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**Original Research Article**

# Role of medical expulsive therapy in lower ureteral calculus

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## ABSTRACT

**Background:** Urolithiasis is a chronic disease with a significant burden on the healthcare system. The aim of this study was to evaluate the role of medical expulsive therapy (tamsulosin alone or in combination with deflazacort) in the treatment of lower ureteric calculi.
**Methods:** This was a prospective, randomized, controlled trial conducted at a tertiary care centre between November 2015 and October 2017. Patients aged more than 18 years solitary ureteral calculus 5–10 mm in size, located at distal ureter were randomized (1:1:1) to receive tamsulosin 0.4 mg once-daily (OD), deflazacort 6 mg twice-daily (BD) and analgesic OD (Group A); tamsulosin 0.4 mg and analgesic OD (Group B); or only analgesic OD (Group C, control Group) for 7 days. The treatment duration was extended to 28 days or until the expulsion of stone. Patients were followed-up weekly during the treatment period.
**Results:** A total of 105 patients were enrolled in the study. Overall, 51.5% of patients in Group A, 48.5% of patients in Group B and 54.3% of patients in Group C had calculus size 7-10 mm. Patients allocated to Group A (80%) and Group B (74.3%) showed higher stone expulsion rate as compared to those in Group C (48.6%). The mean time taken for stone expulsion was around 12 days in Group A, whereas around 15 days in Group B and C.
**Conclusions:** The combination of tamsulosin and deflazacort resulted in higher stone expulsion rate in patients with lower ureteral calculus.

**Keywords:** Deflazacort, Medical expulsive therapy, Tamsulosin, Ureteral calculi

## INTRODUCTION

Ureteral stone is a common problem with significant impact on healthcare system all over the world. The incidence of ureteral stones is estimated to be 1% to 15% of the population and is on rising.[1,2] Among total urolithiasis, 20% accounts for ureteral stones and 70% of the ureteral stones are located in the lower third of the ureter.[3] Spontaneous removal of the stone was associated with the size and location of the stone. The American Urological Association panel recommended that, in general, if the patient has a ureteral calculus of 0.5 cm or less in diameter, there are more chances of spontaneous removal of calculus.[4] When removal of calculus becomes difficult due to its large size, surgical intervention is necessary including ureteroscopy and shock wave lithotripsy. Besides this, other treatment options include medical expulsive therapy, percutaneous antegrade ureteroscopy, and laparoscopic and open surgical ureterolithotomy.[5] According to the location of the stone, there are 48% chances of spontaneous removal for stone in the proximal ureter, 60% for mid ureteral stones, 75% for distal stones, and 79% for ureter vesical junction stones.[6] This paper reports the results of a study that evaluated the role of medical expulsive therapy (tamsulosin alone or in combination with deflazacort) in the treatment of lower ureteric calculi. The study also compared the efficacy of tamsulosin versus tamsulosin

plus deflazacort; and determined the safety of these drugs.

## METHODS

This was a prospective, randomised, controlled trial conducted at a tertiary care centre between November 2015 and October 2017. Patients aged more than 18 years presenting with symptoms of ureteric colic and solitary ureteral calculus 5-10 mm in size, located at distal ureter (below the sacroiliac joint) confirmed by ultrasonography (USG) or non-contrast computerised tomography (NCCT) of kidneys, ureters and bladder (KUB) were included in this study. Patients with fever, pregnancy, not willing for medical treatment, stones in upper or mid-ureter, uncorrected distal obstruction and marked hydronephrosis, acute or chronic renal failure, acute urinary tract infections and history of urinary tract surgery were excluded from the study. The study protocol was reviewed and approved by the Institutional Ethics Committee (17 November 2015; No. BMC/PGs/159/2015-16). The study was conducted in accordance with the approved protocol, and ethical principles that have their origin in the Declaration of Helsinki. Each study participant provided written informed consent before any study-related procedures. Patients medical history, details of physical examination, and routine haematological and biochemical investigations were recorded. Eligible patients were randomised (1:1:1) using closed paper slips into three Groups (A, B, and C) each consisting of 35 patients. Patients from Group A received tamsulosin 0.4 mg OD, deflazacort 6 mg twice-daily (BD) and analgesic OD; patients from Group B received oral tamsulosin 0.4 mg and analgesic once-daily (OD); and patients from Group C received only analgesic OD for 7 days. Treatment was extended for a maximum of 28 days or till the passage of stone (whichever earlier). Each patient was advised to have 2.5 to 3 litres of fluid in 24 hours.

After starting medical expulsive therapy, the patients were followed weekly for 28 days of follow-up period or till the passage of stone whichever was early. The USG or X-ray KUB or CT KUB was done a day after symptom relief and thereafter weekly till the passage of calculus or for 4 weeks. Objective documentation of stone expulsion was done based on follow-up USG KUB. If the patient again complains of colic pain it was managed with analgesics. In case if the stone was not expelled within 28 days, patients were referred for intervention ureteroscopic lithotripsy (URSL). No formal sample size calculation was employed for this study. The data obtained were tabulated, analysed and presented using descriptive statistics - means (standard deviations) for continuous variables and for categorical data number (percentages). The difference of the means of analysis variables was tested using unpaired t test and the difference of the proportion was tested using z test of proportion. P value of <0.05 was considered significant.

