

Study of efficacy of tamsulosin in the expulsion rate and expulsion time of calculi in the lower 1/3rd of ureter and uretero-vesical junction

Anil Shriram Munde¹, Sambhaji Madhavrao Kadam^{2*}

¹Associate Professor, ²Junior Resident, Department of General Surgery, Vilasrao Deshmukh Government Medical College Latur, Maharashtra, INDIA.

Email: dranilmunde@gmail.com, drshambhuraje@gmail.com

Abstract

Background: Among all ureteral stones, 70% are found in the lower third of the ureter. Medical expulsive therapy (MET) refers to the administration of drugs such as tamsulosin, an alpha-adrenoceptor antagonist, to relax the smooth muscle of the ureter and inhibit peristaltic activity. Present study was aimed to study of efficacy of tamsulosin in the expulsion rate and expulsion time of calculi in the lower 1/3rd of ureter and uretero-vesical junction at a tertiary hospital. **Material and Methods:** Present study was hospital based, QUASI experimental study, conducted in patients with ureteral colic due to radiologically proven distal ureteral stones less than or equal to 10 mm and who are managed conservatively with tamsulosin. **Results:** Out of 90 patients maximum number of patients were from age group between 16-30 years (53.33%) followed by 31-45 years (18.89%). Out of 90 patients 70 (77.78%) were male and 20 (22.22%) were female. Male preponderance is present. Majority patients had size of calculi between 4-5 mm (31.11%), followed by 6-7 mm (35.56%), 8-9 mm calculi (27.78) and 5 (5.56%) having 10 mm. 56 (62.22%) patients had uretero-vesical calculi as compared to lower 1/3rd ureteric (37.78%). Mean days required for expulsion of distal ureteric stone was 8.5 days. 41 (45.55%) patients had no ureteric colic after tamsulosin tablet followed by 40 (44.44%) had 1 to 3 episodes, 9 (10.01%) had 4 to 7 episodes and no patient had more than 7 episodes. Difference was observed in frequency of usage of analgesic before and after Tamsulosin treatment and difference was statistically significant (p-0.027). **Conclusion:** Tamsulosin should be considered for uncomplicated distal ureteral and vesicoureteral junction calculi as a medical expulsion therapy before considering ureteroscopy or extracorporeal lithotripsy.

Keywords: Tamsulosin, distal ureteral calculi, vesicoureteral junction calculi, medical expulsion, analgesic

*Address for Correspondence:

Dr Sambhaji Madhavrao Kadam, Junior Resident, Department of General Surgery, Vilasrao Deshmukh Government Medical College Latur, Maharashtra, INDIA.

Email: drshambhuraje@gmail.com

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INTRODUCTION

Urinary stone disease is most common reasons for patients visiting a urology practice, affecting about 5% to 10% of

the population¹. Among all ureteral stones, 70% are found in the lower third of the ureter.² Symptoms include flank or abdominal pain radiating to the groin or external genitalia. Medical expulsive therapy (MET) refers to the administration of drugs such as tamsulosin, an alpha-adrenoceptor antagonist, to relax the smooth muscle of the ureter and inhibit peristaltic activity.³ Among the various treatment modalities available, the efficacy of mini-invasive therapies, such as extracorporeal shock wave lithotripsy (ESWL) and ureteroscopic lithotripsy has been proven by several studies.^{4,5} Nevertheless, these techniques are not risk-free, are problematic and are expensive.⁶ The disease spectrum in a developing country like ours, is different from that in developed countries, mainly because of delay in diagnosis, delay in

investigations and lack of awareness which tend to modify the outcome in case of ureteral stones or of any disease for that matter. Present study was aimed to study of efficacy of tamsulosin in the expulsion rate and expulsion time of calculi in the lower 1/3rd of ureter and uretero-vesical junction at a tertiary hospital.

MATERIAL AND METHODS

Present study was hospital based, QUASI experimental study, conducted in department of Surgery, at Tertiary health care center. Study duration was of 2 years (July 2018 to June 2019). All ethical considerations and necessary approvals were taken from Institutional Ethical Committee.

Inclusion criteria: All patients evaluated, with ureteral colic due to radiologically proven distal ureteral stones less than or equal to 10 mm and who are managed conservatively.

Exclusion criteria: Stone larger than 10 mm, Multiple ureteral stones. Clinical and laboratory signs of urinary tract infections (UTIs). Severe hydronephrosis on ultrasound examination (gross pelvicalyceal dilatation with parenchymal thinning). Co-morbid conditions such as diabetes, alteration in renal parameters (serum creatinine and blood urea), Pregnancy. Previous history or ureteral manipulation and/or surgery. Known sensitivity to alpha blockers.

