age (yr): 44<br>Gender (Male %): 61<br>Race/Ethnicity (%): NR<br>BMI: NR<br>Previous bariatric surgery (%): NR<br>Chronic kidney disease (%): NR | Stone type: calcium 100%<br>Past stone episodes: single 0%, multiple 100%<br>Residual stones/ fragments: NR<br><br>Urine analysis: | 1. Hydrochlorothiazide 25 mg twice daily (n=25)<br>2. Placebo (n=26)<br><br>"Additional potassium" given to those with K <3 mEq/L during study.<br><br>Followup period: 12 mos | 1. Allocation Concealment: unclear, not specified<br>2. Blinding: double, statistical analysis was done independently<br>3. Intention to Treat Analysis: no<br>4. Withdrawals/Dropouts adequately described: yes |

**Appendix C. Table 2. Evidence Table: Thiazide trials for recurrent nephrolithiasis**

| Study/Region / Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics/ Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| supplied thiazide and placebo) | sm. | Serum creatinine (mg/dL): NR<br>Estimated GFR (ml/min/1.73m2): NR<br>Solitary kidney (%): NR<br>History of renal transplant (%): NR<br>Urinary tract anatomic abnormality (%): NR<br><br>Pregnancy: NR<br>History of CAD: NR<br>History of DM: NR<br>History of HTN: NR | Hypercalciuria 12%; hypocitraturia NR%; hyperuricosuria NR%; hyperoxaluria 100%; mixed NR%; no metabolic disorder 0%<br><br>Blood analysis: NR<br><br>Diet characteristics: NR | Study withdrawals (%):<br>• overall: 3 (6)<br>• due to adverse events: 3 (6)<br>• due to loss to follow-up: 0<br><br>Assessment of compliance and adherence to treatment: NR<br><br>Setting (e.g. medicine, urology): NR<br><br>Follow up biochemical measures collected: (y/n): yes | *Quality of harms reporting:*<br>1. Adverse events predefined: no<br>2. Adverse events reported for all participants: yes<br>3. Number of participants with adverse events reported for each study group: yes<br>4. Number of participants with each type of adverse event reported for each study group: yes<br>5. Number of participants that withdrew/lost to followup adequately described: yes |

NR = not reported

**Appendix C. Table 3. Evidence Table: Citrate trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| Fernández-Rodriguez, 2006[9]<br><br>Location: Spain<br><br>Funding Source: NR | Inclusion Criteria:<br>• aged 18-65 years<br>• more than one prior episode of calcium stones in the past 36 months, resolved after stone passage, ESWL (time since ESWL not specified), or surgery (endoscopic and/or open);normal renal function and morphology;<br>• absence of endocrine disease.<br><br>Exclusion Criteria: NR | N=150<br>Age (yr): NR, range 18-65<br>Gender (Male %): NR<br>Race/Ethnicity (%): NR<br>BMI, weight, or percent with obesity: NR<br>Previous bariatric surgery (%): NR<br>Chronic kidney disease (%): 0<br>Serum creatinine (mg/dL): NR<br>Estimated GFR (ml/min/1.73m$^2$): NR<br>Solitary kidney (%): 0% (normal renal morphology)<br>History of renal transplant (%): 0% (normal renal function and morphology)<br>Urinary tract anatomic abnormality: 0% (normal renal morphology)<br><br>Pregnancy: NR<br>History of CAD: NR<br>History of DM: 0% (absence of endocrine disease)<br>History of HTN: NR | Stone type: calcium oxalate 100%<br>Past stone episodes: single 0%, multiple 100% (time since ESWL not reported)<br>Residual stones/ fragments: NR<br><br>Urine analysis: Hypercalciuria 35%; hypocitraturia 15%; hyperuricosuria 4%; hyperoxaluria 2%; mixed 16%; no metabolic disorder 29%<br><br>Blood analysis: NR<br><br>Diet characteristics: NR | 1. Potassium citrate 20 mEq/d + hydrochlorothiazide 50 mg/d (n=50)<br>2. Hydrochlorothiazide 50 mg/d (n=50)<br>3. No treatment (n=50)<br><br>Diet and/or fluid modification: NR<br><br>Followup period: 36 mos<br><br>Study withdrawals (%):<br>• overall: 0<br>• due to adverse events: 0<br>• due to loss to follow-up: 0<br><br>Assessment of compliance and adherence to treatment: NR<br><br>Setting (e.g. medicine, urology): NR<br><br>Follow up biochemical measures collected: | 1. Allocation Concealment: unclear, not specified<br>2. Blinding: not specified<br>3. Intention to Treat Analysis: yes<br>4. Withdrawals/Dropouts adequately described: none reported<br><br>*Quality of harms reporting: No harms data reported*<br>1. Adverse events predefined: no<br>2. Adverse events reported for all participants: no<br>3. Number of participants with adverse events reported for each study group: no<br>4. Number of participants with each type of adverse event reported for each study group: no<br>5. Number of participants that withdrew/lost to followup adequately described: no withdrawals occurred |

**Appendix C. Table 3. Evidence Table: Citrate trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| | | | | (y/n): yes | |
| Soygur, 2002[16]<br><br>Location: Turkey<br><br>Funding Source: none stated | Inclusion criteria:<br>• Patients with lower caliceal calcium oxalate stones who underwent SWL mono-therapy;<br>• stone free or with fragments <5 mm diameter on plain abdominal films and renal ultrasounds 4 weeks later;<br>• Patients with simple renal lithiasis in the presence of normal renal morphology and functions.<br><br>Exclusion criteria:<br>• UTI;<br>• anatomic abnormality of urinary tract<br>• history of urologic surgery, or urolithiasis prior to most recent stone episode;<br>• definitive metabolic disease such as hyper-parathyroidism or renal tubular acidosis. | N=110<br>Age (yr): 42 (18 to 63)<br>Gender (Male %): 67<br>Race/Ethnicity (%): NR<br>BMI, weight, or percent with obesity: NR<br>Previous bariatric surgery: NR<br>Chronic kidney disease (%): 0<br>Serum creatinine (mg/dL): NR<br>Estimated GFR (ml/min/1.73m$^2$): NR<br>Solitary kidney (%): NR<br>History of renal transplant (%): 0<br>Urinary tract anatomic abnormality (%): 0<br><br>Pregnancy: NR<br>History of CAD: NR<br>History of DM: NR<br>History of HTN: NR | Stone type: calcium oxalate 100%<br>Past stone episodes: single 100%, multiple 0%<br>Residual stones/ fragments: 38% with fragment(s) (<5 mm diameter at baseline) 4 weeks after completion of SWLby radiography (abdominal plain films) and ultrasound.<br><br>Urine analysis: Hypercalciuria 20%; hypocitraturia 38%; hyperuricosuria 18%; hyperoxaluria NR; mixed NR; no metabolic disorder NR<br><br>Blood analysis: NR<br><br>Diet characteristics: NR | 1. Potassium citrate 60 mEq/d (n=46)<br>2. Control (n=44)<br><br>Diet and/or fluid modification: Both groups to drink fluid to achieve 2.1 liters/d urine output; avoid oxalate rich and salty foods; limit meat intake; increase fiber.<br><br>Followup period: 12 mos<br><br>Study withdrawals (%):<br>• overall: 20 (18)<br>• due to adverse events: 6 (5)<br>• due to loss to follow-up: 14 (13), including 10 “noncompliance with follow-up” and 4 reluctant to take medication<br><br>Assessment of compliance and adherence to treatment: 4 patients excluded because of | 1. Allocation Concealment: unclear, not specified<br>2. Blinding: outcomes assessor<br>3. Intention to Treat Analysis: no, non-compliant patients, patients with epigastric discomfort, and patients unwilling to receive medication were excluded from analysis<br>4. Withdrawals/Dropouts adequately described: yes<br><br>*Quality of harms reporting:*<br>1. Adverse events predefined: no<br>2. Adverse events reported for all participants: no<br>3. Number of participants with adverse events reported for each study group: no<br>4. Number of participants with each type of adverse event reported for each study group: no<br>5. Number of participants that withdrew/lost to followup adequately described: yes |

**Appendix C. Table 3. Evidence Table: Citrate trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| | | | | "reluctance to receive medication" (treatment groups not reported). Compliance with citrate determined by urinary citrate and potassium reported as "good in all patients"<br><br>Setting (e.g. medicine, urology): NR<br><br>Follow up biochemical measures collected: (y/n): no | |
| Premgamone, 2001[17]<br><br>Location: Thailand<br><br>Funding Source: non-industry (Institute of Thai Traditional Medicine and Ministry of Public Health) | Inclusion Criteria:<br>• Subjects with at least 1 kidney stone ≥10 mm, serum creatinine ≤ 4 mg/dL, no heart disease.<br><br>Exclusion Criteria: NR | N=48<br>Age (yr): NR, range 20 to 60<br>Gender (Male %): 48<br>Race/Ethnicity (%): NR<br>BMI, weight, or percent with obesity: NR<br>Previous bariatric surgery (%): NR<br>Chronic kidney disease (%): NR<br>Serum creatinine (mg/dL): NR<br>Estimated GFR (ml/min/1.73m$^2$): NR<br>Solitary kidney (%): NR<br>History of renal transplant | Stone type: not stated<br>Past stone episodes: not stated<br>Residual stones/ fragments: 100% with retained stone/ fragment(s) >10mm diameter by ultrasound.<br><br>Urine analysis: Hypercalciuria NR; hypocitraturia NR; hyperuricosuria NR; hyperoxaluria NR; | 1. Sodium-potassium citrate 5-10gm/d (n=24)<br>2. *Orthosiphon grandiflorus* extract 5 g/d (n=24)<br><br>Diet and/or fluid modification: NR<br><br>Follow up period: 18 mos<br><br>Study withdrawals (%):<br>• overall: 7 (15)<br>• due to adverse | 1. Allocation Concealment: unclear, not specified<br>2. Blinding: outcomes assessor<br>3. Intention to Treat Analysis: no<br>4. Withdrawals/Dropouts adequately described: yes<br><br>*Quality of harms reporting:*<br>1. Adverse events predefined: no<br>2. Adverse events reported for all participants: yes<br>3. Number of participants with adverse events reported for each study group: yes |

**Appendix C. Table 3. Evidence Table: Citrate trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| | | (%): NR<br>Urinary tract anatomic abnormality (%): NR<br><br>Pregnancy: NR<br>History of CAD: 0% (no heart disease)<br>History of DM: NR<br>History of HTN: NR | mixed NR;<br>no metabolic disorder NR<br><br>Blood analysis: NR<br><br>Diet characteristics: NR | events: 5 (10)<br>• due to loss to follow-up: 2 (4)<br><br>Assessment of compliance and adherence to treatment: NR<br><br>Setting (e.g. medicine, urology): home and private clinic<br><br>Follow up biochemical measures collected: (y/n): yes | 4. Number of participants with each type of adverse event reported for each study group: yes<br>5. Number of participants that withdrew/lost to followup adequately described: yes |
| Ettinger, 1997[18]<br><br>Location: US<br><br>Funding Source: non-industry (US Public Health Service Research) | Inclusion criteria:<br>• Active, recurrent calculous disease;<br>• no secondary cause for nephrolithiasis;<br>• two or more calculi in last 5 years and at least 1 in last 2 years.<br><br>Exclusion criteria:<br>• obstructive uropathy;<br>• chronic urosepsis;<br>• renal failure (serum creatinine >1.8mg/dl, normal 1.5 or less);<br>• renal tubular acidosis;<br>• lithotripsy treatment | N=64<br>Age (yr): 48<br>Gender (Male %): 78<br>Race/Ethnicity (%): NR<br>BMI, weight, or percent with obesity: NR<br>Previous bariatric surgery (%): NR<br>Chronic kidney disease (%): NR<br>Serum creatinine (mg/dL): NR (≤1.8)<br>Estimated GFR (ml/min/1.73m$^2$): NR<br>Solitary kidney (%): NR<br>History of renal transplant (%): NR<br>Urinary tract anatomic | Stone type: calcium oxalate 100%<br>Past stone episodes: single 0%, multiple 100%<br>Residual stones/ fragments: 72% by X-ray.<br><br>Urine analysis: Hypercalciuria NR; hypocitraturia NR; hyperuricosuria NR; hyperoxaluria NR; mixed NR;<br>no metabolic disorder NR | 1. Potassium (42 mEq/d)-magnesium (21 mEq/d) citrate (63 mEq/d) (n=31)<br>2. Placebo (n=33)<br><br>Diet and/or fluid modification: Restricted salt, oxalate, refined sugar and animal protein. Allowed up to 2 servings/day dairy<br><br>Followup period: 37 mos | 1. Allocation Concealment: adequate<br>2. Blinding: double, outcomes assessor<br>3. Intention to Treat Analysis: yes<br>4. Withdrawals/Dropouts adequately described: yes<br><br>*Quality of harms reporting:*<br>1. Adverse events predefined: no<br>2. Adverse events reported for all participants: yes<br>3. Number of participants with adverse events reported for each study group: yes<br>4. Number of participants |

**Appendix C. Table 3. Evidence Table: Citrate trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| | within the previous 6 months. | abnormality (%): NR<br><br>Pregnancy: NR<br>History of CAD: NR<br>History of DM: NR<br>History of HTN: NR | Blood analysis: NR<br><br>Diet characteristics: NR | Study withdrawals (%):<br>• overall: 23 (36)<br>• due to adverse events: 6 (9)<br>• due to loss to follow-up: NR<br><br>Assessment of compliance and adherence to treatment: Medication compliance assessed by pill counts; diet compliance not assessed. Median compliance 86.9% for placebo and 89.0% for citrate group. >70% compliance in 73.1% of placebo group and 80.8% of citrate group.<br><br>Setting (e.g. medicine, urology): none stated<br><br>Follow up biochemical measures collected: (y/n): yes | with each type of adverse event reported for each study group: yes<br>5. Number of participants that withdrew/lost to followup adequately described: no |

**Appendix C. Table 3. Evidence Table: Citrate trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| Hofbauer, 1994[19]<br><br>Location: Austria<br><br>Funding Source: none stated | Inclusion criteria:<br>• patients with recurrent idiopathic calcium oxalate urolithiasis;<br>• at least one stone annually over the previous 3 years.<br><br>Exclusion criteria:<br>• primary hyperparathyroidism;<br>• renal tubular acidosis (type I);<br>• UTI;<br>• hypercalcemia or diseases of the gastrointestinal tract. | N=50<br>Age (yr): 55<br>Gender (Male %): 62<br>Race/Ethnicity (%): NR<br>BMI, weight, or percent with obesity: NR<br>Previous bariatric surgery (%): NR<br>Chronic kidney disease (%): NR<br>Serum creatinine (mg/dL): NR<br>Estimated GFR (ml/min/1.73m$^2$): NR<br>Solitary kidney (%): NR<br>History of renal transplant (%): NR<br>Urinary tract anatomic abnormality (%): NR<br><br>Pregnancy: NR<br>History of CAD: NR<br>History of DM: NR<br>History of HTN: NR | Stone type: calcium oxalate 100%<br>Past stone episodes: single 0%, multiple 100%<br>Residual stones/ fragments: not stated<br><br>Urine analysis: Hypercalciuria 44%; hypocitraturia 69%; hyperuricosuria NR; hyperoxaluria NR; mixed NR;<br>no metabolic disorder NR<br><br>Blood analysis: NR<br><br>Diet characteristics: NR | 1. Sodium-potassium citrate 30 gm/d initially, then adjusted to keep urine pH 7.0-7.2 (n=25)<br>2. Control (n=25)<br><br>Diet and/or fluid modification: Both groups to perform "abundant liquid intake," make unspecified diet restrictions.<br><br>Followup period: 36 mos<br><br>Study withdrawals (%):<br>• overall: 12 (24)<br>• due to adverse events: 4 (8)<br>• due to loss to follow-up: 8 (16); appeared 3 were patient refusal to regularly follow-up and 5 investigators stopped follow-up due to participant noncompliance<br><br>Assessment of compliance and | 1. Allocation Concealment: unclear, not specified<br>2. Blinding: not specified<br>3. Intention to Treat Analysis: no<br>4. Withdrawals/Dropouts adequately described: yes<br><br>*Quality of harms reporting:*<br>1. Adverse events predefined: no<br>2. Adverse events reported for all participants: no<br>3. Number of participants with adverse events reported for each study group: yes<br>4. Number of participants with each type of adverse event reported for each study group: yes<br>5. Number of participants that withdrew/lost to followup adequately described: yes |

**Appendix C. Table 3. Evidence Table: Citrate trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| | | | | adherence to treatment: Reported assessed by participant urinary pH self-monitoring. Noncompliance in 3/25 control group participants ("refused to comply with regular follow-ups" though not specified if this referred to pH monitoring, or other). "Noncompliance" in 5/25 in citrate group.<br><br>Setting (e.g. medicine, urology): NR<br><br>Follow up biochemical measures collected: (y/n): yes | |
| Barcelo, 1993[20]<br><br>Location: Spain<br><br>Funding Source: none stated | Inclusion criteria:<br>• active calcium nephrolithiasis concomitant with idiopathic hypocitraturia;<br>• moderately severe active lithiasis (≥2 stones formed during the previous 2 years | N=57<br>Age (yr): 44<br>Gender (Male %): 44<br>Race/Ethnicity (%): NR<br>BMI, weight, or percent with obesity Previous bariatric surgery (%): NR<br>Chronic kidney disease (%): NR but no renal failure<br>Serum creatinine (mg/dL): | Stone type: calcium oxalate or calcium oxalate + phosphate<br>Past stone episodes: single 0%, multiple 100%<br>Residual stones/ fragments: NR | 1. Potassium citrate scheduled 60 mEq/d, but included in analysis if took 30-60 mEq/d (n=28)<br>2. Placebo (n=29)<br><br>Diet and/or fluid modification: Both groups to increase | 1. Allocation Concealment: unclear, not specified<br>2. Blinding: double<br>3. Intention to Treat Analysis: no<br>4. Withdrawals/Dropouts adequately described: yes<br><br>*Quality of harms reporting:*<br>1. Adverse events predefined: |

**Appendix C. Table 3. Evidence Table: Citrate trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| | composed of calcium oxalate or a mixture of calcium oxalate and calcium phosphate)l<br>• low (<2 mmol/day) or low normal (<3.4 mmol/day) urinary citrate.<br><br>Exclusion criteria:<br>• 3 or more stones in same kidney, in whom stone number was difficult to quantitate;<br>• metabolic abnormalities, such as hypercalciuria, hyperuricosuria or hyperoxaluria;<br>• diabetes mellitus, renal failure, hyperkalemia, active UTI infection, gastrointestinal diseases, medication for stone disease;<br>• pregnancy or lactation | NR<br>Estimated GFR (ml/min/1.73m$^2$): NR<br>Solitary kidney (%): NR<br>History of renal transplant (%): NR<br>Urinary tract anatomic abnormality (%): NR<br><br>Pregnancy: 0%<br>History of CAD: NR<br>History of DM: 0%<br>History of HTN: NR | Urine analysis:<br>Hypercalciuria 0%; hypocitraturia 100%; hyperuricosuria 0%; hyperoxaluria 0%; mixed 0%;<br>no metabolic disorder 0%<br><br>Blood analysis: NR<br><br>Diet characteristics: NR | fluid intake to 2-3L/day, and limit sodium intake<br><br>Followup period: 36 mos<br><br>Study withdrawals (%):<br>• overall: 19 (33)<br>• due to adverse events: 3 (5)<br>• loss to follow-up: 16 (28)<br><br>Assessment of compliance and adherence to treatment: Noncompliance defined as taking fewer than 6 of 12 tablets/day due to inconvenience of dosing regimen (ascertained by interview and pill count). 8/28 noncompliant in potassium citrate group and 8/29 in placebo group.<br><br>Setting (e.g. medicine, urology): NR | no<br>2. Adverse events reported for all participants: no<br>3. Number of participants with adverse events reported for each study group: yes<br>4. Number of participants with each type of adverse event reported for each study group: yes<br>5. Number of participants that withdrew/lost to followup adequately described: yes |

**Appendix C. Table 3. Evidence Table: Citrate trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| | | | | Follow up biochemical measures collected: (y/n): yes | |

CAD = coronary artery disease; DM = diabetes mellitus; ESWL = extracorporeal shock wave lithotripsy; HTN = hypertension; NR = not reported; UTI = urinary tract infection

**Appendix C. Table 4. Evidence Table: Allopurinol trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/ Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics/ Biochemistry | Intervention/Duration | Study Quality |
|---|---|---|---|---|---|
| Borghi, 1993[11]<br><br>Location: Italy<br><br>Funding Source: non-industry (University of Parma) | Inclusion Criteria:<br>• idiopathic recurrent stone formers<br>• Stone type pure CaOx or with less than 20% of CaP,<br>• Hypercalciuria (urine Ca > 300 mg/d in men >250 mg/d in women or >4 mg/kg or Ca/creatinine >0.20 mg/dL for both)<br>• formed at least 1 stone in the previous 3 years<br>• calculi free before treatment.<br><br>Exclusion Criteria: NR | N=75<br>Age (yr): 45<br>Gender (Male %): 79<br>Race/Ethnicity (%): NR<br>Weight (mean, kg): control 74.0, Indapamide 69.1, Indapamide + Allopurinol 76.4<br>Previous bariatric surgery (%): NR<br>Chronic kidney disease (%): NR<br>Serum creatinine (mg/dL): 1.0<br>Estimated GFR (ml/min/1.73m$^2$): NR<br>Solitary kidney (%): NR<br>History of renal transplant (%): NR<br>Urinary tract anatomic abnormality (%): NR<br><br>Pregnancy: NR<br>History of CAD: NR<br>History of DM: NR<br>History of HTN: 26.6% | Stone type: <20% Calcium phosphate, remainder calcium oxalate<br>Past stone episodes: multiple 100%<br>Residual stones/ fragments: 0% on i.v. pyelpgraphy and renal USG<br><br>Urine analysis: Hypercalciuria 100%; hypocitraturia NR ; hyperuricosuria NR; hyperoxaluria NR; mixed NR;<br>no metabolic disorder 0%<br><br>Blood analysis: Hyperuricemia NR<br><br>Diet characteristics: NR | 1. Allopurinol 300 mg/d + Indapamide 2.5 mg/d (n=25).<br>2. Indapamide 2.5 mg/d (n=25).<br>3. Control (n=25)<br><br>Diet and/or fluid modification: All groups instructed to increase fluid intake; limit sodium, calcium, oxalate and purine intake.<br><br>Follow up period: 36 mos<br><br>Study withdrawals (%):<br>• overall n=11 (15%)<br>• due to adverse events 0<br>• loss to follow-up 0<br><br>Assessment of compliance and adherence to treatment: NR<br><br>Setting (e.g. medicine, urology): NR<br><br>Follow up biochemical measures collected: (y/n): Yes | 1. Allocation Concealment: unclear, not specified<br>2. Blinding: open-label, no placebo given to control group<br>3. Intention to Treat Analysis: no<br>4. Withdrawals/Dropouts adequately described: yes<br><br>*Quality of harms reporting:*<br>1. Harms predefined: No<br>2. Harms specified as ALL events collected: No<br>3. Number of participants that withdrew/lost to follow up adequately described: Yes<br>4. Total number of participants affected by harms specified for each study group: Yes<br>5. Number for each type of harm event specified for each study group: Yes |

