Systematic review and meta-analysis

Medical management strategies to prevent recurrent nephrolithiasis are stagnant and stronger evidence is needed to reduce morbidity

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Context

The management of urolithiasis represents a common and costly problem for healthcare services. Up to 15% of the general population may be affected at some point in their lives and 25–50% of cases will recur.[1 2] While minimally invasive surgical treatments can treat most of the upper tract calculi, acute stone events and surgical treatment persist as a significant source of morbidity for patients with recurrent urolithiasis. Consequently, the prevention of stone recurrence is an appealing strategy. Although the benefit of dietary modification in preventing stone formation has long been recognised,[3] drug treatments have been shown to provide additional protection beyond that of dietary measures alone.[4] The goal of this systematic review was to evaluate the evidence for medical management in prevention of recurrent urolithiasis.

Methods

This study uses MEDLINE and Cochrane Library searches to identify English language randomised controlled trials (RCTs) involving dietary or medical treatment to prevent recurrent kidney stones. Relevant articles were reviewed and the strength of evidence was assigned.

Findings

The analysis included 28 RCTs, the majority involving patients with recurrent calcium stones (n=23). Most trials were rated as fair but were limited by unclear descriptions of allocation concealment and failure to report outcomes according to intention to treat principles. The review found that increased fluid reduced the risk for stones (relative risk (RR) 0.45 (95% CI 0.24 to 0.84)), but the evidence was relatively weak due to few RCTs. There was moderate-strength evidence that thiazides (RR 0.52 (95% CI 0.39 to 0.69)), citrates (RR 0.25 (95% CI 0.14 to 0.44)) and allopurinol (RR 0.59 (95% CI 0.42 to 0.84)) reduced stone recurrence beyond increased fluid intake in patients with multiple past calcium stones, but the benefits of allopurinol was limited to patients with baseline hyperuricaemia or hyperuricosuria. There was low-strength evidence that combination therapy involving citrate or allopurinol plus a thiazide was not superior to thiazide alone. Compliance was high for strategies involving fluid intake, but poor in studies involving pharmacological interventions. Outcomes were reported based on mixed outcomes (radiographic findings and/or symptoms).

Commentary

Much of our current understanding and recommendations for managing recurrent urolithiasis are based on flawed RCTs. Most of these studies are from the 1980s and 1990s. The cumulative number of patients analysed is remarkably low for thiazide (n=300) and citrate (n=197) studies. The limitations of these studies include: an inability to stratify patients based on stone composition (most included studies were limited to calcium stones), unknown baseline risk of disease severity or biochemical abnormalities, and an absence of data on the impact of pharmacological or dietary interventions on disease risk factors. The lack of uniformity of outcomes is problematic. CT was unfortunately not available; some patients with 'recurrent' stones may have already harboured the stones at baseline and experienced stone passage rather than progression of disease.

While the field of oncology has advanced with the introduction of risk stratification of cancers, and the identification of molecular mechanisms and targeted therapy, the field of medical management of nephrolithiasis has remained stagnant. No new therapies have been introduced, patients are frequently non-compliant with current therapies and physicians often do not perform even simple evaluations to identify the cause of recurrent stones. This review highlights the gaps in knowledge and the limitations of the current literature. The natural history of stone disease is unclear. There is a lack of a stone classification system such as the tumour, node, metastasis (TNM) classification of malignant tumours, used by clinicians for staging cancer. A very generic risk of recurrence estimate, based on old studies is possible, rather than a specific risk based on baseline clinical and metabolic characteristics. Without better studies that appropriately stratify patients by risk, identify the baseline metabolic or dietary abnormalities and evaluate the impact of intervention on those risk factors, it will be difficult to advance the field. Rational trial design will also be critical to draw appropriate conclusions regarding the outcome of interventions. Finally, an earnest utilisation of current pharmacological agents may serve as an impetus for research and development of new treatment options.

Improving the ability to prevent urolithiasis is an important endeavour. The incidence of stone disease is increasing, perhaps in part due to rising rates of obesity and diabetes, which both contribute to stone formation. This has an important impact not only on patient's morbidity but also on the cost of healthcare. Studies to identify optimal management of patients with recurrent urolithiasis are both timely and necessary.

Competing interests None.

References

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