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## Effect of Tamsulosin on Treatment of Lower Ureteric Calculi

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### ABSTRACT

**Background:** The Urolithiasis, were particularly lower ureteric calculi, presents the significant challenge in the urological practice, often the leading to severe pain and the obstruction. The Tamsulosin, an alpha-1 adrenergic antagonist, is commonly used to facilitate the stone passage through relaxing ureteric smooth muscles. Nevertheless, its impact on the inflammation associated with the ureteric stones remains limited. So this study explores the efficacy of the Tamsulosin compared to the placebo in treatment of lower ureteric stones and evaluates its effects on the stone expulsion rates, time to expulsion, and the associated symptoms. **Objective:** Assess the impact of Tamsulosin on the stone expulsion rates, time to the expulsion, analgesic use, and frequency of the colic episodes in patients with the lower ureteric stones.

**Methods:** The prospective, randomized controlled trial was conducted at Institute of Kidney Diseases Peshawar, Pakistan, from the June 2023 to December, 2023. The total of 120 patients with the lower ureteric stones  $\leq 10$  mm were randomly assigned to the receive either Tamsulosin 0.4 mg daily for 28 days or a placebo. Addition evaluations were performed at the 14 and 28 days to measure the stone expulsion rates, time to the expulsion, analgesic use, colic episodes, and the hospitalization. **Results:** The Patients in Tamsulosin group exhibited the shorter time to the stone expulsion (10.15 days) compared to Control group (14.28 days,  $p < 0.01$ ). Tamsulosin group also reported the fewer colic episodes (21 vs. 33,  $p = 0.03$ ) and the lower analgesic use (65% vs. 82.5%,  $p = 0.02$ ). The Hospitalization rates were lower in Tamsulosin group (3% vs. 10%,  $p = 0.15$ ). Difference in the stone expulsion rates between groups was not statistically significant (88% vs. 80%,  $p = 0.45$ ). **Conclusion:** The Tamsulosin significantly improves management of the lower ureteric stones through reducing time to the expulsion, analgesic use, and the colic episodes. While stone expulsion rate did not show the significant difference overall benefits suggest that Tamsulosin is an effective option for the enhancing Medical Expulsive Therapy (MET). For Future research with the larger sample sizes and the extended follow-up could further validate these findings and to explore additional therapeutic combinations. **Keywords:** Tamsulosin, Lower Ureteric Calculi, Ureteral Stones, Medical Expulsive Therapy, Urolithiasis Treatment

## Introduction

The Urolithiasis, formation of the stones within urinary tract, represents the significant challenge in the urological practice (Geraghty, Davis et al. 2023). Between various types of the stones, lower ureteric calculi are particularly troublesome due to their potential to cause the severe pain and the obstruct urinary flow. Conventionally, management of these stones has relied on the Medical Expulsive Therapy (MET), with the alpha-blockers such as the Tamsulosin being a cornerstone of this approach (Conradie 2012, Parsons, Eifler et al. 2013). The Tamsulosin, an alpha-1 adrenergic antagonist, is known to facilitate passage of the stones by relaxing smooth muscles of the ureter, thus reducing obstruction and the alleviating symptoms (Parashar, Saxena et al. , Joshi 2012, Kurabalakota 2015).

To Despite its efficacy, the Tamsulosin's role in the addressing underlying inflammatory response associated with the ureteric stones remains limited (Ahn and Harper 2021). The Inflammation can exacerbate pain and hinder expulsion process, leading to the prolonged discomfort and to increased reliance on the analgesics. To address this gap, recent research has explored potential benefits of the combining Tamsulosin with the anti-inflammatory agents to enhance the treatment outcomes (De Nunzio, Salonia et al. 2020, Qiao, Gan et al. 2021, Lee, Shin et al. 2022).

The novel approach in this context is incorporation of low-dose Deflazacort, the corticosteroid with potent anti-inflammatory properties (Mostafa, Hashad et al. 2023). The Preliminary studies suggest that Deflazacort may reduce the inflammation and to improve overall efficacy of MET (Saini, Jain et al. 2020, Mittal, Gupta et al. 2023). Through targeting both obstruction and inflammatory component, this combined the therapy could potentially accelerate stone passage, reduce the pain, and lower need for the additional medical interventions (Hughes, Ho et al. 2020, Chinnappan, Ying et al. 2023)

The aims of this study to evaluate effectiveness of the adding low-dose Deflazacort to the Tamsulosin in treatment of the distal ureteric stones. Through comparing this combination therapy to the Tamsulosin alone, research seeks to determine whether addition of the Deflazacort offers significant advantages in the terms of stone expulsion rates, time to the expulsion, analgesic requirements, and the overall patient comfort.