**Appendix C. Table 4. Evidence Table: Allopurinol trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/ Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics/ Biochemistry | Intervention/Duration | Study Quality |
|---|---|---|---|---|---|
| Ettinger, 1986[21]<br><br>Location: US<br><br>Funding Source: Industry and non-industry | Inclusion Criteria:<br>• calculous composition exceeding 79% calcium oxalate<br>• recurrent calculous disease<br>• ≥2 calculi within the previous 5 years and at least 1 calculus within the previous 2 years.<br><br>Exclusion Criteria:<br>• secondary causes of nephrolithiasis (chronic UTI and obstruction, renal failure, renal acidification defects, disorders of calcium metabolism, chronic GI disorders or the use of drugs that could effect calculous disease) | N=72<br>Age (yr): 48<br>Gender (Male %): NR<br>Race/Ethnicity (%): NR<br>BMI (mean): placebo 28.1, treatment 27.4<br>Obesity (%): study stated was present "in half the subjects" without specifying treatment group<br>Previous bariatric surgery (%): NR<br>Chronic kidney disease (%): NR<br>Serum creatinine (mg/dL): NR<br>Estimated GFR (ml/min/1.73m$^2$): NR<br>Solitary kidney (%): NR<br>History of renal transplant (%): NR<br>Urinary tract anatomic abnormality (%): NR<br><br>Pregnancy (%): NR<br>History of CAD (%): NR<br>History of DM (%): NR<br>History of HTN (%): NR | Stone type: 100% of patients with stones comprised of at least 79% calcium oxalate<br>Past stone episodes: multiple 100%<br>Residual stones/ fragments: 42% Allopurinol and 52% placebo groups on abdominal X-ray<br><br>Urine analysis: Hypercalciuria 0%; hypocitraturia NR ; hyperuricosuria 100%; hyperoxaluria NR;<br>mixed NR<br>no metabolic disorder 0%<br><br>Blood analysis: Hyperuricemia NR<br><br>Diet characteristics: NR | 1. Allopurinol 300 mg/d (n=36)<br>2. Placebo (n=36)<br><br>Diet and/or fluid modification: Both groups to "increase fluid intake."<br><br>Follow up period: 24 mos<br><br>Study withdrawals (%):<br>• overall 12 (17%)<br>• due to adverse events 0<br>• due to loss to follow-up 0<br><br>Assessment of compliance and adherence to treatment:<br>By pill count, 89% for placebo, 88% for allopurinol<br><br>Setting (e.g. medicine, urology): none stated<br><br>Follow up biochemical measures collected: (y/n): yes | 1. Allocation Concealment: adequate, block randomization<br>2. Blinding: double blind<br>3. Intention to Treat Analysis: no<br>4. Withdrawals/Dropouts adequately described: yes<br><br>*Quality of harms reporting:*<br>1. Harms predefined: NR<br>2. Harms specified as ALL events collected: NR<br>3. Number of participants that withdrew/lost to follow up adequately described: yes<br>4. Total number of participants affected by harms specified for each study group: yes<br>5. Number for each type of harm event specified for each study group: yes |

**Appendix C. Table 4. Evidence Table: Allopurinol trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/ Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics/ Biochemistry | Intervention/Duration | Study Quality |
|---|---|---|---|---|---|
| Miano, 1985[22]<br><br>Location: Italy<br><br>Funding Source: none stated | Inclusion Criteria:<br>• minimum recurrence rate of 2 stone episodes per year for at least 3 years.<br><br>Exclusion Criteria:<br>• none provided. | N=30, preliminary data on 15 completing 3 years follow up.<br>Age (yr): NR<br>Gender (Male %): NR<br>Race/Ethnicity (%): NR<br>BMI, weight, or percent with obesity: NR<br>Previous bariatric surgery (%): NR<br>Chronic kidney disease (%): NR<br>Serum creatinine (mg/dL): NR<br>Estimated GFR (ml/min/1.73m$^2$): NR<br>Solitary kidney (%): NR<br>History of renal transplant (%): NR<br>Urinary tract anatomic abnormality (%): NR<br><br>Pregnancy (%): NR<br>History of CAD (%): NR<br>History of DM (%): NR<br>History of HTN (%): NR | Stone type: calcium oxalate 100%<br>Past stone episodes: multiple 100%<br>Residual stones/ fragments: NR<br><br>Urine analysis: Hypercalciuria NR; hypocitraturia NR ; hyperuricosuria NR; hyperoxaluria NR; mixed NR<br>no metabolic disorder: NR<br><br>Blood analysis: Hyperuricemia NR<br><br>Diet characteristics: NR | 1. Allopurinol 300 mg/d (n=8)<br>2. Placebo (n=7)<br><br>Data on other 15 subjects not reported<br><br>Diet and/or fluid modification: Both groups to consume ≥1500 mL water daily; limit calcium and purine intake<br><br>Follow up period: 36 mos<br><br>Study withdrawals (%): none reported (preliminary data)<br><br>Assessment of compliance and adherence to treatment: NR<br><br>Setting (e.g. medicine, urology): none stated, authors noted to be affiliated with department of urology<br><br>Follow up biochemical measures collected: (y/n): yes | 1. Allocation Concealment: unclear, not specified<br>2. Blinding: double blind<br>3. Intention to Treat Analysis: no (preliminary results)<br>4. Withdrawals/Dropouts adequately described: unclear; not stated whether any of 15 not completing 3 years followup were dropouts.<br><br>*Quality of harms reporting:*<br>1. Harms predefined: NR<br>2. Harms specified as ALL events collected: NR<br>3. Number of participants that withdrew/lost to follow up adequately described: NR<br>4. Total number of participants affected by harms specified for each study group: NR<br>5. Number for each type of harm event specified for each study group: NR |

**Appendix C. Table 4. Evidence Table: Allopurinol trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/ Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics/ Biochemistry | Intervention/Duration | Study Quality |
|---|---|---|---|---|---|
| Robertson, 1985[23]<br><br>Location: UK<br><br>Funding Source: none stated | Inclusion Criteria:<br>• recurrent idiopathic calcium stone-formers<br><br>Exclusion Criteria:<br>• secondary calcium stones, or with cystine, uric acid or infection stones during pre-treatment observation period. | N=120, preliminary data on 45 participants who first entered the trial.<br>Age (yr): NR<br>Gender (Male %): 100<br>Race/Ethnicity (%): NR<br>BMI, weight, or percent with obesity: NR<br>Previous bariatric surgery (%): NR<br>Chronic kidney disease (%): NR<br>Serum creatinine (mg/dL): NR<br>Estimated GFR (ml/min/1.73m$^2$): NR<br>Solitary kidney (%): NR<br>History of renal transplant (%): NR<br>Urinary tract anatomic abnormality (%): NR<br><br>Pregnancy (%): NR<br>History of CAD (%): NR<br>History of DM (%): NR<br>History of HTN (%): NR | Stone type: calcium oxalate 100%<br>Past stone episodes: multiple 100%<br>Residual stones/ fragments: NR<br><br>Urine analysis: Hypercalciuria NR; hypocitraturia NR ; hyperuricosuria NR; hyperoxaluria NR; mixed NR<br>no metabolic disorder: NR<br><br>Blood analysis: Hyperuricemia NR<br><br>Diet characteristics: NR | 1. Allopurinol 300 mg/d (n=12)<br>2. Control (n=9)<br>24 patients made up 2 more ineligible arms of the study<br><br>Follow up period: up to 60 mos<br><br>Study withdrawals (%): none reported (preliminary data)<br><br>Assessment of compliance and adherence to treatment: NR<br><br>Setting (e.g. medicine, urology): NR<br><br>Follow up biochemical measures collected: (y/n): NR | 1. Allocation Concealment: unclear, not specified<br>2. Blinding: not specified<br>3. Intention to Treat Analysis: no (preliminary results)<br>4. Withdrawals/Dropouts adequately described: unclear; not stated whether any of 75 not included in analyses were dropouts<br><br>*Quality of harms reporting:*<br>1. Harms predefined: NR<br>2. Harms specified as ALL events collected: NR<br>3. Number of participants that withdrew/lost to follow up adequately described: NR<br>4. Total number of participants affected by harms specified for each study group: NR<br>5. Number for each type of harm event specified for each study group: NR |
| Smith, 1977[24]<br><br>Location: US<br><br>Funding Source: none stated | Inclusion Criteria:<br>• not on uricosuric drugs<br>• had passed or had had a minimum of 4 renal calculi in the preceding 3 years, of which there must have been at least 1 crystallographic | N=132<br>Age (yr): NR<br>Gender (Male %): NR<br>Race/Ethnicity (%): NR<br>BMI, weight, or percent with obesity: NR<br>Previous bariatric surgery (%): NR<br>Chronic kidney disease (%): NR<br>Serum creatinine (mg/dL): NR | Stone type: calcium oxalate 100%<br>Past stone episodes: multiple 100%<br>Residual stones/ fragments: NR<br><br>Urine analysis: Hypercalciuria NR; hypocitraturia NR ; hyperuricosuria NR; | 1. Allopurinol (300 mg/d x 1 week, then 100 mg/d) + sodium bicarbonate as needed to keep urine pH >6.5 (n=65)<br>2. Placebo + sodium bicarbonate as needed to keep urine pH >6.5 (n=67) | Allocation Concealment: adequate (pharmacy controlled)<br>Blinding: double<br>Intention to Treat Analysis: no<br>Withdrawals/Dropouts adequately described: yes |

**Appendix C. Table 4. Evidence Table: Allopurinol trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/ Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics/ Biochemistry | Intervention/Duration | Study Quality |
|---|---|---|---|---|---|
| | analysis confirming calcium oxalate<br>• serum uric acid >6mg/dl).<br><br>Exclusion Criteria:<br>• none provided | Estimated GFR (ml/min/1.73m2): NR<br>Solitary kidney (%): NR<br>History of renal transplant (%): NR<br>Urinary tract anatomic abnormality (%): NR<br><br>Pregnancy (%): NR<br>History of CAD (%): NR<br>History of DM (%): NR<br>History of HTN (%): NR | hyperoxaluria NR; mixed NR<br>no metabolic disorder: 0%<br><br>Blood analysis:<br>Hyperuricemia 100%<br><br>Diet characteristics:<br>NR | Diet and/or fluid modification: Both groups to drink adequate fluids, given “simple diet”.<br><br>Follow up period: up to 60 mos<br><br>Study withdrawals (%):<br>• overall 40 (30%)<br>• due to adverse events<br>8 (6.1%)<br>• due to loss to follow-up 13 (9.8%)<br><br>Assessment of compliance and adherence to treatment: Number of remaining pills counted by pharmacy before refills<br><br>Setting (e.g. medicine, urology): none stated, authors noted to be affiliated with department of urology<br><br>Follow up biochemical measures collected: (y/n): NR | |

[a] Total number randomized unclear.
[b] Number randomized to each treatment group unclear.
[c] Total number of withdrawals unclear

**Appendix C. Table 5. Evidence Table: Acetohydroxamic Acid (AHA) trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/Duration | Study Quality |
|---|---|---|---|---|---|
| Griffith, 1991[25]<br><br>Location: USA<br><br>Funding Source: Government | Inclusion Criteria:<br>• presence or history of infection calculi in association with chronic, urea-splitting urinary infection that was recalcitrant to permanent eradication by antimicrobial agents;<br>• serum creatinine <2.5 mg/dL (225 µmol/L);<br>• not suitable for surgical removal of calculi and antimicrobial therapy<br><br>Exclusion Criteria: NR | N=94<br>Age (yr): 79% in age range 25-75y<br>Gender (Male %): 51<br>Race/Ethnicity (%): NR<br>Spinal cord injury: 50%<br>BMI, weight, or percent with obesity: NR<br>Previous bariatric surgery (%): NR<br>Chronic kidney disease (%): NR<br>Serum creatinine (mg/dL): NR<br>Estimated GFR (ml/min/1.73m$^2$): NR<br>Solitary kidney (%): NR<br>History of renal transplant (%): NR<br>Urinary tract anatomic abnormality (%): 64% with prior urinary diversion (ileal conduits)<br><br>Pregnancy: NR<br>History of CAD: NR<br>History of DM: NR<br>History of HTN: NR | Stone type: Struvite 100%<br>Past stone episodes: multiple 100%<br>Residual stones/ fragments: 89% by X-ray.<br>Urine analysis: Hypercalciuria NR; hypocitraturia NR; hyperuricosuria NR; hyperoxaluria NR; mixed NR; no metabolic disorder NR<br><br>Blood analysis: Hyperuricemia NR<br><br>Diet characteristics: NR | 1. AHA 15 mg/kg/d every 6-8 hours (n=45)<br><br>2. Placebo (n=49)<br><br>Other: Antibiotics were prescribed according to the physicians as clinically indicated<br><br>Follow up period: 6-32 mos<br><br>Study withdrawals (%):<br>• overall 65 (69)<br>• due to adverse events 15 (15.9)<br>• due to loss to follow-up 11 (11.7)<br><br>Assessment of compliance and adherence to treatment: Overall > 80% medication compliance as assessed by study nurse<br><br>Setting (e.g. medicine, urology): NR<br><br>Follow up biochemical measures collected: (y/n): NR | 1. Allocation Concealment: unclear, not specified<br>2. Blinding: double blind and radiologist who reviewed radiographs<br>3. Intention to Treat Analysis: yes<br>4. Withdrawals/Dropouts adequately described: yes<br><br>*Quality of harms reporting:*<br>1. Harms predefined: No<br>2. Harms specified as ALL events collected: No<br>3. Number of participants that withdrew/lost to follow up adequately described: Yes<br>4. Total number of participants affected by harms specified for each study group: Yes<br>5. Number for each type of harm event specified for each study group: Yes |

**Appendix C. Table 5. Evidence Table: Acetohydroxamic Acid (AHA) trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/Duration | Study Quality |
|---|---|---|---|---|---|
| Griffith, 1988[26]<br><br>Location: USA<br><br>Funding Source: Government | Inclusion Criteria:<br>• non-progressive spinal cord injury<br>• chronic urinary tract infection with urea-splitting organisms<br>• serum creatinine < 3 mg/dL<br>• acceptance of the logistical requirements of 3-month follow up visits for 2 years<br>• acceptance of the double-blind investigational format.<br><br>Exclusion Criteria:<br>• progressive neuropathy<br>• candidates for surgical lithotomy<br>• nonfunctioning stone-containing kidneys<br>• major coexistent medical problems; having social, economic and logistical problems that would hinder compliance and/or follow up | N=210<br>Age (yr): 49<br>Gender (Male %): 100<br>Race/Ethnicity (%): NR<br>Spinal cord injury: 100%<br>Weight (mean, kg): AHA 79.1, placebo 72.6<br>Previous bariatric surgery (%): NR<br>Chronic kidney disease (%): NR<br>Serum creatinine (mg/dL): 1.0<br>Estimated GFR (ml/min/1.73m$^2$): NR<br>Solitary kidney (%): NR<br>History of renal transplant (%): NR<br>Urinary tract anatomic abnormality (%): NR<br><br>Pregnancy: NR<br>History of CAD: NR<br>History of DM: NR<br>History of HTN: NR | Stone type: Struvite 100%<br>Past stone episodes: single NR, multiple NR<br>Residual stones/ fragments: 88% by excretory urogram.<br><br>Urine analysis: Hypercalciuria NR; hypocitraturia NR ; hyperuricosuria NR; hyperoxaluria NR; mixed NR;<br>no metabolic disorder NR<br><br>Blood analysis: Hyperuricemia NR<br><br>Diet characteristics: NR | 1. Acetohydroxamic acid 0.5-1.0 gm/d (n=121)<br><br>2. Placebo (n=89)<br><br>Follow up period: up to 24 mos<br><br>Study stated that no attempt was made to control antibiotic use during the study.<br><br>Study withdrawals (%): 103 (49)<br><br>Study withdrawals (%):<br>• AHA 62%, placebo 31%<br>• due to adverse events AHA 20%, placebo 5% (severe reactions)<br><br>• due to loss to follow-up NR<br><br>Assessment of compliance and adherence to treatment: Pill count (at least 80% of pills at previous visit), 79-91% in AHA and 84-94% in placebo group | 1. Allocation Concealment: adequate<br>2. Blinding: double and radiologist who reviewed radiographs. Results reviewed by independent monitoring body.<br>3. Intention to Treat Analysis: No<br>4. Withdrawals/Dropouts adequately described: Yes<br><br>*Quality of harms reporting:*<br>1. Harms predefined: No<br>2. Harms specified as ALL events collected: No<br>3. Number of participants that withdrew/lost to follow up adequately described: Yes<br>4. Total number of participants affected by harms specified for each study group: NR<br>5. Number for each type of harm event specified for each study group: NR |

**Appendix C. Table 5. Evidence Table: Acetohydroxamic Acid (AHA) trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/Duration | Study Quality |
|---|---|---|---|---|---|
| | | | | Setting (e.g. medicine, urology): NR<br><br>Follow up biochemical measures collected: (y/n): Yes | |
| Williams, 1984[27]<br><br>Location: USA<br><br>Funding Source: Government and non industry | Inclusion Criteria:<br>• Documented struvite nephrolithiasis concomitant with infection with a urea-splitting organism<br>• > 18 years of age<br>• serum creatinine <3mg/dL<br>• hematocrit > 25%<br>• patients on the phosphate depleting Shor regimen were continued on it<br><br>Exclusion Criteria:<br>• participants unable to understand the protocol<br>• pregnancy<br>• lactation<br>• oral contraceptive use<br>• history of varicose veins, phlebitis or pulmonary | N=39<br>Age (yr): AHA 52, placebo 44<br>Gender (Male %): 17.9<br>Race/Ethnicity (%): NR<br>BMI, weight, or percent with obesity: NR<br>Previous bariatric surgery (%): NR<br>Chronic kidney disease (%): NR<br>Serum creatinine (mg/dL): NR<br>Estimated GFR (ml/min/1.73m$^2$): NR<br>Solitary kidney (%): NR<br>History of renal transplant (%): NR<br>Urinary tract anatomic abnormality (%): AHA 20% and placebo 15.7% had supra vesical dversions (17.9% overall); AHA 5% and placebo 10% had neurogenic bladders (7.7% overall)<br><br>Pregnancy: 0%<br>History of CAD: NR<br>History of DM: NR<br>History of HTN: NR | Stone type: Struvite 100%<br>Past stone episodes: multiple 100%<br>Residual stones/ fragments: NR for all but 7 placebo patients had stones that doubled in area versus 0 for AHA patients (determined by X-ray).<br>Urine analysis: Hypercalciuria NR; hypocitraturia NR ; hyperuricosuria NR; hyperoxaluria NR; mixed NR;<br>no metabolic disorder NR<br><br>Blood analysis: Hyperuricemia NR<br><br>Diet characteristics: NR | 1. Acetohydroxamic acid 15 mg/kg/d (n= 20)<br>2. Placebo (n=19)<br>Other: Both groups treated with suppressive antibiotics throughout study.<br><br>Follow up period: overall mean 18 (up to 30 mos), mean AHA 15.8, mean placebo 19.6<br><br>Study withdrawals (%):<br>• overall 6 (15.3)<br>• due to adverse events AHA 2 (10)<br>• due to loss to follow-up NR<br><br>Assessment of compliance and adherence to treatment:<br>Assessed by pill counts and urine AHA screening; participants | 1. Allocation Concealment: adequate<br>2. Blinding: double and radiologist who reviewed radiographs<br>3. Intention to Treat Analysis: no<br>4. Withdrawals/Dropouts adequately described: yes<br><br>*Quality of harms reporting:*<br>1. Harms predefined: No<br>2. Harms specified as ALL events collected: No<br>3. Number of participants that withdrew/lost to follow up adequately described: Yes<br>4. Total number of participants affected by harms specified for each study group: Yes<br>5. Number for each type of harm event specified for each study group: Yes |

**Appendix C. Table 5. Evidence Table: Acetohydroxamic Acid (AHA) trials for recurrent nephrolithiasis**

| Study/Region/ Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics / Biochemistry | Intervention/Duration | Study Quality |
|---|---|---|---|---|---|
| | embolism. | | | determined by either measure to be taking <50% of medication were withdrawn from the study. 16% of AHA group and 5% of placebo group excluded from 7 to 10 months analysis for noncompliance, but compliance not reported over full study duration.<br><br>Setting (e.g. medicine, urology): NR<br><br>Follow up biochemical measures collected: (y/n): NR | |

