



PROSPECTIVE RANDOMIZED TRIAL COMPARING THE EFFICACY OF TAMSULOSIN AND TAMSULOSIN COMBINED WITH NIFEDIPINE FOR THE MANAGEMENT OF DISTAL URETERIC STONE

General Surgery

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ABSTRACT

Objective: To evaluate the efficacy of tamsulosin compared with the combination of tamsulosin with nifedipine for the management of lower ureteral calculi less than 10 mm in size.

Material And Method: The study included 80 patients with stones less than 10mm in size located in the lower (distal) ureter. The patients were divided into 2 groups. Group 1 patients (N=40) received 0.4mg tamsulosin once daily and nifedipine 5mg once daily. Group 2 (N=40) received 0.4mg tamsulosin once daily. Patients received analgesics and antispasmodics in addition.

Results: The average stone size was similar among the 2 groups. After the treatment with medication, stone expulsion in Group 1 was 34 out of 40. In Group 2 was 30 out of 40. The average time required for the expulsion of stone in Group 1 was 20.2 days and Group 2 was 27.6 days respectively. So, a significantly higher rate of expulsion was noted in Group 1. However, some patients complained of headache, dizziness and postural hypotension.

Conclusion: Study reveals that lower ureteric stones less than 10mm can be effectively managed by medical management. Hence, the combination therapy of tamsulosin with nifedipine is more effective than mono-therapy with tamsulosin.

KEYWORDS

INTRODUCTION

Urolithiasis is a disease affecting 8-15% of the world population¹ urolithiasis is associated with higher risk of recurrence after initial episode. This risk is estimated to be 50% at 5 years and 70% at 9 years², with male :female ratio 2:1 . Ureteric stones invariably originate from kidney and on its course from renal pelvis to bladder gets impacted in any of the anatomical narrowing of ureter³ time to spontaneous expulsion of stone mainly depends on size of the stone and its location in the ureter⁵. 70% are located in lower one third of the ureter⁴. According to the results of a meta-analysis published by American Urological Association, 98% of ureteric calculi having size less than 5 mm in diameter is likely to pass spontaneously without any intervention and requires only observation and symptomatic treatment.⁶

Ureteric colic due to urolithiasis is the most common problem encountered with treatment interventional and expectant treatment are the typical approaches used in management.

The two factors that appear to be most useful in facilitating stone passage are an increase in hydrostatic pressure proximal to a calculus and relaxation of the ureter in the region proximal to the stone. Various drugs used in MET include alpha-1 blockers like tamsulosin, a calcium channel blocker nifedipine, corticosteroids and recently phosphodiesterase 5 (PDE5) inhibitors.

$\alpha 1$ adrenergic receptors are present in the ureter with highest density in lower ureters. $\alpha 1$ adrenergic antagonists inhibit basal tone, peristaltic frequency, and ureteric contractions intramurally, resulting in increased fluid transport and decrease in intra-ureteric pressure⁸ and spontaneous passage of stone and used in MET⁷. In addition to his referred pain is blocked by acting on the c-fibers or sympathetic ganglion^{9,8}.

Nifedipine is a dihydropyridine class of L-type calcium channel blocker that blocks the movement of Ca^{2+} in the cell and is expected to depress ureteric function through its spasmolytic effect. Nifedipine modifies the effect of calcium on ureteric smooth muscle there by reducing the ureteric contraction and ureteric colic⁹.

MATERIALS AND METHODS

In total, 80 patients who presented with stones (<10 mm) located in the distal ureter, were included in the study. The exclusion criteria were: a desire to surgically treat colic, gross back pressure changes, recurrent urinary tract infection, ischemic heart disease, history of previous surgery in the distal ureter, and acute renal failure.

Patients were initially evaluated by performing urinalysis, urine culture and sensitivity, complete hemogram, serum uric acid, USG in

the KUB region. 80 symptomatic cases of lower ureteral calculus were then divided randomly into group 1 and group 2.

Group 1 - The 40 patients in this group received tamsulosin 0.4 mg OD in the night before going to bed until expulsion of the stone, or for 6 weeks, whichever was earlier. An analgesic (diclofenac) and an anti-spasmodic (hyoscine butyl bromide) were administered. Patients were advised to drink plenty of fluids.

Group 2 - The 40 patients in this group received tamsulosin 0.4 mg OD in the night before going to bed and nifedipine (5 mg) once daily in the morning. Analgesic and anti-spasmodic treatments were also administered as needed. Patients were advised to drink plenty of fluids.