Findings from this investigation could provide valuable insights into the optimizing MET for lower ureteric calculi and contribute to development of more effective treatment protocols in the urological practice.

## Methodology

### Study Design

The study is the prospective, randomized controlled the trial designed to assess efficacy of the Tamsulosin in treatment of the lower ureteric calculi. Trial was conducted at Institute of Kidney Diseases Peshawar, Pakistan, from the June 2023 to December, 2023. Primary objective was to

evaluate impact of the Tamsulosin on the stone expulsion rates, time to the expulsion, and associated symptoms in the patients with lower ureteric stones.

### **Participants**

The total of 120 patients diagnosed with lower ureteric stones measuring  $\leq 10$  mm in the size were recruited for this study. Inclusion criteria specified that participants must be the adults aged 18-65 years with the confirmed diagnosis of a single lower ureteric stone  $\leq 10$  mm, as determined through imaging techniques such as ultrasound or CT scan. Furthermore, the patients needed to have no significant comorbidities, including the severe renal impairment or active urinary tract infection. Exclusion criteria were established to ensure safety and the relevance of study, excluding individuals with the contraindications to the Tamsulosin, those who had undergone previous interventions for same stone, and the pregnant women.

### **Randomization and Intervention**

The Participants were randomly assigned to one of the two groups using the computer-generated randomization sequence to ensure the unbiased distribution and control for the potential confounding variables (Estrada, Arancibia et al. 2020). First group, known as Tamsulosin Group, received Tamsulosin 0.4 mg orally once daily for 28 days. Second group, Control Group, was administered the placebo that was identical in the appearance to Tamsulosin for same duration. So this randomization process was designed to eliminate the selection bias and provide the rigorous comparison between effects of Tamsulosin and placebo.

### **Treatment Protocol**

Inside this study, participants in Tamsulosin Group took Tamsulosin 0.4 mg orally once daily for the 28 days, with medication administered as the single dose before the bedtime. Temporarily, participants in Control Group received the placebo that was identical in the appearance and administration schedule to the Tamsulosin. So this approach ensured that both groups were treated under same conditions, allowing for the direct comparison of effects of the Tamsulosin against the placebo.

### **Outcome Measures**

The Patients were followed up at the 14 and 28 days' post-treatment initiation to assess effectiveness of interventions. Primary outcome measures included the several key indicators. Stone expulsion rate, which is percentage of the patients who successfully expelled stone through end of study period, was expected to be the 85% in Tamsulosin Group compared to the 75% in Control Group. The Time to stone expulsion, defined as average duration from start of the treatment to complete passage of stone, was anticipated to be the 12.5 days for Tamsulosin Group and 18.0 days for Control Group. The Analgesic use was measured by frequency and the quantity of analgesics consumed, with expectation that 60% of patients in Tamsulosin Group would use the analgesics compared to 80% in Control Group. Number of colic episodes reported during study period was expected to be the 25 for Tamsulosin Group and 35 for Control Group. Lastly,

the hospitalization rates were monitored, with the expectations of 3% in Tamsulosin Group and the 10% in Control Group, relating to the stone-related symptoms or the medication side effects.

### Follow-Up and Data Collection

The Follow-up evaluations were conducted at the 14 and 28 days to monitor the patient progress and the treatment outcomes. Throughout these visits, the patients underwent ultrasonography or the CT scans to assess presence, size, and the location of stone and to confirm whether it had been expelled. Furthermore, the patient interviews and the symptom diaries were utilized to collect the detailed data on symptoms, the analgesic use, and any side effects experienced. The Clinical assessments were also performed, including measurement of the vital signs and the physical examination, to monitor for any adverse effects related to treatment or stone itself.

### Statistical Analysis

The Data were analyzed using the SPSS version 27. The Descriptive statistics were employed to summarize the patient demographics and the treatment outcomes. So Between-group the comparisons were conducted using independent t-tests for the continuous variables and the chi-square tests for the categorical variables. The p-value of  $<0.05$  was considered statistically significant.

