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# Therapeutic Approaches to Facilitating Expulsion of Distal Ureteric Stones

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## ABSTRACT

Between 5% to 12% of people will get genitourinary stones throughout their lives. Men are more likely to develop calculus than women. Based on data from the Indian population, 12% of people have urinary calculi, and half of them lose their kidney's ability to function. One prevalent ailment that urologists and surgeons see in emergencies is symptomatic urolithiasis. The most common location for ureteric calculus is the bottom third or distal ureter. This study compared the effectiveness of watchful waiting therapy, which only uses non-steroidal anti-inflammatory drugs, with tamsulosin either by itself or in combination with a low-dose corticosteroid (deflazacort) for the management of distal ureteral stones. In this study, there were three times as many males as females. The mean age for men and women was 38.14 and 36.04 years, respectively. In all groups, the mean stone size was about 6 mm. Compared to the right side of the ureter, the left side had greater symptoms. Group B used NSAIDs on average the least. The medical expulsion treatment was more beneficial to group B. We conclude that medical expulsive therapy is a safe and efficient treatment for distal ureteral stones that are symptomatic and not complex. Furthermore, tamsulosin alone, as a medical expulsive medication, may be a viable alternative for individuals who are not candidates for steroid therapy. Deflazacort, even at low dosages, has the same effect as higher dosages.

**Keywords:** MET, Medical expulsion therapy, Tamsulosin, Alpha 1 blockers, Low dose deflazacort for MET

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## Introduction

One of the top three urological conditions is urolithiasis. Between two and three percent of people worldwide suffer from urolithiasis. About 20% of individuals experience a recurrence of urolithiasis [1–3]. In India, 50% of people lose their kidney function, and 12% of people get urinary calculi. The most prevalent ailment that urologists and surgeons see in emergency rooms is symptomatic urolithiasis. The most frequent location for ureteric calculus is the bottom third or distal ureter. Three things happen when kidney stones move through the ureter and into the bladder: 1) a smooth muscular spasm, 2) swelling of the submucosa, and 3) discomfort. The size, shape, and ureteric smooth muscle activity of calculi determine their spontaneous transit. The terminal portion of the ureter, primarily the intramural "detrusor tunnel," is the largest barrier to calculi transit. Many calculi that are 4 mm or less in size pass on their own; however, not without causing the patient pain or expense. Urinary blockage is typically linked to ureteric calculi of any size, and while deciding between active or expectant therapy, we must exercise extreme caution to avoid irreparable kidney damage.

The optimal course of therapy for distal ureteric calculi is still up for dispute. The likelihood of spontaneous stone transit depends on the calculus's initial position and size. Spontaneous ejection is common for distal ureteral calculi with a diameter of 5 to 8 mm [4]. There is a lot of interest in adjuvant pharmacologic therapy for instances of distal ureteral calculi since it can raise the expulsion rate, decrease the need for analgesics, and prevent surgery. The medications used in medical expulsion therapy maintain a tonic contraction of the ureter while lowering the tone of the sphincter and other smooth muscles. Analgesic medications (NSAIDs) can be taken alongside anti-

inflammatory medications, such as corticosteroids. Because corticosteroids reduce inflammation, they lessen the barrier that calculi must overcome, increasing the effectiveness of analgesics.
When considering watchful waiting therapy with only non-steroidal anti-inflammatory drugs (NSAIDs), the primary goal of this prospective study is to assess the effectiveness of α1-blocker (tamsulosin) therapy in the treatment of distal ureteral stones when given as the sole medication or in combination with low-dose corticosteroid (deflazacort).

## Materials and Methods

*Enrolment of patients*
This retrospective investigation was carried out on the first 200 patients with distal ureteral stones between April 1, 2019, and March 31, 2022. The sample size for each group was determined utilizing a standard protocol.

$$[Z (1- a/2) + Z (1- ß)] X [P1Q1 + P2Q2]/e^2 \quad (1)$$

As a result, each group had a minimum of 46 individuals. The SMBT Institute of Medical Sciences and Research Centre, located in Nandi Hills in the hamlet of Dhamangaon, PO-Ghoti, Taluka-Igatpuri, district-Nashik, Maharashtra, India, provided treatment for each patient. Prior clearance was obtained from the SMBT Institute of Medical Sciences and Research Center's Institutional Ethical Committee, with reference number SMBT/IEC/19/090, dated 10/04/2019.

