TAMSULOSIN: URETERIC MOTILITY  Stephen Y. Nakada – University of Wisconsin School of Medicine and Public Health, Madison, WI, USA
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INTRODUCTION
It is well known that most patients with urolithiasis can be managed conservatively. Clinical studies show spontaneous passage rates of 71–98% for small (<5 mm) distal ureteric stones, with stone size and location being the most important predictors of stone passage [1,2]. Not surprisingly, in the last 20 years the most significant advances in managing ureteric stones have been surgical rather than medical. As a result, understanding the dynamics of ureteric stone passage has been a low priority.

So why care about ureteric motility? Is it better to increase or decrease ureteric contractility to facilitate stone passage? How does ureteric stretch affect stone passage? Recently, pharmacological approaches to improving stone passage and reducing the need for surgical intervention have been championed worldwide. Now referred to as ‘medical expulsive therapy’, this new initiative leads to the questions of how it works and why it was not done sooner. Although NSAIDs, calcium-channel blockers and corticosteroids have all been effective medical adjuncts, tamsulosin has been particularly pervasive.

Studies show that both α- and β-adrenergic receptors are present in the human ureter, although α-receptors predominate. More specifically, α1-receptors are important in lower ureteric physiology, and higher densities of α1-receptors have been discovered in the lower ureters of animals and humans [3,4]. Of the known α1-receptor subtypes, α1d-receptors have the most pronounced effect on detrusor contraction and spasm of the lower ureter, particularly the intramural portion. Undoubtedly, alterations in the lower urinary tract, including the bladder neck, trigone and intramural ureter, all have a role in ureteric stone passage.

Peters and Eckstein [5] investigated the effect of adrenergic agents in an obstructed-ureter model. They showed that noradrenaline increased ureteric spasm at the point of obstruction, while decreasing flow. Tachykinins, e.g. substance P, neurokinin A and B, are substances released in response to painful stimuli. Not surprisingly, the presence of neurokinin A, substance P and bradykinin has been associated with increased contractions in the proximal and distal ureter [6].

Urinary colic develops as a result of obstruction, ureteric smooth muscle spasm and subsequent proximal ureteric distension. Physical stimulation of afferent sensory neurones by a stone or stretch is the result, and this effect is intensified by prostaglandins, bradykinin and tachykinins. Increased contractions increase the intraluminal pressure, further intensifying the pain, possibly in part due to local ischaemia. Tamsulosin, selective for the α1a- and α1d-receptors, inhibits basal tone and decreases peristaltic frequency and amplitude in the ureter. Notably, these conditions, with concomitant steroids, have shown significant clinical benefits in patients with ureteric stones.

Dellabella et al. [7] evaluated the efficacy of tamsulosin with corticosteroids in patients with distal ureteric stones. They randomized 60 patients to receive standard treatment, i.e. phloroglucinol-trimethoxybenzene (an oral antispasmyotic) deflazacort and cotrimoxazole, or standard treatment plus tamsulosin 0.4 mg daily. Tamsulosin was beneficial, with a statistically significantly higher stone-expulsion rate (100% vs 70%) with a shorter stone expulsion time (65.7 vs 111.1 h). No drug side-effects were reported and hospital stays were dramatically reduced in the tamsulosin group.

Porpiglia et al. [8] sought to determine if the treatment success of tamsulosin and corticosteroids was a result of a single drug or association of the two. In all, 114 patients with distal ureteric stones of >5 mm were enrolled into four groups. The first group received tamsulosin 0.4 mg daily, the second deflazacort 30 mg daily, the third both medications and the fourth received only analgesics. The treatment duration was 10 days to limit the side-effects of prolonged corticosteroid therapy. The rates of expulsion for the four groups were 60%, 38%, 85% and 33%, respectively. There was a statistically significant difference between the combined tamsulosin and deflazacort group and the other groups. However, the authors concluded that tamsulosin alone can be considered as an alternative treatment for those patients who are unsuitable for steroid therapy.

Hollingsworth et al. [9] provided the most compelling clinical validation by reporting a meta-analysis of randomized trials assessing the efficacy of medical expulsive therapy. Specifically, this meta-analysis showed a clear advantage in stone passage for patients taking α-adrenergic antagonists, as well as calcium-channel blockers. They also concluded that adding corticosteroids might provide an advantage, but the benefit of drug therapy is not lost in those patients in whom corticosteroids might be contraindicated. Our group recently showed that steroids can also independently decrease ureteric contractility [10].

So what can be gleaned from all this? The available scientific evidence supports the view that tamsulosin decreases ureteric contractility. Moreover, several clinical trials have shown that tamsulosin improves stone passage rates, decreases stone expulsion times, and reduces the need for analgesia, hospitalization and surgery. Although tamsulosin appears to be more effective when used in combination with a corticosteroid, it is also effective when used alone.

Regardless of this, medical expulsive agents decrease ureteric contractility, oedema and pain. Therefore, it appears that decreasing ureteric contractility is beneficial to stone passage, even though ureteric contractility increases in response to a stone as a result of the release of pertinent mediators. The subsequent decrease in renal back-pressure probably decreases the acute symptoms of ureteric obstruction, which often requires urgent interventions such as placing a stent, or ureteroscopy. While there is room for a better understanding of the dynamics of ureteric motility and stone passage, medical expulsive therapy is here to stay, which is a good thing for our patients.

CONFLICT OF INTEREST
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REFERENCES


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