

## ORIGINAL ARTICLE

## MEDICAL EXPULSIVE TREATMENT OF DISTAL URETERAL STONE USING TAMSULOSIN

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**Background:** Many minimally invasive interventional techniques as well as expectant treatments exist for the management of lower ureteric calculi. This study was conducted to evaluate the efficacy of tamsulosin as an expulsive pharmacologic therapy for the treatment of distal ureteral stone. **Methods:** This randomized control trial included 100 patients over 18 years of age with stone Size  $\leq 8$ mm in distal 1/3 of ureter. Patients were randomly assigned into two groups (A & B). Group A Patients were given Capsule Tamsulosin 0.4 mg, 1 daily up to 4 weeks while group B patients were given placebo, 1 Capsule daily up to 4 weeks. The primary endpoint was expulsion rate. A written informed consent was taken from all the patients. Expulsion time, need for analgesics, need for hospitalization and drug side effects were secondary endpoints. **Results:** A total of 49 patients in group A and 48 patients in group B reported back, therefore 97 out of 100 patients were evaluated. Mean age of the patients was 36.34 years (range 18–57 years). Mean stone size was 5.78 mm (range 4–8 mm) in greatest dimension. A stone expulsion rate of 85.71% (42 patients) was noted in group A and 54.20% (26 patients) in group B. Group A revealed a statistically significant advantage in term of stone expulsion rate ( $p=0.032$ ). Considering expulsion time in days group A showed statistically significant advantage ( $p=0.015$ ). Regarding age, sex, stone size and stone lateralization (right/left), there was no significant difference between the group A and B. No drug side effects were noted in both the groups. **Conclusion:** By using tamsulosin a higher stone expulsion rates can be achieved in a shorter time. More randomized control trials are required to establish tamsulosin as a standard medical expulsive treatment for small distal ureteric calculus.

**Keywords:** Tamsulosin, expulsive pharmacologic therapy, ureteral stone

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## INTRODUCTION

The goal of the surgical treatment of patients suffering from ureteral calculi is to achieve complete stone clearance with minimal morbidity.<sup>1</sup> Many minimally invasive interventional (e.g., ESWL, ureterorenoscopy, the holmium: YAG laser and basket devices) as well as expectant (watchful waiting) treatments exist for the management of lower ureteric calculi. But the choice of the ideal method to be taken up largely depend on the type of equipment available, location, type and size of stone, needs of the patient and skills of the surgeon.<sup>2</sup> The stone burden remains the primary factor in deciding the appropriate treatment for a patient with ureteral calculi.<sup>3</sup> Most ureteral calculi pass and do not require intervention. Spontaneous passage depends on stone size, shape, location and associated ureteral oedema. Ureteral calculi 4–5 mm in size have a 40–50% chance of spontaneous passage. In contrast, calculi  $>6$  mm have a  $<5\%$  chance of spontaneous passage. This does not mean that a 1cm stone will not pass or that a 1–2 mm stone will always pass uneventfully. The vast majority of stones that pass do so within a 6 weeks period after the onset of symptoms. Ureteral calculi discovered in distal ureter at the time of

presentation have a 50% chance of spontaneous passage, in contrast to a 25% and 10% chance in the mid and proximal ureter, respectively.<sup>4</sup> Ureteral calculi of any size may be associated with renal obstruction, and care must be taken to prevent, irreversible damage to the kidney, whether the patient selects expectant or active treatment.

Several groups have investigated the role of pharmacologic therapy to facilitate spontaneous stone passage. Different drugs (e.g., nifedipine and prednisolone) are used for this purpose.  $\alpha_1$  receptors are the most abundant adrenergic receptors in the ureteral smooth muscle cells. The blockage of adrenergic receptors by a specific antagonist inhibits basal tone, peristaltic activity and ureteral contraction.  $\alpha_1$  receptors are divided into four groups, with  $\alpha_{1D}$  being found mostly on the lower intramural portion of the ureter. Based on these findings, different groups have tried Tamsulosin (selective  $\alpha_1$  adrenergic receptors blocker) to facilitate spontaneous passage of distal ureteral calculi.<sup>5</sup>

Most of the work on the efficacy of tamsulosin in lower ureteral calculi expulsion has been done in the developed countries. In our county the modern interventional facilities are concentrated

at tertiary care centres and are rarely available at district level medical centres. A randomized control trial was planned to compare tamsulosin group with control group in our set up to evaluate the efficacy of tamsulosin as expulsive pharmacologic therapy for the treatment of distal ureteral calculi.