*Patient randomization*
The study's patients were divided into three groups using a straightforward random selection method:
Group A: Tamsulosin and NSAIDs.
Group B: Tamsulosin and deflazacort, and NSAIDs.
Group C (control): only NSAIDs.
The prescribed course of therapy lasted for seven days and was discontinued if the stone went away sooner. To determine if the stone had gone or not, abdominal ultrasonography (USG) was performed. To confirm the stone in situations of dispute, computed tomography (CT) of the kidney, ureter, and bladder (KUB) area was performed.

*Selection of subject*

*Inclusion criteria*
- Patient age: 18 to 65 years.
- Size of the stone: 5 to 8 mm.
- Single distal ureteric stone.

*Exclusion criteria*
- Severe hydronephrosis/forniceal rupture.
- Diabetes/peptic ulcer.
- History of spontaneous passage of stone
- Previous surgical intervention for stones.
- Known hypersensitivity/ contraindication to tamsulosin, steroids, or NSAIDs.
- Not willing to be included in the study.

*Study protocol*
This study comprised patients with distal ureteral stones that met the inclusion criteria and had sizes ranging from 5 to 8 mm. Every patient had a clinical examination. When necessary, full blood counts, urine analyses, abdominal ultrasonography, kidney-ureter-bladder (KUB) plain abdomen x-rays, and plain computed tomography of the KUB area were performed. The first line of therapy for every patient was oral analgesics (diclofenac sodium). Patients who agreed and were prepared to provide written agreement were recruited in the trial if the stone was in the lower ureter, measured between 5 and 8 mm, and if the discomfort subsided. Opioids and smooth muscle relaxants were not administered since they might impede the ejection of stones. Based on the suggested therapy,

three groups were established: For seven days, group C (control group) received just NSAIDs, group B received tamsulosin (0.4 mg) + deflazacort (12 mg) + NSAIDs, and group A received oral tamsulosin (0.4 mg) + NSAIDs. Every patient was encouraged to consume three to four liters of water daily and to utilize an intramuscular or intravenous injection of diclofenac if the oral medication did not relieve their discomfort. Patients were offered the option to stop their current treatment and try alternative treatment methods if they experienced uncontrolled discomfort during the current therapy or a fever. This was seen as a therapeutic failure. The dose of corticosteroids was tapered off after five days. To avoid prejudice, double blinding was used.

Treatment lasted for seven days, after which it was discontinued if the stone went away sooner. It was recommended that all patients follow up after seven days. It was suggested that they report early if they pass the stone earlier. The presence or absence of the stone was verified via USG. If USG is unable to locate the stone, a CT KUB plain was performed to confirm it. Patients who failed the test were offered the option to continue receiving medical care or to pursue alternative therapy methods such as URS and ESWL.

## Results and Discussion

The current investigation comprised two hundred participants in total. The male-to-female ratio was 3:1, with the mean age of the male patients being 38.14 and the mean age of the female patients being 36.04. The majority of patients first complained of abdominal discomfort, which was followed by fever, haematuria, and burning micturition. The left side of the ureter was more symptomatic than the right, and the average stone size across all groups was around 6 mm **(Table 1)**. Patients in group B got the bare minimum of NSAIDs **(Table 2)**, and the medical expulsion treatment was the most beneficial **(Tables 3 and 4)**. Twenty-two patients in the trial were lost to follow-up: four in group A, six in group B, and twelve in group C.