## RESULTS

A total of 105 patients were included and were randomized into three Groups (Group A, n=35), (Group B, n=35), and (Group C, n=35). Baseline and clinical characteristics are shown in (Table 1).

**Table 1: Baseline and clinical characteristics.**

| | Group A (n=35) | Group B (n=35) | Group C (n=35) |
|---|---|---|---|
| **Age (years), mean (SD)/(range)** | **35.45 (13.81)/ (18-66)** | **33.00 (10.38)/ (18-61)** | **34.51 (10.37)/ (18-65)** |
| **Age distribution, n (%)** | | | |
| 18-30 | 15 (42.86) | 20 (57.14) | 14 (40.00) |
| 31-40 | 10 (28.57) | 7 (20.00) | 13 (37.14) |
| 41-50 | 5 (14.29) | 6 (17.14) | 6 (17.14) |
| 51-60 | 2 (5.71) | 1 (2.86) | 1 (2.86) |
| 61-70 | 3 (8.57) | 1 (2.86) | 1 (2.86) |
| Sex, n (%) males | 20 (57.14) | 27 (77.14) | 24 (68.57) |
| **Side of stone, n (%)** | | | |
| Right | 17 (48.57) | 20 (57.14) | 16 (45.71) |
| Left | 18 (51.43) | 15 (42.86) | 19 (54.29) |
| **Localization of stone** | | | |
| VUJ | 19 (54.29) | 21 (60) | 15 (42.86) |
| Lower | 16 (45.71) | 14 (40) | 20 (57.14) |
| Calculus size (mm), mean (SD) | 6.95 (1.46) | 6.91 (1.41) | 6.89 (1.32) |
| **Calculus size distribution, n (%)** | | | |
| 5-5.9 | 7 (20) | 8 (22.9) | 7 (20) |
| 6-6.9 | 10 (28.6) | 10 (28.6) | 9 (25.7) |
| 7-7.9 | 8 (22.9) | 7 (20.0) | 10 (28.6) |
| 8-8.9 | 5 (14.3) | 6 (17.1) | 6 (17.1) |
| 9-10 | 5 (14.3) | 4 (11.4) | 3 (8.6) |

VUJ: Vesico ureteral junction; SD: Standard deviation.

Most of the patients participated in the study were between 18-30 years of age with greater male proportion. The mean age of the patients in Group A, Group B and Group C was 35.45, 33.00, and 34.51, respectively.

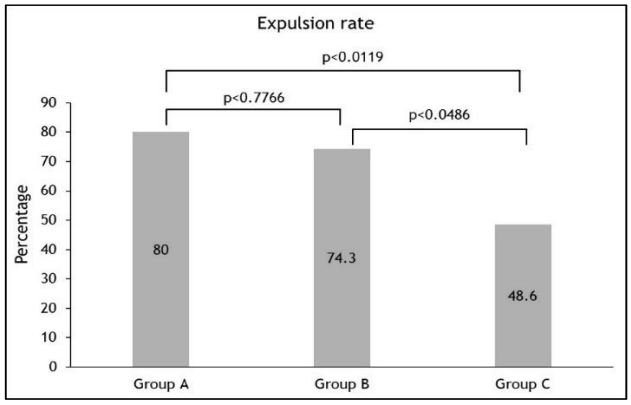


**Figure 1: Expulsion rate of stone.**

There was no statistically significant difference in the side (right/left) and location (vesicoureteral junction [VUJ]/lower ureter) of stone between the three Groups. The mean (SD) calculus size was 6.95 mm (1.46) for Group A, 6.91 mm (1.41) for Group B, and 6.89 mm (1.32) for Group C. Overall, 51.5% of patients in Group A, 48.5% of patients in Group B and 54.3% of patients in Group C had calculus sized 7-10 mm (Table 1). The stone expulsion rate was comparatively higher in Group A (n=28, 80%) and Group B (n=26, 74.3) than in Group C (n=17, 48.6%) (Figure 1). The mean (SD) time for the expulsion of stone was 11.85 (5.1) days in Group A, 14.58 (5.5) days in Group B and 15.12 (6.7) days in Group C (Table 2).

**Table 2: Stone expulsion time.**

| Stone expulsion time (days) | Group A (n=28) | Group B (n=26) | Group C (n=17) |
|---|---|---|---|
| Mean (SD) | 11.85 (5.1) | 14.58 (5.5) | 15.12 (6.7) |
| Median | 10 | 14 | 15 |

SD: Standard deviation

The time taken was significantly less in Group A as compared to that for Group B and C. Overall, both tamsulosin and deflazacort were well tolerated with minimal side effects. Dizziness and vertigo were reported in five patients of Group A and B. Two patients from Group B and one patient from Group A showed signs of hypotension. Retrograde ejaculation was reported in one patient of Group B but these patients did not need to suspend the therapy.

