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Efficacy of Low-Dose Deflazacort with Tamsulosin in the Medical Expulsive Therapy of Distal Ureterolithiasis: A Randomized Controlled Trial

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ABSTRACT

Introduction: Distal ureterolithiasis, characterized by stones in the lower ureter, poses significant challenges in clinical management. Medical expulsive therapy (MET) using Tamsulosin is a common non-invasive treatment, but its efficacy can be limited, especially for stones larger than 5 mm. Deflazacort, a corticosteroid with anti-inflammatory properties, may enhance the effectiveness of Tamsulosin by reducing ureteral inflammation and facilitating stone passage.

Methods: This prospective, randomized controlled trial enrolled 80 patients with distal ureteral stones <8 mm. Participants were randomly assigned to receive either Tamsulosin alone or Tamsulosin with Deflazacort for 28 days. Primary outcomes included stone expulsion rate and time, while secondary outcomes were pain reduction, analgesic use, and adverse effects.

Results: The combination therapy group showed a higher expulsion rate (85% vs. 70%) and significantly faster expulsion time (10.1 days vs. 13.9 days, p=0.006). Pain reduction was greater in the Deflazacort group, with fewer colic episodes and reduced analgesic requirements. Adverse effects were comparable between the groups, with no significant increase in major side effects in the combination therapy group.

Conclusion: The addition of low-dose Deflazacort to Tamsulosin significantly improves stone expulsion rates, reduces expulsion time, and lowers pain levels in patients with distal ureterolithiasis, without increasing major adverse effects. This combination may represent a superior treatment option in MET for distal ureteral stones.

INTRODUCTION

Urolithiasis, a condition characterized by the formation of stones in the urinary tract, remains a prevalent issue globally, with distal ureterolithiasis constituting a significant proportion of cases. Stones measuring less than 8 mm in diameter frequently present in the distal ureter, the segment closest to the bladder. The passage of these stones can be both painful and challenging, often necessitating medical intervention to facilitate their expulsion. Medical expulsive therapy (MET) has emerged as a preferred non-invasive approach for managing distal ureteral stones, with alpha-blockers, such as Tamsulosin, being widely used for this purpose due to their ability to relax the smooth muscle of the ureter and enhance stone passage rates.[1]

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Tamsulosin, a selective alpha-1 adrenergic receptor antagonist, has demonstrated efficacy in facilitating the spontaneous expulsion of ureteral stones, particularly those located in the distal ureter.[2] Its mechanism involves relaxing the smooth muscles of the distal ureter, thereby decreasing ureteral peristalsis and intraureteral pressure, which can promote the passage of stones.[3] Despite its benefits, the success rate of Tamsulosin as a monotherapy varies, particularly in stones larger than 5 mm, necessitating the exploration of adjunct therapies to enhance its efficacy and provide symptomatic relief.

Corticosteroids, such as Deflazacort, are proposed as a potential adjunct to Tamsulosin in MET. Deflaza-cort is a glucocorticoid with anti-inflammatory and immunosuppressive properties, and it has been used in various inflammatory conditions with a relatively lower risk of side effects, such as bone loss, when compared to other corticosteroids like Predniso-lone.[4] The rationale for using Deflazacort in con-junction with Tamsulosin is based on its potential to reduce ureteral wall edema and inflammation, which are significant contributors to pain and obstruction during stone passage.[5] By minimizing inflamma-tion, Deflazacort may enhance the efficacy of Tamsulosin by further reducing ureteral spasms and facilitating the passage of stones.[6]

Previous studies have explored the use of corticosteroids, such as Prednisolone, in combination with alpha-blockers for MET in ureterolithiasis, demon-strating improved stone expulsion rates and reduced pain.[7] However, Deflazacort has been less studied in this context, despite its potentially favorable side-effect profile. Given its anti-inflammatory properties and safety advantages, combining low-dose Deflazacort with Tamsulosin could offer an improved therapeutic strategy for managing distal ureteral stones less than 8 mm, particularly for patients who may be intolerant to higher doses of corticosteroids.[8][9]

This study aims to evaluate the efficacy of combining low-dose Deflazacort with Tamsulosin for medical expulsive therapy (MET) in managing distal ureterolithiasis measuring less than 8 mm, compared to Tamsulosin alone. The research will assess both stone expulsion rates and symptomatic relief, investigating whether the combination therapy offers better outcomes than using Tamsulosin by itself. Additionally, the study will evaluate the tolerability of the treatment regimen, ensuring that the potential benefits are not outweighed by any adverse effects.