## MATERIAL AND METHODS

This randomized controlled trial (RCT) was carried out from 1<sup>st</sup> Jan to 31<sup>st</sup> Oct 2010 in Armed Forces Institute of Urology Rawalpindi, which is a tertiary care centre. The objective was to evaluate the efficacy of tamsulosin as an expulsive pharmacologic therapy for the treatment of distal ureteral stone.

There were 100 patients with 50 patients in each group. We included all patients who fulfilled our inclusion/exclusion criteria during study period after Institutional Review committee approval. Patients were randomly assigned into one of the two groups. A written informed consent was taken from all the patients. All patients with age >18 yrs, stone Size ≤8 mm and stone in distal 1/3 of ureter were included in the study. Patients with ureteric obstruction, distal ureteric stricture, previous ureteral surgery, solitary kidney, aberrant ureteral anatomy (e.g., ureteral ectopia, ureterocele and mega ureter), UTI and radiolucent stone were excluded from the study.

After careful physical examination, basic investigation like Urine R/E, Blood CP, Urine C/S, X-Ray KUB, U/S KUB and IVU (if required), all patients with the diagnosis of ureteral stone in distal 1/3 were recruited in the study. Group A Patients were given Cap Tamsulosin 0.4 mg, 1 daily up to 4 weeks while group B patients were given placebo, 1 Cap daily up to 4 weeks. Both groups were given tab diclofenac Sodium 50 mg, 1 tab 8 hourly for pain control on required basis. Patients were evaluated with plain X-Ray KUB after two weeks and four weeks.

The primary endpoint was expulsion rate. Expulsion time, need for analgesics, need for hospitalization and drug side effects were secondary endpoints. Data was recorded on a Performa. The data analysis was computer based; SPSS-16 was used for analysis. For categoric variables chi-square test was used. For continuous variables independent samples' *t*-test was used. *p*-value <0.05 was considered as significant.

## RESULTS

A total of 49 patients in group A and 48 patients in group B reported back. Three patients lost to follow up, therefore 97 out of 100 patients were evaluated. Mean age of the patients was 36.34 years (rang 18–57 years). Forty-three patients had right ureteral calculus and 54 patients had left ureteral calculus. There was equal distribution of right and left ureteral calculus in both the

group. Mean stone size was 5.78 mm (range 4–8 mm) in greatest dimension.

A stone expulsion rate of 85.71% (42 patients) was noted in group A and 54.20% (26 patients) in group B. Group A revealed a statistically significant advantage in term of stone expulsion rate (*p*=0.032).

In group A 23 patients (46.93%) passed their stone within 7 days of treatment, 13 patients (26.53%) passed stone within 14 days, 4 patients (8.16%) passed stone within 21 days of treatment and 2 patients (4.08%) passed stone within 28 days of treatment. On other hand in group B, 9 patients (18.75%) passed their stone within 7 days of treatment, 5 patients (10.41%) passed stone within 14 days, 2 patients (4.61%) passed stone within 21 days and 10 patients (20.83%) passed their stone within 28 days of treatment. Considering expulsion time in days group A showed statistically significant advantage (*p*=0.015). (Table-1)

Nine patients (18.36%) in group A required analgesic (Diclofenac Na) while in group B, 19 patients (39.58%) required analgesics. There were statistically significant less number of pain episodes in group A as compared to group B (*p*=0.006). None of the patient in group A needed hospitalization while 1 patient in group B was hospitalized during this study. Regarding age, sex, stone size and stone lateralization (right/left), there was no significant difference between the group A and B. No drug side effects were noted in both the groups. All those patients who did not pass stone at the end of 28 days were successfully treated with ureterorenoscopy.