**Table 1.** Distribution of the sample by the mean size of the stone

| | N | Mean | Std. deviation | Std. error | 95% confidence interval for mean | | Min. | Max. | P-value |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | Lower bound | Upper bound | | | |
| A | 65 | 6.12 | 0.992 | 0.123 | 5.88 | 6.37 | 5 | 8 | < 0.001 |
| B | 69 | 6.55 | 0.883 | 0.106 | 6.34 | 6.76 | 5 | 8 | |
| C | 66 | 5.88 | 0.773 | 0.095 | 5.69 | 6.07 | 5 | 7 | |
| **Total** | **200** | **6.19** | **0.926** | **0.065** | **6.06** | **6.32** | **5** | **8** | |

**Table 2.** Shows the Distribution of samples by use of NSAID for the number of days

| | N | Mean (days) | Std. deviation | Std. error | 95% confidence interval for mean | | Min. | Max. | P-value |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | Lower bound | Upper bound | | | |
| A | 61 | 3.18 | 1.162 | 0.149 | 2.88 | 3.48 | 2 | 10 | < 0.001 |
| B | 63 | 2.80 | 0.800 | 0.100 | 2.60 | 3.00 | 1 | 5 | |
| C | 54 | 6.62 | 1.881 | 0.254 | 6.11 | 7.13 | 3 | 10 | |
| **Total** | **178** | **4.09** | **2.142** | **0.160** | **3.78** | **4.41** | **1** | **10** | |

**Table 3.** Mean days of passage of stone

| | N | Mean | Std. deviation | Std. error | 95% confidence interval for mean | | Min. | Max. | P-value |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | Lower bound | Upper bound | | | |
| A | 42 | 8.67 | 0.57 | 0.088 | 8.49 | 8.84 | 7 | 9 | < 0.001 |
| B | 56 | 8.07 | 1.35 | 0.179 | 7.71 | 8.43 | 0 | 10 | |
| C | 25 | 9.65 | 0.49 | 0.095 | 9.46 | 9.85 | 9 | 10 | |
| **Total** | **123** | **8.60** | **1.16** | **0.103** | **8.40** | **8.80** | **0** | **10** | |

**Table 4.** The mean size of stones in patients who passed the stone

| | N | Mean | Std. deviation | Std. error | 95% confidence interval for mean | Min. | Max. | P-value |
|---|---|---|---|---|---|---|---|---|

| | | | | | Lower bound | Upper bound | | | |
|---|---|---|---|---|---|---|---|---|---|
| A | 42 | 5.53 | 0.55 | 0.088 | 5.35 | 5.70 | 5 | 7 | < 0.001 |
| B | 56 | 6.35 | 0.73 | 0.099 | 6.15 | 6.55 | 5 | 8 | |
| C | 25 | 5.08 | 0.28 | 0.055 | 4.97 | 5.20 | 5 | 6 | |
| **Total** | **123** | **5.81** | **0.79** | **0.073** | **5.66** | **5.95** | **5** | **8** | |

In carefully chosen individuals, medical expulsion therapy, or MET, has become a viable conservative treatment option for ureteral stones. To prevent surgery in as many patients as possible, we conducted this study to illustrate different medical care techniques.

Patients with a family history of stone disease and those who are male are three times more likely to get stone disease. The development of stones has been attributed to an imbalance between the stone promoters, such as oxalate, and the stone inhibitors, such as citrate. This may explain why urinary calculi are more common in men. For stones between 5 mm and 10 mm in size, the spontaneous stone passing rate ranges from 25% to 53% [4]. For MET, the majority of studies used a stone size of 5–10 mm [5]. But in our research, we only included patients with stones between 5 and 8 mm in size, and we didn't include any that were smaller or larger than that. In their research, Ye *et al.* [6] considered stone sizes ranging from 4 to 7 mm for MET.

Patients on tamsulosin had a 64% expulsion rate; those taking tamsulosin plus deflazacort had an 88% expulsion rate, and those taking NSAIDs had a 37% expulsion rate. This study can be compared to others. The ejection rate demonstrated by Sinha *et al.* [7] was comparable.

When additional medication was introduced for stone expulsion, the mean daily usage of NSAIDs reduced in our investigation (group II < group I < group III), which predicts a shorter mean time for stone expulsion, as demonstrated by Ali *et al.* [4] and Sinha *et al.* [7] in their investigations.