**Appendix C. Table 6. Evidence Table: Magnesium trials for recurrent nephrolithiasis**

| Study/Region / Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics/ Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| Ettinger, 1988[12]<br><br>Location: US<br><br>Funding Source: Industry and non-industry | Inclusion Criteria:<br>• recurrent calculous disease;<br>• calculous composition exceeding 79% calcium oxalate;<br>• 2 or more calculi within the previous 5 years and at least 1 calculus within the previous 2 years.<br><br>Exclusion Criteria:<br>• secondary causes for nephrolithiasis. | N=124<br>Age (yr): 47<br>Gender (Male %): 88<br>Race/Ethnicity (%): white 94<br>BMI, weight, or percent with obesity: NR<br>Previous bariatric surgery (%): NR<br>Chronic kidney disease (%): NR<br>Serum creatinine (mg/dL):<br>Estimated GFR (ml/min/1.73m$^2$): NR<br>Solitary kidney (%):<br>History of renal transplant (%): NR<br>Urinary tract anatomic abnormality (%): NR<br><br>Pregnancy: NR<br>History of CAD: NR<br>History of DM: NR<br>History of HTN: NR | Stone type: calcium oxalate 100% (stones could be all CaOx or mix of CaOx + CaP)<br>Past stone episodes: single 0%, multiple 100%<br>Residual stones/ fragments: 47% on X-ray<br><br>Urine analysis:<br>Hypercalciuria 36%; hypocitraturia %; NR hyperuricosuria 37%; hyperoxaluria 0%; mixed 23%;<br>no metabolic disorder 50%<br><br>Blood analysis: NR<br><br>Diet characteristics: none stated | 1. Magnesium hydroxide 650 mg/d (n=30)<br>2. Magnesium hydroxide 1300 mg/d (n=21)<br>3. Chlorthalidone 25 mg/d (n=19)<br>4. Chlorthalidone 50 mg/d (n=23)<br>5. Placebo (n=31)<br><br>All groups to drink fluid for urine output of 2L/day; restrict salt, animal protein, and high oxalate foods; increase cereal fiber; avoid vitamin C; consume ≤2 dairy servings/day.<br><br>Followup period: 36 mos<br><br>Study withdrawals (%):<br>• overall: ~32* (possibly 26)<br>• due to adverse events: unclear, range was 3.2% (placebo) to 22.6% (Chlorthalidone 25 mg). None reported for Magnesium hydroxide 650 mg<br>• due to loss to follow-up: 0<br><br>Assessment of compliance and | 1. Allocation Concealment: adequate (identical appearing drugs))<br>2. Blinding: double, outcomes assessor<br>3. Intention to Treat Analysis: no<br>4. Withdrawals/Dropouts adequately described: yes<br><br>*Quality of harms reporting:*<br>1. Adverse events predefined: no<br>2. Adverse events reported for all participants: yes<br>3. Number of participants with adverse events reported for each study group: no<br>4. Number of participants with each type of adverse event reported for each study group: no<br>5. Number of participants that withdrew/lost to followup adequately described: yes |

**Appendix C. Table 6. Evidence Table: Magnesium trials for recurrent nephrolithiasis**

| Study/Region / Funding Source | Inclusion/Exclusion Criteria | Patient Characteristics (expressed in means unless otherwise noted) | Baseline stone characteristics/ Biochemistry | Intervention/ Duration | Study Quality |
|---|---|---|---|---|---|
| | | | | adherence to treatment: Pill counts, no results reported<br><br>Setting (e.g. medicine, urology): NR<br><br>Follow up biochemical measures collected: (y/n): yes<br><br>* Approximate estimate based on the percentages provided in the text by each treatment arm. Actual number of subjects not reported (and it was difficult to calculate the number of patients withdrawing due to the discrepancies between the reported percentages and the numbers in each arm that were reported). | |

NR = not reported

**Appendix C. Table 7. Individual Study Quality – Diet Trials**

| Study ID | Allocation concealment | Blinding | Intention to Treat Analysis | Withdrawals/ described | Study rating |
|---|---|---|---|---|---|
| Dussol 2008 | adequate | outcomes assessor | no | yes | Fair |
| Sarica 2006 | unclear* | none stated | yes | no dropouts | Fair |
| Borghi 2002 | adequate | outcomes assessor | yes | yes | Fair |
| Di Silverio 2000 | unclear* | none stated | no | no dropouts | Fair |
| Kocvara 1999 | unclear* | none stated | no | no | Fair |
| Borghi 1996 | unclear* | none stated | no | no | Fair |
| Hiatt 1996 | unclear* | outcomes assessor | yes | yes | Fair |
| Shuster 1992 | unclear* | controls and outcomes assessor | yes | yes | Fair |

*Methods of concealment not described/reported

**Appendix C. Table 8. Individual Study Quality – Pharmocological Trials**

| Study ID | Allocation concealment | Blinding | Intention to Treat Analysis | Withdrawals/ described | Study rating |
|---|---|---|---|---|---|
| ***Thiazide trials (n=7)*** | | | | | |
| Fernández-Rodriguez 2006 | unclear* | none stated | yes | no dropouts | Fair |
| Ahlstrand 1996 | unclear | open-label | yes | yes | Fair |
| Borghi 1993 | unclear | open-label | no | yes | Fair |
| Ettinger 1988 | unclear** | double, outcomes assessor | no | yes | Fair |
| Ala-Opas 1987 | unclear* | none stated | yes | no dropouts | Fair |
| Laerum 1984 | unclear* | double | yes | yes | Fair |
| Scholz 1982 | unclear* | double | no | yes | Fair |
| ***Citrate trials (n=6)*** | | | | | |
| Fernández-Rodriguez 2006 | unclear* | none stated | yes | no dropouts | Fair |
| Soygur 2002 | unclear* | outcomes assessor | no | yes | Fair |
| Premgamone, 2001 | unclear* | outcomes assessor | no | yes | Fair |
| Ettinger 1997 | adequate | double, outcomes assessor | yes | yes | Good |
| Hofbauer 1994 | unclear* | none stated | no | yes | Fair |
| Barcelo 1993 | unclear* | double | no | yes | Fair |
| ***Allopurinol trials (n=5)*** | | | | | |
| Borghi 1993 | unclear | open-label | no | yes | Fair |
| Ettinger 1986 | adequate | double, outcomes assessor | no | yes | Fair |
| Miano 1985 | unclear* | double | no† | unclear† | Fair |
| Robertson, 1985 | unclear* | none stated | no† | unclear† | Fair |
| Smith 1977 | unclear** | double | no | yes | Fair |
| ***Acetohydroxamic Acid (AHA) trials (n=3)*** | | | | | |
| Griffith 1991 | unclear* | double, outcomes assessor | yes | yes | Fair |
| Griffith 1988 | adequate | double, outcomes assessor | no | yes | Fair |
| Williams 1984 | adequate | double, outcomes assessor | no | yes | Fair |
| ***Magnesium trials (n=1)*** | | | | | |
| Ettinger 1988 | unclear** | double, outcomes assessor | no | yes | Fair |

*Methods of concealment not described/reported;
** Trial had inadequate sequence generation (assigned according to medical record number) which could have revealed assignment to investigators, but assignment may have been concealed from participants (because of identical drug and placebo appearance);
†Both studies reported preliminary results such that it was unclear whether any of randomized participants not included in analyses were dropouts.

# Appendix D

**Appendix D. Table 1. Primary stone recurrence outcomes for the diet trials**

| Study | Definition of Stone Recurrence | Symptomatic Stone Recurrence % (n/N) | | Radiographically detected Stone Recurrence % (n/N) | | Composite Stone Recurrence % (n/N) | |
|---|---|---|---|---|---|---|---|
| | | Diet | Control or Diet B | Diet | Control or Diet B | Diet | Control or Diet B |
| Dussol 2008[1] | Composite: a) symptomatic -passage of stone or stone confirmed radio-logically based on colic or hematuria *or* b) silent- appearance of a new stone or a >50% increase in size of a previously present stone on radiological or ultrasound exams. | NR | NR | NR | NR | Month 24<br>Low animal protein diet<br>34.2% (12/35)<br>High fiber diet<br>40.5% (17/42)<br>P=NS*<br>(all groups)<br><br>Month 48**<br>Low animal protein diet<br>47.8% (11/23)<br>High fiber diet<br>63.0% (17/27)<br>P=NS<br>(all groups) | Month 24<br><br>Usual diet<br>34.2% (12/35)<br><br>Month 48<br><br>47.8% (11/23) |
| Sarica 2006[2] | Radiographic: Plain abdominal X-ray (including renal tomography), kidney sonography or excretory urogram at regular intervals (3, 6, and 12 months after stone disintegration) | NR | NR | Forced fluid<br>8.3% (1/12)†<br>P<0.05 | No intervention<br>55.6% (5/9)† | NR | NR |
| Borghi 2002[3] | Composite: Passage of stone or stone identified by annual ultrasound and abdominal flat-plate examinations | NR | NR | NR | NR | Low calcium diet<br>38.3% (23/60)<br>P=0.03 | Low protein/ low sodium diet<br>20.0% (12/60) |
| Di Silverio 2000[4] | Radiographic: X-ray and abdominal echographic studies upon recruitment and thereafter every 6 months until the onset of | NR | NR | Oligomineral water, calcium 15 mg/l<br>16.7% | Tap water, calcium 55-130 mg/l<br>22.9%<br>(44/192) | NR | NR |

**Appendix D. Table 1. Primary stone recurrence outcomes for the diet trials**

| Study | Definition of Stone Recurrence | Symptomatic Stone Recurrence % (n/N) | | Radiographically detected Stone Recurrence % (n/N) | | Composite Stone Recurrence % (n/N) | |
|---|---|---|---|---|---|---|---|
| | | Diet | Control or Diet B | Diet | Control or Diet B | Diet | Control or Diet B |
| | recurrence. | | | (32/192) P=0.13 | | | |
| Kocvara 1999[5] | Composite: radiography and ultrasonography (but over half of the stones were "asymptomatic") so symptomatic passage also | NR | NR | NR | NR | Tailored diet with evaluation 6.0% (7/113) P<0.01 | General diet recommendations 19.0% (18/94) |
| Borghi 1996[6] | Composite: Passage of stone, renal colic, annual x-ray and ultrasound screening | NR | NR | NR | NR | Achieve daily urine volume >2 liters 12.1% (12/99) P=0.008 | No intervention 27.0% (27/100) |
| Hiatt 1996[7] | Composite: Passage of stone, surgical removal or annual radiological detection of previously unrecognized stone | NR | NR | NR | NR | Low animal protein and high fiber diet 24.0% (12/50) P=0.004 | Standard advice 4.0% (2/49) |
| Shuster 1992[8] | Symptomatic: Self reported stone episode, possibly confirmed by physician | Decrease soft drink consumption 33.7% (170/504) "failed" P=0.023 | No intervention 40.6% (205/505) "failed" | NR | NR | NR | NR |

*P values versus control unless noted; ** of the 39 patients with stone recurrence, 5 patients had silent recurrence; †These results are limited to the subset of subjects who were stone free after SWL. NS = not statistically significant

**Appendix D. Table 2. Primary stone recurrence outcomes for the Thiazide trials**

| Study | Definition of Stone Recurrence | Symptomatic Stone Recurrence % (n/N) | | Radiographically detected Stone Recurrence % (n/N) | | Composite Stone Recurrence % (n/N) | |
|---|---|---|---|---|---|---|---|
| | | Thiazide | Control(s) | Thiazide | Control(s) | Thiazide | Control(s) |
| Fernández-Rodriguez, 2006[9] | Composite: Passage or removal of any stone; radiologically detected new stone (plain x-ray every 6 months for 3 years). | NR | NR | NR | NR | HCTZ monotherapy 32% (16/50) P=0.02 vs. no treatment*,**;<br><br>HCTZ + citrate 30% (15/50) P=0.83 vs. HCTZ monotherapy** | no treatment 56% (28/50) |
| Ahlstrand, 1996[10] | Composite: x-ray examinations annually and "at clinical events" | NR | NR | NR | NR | 53% (9/17) P=0.04; | 86% (19/22) |
| Borghi, 1993[11] | Composite: Passage or removal of any stone; radiologically detected new stone (x-ray abdominal flat plate with renal tomograms at 6 & 12 months, then annually through 3 years). | NR | NR | NR | NR | Indapamide *monotherapy* 15.8% (3/19)* P=0.09 vs. control<br><br>Indapamide+ *allopurinol* 12.5% (3/24)* P=0.04 vs. control P=0.01 for combined Indapamide groups | 42.8% (9/21)* |
| Ettinger, 1988[12] | Composite: Passage of previously unrecognized | NR | NR | NR | NR | chlorthalidone | |

**Appendix D. Table 2. Primary stone recurrence outcomes for the Thiazide trials**

| Study | Definition of Stone Recurrence | Symptomatic Stone Recurrence % (n/N) | | Radiographically detected Stone Recurrence % (n/N) | | Composite Stone Recurrence % (n/N) | |
|---|---|---|---|---|---|---|---|
| | | Thiazide | Control(s) | Thiazide | Control(s) | Thiazide | Control(s) |
| | stone >3 months after baseline; or radiologically detected new stone or enlargement in residual fragment (annual x-ray | | | | | 25 mg/d<br>15.8% (3/19)<br>P=0.06<br>vs. placebo<br>P=0.39<br>vs. $MgOH_2$<br>650 mg<br>P=0.22<br>vs. $MgOH_2$<br>1300 mg<br><br>chlorthalidone<br>50 mg/d<br>13.0% (3/23);<br>P=0.03<br>mg vs.<br>placebo<br>P=0.25<br>vs. $MgOH_2$<br>650 mg<br>P=0.13<br>vs. $MgOH_2$<br>1300 mg<br><br>P=0.007 for combined chlorthalidone groups vs. placebo | 1. placebo<br>45.2% (14/31)<br>2. $MgOH_2$<br>650 mg/d<br>26.7% (8/30)<br>3. $MgOH_2$<br>1300 mg/d<br>33.3% (7/21) |
| Ala-Opas, 1987[13] | Composite: Passage or removal of stone; or radiologically detected new stone (x-ray every 6 months). | NR | NR | NR | NR | HCTZ normocalciuric patients<br>28.6% (4/14) | Control normocalciuric patients<br>22.2% (6/27) |

**Appendix D. Table 2. Primary stone recurrence outcomes for the Thiazide trials**

| Study | Definition of Stone Recurrence | Symptomatic Stone Recurrence % (n/N) | | Radiographically detected Stone Recurrence % (n/N) | | Composite Stone Recurrence % (n/N) | |
|---|---|---|---|---|---|---|---|
| | | Thiazide | Control(s) | Thiazide | Control(s) | Thiazide | Control(s) |
| | | | | | | P=0.71†;<br><br>hypercalciuric patients 14.3% (2/14) P=0.41†<br><br>all patients 21.4% (6/28) P=0.62† | <br><br>hypercalciuric patients 33.3% (6/18)<br><br>all patients 26.7% (12/45) |
| Laerum, 1984[14] | Composite: Passage of new stone; or radiologically detected new stone (annual plain abdominal x-ray plus pyelography and tomography in ambiguous cases). | NR | NR | NR | NR | HCTZ + KCl 21.7% (5/23)** P=0.05 | Placebo 48.0% (12/25) |
| Scholz, 1982[15] | Symptomatic: Passage of new stone. | HCTZ 24.0% (6/25) P=1.0† | Placebo 23.1% (6/26) | NR | NR | NR | NR |

***** n and/or N were calculated from data presented in the manuscript; **P values versus control unless noted; †P-value calculated from data presented in the manuscript

HCTZ = hydrochlorothiazide; HCL = hydrochloride; K = potassium; $MgOH_2$ = magnesium hydroxide; Na phos = sodium phosphate; NS = not significant;

**Appendix D. Table 3. Primary stone recurrence outcomes for the citrate trials**

| Study | Definition of Stone Recurrence | Symptomatic Stone Recurrence % (n/N) | | Radiographically detected Stone Recurrence % (n/N) | | Composite Stone Recurrence % (n/N) | |
|---|---|---|---|---|---|---|---|
| | | Citrate | Control(s) | Citrate | Control(s) | Citrate | Control(s) |
| Fernández-Rodriguez, 2006[9] | Composite: Passage or removal of any stone; radiologically detected new stone (x-ray every 6 months for 3 years). | NR | NR | NR | NR | Citrate + HCTZ 30% (15/50) P= 0.01 vs. no treatment*; P= 0.83 vs. HCTZ** | 1. no treatment 56% (28/50)<br>2. HCTZ 32% (16/50) |
| Soygur, 2002[16] | Composite: Passage of previously unrecognized stone; or any radiologically detected new stone or >2mm increase in residual fragment (ultrasound + plain abdominal x-ray at 1 year post-baseline). | NR | NR | NR | NR | stone free group 0% (0/28); P=0.004 | stone free group 28.6% (8/28) |
| Premgamone, 2001[17] | Radiologic: Percentage reduction in stone diameter per year (ultrasound every 5-7 weeks). | NR | NR | NR | NR | NR | NR |
| Ettinger, 1997[18] | Composite: Passage of previously unrecognized stone >1m after baseline; or radio-logically detected new stone or enlargement in residual fragment (annual x-ray). | NR | NR | NR | NR | 12.9% (4/31)†† P=0.001 | 63.6% (21/33)†† |
| Hofbauer, 1994[19] | Radiologic: Detection by ultrasound + x-ray every 6 months for 3 years. | NR | NR | 68.8% (11/16) | 72.7% (16/22) | NR | NR |
| Barcelo, 1993[20] | Composite: Passage of previously unrecognized stone; new stone requiring SWL or surgery; or | NR | NR | NR | NR | 27.8% (5/18) P=0.003 | 80% (16/20) |

**Appendix D. Table 3. Primary stone recurrence outcomes for the citrate trials**

| Study | Definition of Stone Recurrence | Symptomatic Stone Recurrence % (n/N) | | Radiographically detected Stone Recurrence % (n/N) | | Composite Stone Recurrence % (n/N) | |
|---|---|---|---|---|---|---|---|
| | | Citrate | Control(s) | Citrate | Control(s) | Citrate | Control(s) |
| | radiologically detected new stone (every 6 months, x-ray for 3 years). | | | | | | |

*P values versus control unless noted; ** P-value calculated from data presented in the manuscript; † Recurrence for subjects with residual stones was 55.6% (10/18) and 87.5% (14/16) for the citrate and control groups, respectively (P=0.06); †† n and/or N were calculated from data presented in the manuscript

HCTZ = hydrochlorothiazide; K = potassium; Na = sodium

**Appendix D. Table 4. Primary stone recurrence outcomes for the allopurinol trials**

| Study | Definition of Stone Recurrence | Symptomatic Stone Recurrence % (n/N) | | Radiographically detected Stone Recurrence % (n/N) | | Composite Stone Recurrence % (n/N) | |
|---|---|---|---|---|---|---|---|
| | | **Allopurinol** | **Control(s)** | **Allopurinol** | **Control(s)** | **Allopurinol** | **Control(s)** |
| Borghi, 1993 | Composite: Passage or removal of any stone; radiologically detected new stone (x-ray at 6 & 12 months, then annually through 3 years). | NR | NR | NR | NR | + *indapamide* 12.5% (3/24)* P<0.02 vs. control**; P=0.76 vs. indapamide | 1. control 42.8% (9/21)*<br>2. indapamide 15.8% (3/19)* |
| Ettinger, 1986 | Composite (Beginning 6 months post-baseline): Passage of new stone; or radiologically detected new stone or enlargement of pre-existing stone (annual x-ray). | 10.3% (3/29) | 29.0% (9/31) | 6.9% (2/29) | 6.5% (2/31) | 17.2% (5/29)† | 35.5% (11/31)† |
| Miano, 1985 | Symptomatic: Passage of new stone. | NR | NR | NR | NR | NR | NR |
| Robertson, 1985 | Symptomatic: Passage or removal of any stone. | NR | NR | NR | NR | NR | NR |
| Smith, 1977 | Composite: Passage of new stone; or radiologically detected new stone (study did not report type or frequency of imaging modality utilized). | NR | NR | NR | NR | 42.9% (21/49) P=0.01† | 69.8% (30/43) |

***** n and/or N were calculated from data presented in the manuscript;
**P values versus control unless noted;
†Results indicated here for composite of new symptomatic stones or radiographically detected stones, excluding events reported in the manuscript for stone growth.
HCTZ = hydrochlorothiazide; K = potassium; Mg = magnesium; Na phos. = sodium phosphate; NS = not significant

**Appendix D. Table 5. Primary stone recurrence outcomes for the Acetohydroxamic Acid (AHA) trials**

| Study | Definition of Stone Recurrence | Symptomatic Stone Recurrence % (n/N) | | Radiographically detected Stone Recurrence % (n/N) | | Composite Stone Recurrence % (n/N) | |
|---|---|---|---|---|---|---|---|
| | | AHA | Control(s) | AHA | Control(s) | AHA | Control(s) |
| Griffith, 1991[25] | Radiologic: X-ray. Stone growth (>25% increase in area) or new stone formation detected by x-ray at 3 and 12m, then annually) | NR | NR | 0 (0/3) who were stone free at baseline p= NS* | 28 (2/7) who were stone free at baseline | NR | NR |
| Griffith, 1988[26] | Radiologic: X-ray. Definite (>50% increase in area) or possible (10-50% increase in area) stone growth or new stone formation detected by x-ray every 3 months | NR | NR | 16.6 (2/12) who were stone free at baseline p= NS* | 15.3 (2/13) who were stone free at baseline | NR | NR |
| Williams, 1984[27] | Composite: Radiologically detected new stone or stone growth (>100% increase in area) on x-ray every 3 months or surgical intervention for stone obstruction or infection | NR | NR | 0.0 (0/18) among all patients; no separate results reported by baseline residual stone status | NR | NR | NR |

* NS not significant

**Appendix D. Table 6. Primary stone recurrence outcomes for the Magnesium trials**

| Study | Definition of Stone Recurrence | Symptomatic Stone Recurrence % (n/N) | | Radiographically detected Stone Recurrence % (n/N) | | Composite Stone Recurrence % (n/N) | |
|---|---|---|---|---|---|---|---|
| | | Magnesium | Control(s) | Magnesium | Control(s) | Magnesium | Control(s) |
| Ettinger, 1988 | Composite: Passage of previously unrecognized stone >3 months after baseline; or radiologically detected new stone or enlargement in residual fragment (annual x-ray) | NR | NR | NR | NR | 650 mg/d<br>26.7% (8/30)<br>P=0.15<br>vs. placebo;<br>P=0.39<br>vs. chlorthalidone 25 mg;<br>P=0.25<br>vs. chlorthalidone 50 mg<br><br>1300 mg/d<br>33.3% (7/21)<br>P=0.41<br>vs. placebo;<br>P=0.22<br>chlorthalidone 25 mg;<br>P=0.13<br>vs. chlorthalidone 50 mg<br><br>P=0.14 for combined groups vs. placebo | 1. placebo 45.2% (14/31)<br><br>2. chlorthalidone 25 mg<br>15.8% (3/19)<br><br>3. chlorthalidone 50 mg<br>13.0% (3/23); |