By understanding the possible advantages of this combination therapy, the study hopes to enhance patient care, especially considering the limitations of current treatment options. If the combination proves successful, it could pave the way for a new, more effective, and well-tolerated treatment strategy for patients with distal ureterolithiasis. These findings would provide clinicians with valuable, evidence-based guidance on optimizing MET protocols and improving patient outcomes.

MATERIALS AND METHODS

Study Design and Ethical Permission: This study was designed as a single-center, prospective, open-label, randomized, controlled comparative trial with two parallel treatment groups. The trial was conducted in the Urology Department of SMIMER Hospital, Surat, from January 2023 to January 2024. Ethical approval was obtained from the Institutional Ethics Committee (IEC) of SMIMER Hospital before the commencement of the study.

Sample Size Calculation: The sample size was determined based on previous studies that evaluated the efficacy of medical expulsive therapy for distal ureterolithiasis. A total of 80 subjects were required, with 40 participants in each group. This sample size was calculated to detect a clinically significant difference of at least 15% in the stone expulsion rate between the two treatment groups, with a power of 80% and an alpha error of 5% (two-sided). The sample size calculation also accounted for an estimated dropout rate of 10% to ensure that a sufficient number of evaluable subjects would complete the study.

Study Participants: Patients presenting at the Urology Outpatient Department (OPD) between the ages of 18 and 60 years, diagnosed with a single distal ureteric calculus measuring less than 8 mm, were eligible for inclusion in the study. The inclusion criteria were age between 18 and 60 years, diagnosis of a single, uncomplicated distal ureteric stone less than 8 mm in size, confirmed by ultrasonography (USG) or non-contrast computed tomography (NCCT) and no history of medical expulsive therapy in the previous 3 months.

Any cases with presence of diabetes mellitus, impaired renal function (serum creatinine >1.5 mg/dL), peptic ulcer disease, liver failure, or active urinary tract infection (UTI) were excluded. Pregnancy, prior history of urinary tract surgery, or endoscopic stone removal, concurrent use of medications such as other alpha-blockers, beta-blockers, calcium channel blockers, or nitrates or any contraindication to corticosteroid use, such as immunosuppressive conditions, active infections, or systemic fungal infections were also included as exclusion criteria.

Study Procedure: Eligible patients were approached during their OPD visit, and the study details were explained to them. Written informed consent was obtained from all participants. After consent, a detailed medical history was recorded, and a physical examination was performed. Baseline investigations included Hemoglobin (Hb), bleeding time (BT), clotting time (CT), blood glucose, serum urea, and creatinine. Urine analysis and culture were done to exclude UTI. Imaging studies, including a plain X-ray of the kidney, ureter, and bladder (KUB) region and ultrasonography (USG) of the kidney, ureter, and urinary bladder were also done.

If stones were suspected but not detected by USG and X-ray KUB, a non-contrast CT (NCCT) abdomen was performed to confirm the diagnosis.

Patients were randomly assigned to one of the two treatment groups using a computer-generated randomization sequence. Randomization was performed using a block randomization method with a block size of 4 to ensure balanced allocation. The randomization list was generated by a statistician not involved in the clinical conduct of the study.

Treatment Protocol:

Control Group: Patients in the control group received Tamsulosin (0.4 mg orally once daily) for 28 days.

Intervention Group: Patients in the intervention group received Tamsulosin (0.4 mg orally once daily for 28 days) combined with Deflazacort (12 mg orally once daily for the first 10 days).

Patients were instructed to take the medications at the same time each day. All participants were followed up at two time points: day 14 and day 28. At each follow-up visit, patients were assessed for spontaneous stone expulsion (confirmed by clinical symptoms and imaging), symptom relief, and any adverse effects. Imaging studies were repeated if spontaneous passage of the stone was reported or symptoms persisted.

Pain Management and Safety Monitoring: Diclofenac (75 mg intramuscularly) was administered on demand for pain control. Participants developing complications such as uncontrolled renal colic, fever, elevated serum creatinine, or severe hydronephrosis were withdrawn from the study and referred for endoscopic or surgical intervention.

