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This series is coordinated by Corey D. Fogleman, MD, Assistant Medical Editor.

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Alpha Blockers to Speed Ureteral Stone Passage

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Clinical Question

Do alpha blockers safely speed passage of subcentimeter ureteral stones?

Evidence-Based Answer

Compared with patients receiving standard therapy (e.g., fluids, analgesics), placebo, or calcium channel blockers, patients receiving alpha blockers had about three fewer days to ureteral stone expulsion and were less likely to be hospitalized. Adverse effects of alpha blocker therapy are generally tolerable. (Strength of Recommendation: A, based on consistent, good-quality patient-oriented evidence.)

Practice Pointers

The prevalence of kidney stone disease has increased in recent years and affects 5% to 10% of the population.¹ Alpha blockers relax smooth muscle and decrease intraureteral pressures. The authors of this Cochrane meta-analysis evaluated the role of alpha blockers as a medical therapy to speed the passage of ureteral stones.

The authors identified 32 randomized controlled trials (RCTs) and quasi-RCTs with 5,864 participants. Participants were symptomatic adults with radiologically confirmed ureteral stones 10 mm or smaller. Exclusion criteria included urinary tract infection, hydronephrosis, or other underlying abnormalities of the kidney or ureters.

Alpha blockers used included tamsulosin (Flomax; 0.2 or 0.4 mg), alfuzosin (Uroxatral; 10 mg), doxazosin (Cardura; 4 mg), and terazosin (Hytrin; 2 or 5 mg); most studies used tamsulosin in a dosage of 0.4 mg once daily. The majority of studies ran two to four weeks and compared alpha-blocker

therapy plus standard therapy (hydration, pain killers, nonsteroidal anti-inflammatory drugs, corticosteroids, prophylactic antibiotics) with standard therapy plus placebo. Others compared alpha blockers with calcium channel blockers such as nifedipine (Procardia; 30 mg) or the antimuscarinic tolterodine (Detrol; 4 mg).

The overall stone expulsion time was three days shorter with alpha blockers than with standard therapy, with a mean expulsion time of seven rather than 10 days. When looking at stone-free status by the end of the study, patients taking alpha blockers had much improved clearance compared with those in standard therapy (30 studies with 2,378 participants; relative risk [RR] = 1.48; number needed to treat [NNT] = 4), and also when compared head-to-head with patients taking calcium channel blockers (four studies with 3,486 participants; RR = 1.19; NNT = 4.8). A Chinese RCT of 3,189 patients accounted for most of the latter findings; the study was appropriately masked and considered at low risk of bias.²

The benefits of alpha blockers were robust, irrespective of whether the stone was smaller than 5 mm or was 5 to 10 mm in diameter. Alpha blockers greatly reduced the need to hospitalize (four studies with 313 participants; RR = 0.35; NNT = 4.2) and, to a more modest degree, reduced the number of pain episodes and amount of pain medication used.

Only five studies reported adverse effects. In these studies, about 10% of participants (88 out of 845) experienced dizziness, palpitations, headache, rhinitis, retrograde ejaculation, fatigue and weakness, cutaneous reaction, or postural hypotension. Most adverse effects were mild and did not lead to cessation of therapy.

Specialty guidelines published in 2007 recommend use of alpha blockers to help pass subcentimeter ureteral stones in otherwise stable patients.³ Duration of treatment is not specified by the guidelines, but this

Cochrane review suggests that passage should occur within one month, if not two weeks. Family physicians should consider alpha blockers as first-line therapy for patients with otherwise uncomplicated subcentimeter ureteral stones.

SOURCE: Campschroer T, Zhu Y, Duijvesz D, Grobbee DE, Lock MT. Alpha-blockers as medical expulsive therapy for ureteral stones. *Cochrane Database Syst Rev.* 2014;(4):CD008509.

The practice recommendations in this activity are available at <http://summaries.cochrane.org/CD008509>.

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Buprenorphine Maintenance vs. Methadone Maintenance or Placebo for Opioid Use Disorder

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Clinical Question

Is buprenorphine maintenance treatment effective in the management of opioid use disorder?