# Appendix E

**Appendix E. Table 1a. Secondary Stone recurrence outcomes for the diet trials**

| Study | Definition of Stone Recurrence* | Stone recurrence rate | | Change in stone size | | Residual or Stone fragment clearance | |
|---|---|---|---|---|---|---|---|
| | | Diet | Control or Diet B | Diet | Control or Diet B | Diet | Control or Diet B |
| Dussol 2008[1] | Composite: a) symptomatic - passage of stone or stone confirmed radio-logically based on colic or hematuria *or* b) silent- appearance of a new stone or a >50% increase in size of a previously present stone on radiological or ultrasound exams. | NR | NR | 3 patients had an increase of >50% (silent recurrence) but the authors did not report to which study arms the patients were randomized. | | NR | NR |
| Sarica 2006[2] | Radiographic: Plain abdominal X-ray (including renal tomography), kidney sonography or excretory urogram at regular intervals (3, 6, and 12 months after stone disintegration) | NR | NR | NR | NR | | |
| Borghi 2002[3] | Composite: Passage of stone or stone identified by annual ultrasound and abdominal flat-plate examinations | NR | NR | NR | NR | NR | NR |
| Di Silverio 2000[4] | Radiographic: X-ray and abdominal echographic studies upon recruitment and thereafter every 6 months until the onset of recurrence. | NR | NR | NR | NR | NR | NR |
| Kocvara 1999[5] | Composite: radiography and ultrasonography (but over half of the stones were "asymptomatic") so symptomatic passage also | NR | NR | NR | NR | NR | NR |
| Borghi 1996[6] | Composite: Passage of stone, renal colic, annual x-ray and ultrasound screening | Mean time to 1st recurrence (months) 38.7 (SD 13.2) P=0.016 | Mean time to 1st recurrence (months) 25.1 (SD 16.4) | NR | NR | NR | NR |
| Hiatt 1996[7] | Composite: Passage of stone, | 7.1 per 100 | 1.2 per 100 | | | | |

**Appendix E. Table 1a. Secondary Stone recurrence outcomes for the diet trials**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | surgical removal or annual radiological detection of previously unrecognized stone | person-years P=0.006 | person-years | NR | NR | NR | NR |
| Shuster 1992[8] | Symptomatic: Self reported stone episode, possibly confirmed by physician | NR | NR | NR | NR | NR | NR |

*Full definition in Table x; **P versus control.
NR = not reported

**Appendix E. Table 1b. Health outcomes for the diet trials**

| Study | Pain % (n/N) | | Urinary tract obstruction with acute renal failure % (n/N) | | Infection % (n/N) | | Procedure-related morbidity % (n/N) | |
|---|---|---|---|---|---|---|---|---|
| | Diet | Control or Diet B | Diet | Control or Diet B | Diet | Control or Diet B | Diet | Control or Diet B |
| Dussol 2008[1] | NR | NR | NR | NR | NR | NR | NR | NR |
| Sarica 2006[2] | NR | NR | NR | NR | NR | NR | NR | NR |
| Borghi 2002[3] | NR | NR | NR | NR | NR | NR | NR | NR |
| Di Silverio 2000[4] | NR | NR | NR | NR | NR | NR | NR | NR |
| Kocvara 1999[5] | NR | NR | NR | NR | NR | NR | NR | NR |
| Borghi 1996[6] | NR | NR | NR | NR | NR | NR | NR | NR |
| Hiatt 1996[7] | NR | NR | NR | NR | NR | NR | NR | NR |
| Shuster 1992[8] | NR | NR | NR | NR | NR | NR | NR | NR |

NR = not reported

**Appendix E. Table 1c. Health outcomes for the diet trials (continued)**

| Study | Emergency room treatment related to stone recurrence (e.g. renal colic) % (n/N) | | Hospitalizations related to stone recurrence (e.g. renal colic) % (n/N) | | Quality of life | |
|---|---|---|---|---|---|---|
| | Diet | Control or Diet B | Diet | Control or Diet B | Diet | Control or Diet B |
| Dussol 2008[1] | NR | NR | NR | NR | NR | NR |
| Sarica 2006[2] | NR | NR | NR | NR | NR | NR |
| Borghi 2002[3] | NR | NR | NR | NR | NR | NR |
| Di Silverio 2000[4] | NR | NR | NR | NR | NR | NR |
| Kocvara 1999[5] | NR | NR | NR | NR | NR | NR |
| Borghi 1996[6] | NR | NR | NR | NR | NR | NR |
| Hiatt 1996[7] | NR | NR | NR | NR | NR | NR |
| Shuster 1992[8] | NR | NR | NR | NR | NR | NR |

NR = not reported

**Appendix E. Table 2a. Secondary Stone recurrence outcomes for the Thiazide trials**

| Study | Definition of Stone Recurrence | Stone recurrence rate | | Change in stone size | | Stone fragment clearance | |
|---|---|---|---|---|---|---|---|
| | | Thiazide | Control(s) | Thiazide | Control(s) | Thiazide | Control(s) |
| Fernández-Rodriguez, 2006[9] | Composite: Passage or removal of any stone; radiologically detected new stone (plain x-ray every 6 months for 3 years). | NR | NR | NR | NR | NR | NR |
| Ahlstrand, 1996[10] | Composite: x-ray examinations annually and "at clinical events" | NR | NR | NR | NR | NR | NR |
| Borghi, 1993[11] | Composite: Passage or removal of any stone; radiologically detected new stone (x-ray abdominal falte plate with renal tomograms at 6 & 12 months, then annually through 3 years). | NR | NR | NR | NR | NR | NR |
| Ettinger, 1988[12] | Composite: Passage of previously unrecognized stone >3 months after baseline; or radiologically detected new stone or enlargement in | NR | NR | NR | NR | NR | NR |

**Appendix E. Table 2a. Secondary Stone recurrence outcomes for the Thiazide trials**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | residual fragment (annual x-ray) | | | | | | |
| Ala-Opas, 1987[13] | Composite: Passage or removal of stone; or radiologically detected new stone (x-ray every 6 months). | *Normocalciuric patients* 0.18 stones per patient year; reduction from pretreatment of 0.41 stones per patient year P<0.0005 versus pretreatment<br><br>*Hypercalciuric patients* 0.21 stones per patient year; reduction from pretreatment of 0.30 stones per patient year P<0.10 versus pretreatment | *Normocalciuric patients* 0.17 stones per patient year; reduction from pretreatment of 0.30 stones per patient year P<0.0005 versus pretreatment<br><br>*Hypercalciuric patients* 0.25 stones per patient year; reduction from pretreatment of 0.54 stones per patient year P<0.05 versus pretreatment | NR | NR | NR | NR |
| Laerum, 1984[14] | Composite: Passage of new stone; or radiologically detected new stone (annual plain abdominal x-ray plus pyelography and tomography in ambiguous cases). | NR | NR | NR | NR | NR | NR |
| Scholz, 1982[15] | Symptomatic: Passage of new stone. | NR | NR | NR | NR | NR | NR |

NR = not reported

**Appendix E. Table 2b. Health outcomes for the Thiazide trials**

| Study | Pain % (n/N) | | Urinary tract obstruction with acute renal failure % (n/N) | | Infection % (n/N) | | Procedure-related morbidity % (n/N) | |
|---|---|---|---|---|---|---|---|---|
| | Thiazide | Control(s) | Thiazide | Control(s) | Thiazide | Control(s) | Thiazide | Control(s) |
| Fernández-Rodriguez, 2006[9] | NR | NR | NR | NR | NR | NR | NR | NR |
| Ahlstrand, 1996[10] | NR | NR | NR | NR | NR | NR | NR | NR |
| Borghi, 1993[11] | NR | NR | NR | NR | NR | NR | NR | NR |
| Ettinger, 1988[12] | NR | NR | NR | NR | NR | NR | NR | NR |
| Ala-Opas, 1987[13] | NR | NR | NR | NR | NR | NR | NR | NR |
| Laerum, 1984[14] | NR | NR | NR | NR | NR | NR | NR | NR |
| Scholz, 1982[15] | NR | NR | NR | NR | NR | NR | NR | NR |

NR = not reported

**Appendix E. Table 2c. Health outcomes for the Thiazide trials (continued)**

| Study | Emergency room treatment related to stone recurrence (e.g. renal colic) % (n/N) | | Hospitalizations related to stone recurrence (e.g. renal colic) % (n/N) | | Quality of life | |
|---|---|---|---|---|---|---|
| | Thiazide | Control(s) | Thiazide | Control(s) | Thiazide | Control(s) |
| Fernández-Rodriguez, 2006[9] | NR | NR | NR | NR | NR | NR |
| Borghi, 1993[11] | NR | NR | NR | NR | NR | NR |
| Ettinger, 1988[12] | NR | NR | NR | NR | NR | NR |
| Ala-Opas, 1987[13] | NR | NR | NR | NR | NR | NR |
| Laerum, 1984[14] | NR | NR | NR | NR | NR | NR |
| Scholz, 1982[15] | NR | NR | NR | NR | NR | NR |

NR = not reported

**Appendix E. Table 3a. Secondary Stone recurrence outcomes for the Citrate trials**

| Study | Definition of Stone Recurrence | Stone recurrence rate | | Change in stone size | | Stone fragment clearance | |
|---|---|---|---|---|---|---|---|
| | | Citrate | Control(s) | Citrate | Control(s) | Citrate | Control(s) |
| Fernández-Rodriguez, 2006[9] | Composite: Passage or removal of any stone; radiologically detected new stone (x-ray every 6 months for 3 years). | NR | NR | NR | NR | NR | NR |
| Soygur, 2002[16] | Composite: Passage of previously unrecognized stone; or any radiologically detected new stone or >2mm increase in residual fragment (ultrasound + plain abdominal x-ray at 1 year post-baseline). | NR | NR | NR | NR | NR | NR |
| Premgamone, 2001[17] | Radiologic: Percentage reduction in stone diameter per year (ultrasound every 5-7 weeks). | NR | NR | 38.5% diameter reduction per year at 18 months P*=NS | 40.9% diameter reduction per year at 18 months | NR | NR |
| Ettinger, 1997[18] | Composite: Passage of previously unrecognized stone >1m after baseline; or radio-logically detected new stone or enlargement in residual fragment (annual x-ray). | NR | NR | NR | NR | NR | NR |
| Hofbauer, 1994[19] | Radiologic: Detection by ultrasound + x-ray every 6 months for 3 years. | 0.7 stones per patient year P=0.65* | 0.9 stones per patient year | NR | NR | NR | NR |
| Barcelo, | Composite: Passage of | 0.1 stones | 1.1 stones per | | | | |

**Appendix E. Table 3a. Secondary Stone recurrence outcomes for the Citrate trials**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 1993[20] | previously unrecognized stone; new stone requiring SWL or surgery; or radiologically detected new stone (every 6 months, x-ray for 3 years). | per patient year ($p<0.001$) | patient year | NR | NR | NR | NR |

*P versus control
HCTZ = hydrochlorothiazide NS = not significant

**Appendix E. Table 3b. Health outcomes for the Citrate trials**

| Study | Pain % (n/N) | | Urinary tract infection with acute renal failure % (n/N) | | Infection % (n/N) | | Procedure-related morbidity % (n/N) | |
|---|---|---|---|---|---|---|---|---|
| | Citrate | Control(s) | Citrate | Control(s) | Citrate | Control(s) | Citrate | Control(s) |
| Fernández-Rodriguez, 2006[9] | NR | NR | NR | NR | NR | NR | NR | NR |
| Soygur, 2002[16] | NR | NR | NR | NR | NR | NR | NR | NR |
| Premgamone, 2001[17] | NR | NR | NR | NR | NR | NR | NR | NR |
| Ettinger, 1997[18] | NR | NR | NR | NR | NR | NR | NR | NR |
| Hofbauer, 1994[19] | 9 of 16 (56%) subjects reported spontaneous stone elimination to be painless P=0.001* | 1 of 22 (4%) subjects reported spontaneous stone elimination to be painless | NR | NR | NR | NR | NR | NR |
| Barcelo, 1993[20] | NR | NR | NR | NR | NR | NR | NR | NR |

*versus control

**Appendix E. Table 3c. Health outcomes for the Citrate trials (continued)**

| Study | Emergency treatment related to stone recurrence (e.g. renal colic) % (n/N) | | Hospitalizations related to stone recurrence (e.g. renal colic) % (n/N) | | Quality of life | |
|---|---|---|---|---|---|---|
| | Citrate | Control(s) | Citrate | Control(s) | Citrate | Control(s) |
| Fernández-Rodriguez, 2006[9] | NR | NR | NR | NR | NR | NR |
| Soygur, 2002[16] | NR | NR | NR | NR | NR | NR |
| Premgamone, 2001[17] | NR | NR | NR | NR | NR | NR |
| Ettinger, 1997[18] | NR | NR | NR | NR | NR | NR |
| Hofbauer, 1994[19] | NR | NR | NR | NR | NR | NR |
| Barcelo, 1993[20] | NR | NR | NR | NR | NR | NR |

**Appendix E. Table 4a. Secondary Stone recurrence outcomes for the Allopurinol trials**

| Study | Definition of Stone Recurrence | Stone recurrence rate | | Change in stone size | | Stone fragment clearance | |
|---|---|---|---|---|---|---|---|
| | | Allopurinol | Control(s) | Allopurinol | Control(s) | Allopurinol | Control(s) |
| Borghi, 1993[11] | Composite: Passage or removal of any stone; radiologically detected new stone (x-ray at 6 & 12 months, then annually through 3 years). | NR | NR | NR | NR | NR | NR |
| Ettinger, 1986[21] | Composite (Beginning 6 months post-baseline): Passage of new stone; or radiologically detected new stone or enlargement of pre-existing stone (annual x-ray). | *0.12 stones per patient year;<br><br>*Mean time to first recurrence 33.3 months<br><br>p not reported for stones per patient year; p for time to recurrence <0.05 vs. control | *0.26 stones per patient year;<br><br>*Mean time to first recurrence 27.4 months | 13.8% (4/29) | 22.6% (7/31) | NR | NR |
| Miano, 1985[22] | Symptomatic: Passage of new stone. | 0.96 stones per patient year;<br><br>Mean percent reduction in passed stones 72.2% compared to before treatment<br><br>p not reported for stones per patient year; p =NS for percent reduction in passed stones | 0.66 stones per patient year;<br><br>Mean percent reduction in passed stones 63.2% | NR | NR | NR | NR |

**Appendix E. Table 4a. Secondary Stone recurrence outcomes for the Allopurinol trials**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | vs. placebo | | | | | |
| Robertson, 1985[23] | Symptomatic: Passage or removal of any stone. | 0.54 stones per patient year<br><br>no p values provided | 0.58 stones per patient year | NR | NR | NR | NR |
| Smith, 1977[24] | Composite: Passage of new stone; or radiologically detected new stone (study did not report type or frequency of imaging modality utilized | NR | NR | NR | NR | NR | NR |

*Rate reported only for composite stone recurrence outcome that includes symptomatic and radiographic recurrences as well as incidences of stone growth.
HCTZ = hydrochlorothiazide; NS = not significant

**Appendix E. Table 4b. Health outcomes for the Allopurinol trials**

| Study | Pain % (n/N) | | Urinary tract obstruction with acute renal failure % (n/N) | | Infection % (n/N) | | Procedure-related morbidity % (n/N) | |
|---|---|---|---|---|---|---|---|---|
| | Allopurinol | Control(s) | Allopurinol | Control(s) | Allopurinol | Control(s) | Allopurinol | Control(s) |
| Borghi, 1993[11] | NR | NR | NR | NR | NR | NR | NR | NR |
| Ettinger, 1986[21] | NR | NR | NR | NR | NR | NR | NR | NR |
| Miano, 1985[22] | NR | NR | NR | NR | NR | NR | NR | NR |
| Robertson, 1985[23] | NR | NR | NR | NR | NR | NR | NR | NR |
| Smith, 1977[24] | NR | NR | NR | NR | NR | NR | NR | NR |

**Appendix E. Table 4c. Health outcomes for the Allopurinol trials (continued)**

| Study | Emergency room treatment related to stone recurrence (e.g. renal colic) % (n/N) | | Hospitalizations related to stone recurrence (e.g. renal colic) % (n/N) | | Quality of life | | Other? % (n/N) | |
|---|---|---|---|---|---|---|---|---|
| | Allopurinol | Control(s) | Allopurinol | Control(s) | Allopurinol | Control(s) | Allopurinol | Control(s) |
| Borghi, 1993[11] | NR | NR | NR | NR | NR | NR | NR | NR |
| Ettinger, 1986[21] | NR | NR | NR | NR | NR | NR | NR | NR |
| Miano, 1985[22] | NR | NR | NR | NR | NR | NR | NR | NR |
| Robertson, 1985[23] | NR | NR | NR | NR | NR | NR | NR | NR |
| Smith, 1977[24] | NR | NR | NR | 2.9 (2/67) | NR | NR | NR | NR |

**Appendix E. Table 5a. Secondary Stone recurrence outcomes for the Acetohydroxamic acid (AHA) trials**

| Study | Definition of Stone Recurrence | Stone recurrence rate | | Change in stone size | | Stone fragment clearance | |
|---|---|---|---|---|---|---|---|
| | | AHA | Control(s) | AHA | Control(s) | AHA | Control(s) |
| Griffith, 1991[25] | Radiologic: X-ray. Stone growth (>25% increase in area) or new stone formation detected by abdominal radiographs at 3 and 12m, then annually) | NR | NR | 19.0% (8/42) stone growth* P < 0.05 | 50.0% (21/42) stone growth* | NR | NR |
| Griffith, 1988[26] | Radiologic: X-ray. Definite (>50% increase in area) or possible (10-50% increase in area) stone growth or new stone formation detected by abdominal radiographs every 3 months | NR | NR | 33.3% (14/42) definite or possible stone growth at 1 yr* p=0.017<br><br>41.7% (10/24) definite or possible stone growth at 2 yrs* p=0.26 | 60.5% (26/43) definite or possible stone growth at 1 yr*<br><br>60.0% (21/35) definite or possible stone growth at 2 yrs* | 2.7 (3/109) at 1yr<br><br>3.7 (4/106) at 2yrs<br><br>P=NS at both time intervals | 3.9 (3/76) at 1yr<br><br>1.7 (1/75) at 2yrs |
| Williams, 1984[27] | Composite: Radiologically detected new stone or stone growth (>100% increase in area by planimetry) on x-ray every 3 months or surgical intervention for stone obstruction or infection | NR | NR | 0% (0/18) stone area doubling† P=0.008 | 39% (7/19) stone area doubling† | NR | NR |

*Study reported these results for subset of participants with residual stones at baseline
†Study reported results for all participants, without providing separate results for participants with residual stones at baseline.
NS = not significant

**Appendix E. Table 5b. Health outcomes for the Acetohydroxamic acid trials**

| Study | Pain % (n/N) | | Urinary tract obstruction with acute renal failure % (n/N) | | Infection % (n/N) | | Procedure-related morbidity % (n/N) | |
|---|---|---|---|---|---|---|---|---|
| | AHA | Control | AHA | Control | AHA | Control | AHA | Control |
| Griffith, 1991[25] | NR | NR | NR | NR | NR | NR | NR | NR |
| Griffith, 1988[26] | NR | NR | NR | NR | NR | NR | NR | NR |
| Williams, 1984[27] | NR | NR | NR* | NR* | All patients had UTI at start of the study | All patients had UTI at start of the study | NR | NR |

UTI = urinary tract infection
*Two patients in placebo group and none in the AHA group were stated to have undergone surgery for obstruction or infection.

