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[Intervention Review]

# Alpha-blockers as medical expulsive therapy for ureteral stones

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## ABSTRACT

### Background

Ureteral colic is a common reason for patients to seek medical care. Alpha-blockers are commonly used to improve stone passage through so-called medical expulsive therapy (MET), but their effectiveness remains controversial. This is an update of a 2014 Cochrane review; since that time, several large randomised controlled trials (RCTs) have been reported, making this update relevant.

### Objectives

To assess effects of alpha-blockers compared with standard therapy for ureteral stones 1 cm or smaller confirmed by imaging in adult patients presenting with symptoms of ureteral stone disease.

### Search methods

On 18 November 2017, we searched CENTRAL, MEDLINE Ovid, and Embase. We also searched ClinicalTrials.gov and the WHO Portal/ICTRP to identify all published/unpublished and ongoing trials. We checked all references of included and review articles and conference proceedings for articles relevant to this review. We sent letters to investigators to request information about unpublished or incomplete studies.

### Selection criteria

We included RCTs of ureteral stone passage in adult patients that compared alpha-blockers versus standard therapy.

### Data collection and analysis

Two review authors screened studies for inclusion and extracted data using standard methodological procedures. We performed meta-analysis using a random-effects model. Primary outcomes were stone clearance and major adverse events; secondary outcomes were stone expulsion time, number of pain episodes, use of diclofenac, hospitalisation, and surgical intervention. We assessed the quality of evidence on a per-outcome basis using the GRADE approach.

### Main results

We included 67 studies with 10,509 participants overall. Of these, 15 studies with 5787 participants used a placebo.

Stone clearance: Based on the overall analysis, treatment with an alpha-blocker may result in a large increase in stone clearance (risk ratio (RR) 1.45, 95% confidence interval (CI) 1.36 to 1.55; low-quality evidence). A subset of higher-quality, placebo-controlled trials suggest that the likely effect is probably smaller (RR 1.16, 95% CI 1.07 to 1.25; moderate-quality evidence), corresponding to 116 more (95% CI 51 more to 182 more) stone clearances per 1000 participants.

Major adverse events: Based on the overall analysis, treatment with an alpha-blocker may have little effect on major adverse events (RR 1.25, 95% CI 0.80 to 1.96; low-quality evidence). A subset of higher-quality, placebo-controlled trials suggest that alpha-blockers likely increase the risk of major adverse events slightly (RR 2.09, 95% CI 1.13 to 3.86), corresponding to 29 more (95% CI 3 more to 75 more) major adverse events per 1000 participants.

Patients treated with alpha-blockers may experience shorter stone expulsion times (mean difference (MD) -3.40 days, 95% CI -4.17 to -2.63; low-quality evidence), may use less diclofenac (MD -82.41, 95% CI -122.51 to -42.31; low-quality evidence), and likely require fewer hospitalisations (RR 0.51, 95% CI 0.34 to 0.77; moderate-quality evidence), corresponding to 69 fewer hospitalisations (95% CI 93 fewer to 32 fewer) per 1000 participants. Meanwhile, the need for surgical intervention appears similar (RR 0.74, 95% CI 0.53 to 1.02; low-quality evidence), corresponding to 28 fewer surgical interventions (95% CI 51 fewer to 2 more) per 1000 participants.

A predefined subgroup analysis (test for subgroup differences; P = 0.002) suggests that effects of alpha-blockers may vary with stone size, with RR of 1.06 (95% CI 0.98 to 1.15; P = 0.16; $I^2$ = 62%) for stones 5 mm or smaller versus 1.45 (95% CI 1.22 to 1.72; P < 0.0001; $I^2$ = 59%) for stones larger than 5 mm. We found no evidence suggesting possible subgroup effects based on stone location or alpha-blocker type.

**Authors' conclusions**

For patients with ureteral stones, alpha-blockers likely increase stone clearance but probably also slightly increase the risk of major adverse events. Subgroup analyses suggest that alpha-blockers may be less effective for smaller (5 mm or smaller) than for larger stones (greater than 5 mm).

## PLAIN LANGUAGE SUMMARY

**Alpha-blockers for ureteral stones in adult patients with symptoms of stone disease**

**Review question**

Does medical treatment with alpha-blockers improve the outcomes of patients with stones stuck in their ureter?

**Background**

Stones stuck in the ureter, which is the tube that transports urine from the kidney to the bladder, often cause pain and make people see a doctor. Depending on which part of the ureter the stone is stuck in and the size of the stone, it will often pass into the bladder on its own over the course of weeks. If the stone does not come out by itself, people often need to have procedures done to remove the stone.

Alpha-blockers are medications that relax muscles in the urinary tract and may make the stone pass into the bladder faster. However, they can cause unwanted effects. We updated an existing Cochrane Review from 2014 to look into the effects of alpha-blockers.

**Study characteristics**

Based on our latest search of the literature from November 2017, we included 64 studies with 10,509 participants. Of these, 15 studies compared alpha-blockers with placebo with 5787 participants. A placebo is a pill that looks and tastes exactly like the real medication, so participants did not know what they were getting. These were the higher-quality studies, which we trusted more.

**Key results**

Based on the subset of higher-quality studies that used a placebo, alpha-blockers likely resulted in more people passing their stones. However, these patients are likely to experience slightly more serious unwanted effects of this medication.

People taking alpha-blockers may pass their stones in a shorter time, may use less diclofenac (which is a type of pain medication), and are likely to be admitted to the hospital less often. Meanwhile, the need for surgery for their stones was similar.

Upon completing additional analyses, we found that effects of alpha-blockers may be different in people with small (5 mm or smaller) versus larger (larger than 5 mm) stones. It appears that this medication works better in people with larger stones. We could find no difference in how well alpha-blockers work, no matter where in the ureter the stone is stuck or what type of alpha-blocker is used.

**Authors' conclusions**

For patients with stones stuck in the ureter, alpha-blockers likely make passing the stone easier but cause slightly more unwanted effects. It appears that alpha-blockers work better in people with larger (greater than 5 mm) rather than smaller (5 mm or smaller) stones.

**Quality of the evidence**

The quality of the evidence for most outcomes was moderate or low, meaning that we have moderate or low confidence in most of the reported results.