## DISCUSSION

This prospective randomized study evaluated the role of medical expulsive therapy in the treatment of lower ureteric calculi and found that medical expulsive therapy (tamsulosin alone or in combination with deflazacort) has significantly higher expulsion rate of lower ureteric calculus than the control Group (only analgesic). Results also showed that a combination of tamsulosin and deflazacort was not significantly different than tamsulosin alone.

Urolithiasis is a chronic disease with a significant burden on the healthcare system. Primarily, it affects the younger population and has a high recurrence rate of approximately 50% within 5 years and 75% at 10 years.[7] Though ureteric stones account for around only 20% of total urolithiasis, it is considered most symptomatic and clinically significant. Previous studies have reported that stones less than 5 mm have 71% to 98% of chances of expulsion; however, stones with 5 mm to 10 mm have 25% to 51% of chances of spontaneous expulsion.[8,9]

Management of ureteral stones generally depends on the type, size, location, number and structure of the stone, and the presence of symptoms and complications. The presence of ureteral spasm, mucosal oedema or inflammation, and ureteral anatomy also influences stone expulsion.

Although minimally invasive techniques have significantly advanced over that last few decades, medical expulsive therapy has its own place and is preferred in patients with comparatively small stones and in patients who are not eligible for other options. Additionally, surgical options are costlier. Patients with newly diagnosed ureteral stone less than 10 mm with fewer symptoms which can be managed with analgesics, may be offered medical therapy to facilitate stone passage during the observation period.

Several randomized controlled trials have demonstrated that medical expulsive therapy is beneficial in lower ureteric calculi.[10-12] Various drugs have been studied as medical expulsive therapy including alpha-1 receptor antagonists, calcium channel blockers, corticosteroids and phosphodiesterase inhibitors. Of these, alpha-1 receptor antagonists have shown a higher rate of expulsion than other drugs. In the present study, we used the selective alpha-1a blocker, tamsulosin and corticosteroid, deflazacort to evaluate the efficacy of medical expulsive therapy in lower ureteral calculus 5 to 10 mm size.

In the present study, all three Groups were generally comparable in terms of patient age, sex distribution, stone side, stone size and stone location in all three Groups. The average stone size in our study was 6.95 mm in Group A, 6.91 mm in Group B and 6.89 mm in Group C. The smallest calculus was 5 mm in size, whereas the largest calculus was 10 mm in size. There was no difference in stone size between different Groups.

In the present study, the stone expulsion rate was 80% in Group A and 74.3% in Group B as compared to Group C

where it was only 48.6%. The difference in Group A and B was not statistically significant (p=0.7766) while it was significant between Group A and C and between B and C (0.0486 and 0.0119, respectively). From an analysis of these data, it is evident that tamsulosin on its own has a good expulsion rate in comparison to the control Group (74.3% vs 48.6%). Tamsulosin showed highest expulsion rate (80.00%) when combined with steroids (deflazacort), which was significant in comparison to the other Group C (p=0.0119) but had no significant difference when compared with Group B (p=0.7766). Results from our study were comparable to previous reports (Table 3).

**Table 3: Comparison of expulsion rate.**

| Study | Group A (tamsulosin with deflazacort) | Group B (tamsulosin) | Group C (analgesic) |
|---|---|---|---|
| Porpiglia et al[13] | 84.5% | 66% | 33% |
| Dellabella et al[14] | 96.5% | 90% | 64% |
| Autorino et al[15] | - | 88% | 60% |
| Sio et al[16] | - | 90% | 59% |
| Ramesh A et al[17] | 84% | - | 60% |
| Present study | 80% | 74.3% | 48.6% |

SD: Standard deviation

In the present study, the mean stone expulsion time was 11.85 days in Group A, 14.58 in Group B, and 15.12 days in Group C. This demonstrates that medical expulsive therapy not only facilitates stone passage, but also decreases the stone expulsion time, and analgesic requirement. In a previous study by Porpiglia et al, the mean stone expulsion time was 3 days, 5 days and 7.3 days for tamsulosin with deflazacort Group, tamsulosin Group and analgesic Group, respectively.[13]

In another study by Ramesh et al, the mean stone expulsion time was 3.94 days and 9.84 days for tamsulosin with deflazacort Group, and for the analgesic Group, respectively.17 In our study stone expulsion time was higher compared with previous studies, possibly due to the difference in stone size.

Authors acknowledge the few limitations of the study including a small sample size. Another limitation was that this was a single centre study conducted in Bangalore (India). Hence, the results may not be generalized for other parts, as it could vary due to the difference in dietary habits.

Results from this study demonstrated the effectiveness of medical expulsive therapy with tamsulosin and deflazacort. This study showed significantly higher expulsion rate of lower ureteric calculus in medical expulsive therapy Groups as compared to control Group (analgesic alone). In tamsulosin with deflazacort Group expulsion rate was higher than the tamsulosin Group. Overall, both tamsulosin and deflazacort were well tolerated in this study Group.

## CONCLUSION

The combination of tamsulosin and deflazacort resulted in higher stone expulsion rate in patients with lower ureteral calculus.

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