**Appendix E. Table 5c. Health outcomes for the Acetohydroxamic acid trials (continued)**

| Study | Emergency room treatment related to stone recurrence (e.g. renal colic) % (n/N) | | Hospitalizations related to stone recurrence (e.g. renal colic) % (n/N) | | Quality of life | | Other? % (n/N) | |
|---|---|---|---|---|---|---|---|---|
| | AHA | Control | AHA | Control | AHA | Control | AHA | Control |
| Griffith, 1991[25] | NR | NR | NR | NR | NR | NR | NR | NR |
| Griffith, 1988[26] | NR | NR | NR | NR | NR | NR | NR | NR |
| Williams, 1984[27] | NR | NR | NR | NR | NR | NR | NR | NR |

**Appendix E. Table 6a. Secondary Stone recurrence outcomes for the Magnesium trials**

| Study | Definition of Stone Recurrence* | Stone recurrence rate | | Change in stone size | | Stone fragment clearance | |
|---|---|---|---|---|---|---|---|
| | | Magnesium | Control(s) | Magnesium | Control(s) | Magnesium | Control(s) |
| Ettinger, 1988[12] | Composite: Passage of previously unrecognized stone >3 months after baseline; or radiologically detected new stone or enlargement in residual fragment (annual x-ray) | NR | NR | NR | NR | NR | NR |

*Full definition in Table x;

**Appendix E. Table 6b. Health outcomes for the Magnesium trials**

| Study | Pain % (n/N) | | Urinary tract obstruction with acute renal failure % (n/N) | | Infection % (n/N) | | Procedure-related morbidity % (n/N) | |
|---|---|---|---|---|---|---|---|---|
| | Magnesium | Control(s) | Magnesium | Control(s) | Magnesium | Control(s) | Magnesium | Control(s) |
| Ettinger, 1988[12] | NR | NR | NR | NR | NR | NR | NR | NR |

**Appendix E. Table 6c. Health outcomes for the Magnesium trials (continued)**

| Study | Emergency room treatment related to stone recurrence (e.g. renal colic) % (n/N) | | Hospitalizations related to stone recurrence (e.g. renal colic) % (n/N) | | Quality of life | | Other? % (n/N) | |
|---|---|---|---|---|---|---|---|---|
| | Magnesium | Control(s) | Magnesium | Control(s) | Magnesium | Control(s) | Magnesium | Control(s) |
| Ettinger, 1988[12] | NR | NR | NR | NR | NR | NR | NR | NR |

# Appendix F

**Appendix F. Table 1. Summary of study baseline characteristics for Diet studies**

| **Characteristic** | **Mean (range)** ***Unless otherwise noted*** | **Number of trials reporting** |
|---|---|---|
| Total number of patients evaluated | 2270 (45 to 1009) | 8 |
| Study withdrawals, % of patients | 12 (0 to 58) | 8 |
| Age of subjects, years | 42 (32 to 45) | 7 [a,b,c,d,f,g,h] |
| Gender, male, % of patients | 80 (46 to 100) | 8 |
| Race/ethnicity, white, % of patients | 77 | 1 [g] |
| Weight, pounds | 157.3 (152 to 171) | 3 [a,c,f] |
| Body mass index, kg/m2 | 24.5 (24 to 25.5) | 2 [a,g] |
| Creatinine, mg/dL | 1.0 (1.0 to 1.1) | 2 [a,c] |
| Creatinine clearance | 88 ml/min/1.73m$^2$ to 126 ml/min | 2 [a,c] |
| Stone type, calcium oxalate stones, % of patients (n/N) | 20 (460/2270) | 4 [b,c,f,g] * |
| Stone type, “mixed calcium or other stones,” % of patients (n/N) | 80 (1810/2270) | 4 [a,d,e,h] |
| Multiple past stones, % of patients (n/N) | 54 (1140/2095) | 3 [c,d,h] ** |
| Single past stone, % of patients (n/N) | 46 (955/2095) | 5 [b,e,f,g,h] † |
| Residual stones at baseline, % of patients | 21 [e], 4 trials with 0 [c,d,f,g] | |
| Hypercalciuria at baseline, % of patients | 18 [g], 38 [a], 100 [c], 1 trial with 0 [b], 1 trial with 67 reported only for intervention group [e] | |
| Hypocitraturia at baseline, % of patients | 1 trial with 19 reported only for intervention group [e] | |
| Hyperuricosuria at baseline, % of patients | 1 trial with 27 reported only for intervention group [e], 1 trial with 0 [b] | |
| Hyperoxaluria at baseline, % of patients | 18 [c], 1 trial with 18 reported only for intervention group [e], 2 trials with 0 [a,b] | |
| Hypomagnesuria at baseline, % of patients | 9 | 1 trial reported only intervention group [e] |
| Mixed at baseline, % of patients | 2 trials with 0 [c,d] | |
| No metabolic disorder at baseline (% of patients) | 100 [b], 4 trials with 0 [a,c,e,g] | |

**Appendix F. Table 1. Summary of study baseline characteristics for Diet studies**

| **Characteristic** | **Mean (range)** ***Unless otherwise noted*** | **Number of trials reporting** |
|---|---|---|
| Randomized to low animal protein diet, % of patients (n/N) | 2 (55/2235††) | 1 [a] |
| Randomized to high fiber diet, % of patients (n/N) | 3 (60/2235) | 1 [a] |
| Randomized to low animal protein/high fiber diet, % of patients (n/N) | 2 (50/2235) | 1 [g] |
| Randomized to low protein/low sodium diet, % of patients (n/N) | 3 (60/2235) | 1 [c] |
| Randomized to low calcium diet, % of patients (n/N) | 3 (60/2235) | 1 [c] |
| Randomized to "tailored" diet, % of patients (n/N) | 5 (113/2235) | 1 [e] |
| Randomized to increased fluid or urine output, % of patients (n/N) | 23 (506/2235) | 3 [b,d,f] |
| Randomized to decreased soft drink consumption, % of patients (n/N) | 22 (504/2235) | 1 [h] |
| Randomized to no treatment/usual care, % of patients (n/N) | 37 (827/2235) | 6 [a,b,e,f,g,h] |
| Studies conducted in the US, % of patients (n/N) | 49 (1108/2270) | 2 [g,h] |
| Studies conducted in Europe, % of patients (n/N) | 51 (1162/2270) | 6 [a,b,c,d,e,f] |
| Mean study duration (months) | 39 (19 to 60) | 7 [a,c,d,e,f,g,h] |

* All trials 100%; ** 2 trials 100% (Borghi 2002,[3] Di Silverio 2000[4]); † 4 trials 100% (Sarica 2006,[2] Kocvara 1999,[5] Borghi 1996,[6] Hiatt 1996[7]). †† The denominator for diet allocation includes completers only from Kocvara 1999,[5] number randomized to each arm at baseline not reported. Therefore, there are 207 subjects versus 242 randomized.

[a] Dussol 2008;[1] [b] Sarica 2006;[2] [c] Borghi 2002;[3] [d] Di Silverio 2000;[4] [e] Kocvara 1999;[5] [f] Borghi 1996;[6] [g] Hiatt 1996;[7] [h] Shuster 1992[8]

**Appendix F. Table 2. Summary of baseline characteristics for Thiazide studies**

| Characteristic | Mean (range) *Unless otherwise note* | Trials reporting |
|---|---|---|
| Total number of patients evaluated | 564 (41 to 150) | 7 |
| Study withdrawals, % of patients | 12* (0 to 46) | 7 |
| Study withdrawals due to adverse events, % of patients | 2** (0 to 12) | 7 |
| Age of subjects, years | 45 (35 to 48) | 6 [b,c,d,e,f,g] |
| Gender, male, % of patients | 80 (61 to 88) | 6 [b,c,d,e,f,g] |
| Race/ethnicity, white, % of patients | 94 | 1 [d] |
| Stone type, calcium oxalate stones, % of patients (n/N) | 69† (390/564) | 4 [a,b,c,d,] |
| Stone type, "calcium stones," % of patients (n/N) | 31 (174/564) | 3 [e,f,g] |
| Multiple past stones, % of patients (n/N) | 100 (564/564) | 6 |
| Single past stone, % of patients (n/N) | 0 (0/564) | - |
| Residual stones at baseline, % of patients | 0% [c], 47% [d] | 2 |
| Hypercalciuria at baseline, % of patients | 47 (12 to 100) | 7 |
| Hypocitraturia at baseline, % of patients | 7 (0 to 15) | 4 [a,b,c,e] |
| Hyperuricosuria at baseline, % of patients | 12 (0 to 37) | 6 [a,b,c,d,e,f] |
| Hyperoxaluria at baseline, % of patients | 11 (0 to 100) | 6 [a,b,c,d,e,g] |
| Hypomagnesuria at baseline, % of patients | 10 | 1 [b] |
| Mixed at baseline, % of patients | 11 (0 to 23) | 5 [a,b,c,d,e] |
| No metabolic disorder at baseline (% of patients) | 29 (0 to 56) | 6 [a,b,c,d,e,g] |
| Studies evaluating HCTZ, % of patients (n/N) | 65 (365/564) | 5 [a,b,e,f,g] |
| Studies evaluating chlorthalidone, % of patients (n/N) | 22 (124/564) | 1 [d] |
| Studies evaluating indapamide, % of patients (n/N) | 13 (75/564) | 1 [c] |
| Studies conducted in the US, % of patients (n/N) | 22 (124/564) | 1 [d] |
| Studies conducted in Europe, % of patients (n/N) | 78 (440/564) | 6 [a,b,c,e,f,g] |
| Mean study duration (months) | 34 (12 to 48) | 7 |

*Unclear in the Ettinger 1988[12] trial, possibly 26% overall.** overall due to adverse events for all study groups unclear in the Ettinger 1988[12] trial, the range was 3.2% for placebo up to 22.6% for chlorthalidone 25 mg. None reported for magnesium hydroxide 650 mg.†Two trials (Barcelo[20]) reported either calcium oxalate or a mixture of calcium oxalate and calcium phosphate stones.HCTZ = hydrochlorthiazide [a] Fernandez-Rodriguez 2006;[9] [b] Ahlstrand 1996;[10c] Borghi 1993;[11] [d] Ettinger 1988;[12e] Ala-Opas 1987;[13] [f] Laerum 1984;[14g] Scholz 1982[15]

**Appendix F. Table 3. Summary of baseline characteristics for Citrate studies**

| **Characteristic** | **Mean (range)** ***Unless otherwise note*** | **Number of trials reporting** |
|---|---|---|
| Total number of patients evaluated | 479 (48 to 150) | 6 |
| Study withdrawals, % of patients | 17 (0 to 36) | 6 |
| Study withdrawals due to adverse events, % of patients | 5 (0 to 10) | 6 |
| Age of subjects, years | 46 (42 to 55) | 4 [b,d,e,f] |
| Gender, male, % of patients | 62 (44 to 78) | 5 [b,c,d,e,f] |
| Race/ethnicity, white, % of patients | NR | - |
| Stone type, calcium oxalate stones, % of patients (n/N) | 100* (431/431) | 5 [a,b,d,e,f] of 5 report stone type |
| Multiple past stones, % of patients (n/N) | 74 (321/431) | 4 [a,d,e,f] of 5 report stone history |
| Single past stone, % of patients (n/N) | 26 (110/431) | 1[b] of 5 report stone history |
| Residual stones at baseline, % of patients | 61 (38 to 100) | 3 [b,c,d] |
| Hypercalciuria at baseline, % of patients | 26 (0 to 44) | 4 [a,b,e,f] |
| Hypocitraturia at baseline, % of patients | 26 (0 to 69) | 4 [a,b,e,f] |
| Hyperuricosuria at baseline, % of patients | 8 (0 to 18) | 3 [a,b,f] |
| Hyperoxaluria at baseline, % of patients | 1.5 (0 to 2) | 2 [a,f] |
| Mixed at baseline, % of patients | 12 (0 to 16) | 2 [a,f] |
| No metabolic disorder at baseline, % of patients | 49 (29 to 100) | 2 [a,f] |
| Studies evaluating potassium (K) citrate, % of patients (n/N) | 66 (317/479) | 3 [a,b,f] |
| Studies evaluating sodium/K citrate, % of patients (n/N) | 20 (98/479) | 2 [c,e] |
| Studies evaluating magnesium/K citrate, % of patients (n/N) | 13 (64/479) | 1[d] |
| Studies conducted in the US, % of patients (n/N) | 13 (64/479) | 1[d] |
| Studies conducted in Europe, % of patients (n/N) | 77 (367/479) | 4 [a,b,e,f] |
| Studies conducted in Other, % of patients (n/N) | 10 (48/479) | 1[c] |
| Mean study duration (months) | 29 (12 to 37) | 6 |

*One trial (Barcelo[20]) reported either calcium oxalate or a mixture of calcium oxalate and calcium phosphate stones
NR = not reported
[a] Fernandez-Rodriguez 2006;[9] [b] Soygur 2002;[16] [c] Premgamone 2001;[17] [d] Ettinger 1997;[18] [e] Hofbauer 1994;[19] [f] Barcelo 1993[20]

**Appendix F. Table 4. Summary of baseline characteristics for Allopurinol studies**

| **Characteristic** | **Mean (range)** ***Unless otherwise note*** | **Number of trials reporting** |
|---|---|---|
| Total number of patients evaluated | 339* (15 to 132) | 5 |
| Study withdrawals, % of patients | *23 (15 to 30) | 3 [a,b,e] |
| Study withdrawals due to adverse events, % of patients | 0* | 3 [a,b,e] |
| Age of subjects, years | 46 (45 to 48) | 2 [a,b] |
| Gender, male, % of patients | 87 (79 to 100) | 2 [a,d] |
| Race/ethnicity, white, % of patients | NR | - |
| Stone type, calcium oxalate stones, % of patients | 100% in 3 studies | 3 [c,d,e] |
| Stone type, mixed calcium oxalate stones and calcium phosphate or other, % of patients | 2 studies with ≥80% calcium oxalate only | 2 [a,b] |
| Multiple past stones, % of patients (n/N) | 100% in all studies | 5 |
| Single past stone, % of patients (n/N) | 0% in all studies | 5 |
| Residual stones at baseline, % of patients (n/N) | (0 to 47) | 2 [a,b] |
| Hypercalciuria at baseline, % of patients | 100 | 1 [a] |
| Hypocitraturia at baseline, % of patients | NR | |
| Hyperuricosuria at baseline, % of patients | 100 | 1 [b] |
| Hypeoxaluria at baseline, % of patients | NR | |
| Hyperuricemia at baseline, % of patients | 100 | 1 [e] |
| Mixed at baseline, % of patients | NR | |
| No metabolic disorder at baseline, % of patients | 0 | 3 [a,b,e] |
| Studies conducted in the US, % of patients (n/N) | 60 (204/339) | 2 [b,e] |
| Studies conducted in Europe, % of patients (n/N) | 40 (135/339) | 4 [a,c,d] |
| Mean study duration (months) | 46 (24 to 60) | 5 |

*Two trials, Miano 1985[22] and Robertson 1985[23], reported only preliminary data on 15 patients (of 30 randomized) and 45 (of 120 randomized), respectively. No further data on either of these two studies were identified.

[a] Borghi 1996;[6] [b] Ettinger 1986;[21] [c] Miano 1985;[22] [d] Robertson1985;[23] [e] Smith 1977[24]

**Appendix F. Table 5. Summary of study baseline characteristics for AHA studies**

| **Characteristic** | **Mean (range)** ***Unless otherwise note*** | **Number of trials reporting** |
|---|---|---|
| Total number of patients evaluated | 343 (39 to 210) | 3 |
| Study withdrawals, % of patients | 49 (15 to 69) | 3 |
| Study withdrawals due to adverse events, % of patients | 13 (5 to 16) | 3 |
| Age of subjects, years | 49 (48 to 49) | 2 [b,c] |
| Gender, male, % of patients | 77 (18 to 100) | 3 |
| Race/ethnicity, white, % of patients | NR | |
| Stone type, struvite stones, % of patients | 100% for all trials | |
| Multiple past stones, % of patients (n/N) | 100% for 2 trials | 2 [a, c] |
| Single past stone, % of patients (n/N) | 0% for 2 studies | 2 [a, c] |
| Residual stones at baseline, % of patients (n/N) | 88* (269/304) | 2 [a,b] |
| Hypercalciuria at baseline, % of patients | NR | |
| Hypocitraturia at baseline, % of patients | NR | |
| Hyperuricosuria at baseline, % of patients | NR | |
| Hyperoxaluria at baseline, % of patients | NR | |
| Mixed at baseline, % of patients | NR | |
| No metabolic disorder at baseline, % of patients | NR | |
| Spinal cord injury, % of patients (n/N) | 85** (257/304) | 2 [a,b] |
| Studies conducted in the US | All trials | |
| Mean study duration (months) | 18 months for Williams1984. Only range for follow-up period reported for Griffith 1991 (6-32 mos) and Griffith 1988 reported up to 24 months. | |

[a] Griffith 1991;[25] [b] Griffith 1988;[26] [c] Williams1984[27]

* For Williams1984,[27] residual stones at baseline were not reported for all subjects except for 7 placebo patients who had stones that doubled in area versus 0 for AHA patients (determined by X-ray). **10% of subjects in Williams1984[27] study had neurogenic bladders.

# Appendix G

**Appendix G. Table 1. Withdrawals and adverse events for the diet trials**

| Study | Any study withdrawals n/N (%) | | Any or serious adverse events leading to study withdrawal n/N (%) | | Subjects with at least one adverse event n/N (%) | | Adverse event: (*describe*) n/N (%) | | Adverse event: (*describe*) n/N (%) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Diet** | **Control** | **Diet** | **Control** | **Diet** | **Control** | **Diet** | **Control** | **Diet** | **Control** |
| Dussol 2008[1] | Month 48<br>Low animal protein diet 32/55 (58.0%)<br>High fiber diet 33/60 (55.0%) | Month 48<br>37/60 (61.7%) | NR | NR | NR | NR | NR | NR | | |
| Sarica 2006[2] | 0/12 | 0/9 | 0/12 | 0/9 | NR | NR | NR | NR | | |
| Borghi 2002[3] | Low protein/ Na diet 8/60 (13.3) | Low calcium diet 9/60 (15.0) | Low protein/ Na diet 3/60 (5.0) | Low calcium diet 7/60 (11.7) | NR | NR | HTN† 1/60 (1.7) | HTN† 7/60 (11.7) | Stroke† 1/60 (1.7)<br>Gout† 1/60 (1.7) | Death (accidental) 2/60 (3.3) |
| Di Silverio 2000[4] | Mineral $H_20$ calcium 15 mg/l 0/192 | Tap $H_20$ calcium 55-130 mg/l 0/192 | Mineral $H_20$ calcium 15 mg/l 0/192 | Tap $H_20$ calcium 55-130 mg/l 0/192 | NR | NR | NR | NR | | |
| Kocvara 1999[5] | Not stated per arm, 35 patients (14%) not assessed at year 3 | | NR | NR | NR | NR | NR | NR | | |
| Borghi 1996[6] | 11/99 (11.1) | 10/100 (10.0) | NR | NR | NR | NR | NR | NR | | |
| Hiatt 1996[7] | 9/51 (17.6) | 15/51 (29.4) | NR | NR | NR | NR | NR | NR | | |
| Shuster 1992[8] | 44/504 (8.7) | 28/505 (5.5) | 2/504 (0.4) | 2/505 (0.4) | NR | NR | Death 2/504 (0.4) | Death 2/505 (0.4) | | |

HTN= hypertension; Na = sodium; NR = not reported

†These results refer only to the number of participants who withdrew for these specific reasons. No data were reported on specific adverse effects that did not lead to study withdrawal.

**Appendix G. Table 2. Withdrawals and adverse events for the thiazide trials**

| Study | Any study withdrawals n/N (%) | | Any or serious adverse events leading to study withdrawal n/N (%) | | Subjects with at least one adverse event n/N (%) | | Adverse event: (describe) n/N (%) | | Adverse event: (describe) n/N (%) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Thiazide** | **Control** | **Thiazide** | **Control** | **Thiazide** | **Control** | **Thiazide** | **Control** | **Thiazide** | **Control** |
| Fernández-Rodriguez, 2006[9] | 0/50 | 0/50 | 0/50 | 0/50 | NR | NR | NR | NR | | |
| Ahlstrand, 1996[10] | 10/17 (58.8) | 9/24 (37.5) | 5/17 (29.4) | 0/24 | NR | NR | *Composite A**5/17 (29.4) | NR | | |
| Borghi, 1993[11] | 6/25 (24.0) | Control 4/25 (16.0) Allopurinol 1/25 (4.0) | 2/25 (8.0) | Control 0/25 Allopurinol 0/25 | NR | NR | *Hypotension* 1**/25 (4.0) | NR | *Severe hypokalemia* 1**/25 (4.0) | NR |
| Ettinger, 1988[12] | 17.7% due to loss of interest (not reported separately for each dose) and 22.6% and 18.9% due to AE for 25 and 50 mg dose groups, respectively | Placebo 16.7% $MgOH_2$ 17.7% due to loss of interest (not reported separately for each dose) and 13.3% due to AE (1330 mg dose group only) | 25 mg 22.6% 50 mg 18.9% | Placebo 3.2% $MgOH_2$1300 mg 13.3% | NR | NR | *Composite B** 25 mg 22.6% 50 mg 18.9% | *GI upset* Placebo 3.2% *Diarrhea* $MgOH_2$1300 mg 13.3% | | |
| Ala-Opas, 1987[13] | 0/28 | 0/45 | 0/28 | 0/45 | NR, "Side effects uncommon" | NR | NR | NR | | |
| Laerum, | | | | | | | *Composite* | *Composite* | *Gout* | |

**Appendix G. Table 2. Withdrawals and adverse events for the thiazide trials**

| Study | Any study withdrawals n/N (%) | | Any or serious adverse events leading to study withdrawal n/N (%) | | Subjects with at least one adverse event n/N (%) | | Adverse event: (describe) n/N (%) | | Adverse event: (describe) n/N (%) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Thiazide** | **Control** | **Thiazide** | **Control** | **Thiazide** | **Control** | **Thiazide** | **Control** | **Thiazide** | **Control** |
| 1984[14] | 2/25 (8.0) | 0/25 | 0/25 | 0/25 | 6/25 (24.0) | 2/25 (8.0) | C* 3/25 (12.0) | C* 2/25 (8.0) | 1/25 (4.0) *Hypokalemia* 1/25 (4.0) Impotence 1/25 (4.0) | NR |
| Scholz, 1982[15] | 2/25 (8.0) | 1/26 (3.8) | 2/25 (8.0) | 1/26 (3.8) | 13/25 (52.0) | 6/26 (23.1) | *Composite* D* 11/25 (44.0) | *Composite* D* 5/26 (19.2) | | |

* Composite A = orthostatic reactions, dizziness, GI symptoms, muscle cramp, gout, and erectile dysfunction; Composite B = lassitude, fatigue, impotence, lightheadedness, or muscular symptoms; Composite C = minor adverse events such as slight fatigue and dyspepsia; Composite D = weariness, nausea, symptoms of hypotension. **Patient removed from study.
GI = gastrointestinal; $MgOH_2$ = magnesium hydroxide; NR = not reported

**Appendix G. Table 3. Withdrawals and adverse events for the citrate trials**

| Study | Any study withdrawals n/N (%) | | Any or serious adverse events leading to study withdrawal n/N (%) | | Subjects with at least one adverse event n/N (%) | | Adverse event: Gastrointestinal complaints n/N (%) | | Adverse event: (describe) n/N (%) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Citrate | Control | Citrate | Control | Citrate | Control | Citrate | Control | Citrate | Control |
| Fernández-Rodriguez, 2006[9] | 0/50 | 0/50 | 0/50 | 0/50 | NR | NR | NR | NR | NR | NR |
| Soygur, 2002[16]† | 20 of 110 subjects randomized were excluded but number excluded from each study group was not reported | | 6 subjects withdrew due to epigastric discomfort but number withdrawing from each study group was not reported | | NR | NR | 6 subjects overall | | NR | NR |
| Premgamone, 2001[17] | 5/24 (20.8) | 2/24 (8.3) | 5/24 (20.8) | 0/24 | 8/24 (33.3) | 0/24 | NR | NR | Fatigue or loss of appetite 8/24 (33.3) | 0/24 |
| Ettinger, 1997[18] | 15/31 (48.4) | 8/33 (24.2) | 5/31 (16.1) | 1/33 (3.0) | NR | NR | 13/31 (41.9); 8/31 (25.8%) had more than slight symptoms | 13/33 (39.4); 5/33 (15.2%) had more than slight symptoms | Diarrhea (11.5)* | Diarrhea 0/33 (0) |
| Hofbauer, 1994[19] | 9/25 (36.0) | 3/25 (12.0) | 4/25 (16.0) | 0/25 (0.0) | 4/25 (16.0) | 0/25 (0.0) | 4/25 (16.0) | 0/25 (0.0) | NR | NR |
| Barcelo, 1993[20] | 10/28 (35.7) | 9/29 (31.0) | 2/28 (7.1) | 1/29 (3.4) | NR | NR | 5/28 (17.9) | 1/29 (3.4) | NR | NR |

fu = followup; NR = not reported

* number of subjects unclear/ indeterminable

† Study did not report withdrawal and adverse event data separately for subjects who were stone free at baseline from those who had residual stones at baseline.