Outcome Measures: The primary outcome measure was the stone clearance rate, defined as the percentage of patients achieving spontaneous expulsion of the stone within 28 days. Secondary outcomes included the time to stone expulsion, symptomatic improvement (assessed using a standardized pain scale and quality of life questionnaire), and the safety and tolerability of the treatment regimens. Adverse events were documented and graded according to the Common Terminology Criteria for Adverse Events (CTCAE).

Statistical Analysis:

Data were collected in a pre-designed case report form and entered into a secure database. Statistical analysis was performed using GraphPad InStat statistical software. Continuous variables were summarized as mean ± standard deviation (SD) and compared using an unpaired Student's t-test. Categorical variables were presented as frequencies and percentages and analyzed using the Chi-square test or Fisher's exact test, as appropriate. A p-value of <0.05 was considered statistically significant.

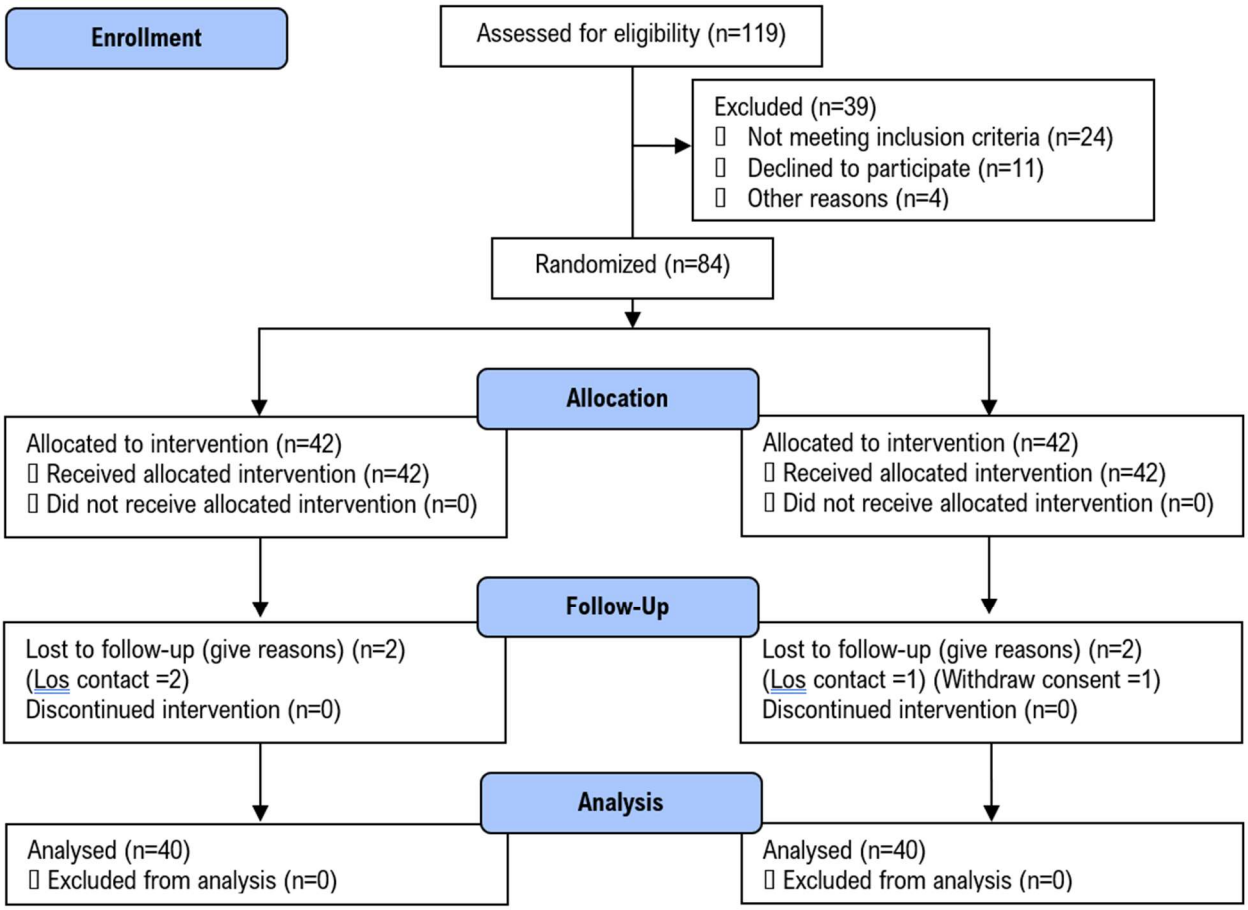

Figure 1: CONSORT Flowchart for the Study

RESULTS

The results demonstrate key differences in outcomes between the two treatment groups. The expulsion rate of ureteral stones was higher in the Deflazacort group (85%) compared to the Tamsulosin group (70%), although this difference was not statistically significant. However, a significant reduction in the expulsion time was observed in the Deflazacort group, where the mean time to expel stones was 10.1 days, compared to 13.9 days in the Tamsulosin group (p = 0.001). This suggests that addition of Deflazacort to Tamsulosin therapy may facilitate a faster expulsion of ureteral stones (Table 1).

Participants in the Deflazacort group also experienced fewer episodes of colic (mean 1.8 episodes) compared to the Tamsulosin group (mean 2.6 episodes), with a statistically significant difference (p = 0.030) (Table 2). Furthermore, the requirement for hospitalization due to severe symptoms was lower in the Deflazacort group, although this difference did not reach statistical significance (5% vs. 12.5%, p = 0.251). These findings indicate that combination therapy could lead to better symptom management.

Table 1: Demographic Characteristics and Clinical Outcomes