**Table-1: Stone expulsion time in days (*p*=0.015)**

Expulsion time in days	Group-A (n= 49) n (%)	Group-B (n=48) n (%)
<7	23 (46.93)	9 (18.75)
8–14	13 (26.53)	5 (10.41)
15–21	4 (8.16)	2 (4.16)
22–28	2 (4.08)	10 (20.83)
Stone not passed	7 (14.29)	22 (45.80)

## DISCUSSION

Flank pain from acute renal colic is a common presenting complaint to emergency departments that is increasing in frequency.<sup>6</sup> Approximately 13% of men and 7% of women will be diagnosed with kidney stone at some time in their life.<sup>7</sup> The majority of ureteral stones cause pain that is intense and rapid in onset, causing patients to seek care acutely.

Recent development in endoscopic urological procedures and fine instruments has largely diverted the management of ureteral stones by open surgery to either minimal invasive methods like ESWL and ureteroscopy or to watchful waiting. The minimally invasive therapies for ureteral stone are now the accepted gold standards. Nevertheless, these techniques are not risk free, are quite expensive and are concentrated at tertiary care centers.<sup>8</sup>

Waiting for the spontaneous passage is an option, only for the smaller ureteral calculi. It may be associated with discomfort of painful episodes. Smaller, more distal and right sided stones are more likely to pass spontaneously.<sup>9</sup> However the expectant approach may result in complications, such as infection of urinary tract, hydronephroureter and renal damage.<sup>10</sup>

In this study the mean stone size was 5.78 mm (range: 4–8 mm) in greatest dimension. Ureteral calculi usually become impacted at three distinct sites where calibre of the ureter narrows: the ureteropelvic junction, the iliac vessels and the ureterovesical junction.  $\alpha 1A$  and  $\alpha 1D$  adrenergic receptors are present more densely in the distal 1/3 of ureter (including intramural part) than other adrenergic receptors.  $\alpha 1$  antagonist can result in inhibition of basal tone, peristaltic wave frequency and ureteral contractions even in the intramural part of ureter. Therefore  $\alpha 1$  antagonists have a crucial role in spontaneous painless passage of stones  $\leq 8$  mm located in distal 1/3 of ureter.

Dellabella and colleagues (2003), in a study performed to investigate the efficacy of tamsulosin in facilitating ureteral stone passage, found that tamsulosin therapy was associated with an increased stone expulsion rate and a decreased time to stone expulsion. In our study a stone expulsion rate of 85.71% was noted in group A and 54.20% in group B. Group A revealed a statistically significant advantage in terms of stone expulsion rate as compared to group B ( $p=0.032$ ). These results are comparable to similar studies by Griwan<sup>2</sup>, De Sio<sup>5</sup> and porpiglia<sup>11</sup>. Considering expulsion time in days group A showed statistically significant advantage as compared to group B ( $p=0.015$ ).

Dellabella *et al*, used tamsulosin as spasmolytic drug during episodes of ureteral colic due to calculi at VUJ, observed an increased stone expulsion rate, decrease in stone expulsion time, decreased need for hospitalization/endoscopic procedures and provided good control of colic pain.<sup>12</sup> In this study 18.36% patients in group A and 39.58% patients required analgesic. Tamsulosin can be used in association with ESWL for larger ureteral calculi, to achieve a higher stone clearance rate.<sup>13</sup> Because the patient symptoms and stone size do not predict loss of renal function, and because there is no clear time threshold for irreversible damage, intervention should

be considered in any patient with ureteral obstruction unless the ability to closely monitor renal function is available.

## CONCLUSION

Medical expulsive therapy should be considered as an option in the management of uncomplicated distal ureteric calculus up to 8 mm in size. By using tamsulosin a higher stone expulsion rates can be achieved in a shorter time. More randomized control trials are required to establish tamsulosin as a standard medical expulsive treatment for small distal ureteric calculus.

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