Diet, fluid, or supplements for secondary prevention of nephrolithiasis: a systematic review and meta-analysis of randomized trials

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CRD summary
The authors concluded that high fluid intake and lowered soft drink intake in patients with high baseline soft drink consumption decreased the risk of nephrolithiasis. Limited data suggested a benefit of dietary calcium. In light of the small number and low quality of available studies and the risk of publication bias, the authors’ conclusions should be treated with caution.

Authors’ objectives
To assess the safety and efficacy of dietary, fluid or supplement interventions on secondary prevention of nephrolithiasis.

Searching
MEDLINE was searched to March 2008 for articles written in English. Search terms were reported. Bibliographies of retrieved trials and review articles were handsearched.

Study selection
Randomised controlled trials (RCTs) that comparing a diet, fluid or supplement intervention with a control in adults (more than 18 years old) living in the community with at least one prior resolved episode of renal colic were eligible for inclusion. Eligible outcomes were secondary prevention of nephrolithiasis (recurrent renal colic, recurrent asymptomatic renal calculi and/or growth or reduction in size of prevalent renal calculi). Follow-up had to be at least three months to be eligible for inclusion. Studies of acute treatment were excluded.

Included studies evaluated high water intake, advice to avoid soft drinks, supplements (orthosiphon grandiflorus extract or phyllanthus niuri extract), sodium potassium citrate or multi-component diets. In one study general dietary advice was compared to dietary advice tailored according to participants’ metabolic evaluations. Duration of interventions ranged from three months to 60 months. Mean age of participants ranged from 38 to 45 years and 85% were male. Outcomes were assessed as symptomatic stone passage, radiographic stone detection by X-rays and/or ultrasound, and/or change in stone size.

Two reviewers independently selected the studies for review. Disagreements were resolved by consensus.

Assessment of study quality
Methodological quality of included studies was assessed according to allocation concealment, blinding of participants and investigators, use of intention-to-treat (ITT) analysis and withdrawals/loss to follow-up.

It appeared that the validity assessment was conducted independently by two reviewers and disagreements were resolved by consensus.

Data extraction
The percentage of participants was extracted for each outcome in each group. The number of adverse events was extracted.

Two reviewers independently extracted data. Differences were resolved through discussion.

Methods of synthesis
Results were grouped according to intervention type. In the absence of clinical or statistical heterogeneity, pooled
relative risks (RR) with 95% confidence intervals (CI) were calculated using a random-effects model. Statistical heterogeneity was calculated with significance set at p<0.10. Where there was clinical or statistical heterogeneity, a narrative synthesis was used.

**Results of the review**

Eight RCTs were included for review (n=1,885). Study size ranged from n=45 to n=1,009. One study had adequate allocation concealment. Participants were blinded in one trial. Outcome assessors were blinded in four trials. Five studies used ITT analysis. Five studies adequately described dropouts; in two trials there were no dropouts.

**Fluid interventions:** Increased fluid intake to more than two litres or two and a half litres per day significantly decreased the risk of stone recurrence by 61% (RR 0.39, 95% CI 0.19 to 0.80; two studies, n=265) compared to no treatment. Decreased soft drink intake significantly reduced incidence of renal colic episodes in men compared to no treatment (34% versus 41%, p=0.023; one study, n=1,009).

**Combination diets:** Results for the impact of combination diets were mixed. One study found that dietary advice tailored to participants' metabolic evaluation significantly reduced recurrence of stones compared to general dietary advice (6% versus 19%, p<0.01; n=242). Men on a high calcium, low animal protein, low sodium diet had significantly less stone recurrence compared to a control group on a low calcium diet (20% versus 38%, p=0.03; n=120). However, one study found that participants on a combination diet of low animal protein, high fruit, vegetables and whole grains, increased bran and low purine had a significantly greater incidence of stone recurrence compared to a control group on standard dietary advice (30% versus 4%, p=0.004; n=102).

**Supplements:** Dietary supplements did not significantly reduce stone recurrence compared to control treatments.

**Authors' conclusions**

High fluid intake decreased risk of recurrent nephrolithiasis. Lowering of soft drink intake decreased risk in patients with high baseline soft drink consumption. Limited data suggested a benefit of dietary calcium.

**CRD commentary**

The review addressed a clear question. Inclusion criteria were clearly stated for participants, study design and outcomes and broad for intervention. Only one database was searched, therefore, important data may have been missed. The search was restricted to studies in English and it appeared that no attempts were made to find unpublished data and so there was a risk of language and publication biases. Appropriate steps were taken in the review process to minimise the risk of reviewer error and bias. A suitable validity assessment was carried out. There were methodological limitations to most trials, which limited the reliability of the findings. The decision to combine most studies in a narrative synthesis was appropriate given the high level of clinical heterogeneity between studies. Most studies were of younger men and it was unclear to what extent the findings may be generalised to other populations. Statistical heterogeneity was not reported for the meta-analysis, which made it difficult for the reader to ascertain the suitability of this analysis. Few studies were available for each intervention, which undermined the strength of the findings. In light of the small number and low quality of available studies and risk of publication bias, the authors' conclusions should be treated with caution.

**Implications of the review for practice and research**

**Practice:** The authors stated that patients with a history of nephrolithiasis should be advised to increase fluid intake to either more than two litres per day or a daily urine output of more than 2.5 litres and to maintain at least regular dietary calcium intake. Patients with high intake of phosphoric acid may be advised to minimise their intake of soft drinks, but maintain adequate total fluid intake.

**Research:** Further research was needed into the effects of reduced dietary intake of animal protein, sodium or oxalate and the effects of increasing dietary calcium, potassium and fruit and/or fibre. There should be consensus as to outcomes to enable comparisons across trials and adverse events. Compliance should be better monitored.
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