**Appendix G. Table 4. Withdrawals and adverse events for the allopurinol trials**

| Study | Any study withdrawals n/N (%) | | Any or serious adverse events leading to study withdrawal n/N (%) | | Subjects with at least one adverse event n/N (%) | | Adverse event: *(describe)* n/N (%) | | Adverse event: *(describe)* n/N (%) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Allopurinol** | **Control** | **Allopurinol** | **Control** | **Allopurinol** | **Control** | **Allopurinol** | **Control** | **Allopurinol** | **Control** |
| Borghi, 1993[11] | Allopurinol + Indapamide 1/25 (4.0) | Control 4/25 (16.0) Indapamide 6/25 (24.0) | Allopurinol + Indapamide 0/25 | Control 0/25 Indapamide 2/25 (8.0) | NR | NR | NR | Control NR; Indapamide *Hypotension* 1/25 (4.0) | NR | Control NR; Indapamide *Severe hypokalemia* 1/25 (4.0) |
| Ettinger, 1986[21] | 7/36 (19.4) | 5/36 (13.8) | 2/36 (5.5) | 2/36 (5.5) | NR | NR | *Gastrointestinal discomfort, rash, or fatigue* 2*/36 (5.6) | *Gastrointestinal discomfort, rash, or fatigue* 2*/36 (5.6) | 1/36 (2.8)maculopapular rash; 2/36 (5.6) intercurrent illness | |
| Miano, 1985[22] | NR** | NR** | NR | NR | NR | NR | NR | NR | | |
| Robertson, 1985[23] | NR** | NR** | NR | NR | NR | NR | NR | NR | | |
| Fellstrom, 1985[28] | 2/33 (6) | NR | 2/33 (6) | NR | NR | NR | *Rash* 2/33 (6) | NR | | |
| Smith, 1977[24] | Before 6 months 16/65 (24.6); Total 24/65 (36.9) | Before 6 months 24/67 (35.8); Total 38/67 (56.7) | "Drug sickness" 2/65 (3.1) | "Drug sickness" 6/67 (9.0) | NR | NR | *Skin rash* 1/65 (1.5) | *Skin rash* 1/67 (1.5) | *Acute gout* 3/65 (4.6) *Leukopenia* 1/65 (1.5) | NR |

* Patients removed from study;
** Study provided only preliminary data on a portion of randomized participants and was unclear regarding whether any of participants not included in analyses had withdrawn.

**Appendix G. Table 5. Withdrawals and adverse events for the Acetohydroxamic Acid (AHA) trials**

| Study | Any study withdrawals n/N (%) | | Any or serious adverse events leading to study withdrawal n/N (%) | | Subjects with at least one adverse event n/N (%) | | Adverse event: *(describe)* n/N (%) | | Adverse event: *(describe)* n/N (%) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **AHA** | **Control** | **AHA** | **Control** | **AHA** | **Control** | **AHA** | **Control** | **AHA** | **Control** |
| Griffith, 1991[25] | 29/45 (64.4)<br><br>Deaths 0/45 (0) | 36/49 (73.5)<br><br>Deaths 1/49 (2.0) | 12/45 (26.6) | 3/49 (6.1) | 35/45 (77.7) | 24/49 (48.9) | Anemia 1/45 (2.2)<br>Phlebitis 1/45 (2.2) | Anemia 0/45 (0)<br>Phlebitis 1/49 (2.0) | Alopecia 4/45 (8.9)<br><br>Headache 4/45 (8.9) | Alopecia 1/49 (2.0)<br><br>Headache 2/49 (4.1) |
| Griffith, 1988[26] | 75/121 (62.0)* | 28/89 (31.5)* | 20%† | 5%† | 75/121 (61.9) | 26/89 (29.2) | Anemia 25/99 (25) | Anemia 10/85 (11.7) | | |
| Williams, 1984[27] | Overall 6/20 (30), of which 2/20 (10) within 3 months | NR | 2/20 (10) | NR | 9/20 (45.0) | 1/19 (5.3) | Tremulousness 5/20 (25)<br><br>Myocardiopathy NR | Tremulousness NR<br><br>Myocardiopathy 1/19 (5%) | Deep vein thrombosis 3/19 (15.7)<br><br>Intolerable headache 1/20 (5) | NR |

* numbers calculated from percentages reported

†Actual numbers not provided by and not possible to determine from original study.

**Appendix G. Table 6. Withdrawals and adverse events for the Magnesium trials**

| Study | Any study withdrawals n/N (%) | | Any or serious adverse events leading to study withdrawal n/N (%) | | Subjects with at least one adverse event n/N (%) | | Adverse event: *(describe)* n/N (%) | | Adverse event: *(describe)* n/N (%) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Magnesium** | **Control** | **Magnesium** | **Control** | **Magnesium** | **Control** | **Magnesium** | **Control** | **Magnesium** | **Control** |
| Ettinger, 1988[12] | †9/51 17.7% due to loss of interest (suspect 3/30 in 650mg group & 6/21 in 1300mg group); 0/27 of remaining 650 mg group and 2/15 (13.3%) remaining 1300 mg group due to GI upset | †Placebo 5/31 (16.7%)<br><br>Thiazide 17.7% due to loss of interest (not reported separately for each dose) and 22.6% and 18.9% due to AE for 650 and 50 mg dose groups, respectively | 1300 mg 13.3% | Placebo 3.2%<br><br>Thiazide 25 mg 22.6%<br><br>50 mg 18.9% | NR | NR | *Diarrhea* 1300 mg 13.3%<br><br>stated as "not a problem" for the 650 mg dose group | *GI upset* Placebo 3.2%<br><br>*Composite** Thiazide 25 mg 22.6%<br><br>50 mg 18.9% | | |

* lassitude, fatigue, impotence, lightheadedness, or muscular symptoms.
†Raw numbers estimated from percentages provided in publication.
GI = gastrointestinal; NR = not reported

# Appendix H

**Appendix H. Table 1. Followup urine biochemical measures for Diet trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| Dussol, 2008[1] | A. Low animal protein diet, decrease intake of animal protein by limiting consumption of meat and fish to 3 servings per week and to not exceed 100 g/day of milk products. The target was to obtain a daily contribution of protein to energy of <13% (n=55).<br>B. High fiber diet, increase intake of fruits and vegetables and to substitute their usual cereals with whole grain dietary products in order to limit the increase in energy. The target was to obtain a 25-g/day increase in fiber intake.<br>Subjects were not instructed to exclude fruits and vegetables particularly rich in oxalate (n=60).<br>C. Controls (usual diet) (n=60)<br><br>24 hour collection | CALCIUM<br>Baseline<br>Mean mmol (SD):<br>A (n=55) 6.8 (3.1)<br>B (n=60) 6.8 (3.1)<br>C (n=60) 6.8 (3.1)<br>% hyperCa: NR<br><br>F/u Time 1: 12 mo.<br>Mean mmol (SD):<br>A (n=41) 6.0 (2.4)<br>B (n=45) 6.9 (3.0)<br>C (n=37) 5.8 (3.0)<br>% hyperCa: NR<br><br>OXALATE<br>Baseline<br>Mean mmol (SD):<br>A (n=55) 0.30 (0.1)<br>B (n=60) 0.31 (0.2)<br>C (n=60) 0.32 (0.1)<br>% hyperOx: NR<br><br>F/u Time 1: 12 mo.<br>Mean mmol (SD):<br>A (n=41) 0.25 (0.1)<br>B (n=45) 0.29 (0.1)<br>C (n=37) 0.27 | URIC ACID<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperUA: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperUA: NR<br>URIC-A SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | PHOSPHATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>CA-P SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | CITRATE<br>Baseline<br>Mean mmol (SD):<br>A (n=55) 2.9 (1.9)<br>B (n=60) 3.3 (3.2)<br>C (n=60) 3.2 (2.5)<br>% hypoCit: NR<br><br>F/u Time 1: 12 mo.<br>Mean mmol (SD):<br>A (n=41) 2.8 (1.1)<br>B (n=45) (2.3 (1.2)<br>C (n=37) 2.6 (1.2)<br>% hypoCit: NR<br><br>SODIUM<br>Baseline<br>Mean mmol (SD):<br>A (n=55) 149 (44)<br>B (n=60) 163 (58)<br>C (n=60) 164 (56)<br>% hyperNa: NR<br><br>F/u Time 1: 12 mo.<br>Mean mmol (SD):<br>A (n=41) 167 (46)<br>B (n=45) 144 (70)<br>C (n=37) 146 (64)<br>% hyperNa: NR<br><br>MAGNESIUM<br>Baseline | POTASSIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoK: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoK: NR<br><br>VOLUME<br>Baseline<br>Mean L (SD):<br>A (n=55) 1.9 (0.8)<br>B (n=60) 2.0 (0.7)<br>C (n=60) 1.8 (0.7)<br><br>F/u Time 1: 12 mo.<br>Mean L (SD):<br>A (n=41) 2.0 (0.9)<br>B (n=45) 2.0 (0.7)<br>C (n=37) 1.8 (0.6)<br><br>pH<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR |

**Appendix H. Table 1. Followup urine biochemical measures for Diet trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | Study reported any data on participant compliance/adherence: No | (0.1)<br>% hyperOx: NR<br><br>CA-OX PRODUCT<br>Baseline<br>N<br>Mean (SD): NR<br>Time 1: mo.<br>N<br>Mean (SD): NR<br>CA-OX SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>Time 1: mo.<br>N<br>Mean (SD): NR | | | N<br>Mean (SD): NR<br>% hypoMg: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoMg: NR | |
| Borghi, 2002[3] | A. Low calcium diet (<10 mmol) (n= 60)<br>B. Low protein (<93 g) and low sodium (50 mmol) diet (n=60)<br><br>24 hour collection<br><br>Study reported any data on participant compliance/adherence: Yes (urine specimen obtained one week after randomization was analyzed to check | CALCIUM<br>Baseline<br>Mean mmol (SD):<br>A (n=60) 11.0 (2.5)<br>B (n=60) 11.5 (2.5)<br>% hyperCa: NR<br><br>F/u Time 1: 12 mo.<br>Mean mmol (SD):<br>A (n=51) 7.6 (2.9)<br>B (n=53) 7.3 (2.5)<br>% hyperCa: NR | URIC ACID<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperUA: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperUA: NR<br>URIC-A SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo. | PHOSPHATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>CA-P SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N | CITRATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoCit: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoCit: NR<br><br>SODIUM<br>Baseline<br>Mean mmol (SD):<br>A (n=60) 227 (59)<br>B (n=60) 241 (67) | POTASSIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoK: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoK: NR<br><br>VOLUME<br>Baseline<br>Mean mL (SD):<br>A (n=60) 1755 (844) |

**Appendix H. Table 1. Followup urine biochemical measures for Diet trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | compliance with the dietary regimen, but no data was reported) | OXALATE<br>Baseline<br>Mean µmol (SD):<br>A (n=60) 367 (136)<br>B (n=60) 411 (132)<br>% hyperOx: NR<br><br>F/u Time 1:12 mo.<br>Mean µmol (SD):<br>A (n=51) 422 (144)<br>B (n=53) 344 (92) [p<0.001]<br>% hyperOx: NR<br><br>CA-OX PRODUCT<br>Baseline<br>Mean molX10-6/L (SD):<br>A (n=60) 2.07 (2.11)<br>B (n=60) 1.82 (1.26)<br><br>Time 1: 12 mo.<br>Mean molX10-6/L (SD):<br>A (n=51) 1.25 (1.17)<br>B (n=53) 0.70 (0.48) [p<0.01] | N<br>Mean (SD): NR | Mean (SD): NR | % hyperNa: NR<br><br>F/u Time 1: 12 mo.<br>Mean mmol (SD):<br>A (n=51) 210 (55)<br>B (n=53) 130 (85) [p<0.001]<br>% hyperNa: NR<br><br>MAGNESIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoMg: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoMg: NR | B (n=60) 1852 (643)<br><br>F/u Time 1: 12 mo.<br>Mean mL (SD):<br>A (n=51) 1905 (713)<br>B (n=53) 2095 (623)<br><br>pH<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR |

**Appendix H. Table 1. Followup urine biochemical measures for Diet trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | | CA-OX SUPERSAT<br>Baseline<br>Mean (SD):<br>A (n=60) 10.1 (5.5)<br>B (n=60) 9.6 (4.2)<br><br>Time 1: 12 mo.<br>Mean (SD):<br>A (n=51) 7.3 (4.3)<br>B (n=53) 5.1 (2.5)<br>[p<0.01] | | | | |
| Di Silverio, 2000[4] | A. "Fiuggi water'" oligo-mineral water with a calcium content of 15 mg/l, 2 liters within a 24-hour period (n=192)<br>B. tap water with a calcium content between 55 and 130 mg/l, 2 liters within a 24-hour period (n=192)<br><br>24 hour collection<br><br>Study reported any data on participant compliance/adherence: No | CALCIUM<br>Baseline<br>Mean mg (SD):<br>A (n=192) 270.67<br>B (n=192) 283.09<br>% hyperCa: NR<br><br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperCa: NR<br><br>OXALATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperOx: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | URIC ACID<br>Baseline<br>Mean mg (SD):<br>A (n=192) 554.95<br>B (n=192) 577.45<br>% hyperUA: NR<br><br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperUA: NR<br>URIC-A SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | PHOSPHATE<br>Baseline<br>Mean mg (SD):<br>A (n=192) 768.92<br>B (n=192) 841.08<br>% hyperP: NR<br><br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>CA-P SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | CITRATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoCit: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoCit: NR<br><br>SODIUM<br>Baseline<br>Mean mmol (SD):<br>A (n=192) 186.3<br>B (n=192) 181.1<br>% hyperNa: NR<br><br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | POTASSIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoK: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoK: NR<br>VOLUME<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>pH<br>Baseline<br>N<br>Mean (SD): NR |

**Appendix H. Table 1. Followup urine biochemical measures for Diet trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | | % hyperOx: NR<br>CA-OX PRODUCT<br>Baseline<br>N<br>Mean (SD): NR<br>Time 1: mo.<br>N<br>Mean (SD): NR<br>CA-OX SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>Time 1: mo.<br>N<br>Mean (SD): NR | | | % hyperNa: NR<br><br>MAGNESIUM<br>Baseline<br>Mean mg (SD):<br>A (n=192) 107.4<br>B (n=192) 105.8<br>% hypoMg: NR<br><br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoMg: NR | F/u Time 1: mo.<br>N<br>Mean (SD): NR |
| Kočvara, 1999[5] | A. Tailored diet (n=113)<br>B. General diet (n=94)<br><br>24 hour collection<br><br>Study reported any data on participant compliance/adherence: No | CALCIUM<br>Baseline<br>Mean mmol (SD):<br>A (n=113) 5.09 (2.36)<br>B (n=94) NR<br>% hyperCa: NR<br><br>F/u Time 1: 6 mo.<br>Mean mmol (SD):<br>A (n=113) 5.77 (2.30) [p<0.01]<br>B (n=94) NR<br>% hyperCa: NR<br><br>OXALATE<br>Baseline | URIC ACID<br>Baseline<br>Mean mmol (SD):<br>A (n=113) 3.74 (1.18)<br>B (n=94) NR<br>% hyperUA: NR<br><br>F/u Time 1: 6 mo.<br>Mean mmol (SD):<br>A (n=113) 3.62 (1.34)<br>B (n=94) NR<br>% hyperUA: NR<br><br>URIC-A SUPERSAT | PHOSPHATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>CA-P SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | CITRATE<br>Baseline<br>Mean mmol (SD):<br>A (n=113) 3.08 (1.54)<br>B (n=94) NR<br>% hypoCit: NR<br><br>F/u Time 1: 6 mo.<br>Mean mmol (SD):<br>A (n=113) 2.99 (1.43)<br>B (n=94) NR<br>% hypoCit: NR<br><br>SODIUM<br>Baseline | POTASSIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoK: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoK: NR<br><br>VOLUME<br>Baseline<br>Mean mL (SD):<br>A (n=113) 2354 (645)<br>B (n=94) NR |

**Appendix H. Table 1. Followup urine biochemical measures for Diet trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | | Mean µmol (SD):<br>A (n=88) 351 (156)<br>B (n=94) NR<br>% hyperOx: NR<br><br>F/u Time 1:6 mo.<br>Mean µmol (SD):<br>A (n=88) 334 (138)<br>B (n=94) NR<br>% hyperOx: NR<br><br>CA-OX PRODUCT<br>Baseline<br>N<br>Mean (SD): NR<br>Time 1: mo.<br>N<br>Mean (SD): NR<br>CA-OX SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>Time 1: mo.<br>N<br>Mean (SD): NR | Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | | N<br>Mean (SD): NR<br>% hyperNa: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperNa: NR<br><br>MAGNESIUM<br>Baseline<br>Mean mmol (SD):<br>A (n=113) 4.13 (1.44)<br>B (n=94) NR<br>% hypoMg: NR<br><br>F/u Time 1: 6 mo.<br>Mean mmol (SD):<br>A (n=113) 4.78 (1.94) [p<0.01]<br>B (n=94) NR<br>% hypoMg: NR | F/u Time 1: 6 mo.<br>Mean mL (SD):<br>A (n=113) 2342 (693)<br>B (n=94) NR<br><br>pH<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR |
| Borghi, 1996[6] | A. Achieve urine volume >2 liters/day. Urine volume to be measured every 2 months to ensure high | CALCIUM<br>Baseline<br>Mean mg (SD):<br>A (n=110) 244 (109) | URIC ACID<br>Baseline<br>Mean mg (SD):<br>A (n=110) 588 (183) | PHOSPHATE<br>Baseline<br>N<br>Mean mg (SD):<br>NR | CITRATE<br>Baseline<br>Mean mg (SD):<br>A (n=110) 512 (207) | POTASSIUM<br>Baseline<br>Mean mmol (SD):<br>A (n=110) 47 (14)<br>B (n=110) 47 (15) |

**Appendix H. Table 1. Followup urine biochemical measures for Diet trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | volume (n=110)<br>B. No treatment (n=110)<br><br>24 hour collection<br><br>Study reported any data on participant compliance/adherence: No | B (n=110) 266 (112)<br>% hyperCa: NR<br><br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperCa: NR<br><br>OXALATE<br>Baseline<br>Mean mg (SD):<br>A (n=110) 28.7 (9.5)<br>B (n=110) 28.6 (10.5)<br>% hyperOx: NR<br><br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperOx: NR<br><br>CA-OX PRODUCT<br>Baseline<br>N<br>Mean (SD): NR<br>Time 1: mo.<br>N<br>Mean (SD): NR<br><br>CA-OX SUPERSAT<br>Baseline | B (n=110) 572 (211)<br>% hyperUA: NR<br><br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperUA: NR<br><br>URIC-A SUPERSAT<br>Baseline<br>Mean (SD):<br>A (n=110) 3.48 (2.95)<br>B (n=110) 3.64 (3.08)<br><br>F/u Time 1: 12 mo.<br>Mean (SD):<br>A (n=110) 1.72 (1.49) [p<0.001]<br>B (n=110) 2.66 (2.3) | A (n=110) 707 (250)<br>B (n=110) 670 (255)<br>% hyperP: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>CA-P SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | B (n=110) 530 (259)<br>% hypoCit: NR<br><br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoCit: NR<br><br>SODIUM<br>Baseline<br>Mean mmol (SD):<br>A (n=110) 158 (52)<br>B (n=110) 162 (55)<br>% hyperNa: NR<br><br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperNa: NR<br><br>MAGNESIUM<br>Baseline<br>Mean mg (SD):<br>A (n=110) 85 (31)<br>B (n=110) 88 (33)<br>% hypoMg: NR<br><br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoMg: NR | % hypoK: NR<br><br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoK: NR<br><br>VOLUME<br>Baseline<br>Mean mL (SD):<br>A (n=110) 1068 (240)<br>B (n=110) 1008 (231)<br><br>F/u Time 1: mo.<br>Mean mL (SD):<br>A (n=110) 2127 (546) [p<0.0001]<br>B (n=110) 1258 (292)<br><br>pH<br>Baseline<br>N<br>Mean (SD):<br>A (n=110) 5.91 (0.49)<br>B (n=110) 5.90 (0.5)<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR |

**Appendix H. Table 1. Followup urine biochemical measures for Diet trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | | Mean (SD):<br>A (n=110) 10.1 (4.9)<br>B (n=110) 11.2 (5.3)<br><br>Time 1: 12 mo.<br>Mean (SD):<br>A (n=110) 5.2 (3.2) [p<0.0001]<br>B (n=110) 8.1 (5.2) | | | | |
| Hiatt, 1996[7] | A. Low animal protein and high fiber diet: Decrease intake of animal protein (56 to 64 gm/day) and of purine containing foods (75 mg/day); increase fruits,vegetables, and whole grains; and add 1/4 cup bran/day (n= 51, 50 included in study, 1 excluded post randomization)<br>B. Standard advice instructed on fluid intake and adequate calcium intake (n=51, 49 included in study 2 excluded post randomization)<br><br>24 hour collection | CALCIUM<br>Baseline<br>Mean mmol (SD):<br>A (n=42) 5.21 (0.36)<br>B (n=37) 5.24 (0.49)<br>% hyperCa: NR<br><br>F/u Time 1: 6 mo.<br>Mean mmol (SD):<br>A (n=31) 5.5<br>B (n=28) 5.9<br>% hyperCa: NR<br><br>OXALATE<br>Baseline<br>Mean mmol (SD):<br>A (n=41) 445 (32)<br>B (n=35) 474 (43)<br>% hyperOx: NR<br><br>F/u Time 1: 6 mo. | URIC ACID<br>Baseline<br>Mean mmol (SD):<br>A (n=43) 4.36 (0.22)<br>B (n=37) 4.40 (0.29)<br>% hyperUA: NR<br><br>F/u Time 1: 6 mo.<br>Mean mmol (SD):<br>A (n=32) 3.8<br>B (n=28) 4.2<br>% hyperUA: NR<br><br>URIC-A SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | PHOSPHATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>CA-P SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | CITRATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoCit: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoCit: NR<br>SODIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperNa: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperNa: NR<br>MAGNESIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoMg: NR | POTASSIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoK: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoK: NR<br><br>VOLUME<br>Baseline<br>Mean mL (SD):<br>A (n=43) 1510 (111)<br>B (n=37) 1459 (105)<br><br>F/u Time 1: 6 mo.<br>Mean mL (SD):<br>A (n=29) 1800<br>B (n=32) 1950 |