Lower ureteral stones are often treated by ureteroscopy. With the use of strong energy sources (such as holmium and thulium lasers) and current technological advancements, ureteroscopic intervention can achieve a success rate of up to 94% [8]. Although ureteroscopy is both safe and efficient, it necessitates double J-stenting and anesthesia. Additional ramifications include exorbitant expenses, reduced quality of life, usual activities being suspended, and the likelihood of problems such as ureteric stricture development and ureteric perforation [9]. These factors are crucial when considering the treatment of a distal ureteral stone that is symptomatic and amenable to expulsion therapy. For these reasons, some organizations have suggested using an adjuvant pharmacologic intervention in addition to analgesics during conservative therapy. Increasing the rate at which ureteral calculi in the lower ureter are expelled is the goal.

Pharmacologic medications are utilized to preserve the ureter's tonic activity, reduce the tonic contraction of smooth muscles during the peristaltic phase, and aid in preventing the development of ureteral mucosal oedema around the stones [4]. Steroid administration is justified by the fact that a ureter stone generates an inflammatory response of the mucosa, resulting in different types of oedema of varying degrees of severity. Steroids help the stone move through and keep this oedematous response from happening. Additional pharmacological therapies that can reduce spasmodic contraction of the ureter include beta-adrenergic agonists, calcium antagonists (nifedipine), and alpha1-blockers. Steroid pharmaceuticals such as prednisolone, deflazacort, and methylprednisolone are commonly used as anti-oedema treatments. Since they speed up the pace of evacuation, alpha1-blockers and corticosteroids are the best treatments for distal ureteral stones, based on the information that is currently available [10, 11].

Deflazacort was utilized at extremely high dosages or in conjunction with commercially available tamsulosin and deflazacort in all of the trials where its effects were detected. Deflazacort was utilized in our research at extremely low dosages of 12 mg daily, however, in contrast to previous studies that employed a dosage of 30 mg daily. Comparing our findings to those of previous research, we found that the ejection rate remained constant, even at reduced dosages. Based on our study's findings, we may conclude that corticosteroids work just as well at low dosages as they do at high ones. When contrasted to large dosages, this could lessen the steroids' adverse impact profile. In their investigation, Phukan *et al.* [12] also utilized modest doses of deflazacort, and this did not affect the stone's ejection rate.

Patients having symptoms of lower ureteral calculi 5-8 mm in size are the subject of our investigation. Our investigation included tamsulosin because the distal ureter contains the largest concentration of α1-receptors. Good anti-oedema medication of deflazacort has fewer adverse effects and a high tolerance. To avoid steroidal

pharmacological agents, the therapy was recommended for a maximum of seven days. Additionally, the aforementioned treatment regimen is most effective during the first several days.

The data analysis indicates that individuals taking α-blockers in combination with steroidal drugs and those taking α-blockers alone had a good rate of stone expulsion compared to patients taking NSAIDs alone (88%, 64% vs. 37%). Furthermore, when the mean day of passing of the stone was compared, the mean reduction in analgesic intake was lower in group II (8.07, 8.67 vs. 9.65), and it was higher (2.80, 3.18 vs. 6.62 days). When administered as a single medication to patients with diabetes, peptic ulcers, or steroidal contraindications, α-blockers also effectively reduce the ejection of stones and need to be utilized in these situations.

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## Conclusion

Medical expulsion treatment is both safe and effective for symptomatic and uncomplicated distal ureteral calculi. Tamsulosin can be used safely as a stand-alone therapeutic option for people who are allergic to steroids. Even at modest dosages, Deflazacort can be used efficiently for stone ejection. A prospective randomized multicenter research should be developed to corroborate these results.

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**Conflict of Interest:** None

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**Ethics Statement:** This study was approved by the Ethics Committee of SMBT Institute of Medical Sciences & Research Center, Dhamangaon, Nashik, Maharashtra, India. The patients provided written consent.

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