

MEDICAL MYTHOLOGY

Myth: Nephrolithiasis and medical expulsive therapy

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ABSTRACT

There is a medical myth that ureteral stones larger than 5 mm will not pass spontaneously and require urological intervention for removal. Recent findings indicate that medical expulsive therapy can facilitate spontaneous passage for stones up to 10 mm. For the management of ureteral stones, we recommend administering tamsulosin and a corticosteroid (deflazacort or prednisone) along with the standard therapy of analgesics, antibiotics and hydration.

Key words: renal colic, medical therapy, expulsive therapy, kidney stone

RÉSUMÉ

Selon un mythe médical, les calculs urétéraux de plus de 5 mm ne pourraient pas passer spontanément et nécessiteraient une intervention urologique. Des études récentes montrent cependant qu'un traitement expulsif peut faciliter le passage spontané de calculs de 10 mm ou moins. Nous recommandons, pour la prise en charge de calculs urétéraux, l'administration de la tamsulosine et de corticostéroïdes (deflazacort ou prednisone) en combinaison avec un traitement standard d'analgésiques, d'antibiotiques et d'hydratation.

Background

Ureteral stones are a common problem, with over 1 million visits to US emergency departments (EDs) annually.¹ Stone size is an important factor in determining treatment, and recommendations in emergency medicine textbooks do not reflect current literature or evolving urological practice.^{2,3} Recent research shows that medical expulsive therapy in the ED can increase the expulsion rate and decrease the expulsion time thereby reducing lost workdays, urological visits and (avoidable) stone removal procedures.³⁻⁸

Rosen's textbook of emergency medicine suggests that 90% of stones less than 5 mm and 15% of stones

between 5 mm and 8 mm will pass spontaneously within 4 weeks, while 95% of those larger than 8 mm will require urological intervention. Recommended management includes analgesics, antibiotics and hydration for stones less than 5 mm or urology referral with consideration of extracorporeal shock wave lithotripsy, percutaneous nephrolithotomy or surgical removal for larger stones.²

Recent research on medical expulsion therapy

Emergency physicians can do more to facilitate stone passage. New research on medical expulsive therapy shows that calcium channel blockers, alpha-1-adrenergic blockers

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and steroids increase expulsion rates and reduce stone passage time (Box 1).^{4,9}

Calcium channel blockers

The ureter is lined by smooth muscle cells that respond to changes in calcium ion concentrations. Increasing calcium levels cause ureteral muscle contraction and decreases cause relaxation. When renal calculi induce ureteral spasms that interfere with stone expulsion, calcium channel blockers can reduce these spasms.¹⁰ In a 2000 study of the efficacy of nifedipine and deflazacort on the management of distal ureter stones, stone expulsion occurred in 79% of the treatment group and only 35% of control subjects. The average stone size was 5.8 (standard deviation [SD] 1.8) mm (range 3.5–10 mm) for the treatment group and 5.5 (SD 1.4) mm (range 3–10 mm) for the control group. No correlation was found between stone size and expulsion time for patients in the treatment group.⁵ This study⁵ and others^{7,9} suggest that calcium channel blockers can facilitate spontaneous passage for stones up to 10 mm, contrary to information provided in emergency medicine textbooks.

Alpha-1-adrenergic receptor blockers

Ureteral smooth muscle is densely populated by alpha-1-adrenergic receptors. Similarly, the proximal urethra, prostate and bladder outlet contain high concentrations of alpha-1A-receptors while the detrusor and lower ureter contain alpha-1d-receptors. Alpha receptor blockade inhibits basal smooth muscle tone, peristaltic frequency and ureteral contraction thus facilitating the passage of ureteral stones.⁹ In a recent study assessing the efficacy of tamsulosin in the management of renal colic, the stone

expulsion rate was 100% for the treatment group and 70% for control subjects. Mean expulsion time was 65.7 (SD 66.5) hours for the treatment group (range 2–288) compared with 111.1 (SD 65.5) hours for control subjects (range 12–240). In this study, mean stone size was 6.7 (SD 2.1) mm in the treatment group, compared with 5.8 (SD 1.3) mm in control subjects ($p = 0.047$).⁶ This and other studies indicate that tamsulosin therapy initiated in the ED can increase passage rates and reduce passage time for stones up to 10 mm.^{6–8,12}

Corticosteroids

Investigators have shown that larger stones tend to cause more intense ureteral inflammatory reactions and that submucosal edema in the vicinity of a stone may aggravate urinary obstruction and calculus retention.^{13,14} Corticosteroids stabilize neutrophil lysosomes, therefore decreasing inflammation and edema related to mechanical irritation.¹⁵ Steroids, notably deflazacort and prednisone,^{4–6,8} can be used in conjunction with the medical expulsive therapies discussed above. In a recent study of patients treated with tamsulosin, the addition of deflazacort reduced mean (SD) expulsion time from 139.2 (113.8) hours to 103.3 (136.2) hours ($p = 0.04$) but had minimal positive effect on stone expulsion rates (90.0% v. 96.7%). Median stone size was 6.9 mm (range 5.5–7.8) in deflazacort recipients, compared with 6.4 mm (range 5–8) in control subjects, suggesting that corticosteroids may be beneficial for reducing expulsion time with larger stones.

We were unable to identify any trials examining the role of corticosteroids alone in the treatment of renal colic, and no studies have yet assessed the combination of corticosteroids and calcium channel blockers, although they are now often used concurrently.¹⁶

Calcium channel blockers versus alpha-1-adrenergic receptors

The above-mentioned research suggests that both classes of drugs are potentially beneficial for patients with renal colic, but direct comparative data are limited. In one study, Dellabella and colleagues compared nifedipine with tamsulosin in 140 patients with renal colic (70 patients in each group), reporting expulsion rates of 97.1% in the tamsulosin group and 77.1% in the nifedipine group ($p < 0.001$). Average expulsion times were 72 hours and 120 hours ($p < 0.001$) in the 2 groups, respectively, despite larger stones in the tamsulosin group (tamsulosin 7.2 mm v. nifedipine 6.2 mm; $p = 0.002$).⁸ These data suggest that tamsulosin may be the first line agent for medical expulsive therapy.^{8,17}

Box 1. Recommendations for medical expulsive therapy*

- Tamsulosin 0.4 mg daily (with side effects including hypotension, asthenia, dizziness, malaise and diarrhea).¹²
Or
- Nifedipine XL 30 mg daily (with side effects including hypotension, palpitations, stomach, headache, edema and asthenia).⁵
Either of the following *may* be considered in addition to the above:
 - Deflazacort 30 mg daily (maximum 10 days)†
 - Prednisone 10 mg twice daily (5 days burst without taper)†

*Patients receiving medical expulsive therapy who do not pass their stones within 4 weeks should be referred to a urologist since longer observation may increase the rate of complications, including renal dysfunction, urosepsis and intractable pain.¹⁸

†Corticosteroid adverse effects include hyperglycemia, bone loss and Cushing's syndrome.

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