**Appendix H. Table 1. Followup urine biochemical measures for Diet trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | Study reported any data on participant compliance/adherence: No | Mean mmol (SD):<br>A (n=32) 470<br>B (n=28) 620<br>% hyperOx: NR<br><br><u>CA-OX PRODUCT</u><br><u>Baseline</u><br>N<br>Mean (SD): NR<br><u>Time 1</u>: mo.<br>N<br>Mean (SD): NR<br><u>CA-OX SUPERSAT</u><br><u>Baseline</u><br>N<br>Mean (SD): NR<br><u>Time 1</u>: mo.<br>N<br>Mean (SD): NR | | | <u>F/u Time 1</u>: mo.<br>N<br>Mean (SD): NR<br>% hypoMg: NR | <u>pH</u><br><u>Baseline</u><br>N<br>Mean (SD): NR<br><u>F/u Time 1</u>: mo.<br>N<br>Mean (SD): NR |

**Appendix H. Table 2. Followup urine biochemical measures for Thiazide trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| Fernandez-Rodriguez, 2006[9] | A. Hydrochlorothiazide 50 mg/d (n=50)<br>B. Potassium citrate 20 mEq/d + hydrochlorothiazide 50 mg/d + (n=50)<br>C. No treatment (n= 50)<br><br>Urine collection method not specified<br><br>Study reported any data on participant compliance/adherence: No | CALCIUM<br>Baseline<br><br>Mean (SD): NR<br><br>% hyperCa:<br>A – 42%<br>B – 28%<br>C – 34%<br><br>F/u Time 1: 12 mo.<br><br>Mean (SD): NR<br><br>% hyperCa:<br>A – 16%<br>B – 4%<br>C – 26%<br><br>OXALATE<br>Baseline<br><br>Mean (SD): NR<br><br>% hyperOx:<br>A – NR<br>B – 2%<br>C – 2%<br><br>F/u Time 1:12 mo.<br><br>Mean (SD): NR<br><br>% hyperOx:<br>A – NR | URIC ACID<br>Baseline<br><br>Mean (SD): NR<br><br>% hyperUA:<br>A – 2%<br>B – 6%<br>C – 4%<br><br>F/u Time 1: 12 mo.<br><br>Mean (SD): NR<br><br>% hyperUA:<br>A – NR<br>B – 16%<br>C – 2%<br><br>URIC-A SUPERSAT<br>Baseline<br><br>Mean (SD): NR<br>F/u Time 1: mo.<br><br>Mean (SD): NR | PHOSPHATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperP:<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperP:<br>CA-P SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | CITRATE<br>Baseline<br><br>Mean (SD): NR<br><br>% hypoCit:<br>A – 14%<br>B – 16%<br>C – 14%<br><br>F/u Time 1: 12 mo.<br><br>Mean (SD): NR<br><br>% hypoCit:<br>A – 22%<br>B – 16%<br>C – 14%<br><br>SODIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperNa: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperNa: NR<br>MAGNESIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoMg: NR<br>F/u Time 1: mo. | POTASSIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoK: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoK: NR<br>VOLUME<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>pH<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR |

**Appendix H. Table 2. Followup urine biochemical measures for Thiazide trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | | B – 2%<br>C – 4%<br><br><u>CA-OX PRODUCT</u><br><u>Baseline</u><br>N<br>Mean (SD): NR<br><u>Time 1</u>: mo.<br>N<br>Mean (SD): NR<br><u>CA-OX SUPERSAT</u><br><u>Baseline</u><br>N<br>Mean (SD): NR<br><u>Time 1</u>: mo.<br>N<br>Mean (SD): NR | | | N<br>Mean (SD): NR<br>% hypoMg: NR | |
| Borghi, 1993[11] | A. Indapamide 2.5 mg/d (n=25).<br>B. Allopurinol 300 mg/d + Indapamide 2.5 mg/d (n=25).<br>C. Control (diet/increased fluid treatment) (n=25)<br><br>24 hour collection<br><br>Study reported any data on participant compliance/adherence: No | <u>CALCIUM</u><br><u>Baseline</u><br>Mean mg/24 hr(SD):<br>A (n=19) 387 (121);<br>B (n=24) 410 (154);<br>C (n=21) 381 (156)<br><br>% hyperCa: NR<br><br><u>F/u Time 1</u>: 6 mo.<br>Mean mg/24 hr(SD):<br>A (n=19) 237 (96) [p<0.001];<br>B (n=24) 231 (115) [p<0.001];<br>C (n=21) 284 (99) [p<0.01] | <u>URIC ACID</u><br><u>Baseline</u><br>Mean mg/24 hr(SD):<br>A (n=19) 642 (191);<br>B (n=24) 811 (351);<br>C (n=21) 788 (210)<br><br>% hyperUA: NR<br><br><u>F/u Time 1</u>: 6 mo.<br>Mean mg/24 hr(SD): | <u>PHOSPHORUS</u><br><u>Baseline</u><br>Mean mg/24 hr(SD):<br>A (n=19) 812 (189);<br>B (n=24) 936 (314);<br>C (n=21) 884 (262)<br><br>% hyperP: NR<br><br><u>F/u Time 1</u>: 6 mo.<br>Mean mg/24 hr(SD):<br>A (n=19) 776 | <u>CITRATE</u><br><u>Baseline</u><br>Mean mg/24 hr(SD):<br>A (n=19) 484 (172);<br>B (n=24) 535 (271);<br>C (n=21) 637 (391)<br><br>% hypoCit: NR<br><br><u>F/u Time 1</u>: 6 mo.<br>Mean mg/24 hr(SD): | <u>POTASSIUM</u><br><u>Baseline</u><br>Mean mM/24 hr(SD):<br>A (n=19) 54 (15);<br>B (n=24) 54 (15);<br>C (n=21) 50 (13)<br><br>% hypoK: NR<br><br><u>F/u Time 1</u>: 6 mo.<br>Mean mM/24 hr(SD): |

**Appendix H. Table 2. Followup urine biochemical measures for Thiazide trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | | % hyperCa: NR<br><br>OXALATE<br>Baseline<br>Mean mg/24 hr(SD):<br>A (n=19) 29 (13);<br>B (n=24) 33 (15);<br>C (n=21) 25 (8)<br><br>% hyperOx: NR<br><br>F/u Time 1: 6 mo.<br>Mean mg/24 hr(SD):<br>A (n=19) 27 (14);<br>B (n=24) 28 (11);<br>C (n=21) 24 (13)<br><br>% hyperOx: NR<br><br>CA-OX PRODUCT<br>Baseline<br>Mean (SD): NR<br><br>Time 1: mo.<br>Mean (SD): NR<br><br>CA-OX SUPERSAT<br>Baseline<br>Mean (SD): NR<br><br>Time 1: mo.<br>Mean (SD): NR | A (n=19) 692 (319);<br>B (n=24) 535 (255) [p<0.001];<br>C (n=21) 613 (193) [p<0.01]<br><br>% hyperUA: NR<br><br>URIC-A SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | (265);<br>B (n=24) 911 (263);<br>C (n=21) 772 (237) [p<0.05]<br><br>% hyperP: NR<br><br>CA-P SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | A (n=19) 491 (214);<br>B (n=24) 484 (234);<br>C (n=21) 557 (247)<br><br>% hypoCit: NR<br><br>SODIUM<br>Baseline<br>Mean mM/24 hr(SD):<br>A (n=19) 210 (61);<br>B (n=24) 218 (80);<br>C (n=21) 201 (64)<br><br>% hyperNa: NR<br><br>F/u Time 1: 6 mo.<br>Mean mM/24 hr(SD):<br>A (n=19) 208 (80);<br>B (n=24) 190 (76);<br>C (n=21) 159 (51) [p<0.05]<br><br>% hyperNa: NR | A (n=19) 51 (22);<br>B (n=24) 58 (25);<br>C (n=21) 51 (15)<br><br>% hypoK: NR<br><br>VOLUME<br>Baseline<br>Mean mL/24 hr(SD):<br>A (n=19) 1813 (480);<br>B (n=24) 1995 (772);<br>C (n=21) 1541 (774)<br><br>F/u Time 1: 6 mo.<br>Mean mL/24 hr(SD):<br>A (n=19) 2045 (807);<br>B (n=24) 2193 (897);<br>C (n=21) 1509 (646)<br><br>pH<br>Baseline<br>Mean 24 hr(SD): |

**Appendix H. Table 2. Followup urine biochemical measures for Thiazide trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | | | | | MAGNESIUM<br>Baseline<br>Mean mg/24 hr(SD):<br>A (n=19) 106 (37);<br>B (n=24) 116 (36);<br>C (n=21) 108 (33)<br><br>% hypoMg: NR<br><br>F/u Time 1: 6 mo.<br>Mean mg/24 hr(SD):<br>A (n=19) 94 (38);<br>B (n=24) 104 (44);<br>C (n=21) 81 (28) [p<0.001]<br><br>% hypoMg: NR | A (n=19) 5.83 (0.43);<br>B (n=24) 5.75 (0.46);<br>C (n=21) 5.86 (0.51)<br><br>F/u Time 1: 6 mo.<br>Mean 24 hr(SD):<br>A (n=19) 5.95 (0.49);<br>B (n=24) 6.06 (0.59) [p<0.005];<br>C (n=21) 5.90 (0.53) |
| Ettinger, 1988[12] | A. Chlorthalidone 25 mg/d (n=19)<br>B. Chlorthalidone 50 mg/d (n=23)<br>C. Magnesium hydroxide 650 mg/d (n=30)<br>D. Magnesium hydroxide 1300 mg/d (n=21) | CALCIUM<br>Baseline<br>Mean mg/24 hr(SD):<br>A (n=19) 271 (125)<br>B (n=23) 299 (138)<br>C (n=30) 275 (127)<br>D (n=21) 247 (136)<br>E (n=31) 232 (117)<br><br>% hyperCa: | URIC ACID<br>Baseline<br>Mean mg/24 hr(SD):<br>A (n=19) 768 (207)<br>B (n=23) 826 (206)<br>C (n=30) 837 (257) | PHOSPHATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>CA-P | CITRATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoCit: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoCit: NR<br>SODIUM | POTASSIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoK: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoK: NR |

**Appendix H. Table 2. Followup urine biochemical measures for Thiazide trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | E. Placebo (n=31)<br><br>24 hour collection<br><br>Study reported any data on participant compliance/adherence: Yes (medication compliance confirmed by tablet count – no results reported) | A (n=19) 15.8<br>B (n=23) 13.0<br>C (n=30) 13.3<br>D (n=21) 14.3<br>E (n=31) 9.7<br><br>F/u Time 1: 24 mo.<br>Mean (SD):<br>A (n=19) 196 [p<0.01]<br>B (n=23) 233 [p<0.01]<br>C (n=30) no signif change<br>D (n=21) no signif change<br>E (n=31) no signif change<br><br>% hyperCa: NR<br><br>OXALATE<br>Baseline<br>Mean mg/24 hr(SD):<br>A (n=19) 21 (16)<br>B (n=23) 19 (12)<br>C (n=30) 29 (19)<br>D (n=21) 28 (19)<br>E (n=31) 23 (15)<br><br>% hyperOx: NR<br><br>F/u Time 1: 24 mo.<br>Mean mg/24 hr(SD):<br>A (n=19) 8 [p<0.05]<br>B (n=23) 14 [not signif] | D (n=21) 734 (181)<br>E (n=31) 699 (210)<br><br>% hyperUA:<br>A (n=19) 21.1<br>B (n=23) 26.1<br>C (n=30) 6.7<br>D (n=21) 9.5<br>E (n=31) 9.7<br><br>F/u Time 1: mo.<br>Mean mg/24 hr(SD):<br>All groups- no signif change<br><br>% hyperUA: NR<br><br>URIC-A SUPERSAT<br>Baseline<br>Mean (SD): NR<br><br>F/u Time 1: mo.<br>Mean (SD): NR | SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | Baseline<br>N<br>Mean (SD): NR<br>% hyperNa: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperNa: NR<br>MAGNESIUM<br>Baseline<br>Mean mg/24 hr(SD):<br>A (n=19) 93 (33)<br>B (n=23) 97 (38)<br>C (n=30) 91 (27)<br>D (n=21) 97 (27)<br>E (n=31) 95 (45)<br><br>% hypoMg: NR<br><br>F/u Time 1: 24 mo.<br>Mean mg/24 hr(SD):<br>A (n=19) no signif change<br>B (n=23) no signif change<br>C (n=30) 137 [p<0.001]<br>D (n=21) 148 [p<0.001]<br>E (n=31) no | VOLUME<br>Baseline<br>Mean mL/24 hr(SD):<br>A (n=19) 1744 (720)<br>B (n=23) 1671 (690)<br>C (n=30) 1894 (814)<br>D (n=21) 1579 (675)<br>E (n=31) 1482 (671)<br><br>F/u Time 1: 24 mo.<br>Mean mL/24 hr(SD):<br>All groups- no signif change<br><br>pH<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR |

**Appendix H. Table 2. Followup urine biochemical measures for Thiazide trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | | C (n=30) no signif change<br>D (n=21) no signif change<br>E (n=31) no signif change<br><br>% hyperOx: NR<br><br><u>CA-OX PRODUCT</u><br><u>Baseline</u><br>N<br>Mean (SD): NR<br><u>Time 1</u>: mo.<br>N<br>Mean (SD): NR<br><u>CA-OX SUPERSAT</u><br><u>Baseline</u><br>N<br>Mean (SD): NR<br><u>Time 1</u>: mo.<br>N<br>Mean (SD): NR | | | signif change<br><br>% hypoMg: NR | |
| Ala-Opas, 1987[13] | A. Hydrochlorothiazide 100mg/day for first 5 months (+ bran) (n=28) [hypercalciuric [HU] = 14, normocalciuric [NU] = 14]<br>B. Control (bran) (n=45) [hypercalciuric [HU] = 18, normocalciuric [NU] = | <u>CALCIUM/CREATININE</u><br><u>Baseline</u><br>Mean mmol/mmol (SD):<br>A[HU] (n=14) 0.64 (0.17)<br>B[HU] (n=18) 0.57 (0.12)<br>A[NU] (n=14) 0.36 (0.14)<br>B[NU] (n=27) 0.37 | <u>URIC ACID</u><br><u>Baseline</u><br>Mean (SD): NR<br>% hyperUA: NR<br><u>F/u Time 1</u>: mo.<br>Mean (SD): NR<br>% hyperUA: NR<br><u>URIC-A SUPERSAT</u><br><u>Baseline</u><br>Mean (SD): NR | <u>PHOSPHATE</u><br><u>Baseline</u><br>N<br>Mean (SD): NR<br>% hyperP: NR<br><u>F/u Time 1</u>: mo.<br>N<br>Mean (SD): NR<br>% hyperP: NR<br><u>CA-P SUPERSAT</u> | <u>CITRATE</u><br><u>Baseline</u><br>Mean (SD): NR<br>% hypoCit: NR<br><u>F/u Time 1</u>: mo.<br>Mean (SD): NR<br>% hypoCit: NR<br><u>SODIUM</u><br><u>Baseline</u><br>Mean mmol (SD): | <u>POTASSIUM</u><br><u>Baseline</u><br>Mean (SD): NR<br>% hypoK: NR<br><u>F/u Time 1</u>: mo.<br>Mean (SD): NR<br>% hypoK: NR<br><u>VOLUME</u><br><u>Baseline</u><br>Mean (SD): NR |

**Appendix H. Table 2. Followup urine biochemical measures for Thiazide trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | 27]<br><br>24 hour collection<br><br>Study reported any data on participant compliance/adherence: No | (0.08)<br><br>% hyperCa: 41.0<br><br><u>F/u Time 1</u>: 6 mo.<br>Mean mmol/mmol (SD):<br>A[HU] (n=14) 0.34 (0.15) [p<0.05]<br>B[HU] (n=18) 0.37 (0.13) [p<0.05]<br>A[NU] (n=14) 0.19 (0.08)<br>B[NU] (n=27) 0.29 (0.16)<br>% hyperCa:<br><u>OXALATE</u><br><u>Baseline</u><br>Mean µmol (SD):<br>A[HU] (n=14) 256 (101)<br>B[HU] (n=18) 276 (153)<br>A[NU] (n=14) 167 (71)<br>B[NU] (n=27) 219 (111)<br>% hyperOx: NR<br><br><u>F/u Time 1</u>: 6 mo.<br>Mean µmol (SD):<br>A[HU] (n=14) 194 (70)<br>B[HU] (n=18) 281 (189)<br>A[NU] (n=14) 279 (136)<br>B[NU] (n=27) 334 (86)<br>% hyperOx: NR<br><br><u>CA-OX PRODUCT</u><br><u>Baseline</u><br>Mean (SD): NR | <u>F/u Time 1</u>: mo.<br>Mean (SD): NR | <u>Baseline</u><br>N<br>Mean (SD): NR<br><u>F/u Time 1</u>: mo.<br>N<br>Mean (SD): NR | A[HU] (n=14) 156 (88)<br>B[HU] (n=18) 158 (62)<br>A[NU] (n=14) 113 (33)<br>B[NU] (n=27) 135 (53)<br>% hyperNa: NR<br><br><u>F/u Time 1</u>: 6 mo.<br>Mean µmol (SD):<br>A[HU] (n=14) 149 (71)<br>B[HU] (n=18) 144 (53)<br>A[NU] (n=14) 130 (52)<br>B[NU] (n=27) 138 (70)<br>% hyperNa: NR<br><br><u>MAGNESIUM</u><br><u>Baseline</u><br>Mean mmol (SD):<br>A[HU] (n=14) 4.1 (2.1)<br>B[HU] (n=18) 3.0 (1.4)<br>A[NU] (n=14) 3.7 (1.6)<br>B[NU] (n=27) | <u>F/u Time 1</u>: mo.<br>Mean (SD): NR<br><u>pH</u><br><u>Baseline</u><br>Mean (SD): NR<br><u>F/u Time 1</u>: mo.<br>Mean (SD): NR |

**Appendix H. Table 2. Followup urine biochemical measures for Thiazide trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | | Time 1: mo.<br>Mean (SD): NR<br>CA-OX SUPERSAT<br>Baseline<br>Mean (SD): NR<br>Time 1: mo.<br>Mean (SD): NR | | | 4.0 (1.6)<br>% hypoMg: NR<br><br>F/u Time 1: 6 mo.<br>Mean µmol (SD):<br>A[HU] (n=14) 3.4 (1.4)<br>B[HU] (n=18) 3.6 (1.4)<br>A[NU] (n=14) 3.5 (1.4)<br>B[NU] (n=27) 3.7 (1.4)<br>% hypoMg: NR | |
| Laerum, 1984[14] | A. Hydrochlorothiazide 50 mg/d + potassium chloride 1.2 gm/d (n=23)<br>B. Placebo (n=25)<br><br>24 hour collection<br><br>Study reported any data on participant compliance/adherence: No | CALCIUM<br>Baseline<br>Mean mmol (SD):<br>A (n=23) 4.3 (0.55)<br>B (n=25) 4.92 (0.42)<br><br>% hyperCa: 27.1<br><br>F/u Time 1: 10 mo.<br>Mean mmol (SD):<br>A (n=17) 3.79 (0.46)<br>B (n=21) 5.0 (0.44)<br>[p<0.05 A vs B]<br><br>% hyperCa: NR<br><br>OXALATE<br>Baseline<br>Mean (SD): NR | URIC ACID<br>Baseline<br>Mean mmol (SD):<br>A (n=23) 3.2 (0.25)<br>B (n=25) 3.1 (0.21)<br><br>% hyperUA: 25.0<br><br>F/u Time 1: 10 mo.<br>Mean mmol (SD):<br>A (n=17) 3.3 (0.28)<br>B (n=21) 3.5 (0.19)<br><br>% hyperUA: NR | PHOSPHATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>CA-P<br>SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | CITRATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoCit: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoCit: NR<br>SODIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperNa: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperNa: NR<br>MAGNESIUM | POTASSIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoK: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoK: NR<br>VOLUME<br>Baseline<br>Mean mL (SD):<br>A (n=23) 1522 (114)<br>B (n=25) 1374 (108)<br><br>F/u Time 1: 10 |

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| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | | % hyperOx: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperOx: NR<br>CA-OX PRODUCT<br>Baseline<br>N<br>Mean (SD): NR<br>Time 1: mo.<br>N<br>Mean (SD): NR<br>CA-OX SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>Time 1: mo.<br>N<br>Mean (SD): NR | URIC-A SUPERSAT<br><br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | | Baseline<br>Mean mmol (SD):<br>A (n=23) 3.79 (0.26)<br>B (n=25) 4.20 (0.22)<br><br>% hypoMg: NR<br><br>F/u Time 1: 10 mo.<br>Mean mmol (SD):<br>A (n=17) 4.28 (0.26)<br>B (n=21) 4.40 (0.22)<br><br>% hypoMg: NR | mo.<br>Mean mL (SD):<br>A (n=17) 1492 (95)<br>B (n=21) 1638 (96)<br><br>pH<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR |
| Scholz, 1982[15] | A. Hydrochlorothiazide 50 mg/d (n=25)<br>B. Placebo (n=26)<br><br>24 hour collection<br><br>Study reported any data on participant compliance/adherence: No | CALCIUM<br>Baseline<br>Mean mg (SD):<br>A (n=25) 249 (20)<br>B (n=20) 272 (32)<br>% hyperCa: NR<br><br>F/u Time 1: 12 mo.<br>Mean mg (SD):<br>A (n=25) 153 (22) [p<0.001]<br>B (n=20) 235 (26)<br>% hyperCa: NR<br><br>OXALATE | URIC ACID<br>Baseline<br>Mean mg (SD):<br>A (n=25) 641 (45)<br>B (n=19) 699 (37)<br>% hyperUA: NR<br><br>F/u Time 1: 12 mo.<br>Mean mg (SD):<br>A (n=25) 593 (50)<br>B (n=19) 551 (33)<br>% hyperUA: NR<br><br>URIC-A | PHOSPHATE<br>Baseline<br>Mean mg (SD):<br>A (n=25) 784 (70)<br>B (n=19) 824 (75)<br>% hyperP: NR<br><br>F/u Time 1: 12 mo.<br>Mean mg (SD):<br>A (n=25) 737 (46)<br>B (n=19) 759 (44)<br>% hyperP: NR<br><br>CA-P | CITRATE<br>Baseline<br>Mean mg (SD):<br>A (n=16) 345 (74)<br>B (n=16) 350 (46)<br>% hypoCit: NR<br><br>F/u Time 1: 12 mo.<br>Mean mg (SD):<br>A (n=16) 332 (70)<br>B (n=16) 309 | POTASSIUM<br>Baseline<br>Mean mEq (SD):<br>A (n=25) 61 (5)<br>B (n=19) 64 (7)<br>% hypoK: NR<br><br>F/u Time 1: 12 mo.<br>Mean mEq (SD):<br>A (n=25) 60 (5)<br>B (n=19) 50 (4)<br>% hypoK: NR |