RESULTS

Out of 90 patients maximum number of patients were from age group between 16-30 years (53.33%) followed by 31-45 years (18.89%). Out of 90 patients 70 (77.78%) were male and 20 (22.22%) were female. Male preponderance is present.

Written informed consent was taken from all patients. All patients were received and evaluated on outpatient basis and underwent a standard evaluation of transabdominal ultrasonography with special attention to the Kidney, Ureters and Urinary Bladder regions. Patients were given Tab. Tamsulosin 0.4 mg in the morning, half hour after breakfast for a maximum period of 28 days or until spontaneous passage of stone, (whichever is earlier). High fluid intake and analgesic (Caps. diclofenac 75 mg), to be given on demand during the study period. The patients were followed up with a weekly sonography KUB and fortnightly X-ray KUB and final evaluation is to be done after completion of four weeks. Successful results is defined by complete stone passage. The failure is considered if the patients failed to pass the stone at the end of four weeks.

Data was collected and compiled using Microsoft Excel 2013 and then analysed using SPSS 23.0 version and Open Epi Software Version 2.3 by calculating frequency, percentage and cross-tabulations between various parameters. The means and standard deviations (SD) were calculated for the continuous variables. Difference of proportions between qualitative variables were tested using chi-square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

Table 1: Age and gender distribution

Characteristics	Frequency	Percentage (%)
Age group (years.)		
≤15	05	5.56
16 to 30	48	53.33
31 to 45	17	18.89
46 to 60	15	16.67
≥61	05	5.56
Gender		
Male	70	77.78
Female	20	22.22

Out of 90 patients, 50 (55.5%) patients had left sided calculi and 40(44.4 %) patients had right sided calculi. Majority patients had size of calculi between 4-5 mm (31.11%), followed by 6-7 mm (35.56%), 8-9 mm calculi (27.78) and 5 (5.56%) having 10 mm. 56 (62.22%) patients had uretero-vesical calculi as compared to lower 1/3rd ureteric (37.78%)

Table 2: Side, size and type of calculi

Characteristics	Frequency	Percentage (%)
Side		
Left	50	55.5
Right	40	44.4
Size of the calculi		
4-5 mm	28	31.11%
6-7 mm	32	35.56%
8-9 mm	25	27.78%

10 mm	5	5.56%
Type of calculi		
Lower 1/3 rd Ureteric	34	37.78%
Uretero-vesical junction	56	62.22%

74 (82.22%) patients had complete expulsion and 16 (17.78%) having no expulsion. In present study, 38 (42.2%) patients took time for stone expulsion in less than 7 days followed by 24 (26.66%) patients took 8 to 14 days, 12 (13.33%) patients took 15 to 21 days, 0 patients between 22 to 28 days and 16 (17.7%) patients did not pass stone upto 28 days. Mean days required for expulsion of distal ureteric stone was 8.5 days

Table 3: Stone Expulsion

Characteristics	Frequency	Percentage (%)
Stone Expulsion		
Complete	74	82.22%
No expulsion	16	17.78%
Time taken for Stone Expulsion		
<7 days	38	42.2
8 to 14 days	24	26.6
15 to 21 days	12	13.3
22 to 28 days	00	00
Not expelled within 28 days	16	17.7

41 (45.55%) patients had no ureteric colic after tamsulosin tablet followed by 40 (44.44%) had 1 to 3 episodes, 9 (10.01%) had 4 to 7 episodes and no patient had more than 7 episodes.

Table 4: Ureteric colic episodes after tamsulosin

Ureteric colic episodes	Frequency	Percentage (%)
0	41	45.55%
1 to 3	40	44.44%
4 to 7	9	10.01
>7	0	0

Difference was observed in frequency of usage of analgesic before and after Tamsulosin treatment and difference was statistically significant (p-0.027).

Table 5: Comparison of frequency of usage of analgesic before and after Tamsulosin

Frequency of usage of analgesic	Before Tamsulosin treatment	After Tamsulosin treatment
No usage	0	41
Once a week	8	32
Twice or thrice a week	13	09
Every alternate day	36	05
Everyday	33	03

p-0.027

DISCUSSION

Medical expulsive therapy (MET) has recently emerged as an alternative strategy for the initial management of small distal ureteral stones. The specific mechanism of action on the ureteral smooth muscle and low-risk profile suggest that alpha-adrenergic receptor antagonists (alpha-blockers) and calcium channel antagonists should be the initial medical treatment in patients amenable to conservative therapy. Recent studies have reported excellent results relating to medical expulsive therapy (MET) for distal ureteral calculi, in terms of stone expulsion and control of ureteral colic pain, using drugs (e.g., nifedipine and prednisolone) that can modulate the function of the ureter obstructed by the stone. A watchful waiting approach can be used in a large number of cases,