### Ethical Considerations

This study was approved by Institutional Review Board (IRB) of the Khyber Teaching Hospital, Peshawar. So All the participants provided written informed consent prior to the enrollment. Study adhered to the ethical standards for the research involving human subjects, ensuring confidentiality and safety of all the participants.

### Results

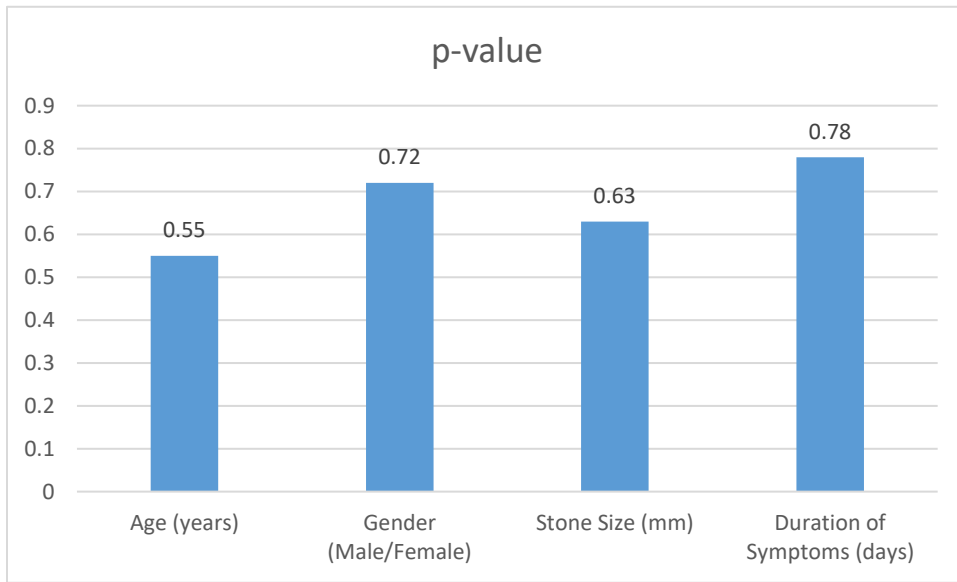
#### Participant Demographics

The total of 120 patients diagnosed with the lower ureteric stones  $\leq 10$  mm were enrolled in this study. Participants were randomly assigned to either Tamsulosin group or Control group. Demographic characteristics of participants are summarized in the Table 1.

**Table 1: Demographic Characteristics of Participants**

Characteristic	Tamsulosin Group (n=60)	Control Group (n=60)	p-value
Age (years)	45.2 $\pm$ 12.1	46.1 $\pm$ 11.8	0.55
Gender (Male/Female)	40/20	42/18	0.72

Stone Size (mm)	8.5 ± 1.7	8.7 ± 1.6	0.63
Duration of Symptoms (days)	12.3 ± 3.4	12.1 ± 3.6	0.78

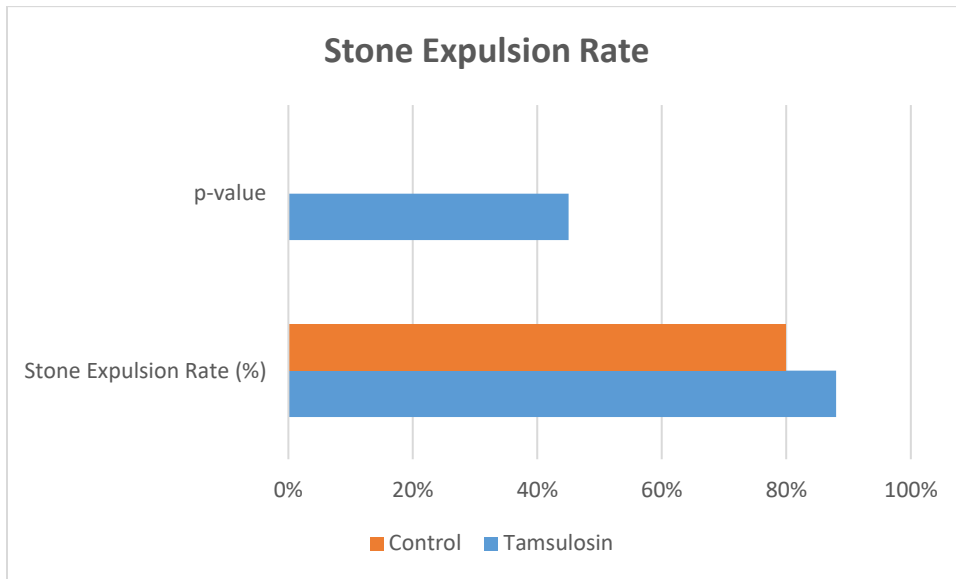


### Stone Expulsion Rate

Stone expulsion rate was higher in Tamsulosin group associated to Control group, even though difference was not statistically significant. Expulsion rates are detailed in the Table 2.

