

# Review: Medical therapy with calcium-channel blockers or $\alpha$ -blockers helps patients to pass urinary stones

Hollingsworth JM, Rogers MA, Kaufman SR, et al. Medical therapy to facilitate urinary stone passage: a meta-analysis. *Lancet*. 2006;368:1171-9.

**Clinical impact ratings:** Emergency Med ★★★★★☆ GIM/FP/GP ★★★★★☆ Hospitalists ★★★★★☆

**QUESTION**

In patients with urolithiasis, are calcium-channel blockers or  $\alpha$ -blockers more effective than standard therapy for helping patients pass urinary stones?

**METHODS**

**Data sources:** MEDLINE, PREMEDLINE, CINAHL, EMBASE/Excerpta Medica, abstracts from annual meetings, study authors, and drug manufacturers.

**Study selection and assessment:** Randomized controlled trials (RCTs) that evaluated calcium-channel blockers or  $\alpha$  blockers as the main treatment for ureteral-stone disease (mean size 3.9 to 7.8 mm) and had  $\geq$  1-week follow-up (range 15 to 48 d). Studies were excluded if medical therapy was an adjunct to surgery. 9 RCTs ( $n = 693$ , mean age range 34 to 47 y, 25% to 60% women) met the selection criteria. In 3 RCTs, corticosteroids were given to the treatment groups with the calcium-channel blocker nifedipine. Non-steroidal antiinflammatory drugs were given to both treatment and control groups in 7 RCTs. RCTs were pooled using a fixed-effects model. Quality assessment of the stud-

ies included method of randomization, concealment of allocation, blinding, loss to follow-up, and intention-to-treat analysis.

**Outcomes:** Proportion of patients who passed stones.

**MAIN RESULTS**

More patients in the treatment group than in the control group passed stones (Table). 5 additional RCTs did not have a true control comparator (i.e., calcium-channel blockers or  $\alpha$ -blockers were compared with a treatment that was potentially active [e.g., corticosteroids]); when these RCTs were added to the meta-analysis, the effect for medical therapy with calcium-channel blockers or  $\alpha$ -blockers remained (relative benefit increase

52%, 95% CI 39 to 65). Mean time to passage ranged from 6 days in several treatment groups to 20 days in 1 control group.

**CONCLUSION**

In patients with urolithiasis, medical therapy with calcium-channel blockers or  $\alpha$ -blockers may increase the chance of passing ureteral stones.

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**Medical therapy (calcium-channel blockers or  $\alpha$ -blockers) vs no medical therapy for urolithiasis at 15 to 48 days\***

Outcome	Number of trials (n)	Medical therapy	No medical therapy	Weighted event rates	
				Weighted RBI (95% CI)	NNT (CI)
Urinary stone passage	9 (693)	78%†	47%	65% (45 to 88)	4 (3 to 4)

\*Abbreviations defined in Glossary.

†Weighted event rate and CI for NNT calculated from data in article. A fixed-effects model was used.

**COMMENTARY**

Ureteral colic is an extremely painful and costly medical condition. Despite this, surprisingly few RCTs have examined noninvasive methods to speed stone passage. Traditionally, increased fluids (orally or intravenously) and pain control have been the mainstay of treatment. However, the benefits of increased fluids are uncertain (1). While urologic intervention is nearly always effective, the associated discomfort, risks, and costs preclude this treatment as routine first-line therapy.

The meta-analysis by Hollingsworth and colleagues highlights 2 inexpensive and widely available medications that increased the likelihood of stone passage. However, several issues should be considered. First, in the setting of uncontrollable pain or infection, emergent urologic intervention should not be delayed. Second, the long-term effect on renal function of prolonged partial or complete ureteral obstruction needs clarification. It is not only the proportion of stones that eventually pass, but also the time to passage that matters. Third, the role of the other therapies used with the study drugs is uncertain. For several studies,  $\geq$  1 intervention was used, thus making it difficult to separate the independent effect of the drugs of interest. Fourth, the costs associated with delaying the urological intervention need to be determined. For

example, do patients require more analgesics and still have to miss work while waiting for the stone to pass? Fifth, while the title of the meta-analysis refers to “medical therapy,” it only addresses the role of calcium-channel blockers and  $\alpha$  blockers. In fact, the only calcium-channel blocker studied was nifedipine and the results cannot necessarily be extrapolated to other calcium-channel blockers. Finally, the authors conclude that “a high-quality randomized trial is necessary to confirm the efficacy of [these drugs],” implying that the studies included in the meta-analysis were not “high-quality.” I agree that this research question warrants further study because if these drugs are truly effective, they should become part of the standard treatment of ureteral-stone disease. Based on the available evidence, it seems reasonable to try nifedipine or an  $\alpha$  blocker to facilitate ureteral stone passage while waiting for definitive studies.

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**Reference**

1. Worster A, Richards C. Fluids and diuretics for acute ureteric colic. *Cochrane Database Syst Rev*. 2005;(3):CD004926.