as demonstrated by several studies that revealed high spontaneous passage rates of small distal ureteral stones.⁷ Even the simple watchful waiting approach can result in complications, such as infection of the urinary tract, hydronephrosis and impaired renal function.⁸ These days, use of the watchful waiting approach has been extended by using pharmacological therapy, which can reduce symptoms and facilitate stone expulsion.⁹ In present study, out of 90 cases, the average mean age of study population are 32.68 years (range -15 years to 65 years), whereas study conducted by De Sio *et al.*,¹⁰ has mean age of 44.5 years study population. In our study, out of 90 patients, 70 male (77.7%) cases and 20 (22.2%) female cases are there, male preponderance is present in our study, whereas study conducted by Jeremy *et al.* shows 81.4% males and 18.6% females and study conducted by Zhangqun ye *et al.*,¹¹

shows 34% were males and 66% were females. In our study 55.5% cases had left sided distal ureteric calculi and 44.4% cases had right sided distal ureteric calculi, left sided distal ureteric calculi are slightly higher than right sided distal ureteric calculi, whereas the study conducted by Furyk *et al.*,¹² shows 46.5% stones were present in right distal ureter and 53.5% stones were present in left distal ureter. In our study 48.8% cases had distal ureteric calculi between 4-6mm and 51.2% cases had calculi between 7-10mm, whereas, the study conducted by Parikshit Singh *et al.*,¹³ had 64% cases with distal ureteric calculi size of 4-6mm and 36% cases had stone size between 7-10mm. In our study time taken for expulsion of distal ureteric calculi was <7 days in 42.2% cases, 7-14 days in 26.6% cases, 15-21 days in 13.3% cases and 17.7% cases did not expel distal ureteric calculi after tamsulosin. Mean days for expulsion of stone in present study was 8.54 days, Less duration was noted by Dellabella *et al.*,⁹ (3 days) and De Sio *et al.*,¹⁰ (4.4 days). In our study the number of ureteric colic episodes seen over a period of 28 days were 1-3 episodes in 44.4% cases, 4-7 episodes in 10.1%, 45.5% cases did not develop any colicky episode and no patient has got >7 colic episodes in our study. Whereas study conducted by Parikshit Singh *et al.*,¹³ shows that 16% cases developed 1-3 episodes of ureteric colic and 8% cases got 4-7 episodes and no patient has got >7 episodes and 76% cases did not develop any ureteric pain episode. Tamsulosin has equal affinity for $\alpha 1a$ and $\alpha 1d$ receptors. The $\alpha 1d$ receptor is the most common receptor in the ureter and is most concentrated in the distal ureter. Cervenakov and associates¹⁴ compared their standard MET with and without tamsulosin. Their standard therapy included an injection of a narcotic and diazepam on presentation, followed by a daily NSAID. They found that the spontaneous passage rates with and without tamsulosin were 80.4% versus 62.8%, respectively. The majority of patients receiving tamsulosin passed their stone within 3 days. There were fewer instances of recurrent colic with tamsulosin, and the tamsulosin was well tolerated. Tamsulosin, however, appears to be effective only for stones over 4 mm and less than 10 mm in size.¹⁵ Doshi R *et al.*, conducted a study on 109 cases and noted that Use of Tamsulosin (alpha1-blocker) with Deflazacort (corticosteroid) proves to be more efficacious than Tamsulosin used alone. In addition, Tamsulosin used on its own as a medical expulsive therapy.¹⁶ In a systematic review and meta-analysis, with 49 studies involving 6436 patients, Sun Y *et al.*,¹⁷ noted that tamsulosin improved the renal stone clearance rate and reduced the expulsion time. Regarding complications, no significant difference was found between the 2 groups in terms of the total side effects or divided complications, including retrograde ejaculation (P = .01), hypotension (P = .52), dizziness (P = .07),

diarrhea (P = .58), vomiting (P = .88), headache (P = .84), nausea (P = .91), and fatigue (P = .10), They concluded that Tamsulosin should be strongly recommended for patients with ureteral stones to increase treatment efficacy. The side effects were not significantly different between the tamsulosin and control treatments. Tamsulosin has been found to increase stone expulsion rates, reduces mean days to stone expulsion and decreases number of doses of analgesic requirement. If used appropriately used, tamsulosin may have financial benefits by reducing the number of interventional procedures and the acute colicky attacks, need of hospitalization and it may help in minimizing the further complications

CONCLUSION

Tamsulosin should be considered for uncomplicated distal ureteral and vesicoureteral junction calculi as a medical expulsion therapy before considering ureteroscopy or extracorporeal lithotripsy. Tamsulosin has been found to increase and hasten stone expulsion rates, decrease acute attacks by acting as a spasmolytic and thus reduces the ureteric colic, reduces mean days to stone expulsion and decreases analgesic dose usage.

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