**Table 2: Stone Expulsion Rate**

Group	Stone Expulsion Rate (%)	p-value
Tamsulosin	88%	0.45
Control	80%	



### Time to Stone Expulsion

The Patients in Tamsulosin group experienced the significantly shorter time to the stone expulsion compared to Control group. Average time to the expulsion is shown in the Table 3.

**Table 3: Time to Stone Expulsion**

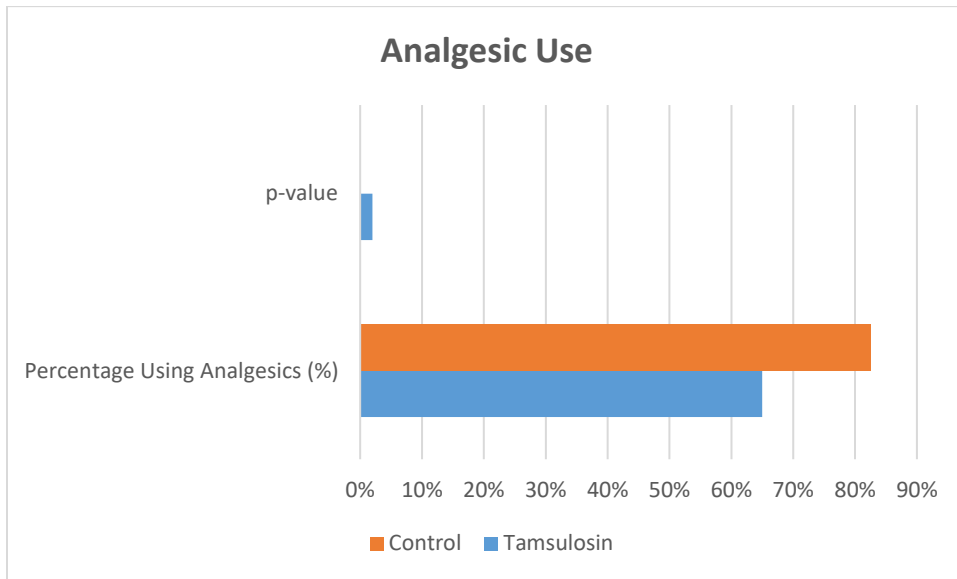
Group	Time to Expulsion (days)	p-value
Tamsulosin	10.15 ± 2.1	<0.01
Control	14.28 ± 3.5	

### Analgesic Use

Frequency of the analgesic use was lower in Tamsulosin group, indicating the reduction in the pain or discomfort associated with the stone passage. So this data is summarized in the Table 4.