Patients were followed up weekly with direct X-ray of the KUB region and ultrasonography of the KUB region. Time to pass the stone, the size of stone, the need for analgesic and anti-spasmodic treatments, as well as the number of colic episodes experienced were evaluated.

RESULTS

	Group 1	Group 2
Patient No.	40	40
Male: Female	31:9	33:7
Mean age (years)	35.5	33.4
Mean stone size (mm)	6.50	6.72
Mean time for stone passage (days)	20.2	27.6
Spontaneous expulsion (%)	85%	75%

In total, 80 patients were included in the study. They were randomized to 2 groups that had no significant demographic difference (Table 1). Spontaneous stone expulsion was noted in 34 of 40 patients in group 1 (85%), and 30 of 40 patients in group 2 (75%). A significant difference was noted between the two groups.

The average time to stone expulsion was 20.2 days in group 1, and 27.6 days in Group 2. Patient in both groups experienced side effects, which included nausea, vertigo, postural hypotension, retrograde ejaculation, headache, and gastritis acidity. All these side effects subsided in both groups, and no patients had to be excluded.

On an average, 2-3 episodes of ureteric colic was noted in each group. In group 1, 17 out of 40 patients received the analgesic, diclofenac. In group 2, 21 out of 40 patients required diclofenac. In both groups, the number of times the medication had to be administered was similar. There was no significant difference between group 1 and group 2 regarding the number of episodes of ureteric colic and the need for an analgesic or anti-spasmodic. Side effects patient complained of headache, nausea, postural hypotension and acidity. intensity

decreased by time so no people dropped out of study .

DISCUSSION

Prevalence of urolithiasis in India ranges from 4-20% with a male: female ratio of 2:1. Ureteric stones account for approximately 20% of urolithiasis cases, out of which 70% are located in the lower one third of the ureter². The time for spontaneous expulsion of stones depends on the size of the stone and its location. Stones with sizes less than 6 mm require 42 days for spontaneous expulsion. They can be managed conservatively using pharmacological intervention to control pain, ureteric spasm, edema and infection, accelerating stone expulsion. MET with active monitoring is an option for stones up to 10 mm especially for distal ureteric calculus¹⁰. It is a cost-effective strategy before opting for active stone removal. The EUA/AUA 2007 guidelines suggest tamsulosin and nifedipine for MET¹¹. MET can potentially prevent hospitalization for treatment, cutting risks, and being cost saving. In this randomized prospective clinical study, a combination of tamsulosin and nifedipine was compared with a monotherapy of tamsulosin to assess its efficacy and safety. MET can be used in cutting down cost and risks and hospitalization^{12,8}

A recent meta-analysis considered all randomized controlled trials in which calcium channel blocker or alpha blockers were used to treat urethral stones¹³. The subgroup analysis indicated no statistically significant difference between the drugs with regard to minor or major adverse effects fixed-effect. This meta-analysis demonstrated that tamsulosin was more effective than nifedipine in patients with lower ureteric stones, as evidenced by the higher stone expulsion rate.

In another study, there was a 65% greater likelihood of stone passage in the treated patients. In two published comparisons of tamsulosin and nifedipine, tamsulosin had superiority over nifedipine in terms of the rate of stone passage, time to stone passage and reduced narcotic use in one study. Steroids had a slight added benefit but do not appear to be as important as the alpha- or calcium channel blocker¹⁴.

Ureteral calculus can lead to urinary tract infection, hydronephrosis and renal function deterioration. In case of complete ureteral obstruction by calculus, signs of kidney damage will appear within 3-4 weeks. We extended our study to 6 weeks to monitor renal function and the progress of stone movement.

Alpha-blockers, being predominant in lower ureter, are more effective for distal or lower ureteric stones, whereas calcium channel blocker acts along the entire length of ureter. Both the drugs work in synergy to reduce the force of ureteric spasm and increasing the hydrostatic pressure proximal to the stone, and relaxing the ureter both at the site of the calculus and distal to it, thus causing expulsion of stone.

CONCLUSION

The results of this study demonstrate superiority of the combination (Group 1) over monotherapy (Group 2). The combination of tamsulosin with nifedipine had a statistically significant higher rate of expulsion and reduction in duration to expulsion than tamsulosin monotherapy. The combination of tamsulosin and nifedipine can be used as monotherapy with tamsulosin in patients as MET for lower ureteric stones of 5 to 10 mm, who are amenable to waiting management.

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