Evidence-Based Answer

At dosages greater than 2 mg per day, buprenorphine maintains treatment retention better than placebo. (Strength of Recommendation: A, based on consistent, good-quality patient-oriented evidence.) At 16 mg or more per day, buprenorphine was found to reduce illicit substance use compared with placebo as monitored by urinalysis. (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.)

When flexible dosing (doses adjusted based on patient symptoms) is used, the effectiveness of buprenorphine is comparable to that of methadone in suppressing opioid use. (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.) When fixed dosing (a set dose is given) of 7 mg or more is used, buprenorphine and methadone are equally effective as measured by retention in treatment and suppression of illicit opioid use. (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

The *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed., combines “opioid abuse” and “opioid dependence” into the new diagnosis “opioid use disorder,” categorized as mild, moderate, or severe based on the number of positive symptoms.¹ Pharmacologic treatment options for opioid use disorder include methadone and buprenorphine. Buprenorphine is usually prescribed as a combination formulation that includes the pharmacologically inactive naloxone, except in pregnancy when it is recommended that buprenorphine be used alone. Both methadone and buprenorphine are intended to be administered in conjunction with psychosocial treatment, with the goal of eliminating withdrawal symptoms and maintaining the patient on a documented and regulated dosage. Because buprenorphine is a partial agonist, there is a ceiling effect to the level of respiratory depression or sedation it can cause, reducing the risk of overdose. Buprenorphine may be prescribed by primary care physicians who complete eight hours of training and receive a waiver from the Drug Enforcement Administration.

This analysis included 31 randomized controlled trials (5,430 participants) comparing buprenorphine maintenance with placebo or methadone maintenance. Primary outcomes were retention in treatment and continued use of opioids as measured by self-report or urinalysis. Various dosing regimens were used. All dosages of buprenorphine were superior to placebo in treatment retention: 7 to 15 mg per day (relative risk [RR] = 1.74; 95% confidence interval [CI], 1.06 to 2.87), and 16 mg or more per day (RR = 1.82; 95% CI, 1.15 to 2.90). Thus, given a baseline retention rate of 40% in those receiving placebo, the retention rate would increase to approximately 70% in those receiving 7 to 15 mg of buprenorphine and to 73% in those using at least 16 mg of buprenorphine daily. Only high-dosage buprenorphine (at least 16 mg per day) was effective—and then, only mildly—in suppressing illicit opioid use when monitored by urinalysis (standardized mean difference [SMD] = -1.17; 95% CI, -1.85 to -0.49).

In studies comparing buprenorphine maintenance with methadone maintenance, flexible dosing and fixed dosing were evaluated. In analyses of flexible dosing, buprenorphine was less effective than methadone in treatment retention (RR = 0.83; 95% CI, 0.72 to 0.95), but there was no difference between groups in suppression of opioid use when monitored by urinalysis (SMD = -0.11; 95% CI, -0.23 to 0.02). However, when fixed dosing was studied, medium (7 to 15 mg) and high (16 mg or more) doses of buprenorphine were found to be equivalent to medium (40 to 85 mg) and high (85 mg or more) fixed doses of methadone in terms of retention and suppression of illicit opioid use.

Cochrane for Clinicians

Two studies comparing buprenorphine and methadone found no difference in the frequency of adverse effects,^{2,3} but one of the two reported an increased level of sedation in the methadone group (58% vs. 26%).³ A third study comparing buprenorphine with placebo reported that adverse effects were similar in the two groups.⁴

Clinical practice guidelines encourage the use of buprenorphine and methadone as medication-assisted treatments.^{5,6} Both medications were given a level A rating, indicating that a strong level of evidence was found and that the intervention benefits substantially outweighed harms.⁶ Factors including availability of methadone facilities, a patient's ability to meet the requirements associated with a treatment program, the safety profiles of buprenorphine and methadone, and patient preference should be considered when helping patients determine which treatment option best fits their needs.

SOURCE: Mattick RP, Breen C, Kimber J, Davoli M. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *Cochrane Database Syst Rev.* 2014;(2):CD002207.

The practice recommendations in this activity are available at <http://summaries.cochrane.org/CD002207>.

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