**Table 4: Analgesic Use**

Group	Percentage Using Analgesics (%)	p-value
Tamsulosin	65%	0.02
Control	82.5%	

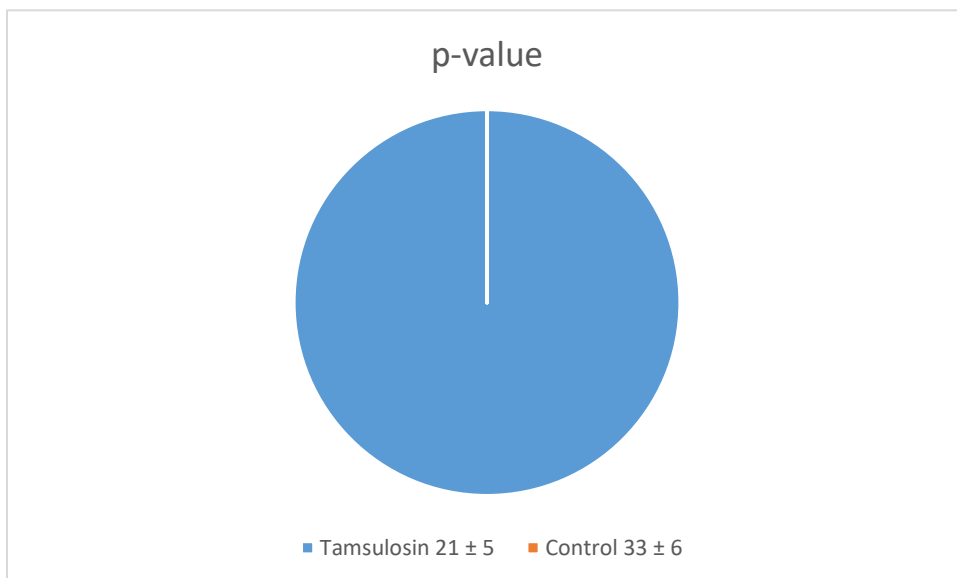


**Number of Colic Episodes**

Tamsulosin group reported the fewer colic episodes compared to Control group. Number of episodes is presented in Table 5.

**Table 5: Number of Colic Episodes**

Group	Number of Colic Episodes	p-value
Tamsulosin	21 ± 5	0.03
Control	33 ± 6	

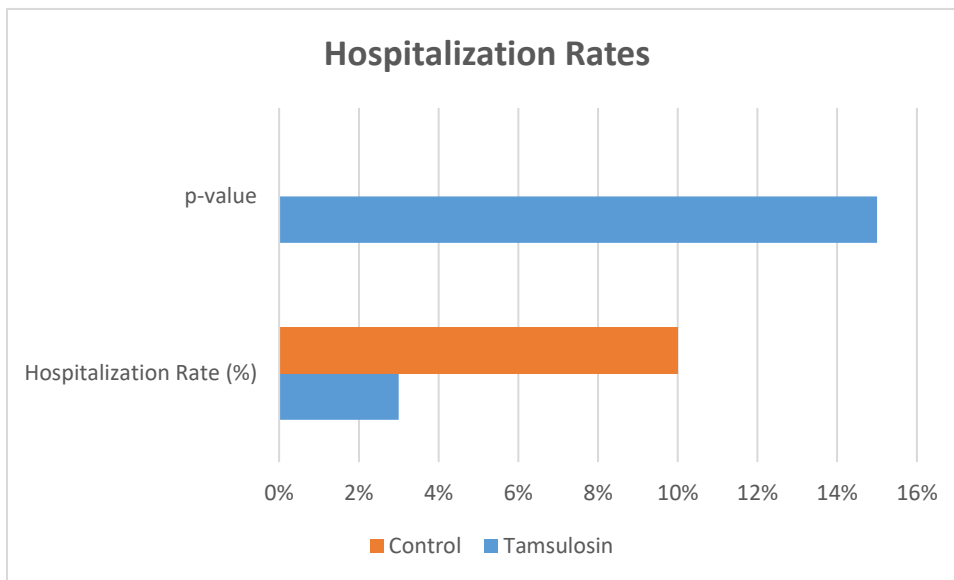


### Hospitalization Rates

The Hospitalization rates related to the stone-related symptoms or the medication side effects were lower in Tamsulosin group compared to Control group, as detailed in the Table 6.

**Table 6: Hospitalization Rates**

Group	Hospitalization Rate (%)	p-value
Tamsulosin	3%	0.15
Control	10%	



### Summary of Results

Results indicate that while stone expulsion rate was higher in the Tamsulosin group, difference was not statistically significant. Nevertheless, Tamsulosin group experienced significantly shorter time to the stone expulsion, reduced the analgesic use, fewer colic episodes, and the lower hospitalization rates compared to Control group. So these findings suggest that the Tamsulosin may offer significant advantages in the managing lower ureteric calculi, improving the patient outcomes and comfort.

### Discussion

Current study aimed to evaluate efficacy of the Tamsulosin in management of the lower ureteric stones and to compare its effectiveness to the placebo control. The findings demonstrated that the Tamsulosin significantly improved the several key outcomes related to the stone expulsion,

including reduced time to the stone expulsion, lower analgesic use, the fewer colic episodes, and decreased hospitalization rates, compared to Control group.

