Alpha-blockers for expulsion of ureteral stones

A Cochrane review reports that alpha-blockers are more effective at expelling ureteral stones less than 10 mm in diameter than standard therapy or calcium channel blockers.

**Overview:** Kidney stones are caused by the build-up of calcium, ammonia, uric acid or cystine in the kidney (NHS Choices 2014). These stones can pass from the kidney and become lodged in the ureter as ureteral stones (urolithiasis). Ureteral stones may cause symptoms known as renal colic, characterised by flank or abdominal pain radiating to the groin or external genitalia.

Small ureteral stones usually pass spontaneously: 68% of stones 5 mm in diameter or less and 47% of stones between 5 mm and 10 mm in size are passed spontaneously (Preminger et al. 2007). However, medical expulsive therapy with alpha-blockers, calcium channel blockers, corticosteroids, or some combination of these drugs may be offered to facilitate passage of the stone. Alpha-blockers inhibit muscle tone in the ureter to reduce intra-ureteral pressure and increase movement of fluid, boosting the likelihood of stone passage. Faster stone expulsion may decrease the rate of complications, such as urinary tract infections, and reduce the need for interventions to remove the stone.

**Current advice:** Guidance on urolithiasis from the European Association of Urology recommends that people with newly diagnosed ureteral stones less than 10 mm in diameter should undergo observation with periodic evaluation as standard treatment. Patients may be offered medical expulsive therapy with alpha-blockers to facilitate stone passage during observation if they are comfortable with this approach.

The guidance adds that ureteral stones should be actively removed in people with:

- stones with low likelihood of spontaneous passage
- persistent pain despite adequate analgesic medication
- persistent obstruction
- renal insufficiency (renal failure, bilateral obstruction, or single kidney).

**New evidence:** A Cochrane review by Campschroer et al. (2014) assessed the effect of alpha-blockers compared with standard therapy (hydration and painkillers, with or without prophylactic antibiotics), other drugs or placebo on the expulsion of ureteral stones. The authors identified 32 randomised controlled trials and quasi-randomised controlled trials (n=5864) of alpha-blockers in adults with ureteral stones less than 10 mm and confirmed by imaging.

Alpha-blockers were associated with a higher stone clearance rate than standard therapy with hydration and painkillers, with or without prophylactic antibiotics (risk ratio [RR]=1.48, 95% confidence interval [CI] 1.33 to 1.64, p=0.00001; 30 studies, n=2378). The rate of stone expulsion was also significantly higher when alpha-blockers were compared with calcium channel blockers (RR=1.19,
95% CI 1.05 to 1.35, p=0.006; 4 studies, n=3486), but not when compared with placebo (RR=1.22, 95% CI 0.99 to 1.51, p=0.062; 6 studies, n=629).

Time to stone expulsion was nearly 3 days less with alpha-blockers than with standard therapy (mean difference [MD]=–2.91 days, 95% CI –4.00 to –1.81 days, p<0.00001; 18 studies, n=1388), and the number of pain episodes was slightly less than with any of the control treatments (MD=–0.48, 95% CI 0.94 to –0.01, p=0.04; 6 studies, n=555). People on alpha-blockers were more likely to experience adverse effects than those on standard therapy (RR=2.74, 95% CI 1.38 to 5.45, p=0.004; 13 studies, n=1126) or placebo (RR=2.73, 95% CI 1.50 to 4.96, p=0.001; 5 studies, n=507). However, only 10.4% of people on alpha-blockers experienced adverse effects and these effects were mostly mild.

Limitations of this analysis include that most studies were small single-centre trials, few (22%) were double blind, and most (81%) were at high or unclear risk of bias. Most studies (91%) were in people with distal ureteral stones, so no conclusions can be drawn on the effects of alpha-blockers on proximal or mid-ureteral stones. In addition, none of the drugs studied are licenced for use in urolithiasis in the UK.

Commentary: “This latest Cochrane review confirms what has entered common practice in urology despite limitations of the evidence. Alpha-blockers have emerged as consistently providing a benefit in patients with acute renal colic when compared with other medications. However, the trials are not as high quality as would be desirable. To this end, a multicentre, randomised, placebo-controlled UK trial is underway to compare alpha-blockers, calcium channel blockers and placebo in the management of symptomatic ureteral stones (SUSPEND). This trial has closed recruitment and should report next year.

“Increasing the passage of ureteral stones clearly avoids the cost of intervention – for example, extracorporeal shock wave lithotripsy or ureteroscopy for the NHS – and potential complications for the patient. As these stones are often found in a young, active, working population, improving stone expulsion also reduces the burden on society by meaning patients can return to work more quickly. Evidence from further trials is keenly awaited.” – Miss Kay Thomas, Clinical Lead for Urology, Guy’s and St Thomas’ NHS Foundation Trust and Honorary Senior Lecturer, Kings College London

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