Medical expulsive therapy for urolithiasis

Urolithiasis or urinary stone disease is one of the most common conditions encountered in daily urological practice. Patients may be asymptomatic or present to emergency departments or an outpatient setting with renal colic. The two factors most likely to predict successful stone passage are stone size - stones < 10mm are more likely to pass spontaneously, and secondly, stone location - distal stones are more likely to pass compared to proximal stones. There is a high rate of spontaneous passage (ranging from 71-98%) for small stones < 5mm in size, located in the distal ureter. Depending on the extent of renal compromise caused by the stone and pain experienced by the patient, a trial of non-surgical means to facilitate passage is a useful treatment option, given the high rate of spontaneous stone passage and the fact that surgery and anaesthesia are not without risks. Interest in the use of medications to assist in spontaneous stone passage has increased in recent times. The theoretical mechanism behind using medications to promote stone passage is relaxation of the ureter in the region of the stone, and an increase the hydrostatic pressure proximal to the stone to promote expulsion. These effects are mediated via active calcium-channel pumps and adrenergic alpha-1 receptors present in the ureteral smooth muscle.

In 2006, a meta-analysis of nine randomised controlled trials (RCT) assessing calcium channel blockers (CCB) and alpha-blockers to treat ureteral stones was published in *The Lancet*. The meta-analysis included studies with a total of 693 patients treated in an outpatient setting. The mean age of patients varied from 34.4 - 46.5 years. The mean stone size was 3.9 - 7.8mm, and 8/9 studies included patients with stones located in the distal third of the ureter. Treatment duration with a calcium channel blocker (nifedipine) or alpha-blocker (tamsulosin) therapy ranged from seven days to six weeks, or until stone passage (if the stone was passed before six weeks elapsed). Treatment and control groups received an anti-inflammatory for pain in 7/9 studies. The primary outcome of the meta-analysis was the proportion of patients with successful stone passage. In all the studies, the proportion of patients with successful stone passage was greater in the treatment group compared to controls. There was a 65% greater likelihood of spontaneous stone passage with medical expulsive therapy (MET) with the mean time for stone passage ranging from 6-20 days. Other reported benefits included decreased time to stone passage, decreased pain episodes, decreased analogue pain scores and decreased doses of analgesics. The meta-analysis does not differentiate between the effectiveness of nifedipine and tamsulosin.

In 2010, a multi-centre, prospective, randomised trial comparing the efficacy of nifedipine and tamsulosin for MET in patients with distal ureteric stones and renal colic. The study included 3189 patients with a single ureteral stone of 4-7mm. Fever, UTI, severe hydronephrosis, multiple renal stones and renal insufficiency were some of the exclusion criteria. Patients from 10 medical centres in China were enrolled and randomly assigned to treatment with tamsulosin 400 microgram per day (n=1596) or nifedipine 10mg three times a day (n=1593) over four weeks. The primary outcome was overall stone expulsion rate. Those who received tamsulosin experienced a higher stone expulsion rate (95.9%) compared to nifedipine (75.5%). There were no significant differences in side effects reported with tamsulosin (5.6%) compared to nifedipine (6.2%). Specific side effects were not reported in the study, but details of blood pressure in each arm would be of interest, as nifedipine is a known peripheral vasodilator and tamsulosin is an alpha-blocker specific to the urinary tract.

The urology department at the RGH have recently adopted the use an alpha-blocker specific to the smooth muscle of the urinary tract for the off-label use of MET in urolithiasis. Given the elderly patient demographic at RGH, multiple co-morbidities and polypharmacy can contribute to risks where additional vasodilators may increase falls risk. Ultimately, the risk of surgery need to be weighed against the costs of the off-label use of medications in each individual, but MET does present a reasonable treatment alternative for patients amenable to conservative management of urolithiasis.

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FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: chris.alderman@rgh.sa.gov.au

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