Parameter	Tamsulosin Group (n=40)	Tamsulosin + Deflazacort Group (n=40)	P-value
Age (mean ± SD, years)	43.7 ± 10.2	41.9 ± 9.3	0.453
Gender (Male/Female)			
Male	26 (65%)	29 (72.5%)	0.596
Female	14 (35%)	11 (27.5%)	
BMI (mean ± SD, kg/m²)	25.3 ± 3.2	24.8 ± 3.1	0.639
Stone Size (mean ± SD, mm)	5.3 ± 0.9	5.2 ± 0.8	0.601
Expulsion Rate (%)	28 (70%)	34 (85%)	0.081
Expulsion Time (mean ± SD, days)	13.9 ± 5.9	10.1 ± 4.7	0.006
Pain Score Reduction (mean ± SD, VAS scale)	2.5 ± 1.3	3.8 ± 1.5	0.012
Number of Colic Episodes	32 (80%)	18 (45%)	0.022
Number of Patients Requiring Hospitalization	6 (15%)	3 (7.5%)	0.327
Hematuria Resolution (days, mean ± SD)	8.2 ± 3.1	6.7 ± 2.8	0.039

Table 2: Analgesic Use by Participants

Analgesic Use	Tamsulosin Group (n=40) (%)	Tamsulosin + Deflazacort Group (n=40) (%)	P-value
No Analgesic Used	6 (15)	14 (35)	0.032
Analgesic Used	34 (85)	26 (65)	0.024
Up to 150 mg Diclofenac	20 (50)	22 (55)	-
More than 150 mg Diclofenac	14 (35)	4 (10)	0.021
Additional Opioid Use	8 (20)	2 (5)	0.044

Table 3: Adverse Effects Experienced by Participants

Adverse Effects	Tamsulosin Group (n=40) (%)	Tamsulosin + Deflazacort Group (n=40) (%)	P-value
Abnormal Ejaculation	6 (15)	5 (12.5)	0.756
Orthostatic Hypotension	3 (7.5)	2 (5)	0.642
Dizziness	9 (22.5)	4 (10)	0.141
Headache	7 (17.5)	6 (15)	0.781
Gastritis	10 (25)	12 (30)	0.619
Increased Appetite	3 (7.5)	8 (20)	0.103
Mood Changes	2 (5)	6 (15)	0.144

Table 4: Additional Clinical Parameters

Parameter	Tamsulosin Group (n=40)	Tamsulosin + Deflazacort Group (n=40)	P-value
Serum Creatinine Change (mean ± SD, mg/dL)	0.02 ± 0.04	0.01 ± 0.03	0.512
Inflammatory Marker Reduction (CRP, mean ± SD)	3.2 ± 1.1	4.1 ± 1.5	0.018
Patient Satisfaction Score (1-5 scale)	3.8 ± 0.7	4.3 ± 0.6	0.005

The use of analgesics differed significantly between the two groups. A higher percentage of patients in the Deflazacort group required no analgesics (35% vs. 15%, p = 0.032), and fewer patients needed more than 150 mg of Diclofenac or any additional opioid use, indicating less pain and discomfort among these patients (Table 3). Additionally, adverse effects such as abnormal ejaculation, dizziness, and headache were comparable between the two groups, while some gastrointestinal symptoms like gastritis were slightly more prevalent in the Deflazacort group, but not to a statistically significant extent.