**Appendix H. Table 2. Followup urine biochemical measures for Thiazide trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | | Baseline<br>Mean mg (SD):<br>A (n=16) 42 (6)<br>B (n=13) 47 (6)<br>% hyperOx: NR<br><br>F/u Time 1:12 mo.<br>Mean mg (SD):<br>A (n=16) 35 (6)<br>B (n=13) 22 (6) [p<0.05]<br>% hyperOx: NR<br><br>CA-OX PRODUCT<br>Baseline<br>Mean (SD):<br>A (n=16) 0.96 (0.07)<br>B (n=13) 0.98 (0.06)<br><br>Time 1: 12 mo.<br>Mean (SD):<br>A (n=16) 0.71 (0.08) [p<0.05]<br>B (n=13) 0.71 (0.08) [p<0.05]<br><br>CA-OX SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>Time 1: mo.<br>N<br>Mean (SD): NR | SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | (41)<br>% hypoCit: NR<br><br>SODIUM<br>Baseline<br>Mean mEq (SD):<br>A (n=25) 197 (15)<br>B (n=19) 184 (13)<br>% hyperNa: NR<br><br>F/u Time 1: 12 mo.<br>Mean mEq (SD):<br>A (n=25) 173 (14)<br>B (n=19) 142 (11) [p<0.05]<br>% hyperNa: NR<br><br>MAGNESIUM<br>Baseline<br>Mean mg (SD):<br>A (n=25) 103 (9)<br>B (n=20) 102 (9)<br>% hypoMg: NR<br><br>F/u Time 1: 12 mo.<br>Mean mg (SD):<br>A (n=25) 89 (9)<br>B (n=20) 85 (5) | VOLUME<br>Baseline<br>Mean mL (SD):<br>A (n=25) 1820 (136)<br>B (n=20) 1891 (116)<br><br>F/u Time 1: 12 mo.<br>Mean mL (SD):<br>A (n=25) 1820 (166)<br>B (n=20) 1658 (142)<br><br>pH<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR |

**Appendix H. Table 2. Followup urine biochemical measures for Thiazide trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | | | | | [p<0.05]<br>% hypoMg: NR | |

**Appendix H. Table 3. Followup urine biochemical measures for Citrate trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| Fernandez-Rodriguez, 2006[9] | A. Hydrochlorothiazide 50 mg/d (n=50)<br>B. Potassium citrate 20 mEq/d + hydrochlorothiazide 50 mg/d + (n=50)<br>C. No treatment (n= 50)<br><br>Urine collection method not specified<br><br>Study reported any data on participant compliance/adherence: No | CALCIUM<br>Baseline<br><br>Mean (SD): NR<br><br>% hyperCa:<br>A – 42%<br>B – 28%<br>C – 34%<br><br>F/u Time 1: 12 mo.<br><br>Mean (SD): NR<br><br>% hyperCa:<br>A – 16%<br>B – 4%<br>C – 26%<br><br>OXALATE<br>Baseline<br><br>Mean (SD): NR<br><br>% hyperOx:<br>A – NR<br>B – 2%<br>C – 2%<br><br>F/u Time 1:12 mo.<br><br>Mean (SD): NR<br><br>% hyperOx: | URIC ACID<br>Baseline<br><br>Mean (SD): NR<br><br>% hyperUA:<br>A – 2%<br>B – 6%<br>C – 4%<br><br>F/u Time 1: 12 mo.<br><br>Mean (SD): NR<br><br>% hyperUA:<br>A – NR<br>B – 16%<br>C – 2%<br><br>URIC-A SUPERSAT<br>Baseline<br><br>Mean (SD): NR<br>F/u Time 1: mo.<br><br>Mean (SD): NR | PHOSPHATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperP:<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperP:<br>CA-P SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | CITRATE<br>Baseline<br><br>Mean (SD): NR<br><br>% hypoCit:<br>A – 14%<br>B – 16%<br>C – 14%<br><br>F/u Time 1: 12 mo.<br><br>Mean (SD): NR<br><br>% hypoCit:<br>A – 22%<br>B – 16%<br>C – 14%<br><br>SODIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperNa: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperNa: NR<br>MAGNESIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoMg: NR<br>F/u Time 1: mo. | POTASSIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoK: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoK: NR<br>VOLUME<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>pH<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR |

**Appendix H. Table 3. Followup urine biochemical measures for Citrate trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | | A – NR<br>B – 2%<br>C – 4%<br><br><u>CA-OX PRODUCT</u><br><u>Baseline</u><br>N<br>Mean (SD): NR<br><u>Time 1</u>: mo.<br>N<br>Mean (SD): NR<br><u>CA-OX SUPERSAT</u><br><u>Baseline</u><br>N<br>Mean (SD): NR<br><u>Time 1</u>: mo.<br>N<br>Mean (SD): NR | | | N<br>Mean (SD): NR<br>% hypoMg: NR | |
| Ettinger, 1997[18] | A. Potassium (42 mEq/d)-magnesium (21 mEq/d) citrate (63 mEq/d) (n=31)<br>B. Placebo (n=33)<br><br>24 hour collection<br><br>Study reported any data on participant compliance/adherence: Yes (counting tablets) | <u>CALCIUM</u><br><u>Baseline</u><br>Mean mg (SD):<br>A (n=31) 237 (120)<br>B (n=33) 275 (131)<br>% hyperCa: NR<br><br><u>F/u Time 1</u>: 36 mo.<br>Mean mg (SD):<br>A (n=16) 225 (92)<br>B (n=25) 261 | <u>URIC ACID</u><br><u>Baseline</u><br>Mean mg (SD):<br>A (n=31) 722 (239)<br>B (n=33) 695 (227)<br>% hyperUA: NR<br><br><u>F/u Time 1</u>: 36 mo.<br>Mean mg (SD):<br>A (n=16) 726 (210) | <u>PHOSPHATE</u><br><u>Baseline</u><br>N<br>Mean (SD): NR<br>% hyperP: NR<br><u>F/u Time 1</u>: mo.<br>N<br>Mean (SD): NR<br>% hyperP: NR<br><br><u>CA-P SUPERSAT</u><br><u>Baseline</u><br>N<br>Mean (SD): NR | <u>CITRATE</u><br><u>Baseline</u><br>Mean mg (SD):<br>A (n=31) 587 (37.4)<br>B (n=33) 549 (280)<br>% hypoCit: NR<br><br><u>F/u Time 1</u>: 36 mo.<br>Mean mg (SD):<br>A (n=16) 769 (289) [p<0.05] | <u>POTASSIUM</u><br><u>Baseline</u><br>Mean mEq (SD):<br>A (n=31) 56 (25)<br>B (n=33) 58 (20)<br>% hypoK: NR<br><br><u>F/u Time 1</u>: 36 mo.<br>Mean mEq (SD):<br>A (n=16) 89 (27) [p<0.001]<br>B (n=25) 58 (17)<br>% hypoK: NR |

**Appendix H. Table 3. Followup urine biochemical measures for Citrate trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | | (123)<br>% hyperCa: NR<br><br>OXALATE<br>Baseline<br>Mean mg (SD):<br>A (n=31) 37 (13)<br>B (n=33) 36 (12)<br>% hyperOx: NR<br><br>F/u Time 1: 36 mo.<br>A (n=16) 44 (21) [p<0.05]<br>B (n=25) 39 (10)<br>% hyperOx: NR<br><br>CA-OX PRODUCT<br>Baseline<br>Mean m2 X 10-8 (SD):<br>A (n=31) 1.40 (0.76)<br>B (n=33) 1.77 (0.87)<br><br>Time 1: 36 mo.<br>Mean m2 X 10-8 (SD):<br>A (n=16) 1.48 (0.75)<br>B (n=25) 1.72 (0.53) | B (n=25) 694 (194)<br>% hyperUA: NR<br><br>URIC-A SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | F/u Time 1: mo.<br>N<br>Mean (SD): NR | B (n=25) 548 (265)<br>% hypoCit: NR<br><br>SODIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperNa: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperNa: NR<br><br>MAGNESIUM<br>Baseline<br>Mean mg (SD):<br>A (n=31) 116 (44)<br>B (n=33) 121 (47)<br>% hypoMg: NR<br><br>F/u Time 1: 36 mo.<br>Mean mg (SD):<br>A (n=16) 142 (42) [p<0.05]<br>B (n=25) 105 (32)<br>% hypoMg: NR | VOLUME<br>Baseline<br>Mean L (SD):<br>A (n=31) 1.98 (1.15)<br>B (n=33) 1.74 (0.70)<br><br>F/u Time 1: 36 mo.<br>Mean L (SD):<br>A (n=16) 2.01 (1.00)<br>B (n=25) 1.79 (0.84)<br><br>pH<br>Baseline<br>Mean (SD):<br>A (n=31) 6.01 (0.46)<br>B (n=33) 5.96 (0.41)<br><br>F/u Time 1: 36 mo.<br>Mean (SD):<br>A (n=16) 6.29 (0.58)<br>B (n=25) 6.02 (0.32) |

**Appendix H. Table 3. Followup urine biochemical measures for Citrate trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | | CA-OX SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>Time 1: mo.<br>N<br>Mean (SD): NR | | | | |
| Hofbauer, 1994[19] | A. Sodium-potassium citrate 30 gm/d initially, then adjusted to keep urine pH 7.0-7.2 (n=25)<br>B. Control (n=25)<br><br>24 hour collection<br><br>Study reported any data on participant compliance/adherence: No | CALCIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperCa:<br>A (n=25) 48%<br>B (n=25) 40%<br><br>F/u Time 1: 36 mo.<br>N<br>Mean (SD): NR<br>% hyperCa:<br>A (n=16) 25%<br>B (n=22) 45%<br><br>OXALATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperOx: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperOx: NR<br>CA-OX | URIC ACID<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperUA: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperUA: NR<br>URIC-A SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | PHOSPHATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>CA-P SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | CITRATE<br>Baseline<br>Mean mmol/L (SD):<br>A (n=25) 1.3 (0.8)<br>B (n=25) 1.27 (0.9)<br>% hypoCit:<br>A (n=25) 72%<br>B (n=25) 65%<br><br>F/u Time 1: 36 mo.<br>Mean mmol/L (SD):<br>A (n=16) 2.28 (0.8)<br>B (n=22) 1.47 (0.9)<br>% hypoCit:<br>A (n=16) 25%<br>B (n=22) 55%<br><br>SODIUM<br>Baseline<br>N | POTASSIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoK: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoK: NR<br>VOLUME<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>pH<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR |

**Appendix H. Table 3. Followup urine biochemical measures for Citrate trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | | PRODUCT<br>Baseline<br>N<br>Mean (SD): NR<br>Time 1: mo.<br>N<br>Mean (SD): NR<br>CA-OX<br>SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>Time 1: mo.<br>N<br>Mean (SD): NR | | | Mean (SD): NR<br>% hyperNa: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperNa: NR<br>MAGNESIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoMg: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoMg: NR | |
| Barcelo, 1993[20] | A. Potassium citrate 30-60 mEq/d (n=28)<br>B. Placebo (n=29)<br><br>24 hour collection<br><br>Study reported any data on participant compliance/adherence: Yes (interview and pill count) | CALCIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperCa: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperCa: NR<br>OXALATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperOx: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperOx: NR<br>CA-OX | URIC ACID<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperUA: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperUA: NR<br>URIC-A<br>SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | PHOSPHATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>CA-P SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | CITRATE<br>Baseline<br>Mean nmol/day(SD):<br>A (n=28) 1.9 (0.5)<br>B (n=29) NR<br>% hypoCit: NR<br><br>F/u Time 1: 36 mo.<br>Mean nmol/day(SD):<br>A (n=18) 3.3 (0.5) [p<0.01]<br>B (n=20) NR<br>% hypoCit: NR<br><br>SODIUM<br>Baseline | POTASSIUM<br>Baseline<br>Mean mEq/day(SD):<br>A (n=28) 61 (17)<br>B (n=29) NR<br>% hypoK: NR<br><br>F/u Time 1: 36 mo.<br>Mean mEq/day(SD):<br>A (n=18) 105 (41) [p<0.01]<br>B (n=20) NR<br>% hypoK: NR<br><br>VOLUME<br>Baseline |

**Appendix H. Table 3. Followup urine biochemical measures for Citrate trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | | PRODUCT<br>Baseline<br>N<br>Mean (SD): NR<br>Time 1: mo.<br>N<br>Mean (SD): NR<br>CA-OX SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>Time 1: mo.<br>N<br>Mean (SD): NR | | | N<br>Mean (SD): NR<br>% hyperNa: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperNa: NR<br>MAGNESIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoMg: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoMg: NR | N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br><br>pH<br>Baseline<br>Mean (SD):<br>A (n=28) 5.4 (0.5)<br>B (n=29) NR<br><br>F/u Time 1: 36 mo.<br>Mean (SD):<br>A (n=18) 6.4 (0.3) [p<0.01]<br>B (n=20) NR |

**Appendix H. Table 4. Followup urine biochemical measures for Allopurinol trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| Ettinger, 1986[21] | A. Allopurinol 300 mg/d (n=36)<br>B. Placebo (n=36)<br><br>24 hour collection<br><br>Study reported any data on participant compliance/adherence: Yes (tablet counts) | CALCIUM<br>Baseline<br>Mean mg (SD):<br>A (n=29) 238 (74)<br>B (n=31) 211 (83)<br>% hyperCa: NR<br><br>F/u Time 1: 6 mo.<br>Mean mg (SD):<br>A (n=29) no signif change<br>B (n=31) no signif change<br>% hyperCa: NR<br><br>OXALATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperOx: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperOx: NR<br>CA-OX PRODUCT<br>Baseline<br>N<br>Mean (SD): NR<br>Time 1: mo.<br>N<br>Mean (SD): NR<br>CA-OX SUPERSAT<br>Baseline | URIC ACID<br>Baseline<br>Mean mg (SD):<br>A (n=29) 1017 (214)<br>B (n=31) 935 (134)<br>% hyperUA: NR<br><br>F/u Time 1: 6 mo.<br>Mean mg (SD):<br>A (n=29) 660 (55)<br>B (n=31) 885 (50)<br>% hyperUA: NR<br><br>URIC-A SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | PHOSPHATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>CA-P SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | CITRATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoCit: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoCit: NR<br>SODIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperNa: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperNa: NR<br>MAGNESIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoMg: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoMg: NR | POTASSIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoK: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoK: NR<br>VOLUME<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>pH<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR |

**Appendix H. Table 4. Followup urine biochemical measures for Allopurinol trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | | N<br>Mean (SD): NR<br>Time 1: mo.<br>N<br>Mean (SD): NR | | | | |
| Miano, 1985[22] | A. Allopurinol 300 mg/d (n=8)<br>B. Placebo (n=7)<br><br>24 hour collection<br><br>Study reported any data on participant compliance/adherence: No | CALCIUM<br>Baseline<br>Mean mg (SD):<br>A (n=8) 203 (34)<br>B (n=7) 218 (14)<br>% hyperCa: NR<br><br>F/u Time 1: 36 mo.<br>Mean mg (SD):<br>A (n=8) 210 (44)<br>B (n=7) 218 (31)<br>% hyperCa: NR<br><br>OXALATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperOx: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperOx: NR<br>CA-OX PRODUCT<br>Baseline<br>N<br>Mean (SD): NR<br>Time 1: mo. | URIC ACID<br>Baseline<br>Mean mg (SD):<br>A (n=8) 513 (136)<br>B (n=7) 421 (55)<br>% hyperUA: NR<br><br>F/u Time 1: 36 mo.<br>Mean mg (SD):<br>A (n=8) 444 (103)<br>B (n=7) 482 (67)<br>% hyperUA: NR<br><br>URIC-A SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | PHOSPHATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>CA-P SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | CITRATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoCit: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoCit: NR<br>SODIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperNa: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperNa: NR<br>MAGNESIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoMg: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoMg: NR | POTASSIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoK: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoK: NR<br><br>VOLUME<br>Baseline<br>Mean mL (SD):<br>A (n=8) 1314 (497)<br>B (n=7) 1439 (368)<br><br>F/u Time 1: 36 mo.<br>Mean mL (SD):<br>A (n=8) 1389 (312)<br>B (n=7) 1653 (413)<br><br>pH<br>Baseline<br>N |

**Appendix H. Table 4. Followup urine biochemical measures for Allopurinol trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | | N<br>Mean (SD): NR<br>CA-OX SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>Time 1: mo.<br>N<br>Mean (SD): NR | | | | Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR |

**Appendix H. Table 5. Followup urine biochemical measures for magnesium trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| Ettinger, 1988[12] | A. Chlorthalidone 25 mg/d (n=19)<br>B. Chlorthalidone 50 mg/d (n=23)<br>C. Magnesium hydroxide 650 mg/d (n=30)<br>D. Magnesium hydroxide 1300 mg/d (n=21)<br>E. Placebo (n=31)<br><br>24 hour collection<br><br>Study reported any data on participant compliance/adherence: Yes (medication compliance confirmed by tablet count – no results reported) | CALCIUM<br>Baseline<br>Mean mg/24 hr(SD):<br>A (n=19) 271 (125)<br>B (n=23) 299 (138)<br>C (n=30) 275 (127)<br>D (n=21) 247 (136)<br>E (n=31) 232 (117)<br><br>% hyperCa:<br>A (n=19) 15.8<br>B (n=23) 13.0<br>C (n=30) 13.3<br>D (n=21) 14.3<br>E (n=31) 9.7<br><br>F/u Time 1: 24 mo.<br>Mean (SD):<br>A (n=19) 196 [p<0.01]<br>B (n=23) 233 [p<0.01]<br>C (n=30) no signif change<br>D (n=21) no signif change<br>E (n=31) no signif change | URIC ACID<br>Baseline<br>Mean mg/24 hr(SD):<br>A (n=19) 768 (207)<br>B (n=23) 826 (206)<br>C (n=30) 837 (257)<br>D (n=21) 734 (181)<br>E (n=31) 699 (210)<br><br>% hyperUA:<br>A (n=19) 21.1<br>B (n=23) 26.1<br>C (n=30) 6.7<br>D (n=21) 9.5<br>E (n=31) 9.7<br><br>F/u Time 1: mo.<br>Mean mg/24 hr(SD):<br>All groups- no signif change<br><br>% hyperUA: NR<br><br>URIC-A SUPERSAT<br>Baseline<br>Mean (SD): NR | PHOSPHATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperP: NR<br>CA-P SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR | CITRATE<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoCit: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoCit: NR<br>SODIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hyperNa: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hyperNa: NR<br>MAGNESIUM<br>Baseline<br>Mean mg/24 hr(SD):<br>A (n=19) 93 (33)<br>B (n=23) 97 (38)<br>C (n=30) 91 (27)<br>D (n=21) 97 (27)<br>E (n=31) 95 (45)<br><br>% hypoMg: NR<br><br>F/u Time 1: 24 mo.<br>Mean mg/24 hr(SD):<br>A (n=19) no signif | POTASSIUM<br>Baseline<br>N<br>Mean (SD): NR<br>% hypoK: NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR<br>% hypoK: NR<br><br>VOLUME<br>Baseline<br>Mean mL/24 hr(SD):<br>A (n=19) 1744 (720)<br>B (n=23) 1671 (690)<br>C (n=30) 1894 (814)<br>D (n=21) 1579 (675)<br>E (n=31) 1482 (671)<br><br>F/u Time 1: 24 mo.<br>Mean mL/24 hr(SD):<br>All groups- no signif change<br><br>pH<br>Baseline<br>N |

**Appendix H. Table 5. Followup urine biochemical measures for magnesium trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | | % hyperCa: NR<br><br>OXALATE<br>Baseline<br>Mean mg/24 hr(SD):<br>A (n=19) 21 (16)<br>B (n=23) 19 (12)<br>C (n=30) 29 (19)<br>D (n=21) 28 (19)<br>E (n=31) 23 (15)<br><br>% hyperOx: NR<br><br>F/u Time 1: 24 mo.<br>Mean mg/24 hr(SD):<br>A (n=19) 8 [p<0.05]<br>B (n=23) 14 [not signif]<br>C (n=30) no signif change<br>D (n=21) no signif change<br>E (n=31) no signif change<br><br>% hyperOx: NR<br><br>CA-OX PRODUCT | F/u Time 1: mo.<br>Mean (SD): NR | | change<br>B (n=23) no signif change<br>C (n=30) 137 [p<0.001]<br>D (n=21) 148 [p<0.001]<br>E (n=31) no signif change<br><br>% hypoMg: NR | Mean (SD): NR<br>F/u Time 1: mo.<br>N<br>Mean (SD): NR |

**Appendix H. Table 5. Followup urine biochemical measures for magnesium trials**

| Study | Treatment Groups, Urine Collection Method | Calcium, Oxalate, Ca-Ox Product, Ca-Ox Supersaturation | Uric acid, Uric-A Supersaturation | Phosphate, Ca-P Supersaturation | Citrate, Sodium, Magnesium | Potassium (K), Volume, pH |
|---|---|---|---|---|---|---|
| | | Baseline<br>N<br>Mean (SD): NR<br>Time 1: mo.<br>N<br>Mean (SD): NR<br>CA-OX SUPERSAT<br>Baseline<br>N<br>Mean (SD): NR<br>Time 1: mo.<br>N<br>Mean (SD): NR | | | | |

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