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, 199126  Location: USA  Funding Source: Government | Inclusion Criteria:   * presence or history of infection calculi in association with chronic, urea-splitting urinary infection that was recalcitrant to permanent eradication by antimicrobial agents; * serum creatinine <2.5 mg/dL (225 μmol/L); * not suitable for surgical removal of calculi and antimicrobial therapy   Exclusion Criteria: NR | N=94  Age (yr): 79% in age range 25-75y  Gender (Male %): 51 Race/Ethnicity (%): NR  Spinal cord injury: 50%  BMI, weight, or percent with obesity: NR  Previous bariatric surgery (%): NR Chronic kidney disease (%): NR  Serum creatinine (mg/dL): NR  Estimated GFR (ml/min/1.73m2): NR Solitary kidney (%): NR  History of renal transplant (%): NR  Urinary tract anatomic abnormality (%): 64% with prior urinary diversion (ileal conduits)  Pregnancy: NR  History of CAD: NR  History of DM: NR  History of HTN: NR | Stone type: Struvite 100%  Past stone episodes: multiple 100%  Residual stones/ fragments: 89% by X-ray.  Urine analysis:  Hypercalciuria NR; hypocitraturia NR; hyperuricosuria NR; hyperoxaluria NR;  mixed NR;  no metabolic disorder NR  Blood analysis:  Hyperuricemia NR  Diet characteristics: NR | 1. AHA 15 mg/kg/d every 6-8 hours (n=45)  2. Placebo (n=49)  Other: Antibiotics were prescribed according to the physicians as clinically indicated   Follow up period: 6-32 mos  Study withdrawals (%):   * overall 65 (69) * due to adverse events 15 (15.9) * due to loss to follow-up 11 (11.7)   Assessment of compliance and adherence to treatment: Overall > 80% medication compliance as assessed by study nurse  Setting (e.g., medicine, urology): NR  Follow up biochemical measures collected: (y/n): NR | 1. Allocation Concealment: unclear, not specified 2. Blinding: double blind and radiologist who reviewed radiographs 3. Intention to Treat Analysis: yes 4. Withdrawals/Dropouts adequately described: yes  *Quality of harms reporting:*  1. Harms predefined: No  2. Harms specified as ALL events collected: No  3. Number of participants that withdrew/lost to follow up adequately described: Yes  4. Total number of participants affected by harms specified for each study group: Yes  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 (continued) | | | | | |
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| **Study/Region/**  **Funding Source** | **Inclusion/Exclusion Criteria** | **Patient Characteristics (expressed in means unless otherwise noted)** | **Baseline Stone Characteristics /**  **Biochemistry** | **Intervention/Duration** | **Study Quality** |
| Griffith, 198827  Location: USA  Funding Source: Government | Inclusion Criteria:   * non-progressive spinal cord injury * chronic urinary tract infection with urea-splitting organisms * serum creatinine < 3 mg/dL * acceptance of the logistical requirements of 3-month follow up visits for 2 years * acceptance of the double-blind investigational format.   Exclusion Criteria:   * progressive neuropathy * candidates for surgical lithotomy * nonfunctioning stone-containing kidneys * major coexistent medical problems; having social, economic and logistical problems that would hinder compliance and/or follow up | N=210  Age (yr): 49  Gender (Male %): 100 Race/Ethnicity (%): NR  Spinal cord injury: 100%  Weight (mean, kg): AHA 79.1, placebo 72.6  Previous bariatric surgery (%): NR Chronic kidney disease (%): NR  Serum creatinine (mg/dL): 1.0  Estimated GFR (ml/min/1.73m2): NR Solitary kidney (%): NR  History of renal transplant (%): NR  Urinary tract anatomic abnormality (%): NR  Pregnancy: NR  History of CAD: NR  History of DM: NR  History of HTN: NR | Stone type: Struvite 100%  Past stone episodes: single NR, multiple NR  Residual stones/ fragments: 88% by excretory urogram.  Urine analysis:  Hypercalciuria NR; hypocitraturia NR ; hyperuricosuria NR; hyperoxaluria NR;  mixed NR;  no metabolic disorder NR  Blood analysis:  Hyperuricemia NR  Diet characteristics: NR | 1. Acetohydroxamic acid 0.5-1.0 gm/d (n=121)  2. Placebo (n=89)  Follow up period: up to 24 mos  Study stated that no attempt was made to control antibiotic use during the study.  Study withdrawals (%): 103 (49)  Study withdrawals (%):   * AHA 62%, placebo 31% * due to adverse events AHA 20%, placebo 5% (severe reactions) * due to loss to follow-up NR   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  Setting (e.g., medicine, urology): NR  Follow up biochemical measures collected: (y/n): Yes | 1. Allocation Concealment: adequate 2. Blinding: double and radiologist who reviewed radiographs. Results reviewed by independent monitoring body.  3. Intention to Treat Analysis: No 4. Withdrawals/Dropouts adequately described: Yes  *Quality of harms reporting:*  1. Harms predefined: No  2. Harms specified as ALL events collected: No  3. Number of participants that withdrew/lost to follow up adequately described: Yes  4. Total number of participants affected by harms specified for each study group: NR  5. Number for each type of harm event specified for each study group: NR |
| Williams, 198428  Location: USA  Funding Source: Government and non industry | Inclusion Criteria:   * Documented struvite nephrolithiasis concomitant with infection with a urea-splitting organism * > 18 years of age * serum creatinine <3mg/dL * hematocrit > 25% * patients on the phosphate depleting Shor regimen were continued on it   Exclusion Criteria:   * participants unable to understand the protocol * pregnancy * lactation * oral contraceptive use * history of varicose veins, phlebitis or pulmonary embolism. | N=39  Age (yr): AHA 52, placebo 44  Gender (Male %): 17.9 Race/Ethnicity (%): NR  BMI, weight, or percent with obesity: NR  Previous bariatric surgery (%): NR Chronic kidney disease (%): NR  Serum creatinine (mg/dL): NR  Estimated GFR (ml/min/1.73m2): NR Solitary kidney (%): NR  History of renal transplant (%): NR  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)  Pregnancy: 0%  History of CAD: NR  History of DM: NR  History of HTN: NR | Stone type: Struvite 100%  Past stone episodes: multiple 100%  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).  Urine analysis:  Hypercalciuria NR; hypocitraturia NR ; hyperuricosuria NR; hyperoxaluria NR;  mixed NR;  no metabolic disorder NR  Blood analysis:  Hyperuricemia NR  Diet characteristics: NR | 1. Acetohydroxamic acid 15 mg/kg/d (n= 20)  2. Placebo (n=19)  Other: Both groups treated with suppressive antibiotics throughout study.  Follow up period: overall mean 18 (up to 30 mos), mean AHA 15.8, mean placebo 19.6  Study withdrawals (%):   * overall 6 (15.3) * due to adverse events AHA 2 (10) * due to loss to follow-up NR   Assessment of compliance and adherence to treatment:  Assessed by pill counts and urine AHA screening; participants 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.  Setting (e.g., medicine, urology): NR  Follow up biochemical measures collected: (y/n): NR | 1. Allocation Concealment: adequate 2. Blinding: double and radiologist who reviewed radiographs 3. Intention to Treat Analysis: no 4. Withdrawals/Dropouts adequately described: yes  *Quality of harms reporting:*  1. Harms predefined: No  2. Harms specified as ALL events collected: No  3. Number of participants that withdrew/lost to follow up adequately described: Yes  4. Total number of participants affected by harms specified for each study group: Yes  5. Number for each type of harm event specified for each study group: Yes |