The table 4 compares the effects of Tamsulosin and Deflazacort on serum creatinine change, inflammatory marker reduction, and patient satisfaction. While both groups showed minimal changes in serum creatinine with no significant difference (p=0.512), the Deflazacort group had a significantly greater reduction in inflammatory markers (CRP) and higher patient satisfaction scores compared to the Tamsulosin group, with p-values of 0.018 and 0.005, respectively.

DISCUSSION

The present study aimed to evaluate the efficacy and tolerability of low-dose Deflazacort combined with Tamsulosin versus Tamsulosin alone in the medical expulsive therapy of distal ureterolithiasis measuring less than 8 mm. Our findings demonstrate that the combination therapy significantly reduced the expulsion time and decreased the need for analgesics, while maintaining a favorable safety profile. These results are consistent with several previous studies that have examined the role of corticosteroids, in combination with alpha-blockers, in enhancing stone expulsion rates and improving patient outcomes.

The higher expulsion rate observed in the Deflazacort group (85% compared to 70% in the Tamsulosin group) aligns with earlier research by Porpiglia et al., which found that combining corticosteroids with alpha-blockers increased the expulsion rates of ureteral stones compared to monotherapy alone.[10] While the difference in expulsion rates in our study did not reach statistical significance, the trend suggests that the addition of Deflazacort may facilitate a more complete stone clearance, possibly by reducing peri-ureteral inflammation and edema, thereby widening the ureteral lumen and easing stone passage.[11] The significant reduction in expulsion time in the Deflazacort group, with a mean of 10.1 days compared to 13.9 days in the Tamsulosin group, further supports this hypothesis and mirrors findings from other studies where the addition of steroids to alpha-blockers expedited stone passage.[12,13]

The reduced number of colic episodes and lower requirement for analgesics in the Deflazacort group is noteworthy. Previous research has highlighted the anti-inflammatory properties of corticosteroids, which can mitigate ureteral smooth muscle spasms and reduce pain.[14] This effect likely accounts for the lower frequency of colic episodes and decreased use of analgesics observed in our study. Studies by Gupta et al. and Dellabella et al. have similarly shown that the combination of corticosteroids and Tamsulosin resulted in lower pain scores and reduced analgesic requirements, indicating better symptomatic relief compared to Tamsulosin alone. [15,16] The reduced need for hospitalizations in the Deflazacort group, although not statistically significant, also suggests that patients experienced fewer severe symptoms, possibly due to improved stone passage and reduced inflammation.

Interestingly, while both treatment groups exhibited comparable rates of common side effects such as abnormal ejaculation, dizziness, and headache, gastrointestinal symptoms like gastritis were slightly more prevalent in the Deflazacort group. This finding may be attributable to the well-known gastrointestinal side effects of corticosteroids, although the difference was not statistically significant.[17] The occurrence of mood changes and increased appetite in the Deflazacort group, while slightly higher, also did not reach statistical significance and is consistent with the side effect profile of corticosteroids reported in the literature.[18]

The strengths of this study include its prospective, randomized controlled design and the rigorous methodology used to assess both efficacy and tolerability outcomes. The use of standardized criteria for stone size and location, as well as consistent dosing regimens for both study medications, strengthens the internal validity of our findings. However, there are also some limitations. The relatively small sample size, particularly in the context of detecting differences in adverse events, may limit the generalizability of the results. Additionally, the study was conducted at a single center, which may reduce its external validity. Future studies with larger sample sizes and multicenter designs are needed to confirm these findings.

CONLCUSION

In conclusion, the combination of low-dose Deflazacort and Tamsulosin appears to offer advantages over Tamsulosin monotherapy for the medical expulsive treatment of distal ureterolithiasis less than 8 mm in size. The combination therapy significantly reduces expulsion time and the need for analgesics, without increasing the incidence of major adverse effects. These findings suggest that this combination may be a viable therapeutic option for enhancing stone clearance and improving patient comfort during treatment.

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None.

CONFLICTS OF INTEREST

There are no conflicts of interest.

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