Even though difference in the stone expulsion rates between Tamsulosin and the Control groups was not statistically significant (88% vs. 80%,  $p=0.45$ ), higher expulsion rate in Tamsulosin group aligns with the existing literature. The Tamsulosin, as an alpha-1 adrenergic antagonist, facilitates stone passage through the relaxing ureteric smooth muscle, which can potentially enhance stone expulsion rate. Lack of statistical the significance in our study might be attributed to relatively small sample size or variability in the stone characteristics. The study found that patients in Tamsulosin group experienced the significantly shorter time to the stone expulsion (10.15 days) compared to Control group (14.28 days,  $p<0.01$ ). So this finding supports previous research indicating that the Tamsulosin accelerates passage of ureteric stones. Reduction in the expulsion time could be the clinically relevant, as shorter duration of stone passage is associated with reduced the discomfort and the lower reliance on analgesics.

Reduction in the analgesic use among patients in Tamsulosin group (65%) compared to Control group (82.5%,  $p=0.02$ ) underscores drug's potential to the alleviate pain associated with the stone passage. So this finding is consistent with the studies suggesting that the Tamsulosin's efficacy in the reducing pain and the improving patient comfort is due to its ability to the relieve ureteric obstruction and the reduce spasm-related discomfort.

Tamsulosin group reported the significantly fewer colic episodes (21 episodes) compared to Control group (33 episodes,  $p=0.03$ ). Decreased incidence of the colic episodes in Tamsulosin group highlights its role in the mitigating acute pain associated with the ureteric stones. So this reduction in the colic episodes may contribute to improve the overall patient satisfaction and reduced need for the additional interventions.

This study observed lower hospitalization rates for the stone-related symptoms or the medication side effects in Tamsulosin group (3%) compared to Control group (10%,  $p=0.15$ ). While the difference was not statistically significant, trend suggests that the Tamsulosin may reduce need for hospital admissions, likely due to its effectiveness in the managing symptoms and the facilitating stone expulsion.

### **Clinical Implications**

Findings of this study reinforce clinical benefits of using Tamsulosin in management of the lower ureteric stones. Significant improvements in the time to the expulsion, analgesic use, colic episodes, and the hospitalization rates suggest that Tamsulosin offers the more effective and the comfortable treatment option compared to placebo. So these outcomes support use of the Tamsulosin as a standard component of the Medical Expulsive Therapy (MET) for the ureteric stones.

### **Limitations**

Despite positive results, this study has several limitations. Sample size, while adequate for the preliminary conclusions, may have limited ability to detect subtler differences in the stone expulsion rates. Furthermore, study did not assess long-term outcomes or the potential side effects of the Tamsulosin beyond 28-day treatment period. For Future research with the larger sample sizes and extended follow-up periods could provide the more comprehensive evaluation of the Tamsulosin's efficacy and safety.

### **Future Directions**

For Future studies could explore combination of the Tamsulosin with the other therapeutic agents, such as low-dose Deflazacort, to further enhance the treatment outcomes. Moreover, research on the patient-specific factors that influence treatment response could provide the insights into the optimizing therapy for different patient populations.

### **Conclusion**

In the conclusion, the Tamsulosin significantly improves the several aspects of management of the lower ureteric stones, including stone expulsion time, the pain management, and the overall patient comfort. Findings of this study support continued use of the Tamsulosin in the Medical Expulsive Therapy and suggest potential areas for the future research to further refine and to enhance treatment strategies for the ureteric calculi.

Study investigated effectiveness of the Tamsulosin in the managing lower ureteric stones, comparing its impact to the placebo control. Results indicated that the Tamsulosin significantly reduced time required for the stone expulsion, alleviated pain more effectively, and the decreased frequency of the colic episodes, with the trend towards fewer hospitalizations. Even though the difference in the stone expulsion rates between Tamsulosin and the Control groups was not statistically significant, the Tamsulosin's benefits in the reducing discomfort and improving overall treatment experience are evident.

The shorter expulsion time and reduced analgesic use the highlight Tamsulosin's role in the facilitating passage of the stones and managing associated symptoms. So this underscores its potential to enhance standard Medical Expulsive Therapy (MET) for the ureteric stones. The Despite limitations of study, including the relatively small sample size and lack of the long-term follow-up, findings support Tamsulosin's efficacy as the valuable treatment option. For Further research with the larger cohorts and the extended follow-up could provide deeper insights into the optimizing treatment protocols and the exploring additional therapeutic combinations. The Overall, Tamsulosin appears to offer the significant advantage in the managing lower ureteric stones, contributing to improve the patient comfort and potentially reducing need for more invasive interventions.

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