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MIRABEGRON VS ALPHA BLOCKERS IN MEDICAL EXPULSIVE THERAPY IN DISTAL URETERIC CALCULUS

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Abstract

Background:

Medical Expulsive Therapy (MET) enhances the rapid removal of stones with ureteral blockage avoidance and ureteral colic relief. Mirabegron and Tamsulosin both have been helpful as MET for ureteric calculus (UC).

Objective:

To compare the effectiveness of Mirabegron and Tamsulosin in distal ureteral stone expulsion (SE) in patients presenting with distal UC.

Method:

This is a randomized controlled trial conducted at the Urology Department of Indus Hospital and Health Networks, Korangi campus, Karachi from April 2024 to February 2025. Participants were randomly divided into groups A and B. Patients in group A received Mirabegron 50mg, Drotaverine 40mg, and Diclofenac 50mg. Group B patients received Tamsulosin 0.4mg, Drotaverine 40mg, and Diclofenac 50mg. After 4 weeks, Computed Tomography (CT) was done to evaluate the presence or absence of ureteral stone. The chi-square test was employed to compare the effectiveness between the two groups with a p-value of ≤0.05 considered statistically significant.

Results:

A total of 94 patients (47 in each group) were enrolled in this study with an average age of 31 years. SE was observed in 27 patients (52.9%) who received tamsulosin and 24 patients (47.1%) who received Mirabegron treatment. No major effect on SE was seen in either treatment group.

Conclusion:

More studies with bigger sample numbers and a wider range of demographics could help confirm these results and investigate Mirabegron's long-term effects on ureteral SE. Ultimately, this study emphasizes how critical it is to keep researching and contrasting different medical treatments to improve patient care for urolithiasis management.

INTRODUCTION

Urolithiasis is a common condition that affects roughly 10% of people worldwide and is becoming more common (1). The main treatments for ureteral calculi include extracorporeal shock wave lithotripsy (ESWL), ureteroscopy, percutaneous nephrolithotomy, open and laparoscopic procedures, and medical expulsive therapy (MET). Enhancing the rapid removal of stones along the ureter is the main goal of MET to avoid ureteral blockage and relieve ureteral colic. This strategy seeks to avoid the need for more intrusive procedures and surgery, both of which could have unfavourable effects (1).

According to the research, several medications, including calcium channel blockers, alpha-1 receptor blockers (Tamsulosin), and phosphodiesterase-5 inhibitors, have been employed as medical expulsive therapy (MET) for distal ureteric stones (2). Beta-3 adrenergic receptors (β3-AR, Mirabegron) are found in the ureter's smooth muscles. By influencing urothelial function, their activation causes smooth muscles to relax (3). A meta-analysis comparing the control group with Mirabegron revealed that the latter greatly increased the removal percentage of stones less than 5 mm (60% vs. 83%) (4). Whereas, literature also stated that Tamsulosin substantially facilitates the removal of bigger ureteral stones, which measure 5 to 10 mm(5).

European Association of Urology recommended alpha blockers mainly in MET for stone expulsion (SE). However, few studies have been done on Mirabegron, which is also helpful in SE with fewer pain episodes (6, 7). In our setup, we commonly see patients with ureteric calculus (UC) presenting in the emergency department (ED) and those having affordability issues. Mirabegron is cheaper compared to alpha blockers and needs less analgesia. This study aimed to compare the effectiveness of Mirabegron and Tamsulosin in distal ureteral SE in patients presenting with distal UC.

METHODOLOGY:

A randomized controlled trial was conducted in the Urology Department at the Indus Hospital and Health Networks, Korangi campus, Karachi from April 2024 to February 2025. The study was ethically approved by the College of Physicians and Surgeons of Pakistan (CPSP) and the Institutional Review Board of Indus Hospital and Health Networks, Korangi campus, Karachi. The study duration was six months. Non-probability sampling technique was used. For sample size calculation, a hypothesized frequency of 89.6% and 61.2% was taken from the effect of Mirabegron 50mg and Tamsulosin 0.4mg on SE (6, 8). By applying 90% power and a 95% confidence interval, a sample size of 94 (47 in each group) was calculated. Patients of age >14 and <80 years; either gender; with symptoms suggestive of renal colic; with calculus >4mm and <10mm demonstrated in the distal ureter [stone size was measured on Computed Topography (CT) scan], and consented to participate in the study were included. Patients were excluded if they had a calculus larger than 10 mm, multiple renal calculi, were already taking alpha-blockers for benign prostatic hyperplasia, had a solitary functioning kidney or a transplanted kidney, a history of ureteral stricture, an allergy to any of the study drugs, or were pregnant.

Patients who came in the Emergency, Outpatient Department (OPD) or were seen as inpatients and diagnosed as distal UC on CT of Kidneys, Ureters, and Bladder (KUB), fulfilling the inclusion criteria were enrolled in the study. Before enrollment, all risks and benefits of the study were explained to patients, and informed consent was taken. After obtaining consent, a thorough medical history from patients was taken, including demographic details and clinical history in ED and OPD.

All patients were randomly divided into two groups by using the opaque seal envelope method. Patients in group A received capsule Mirabegron 50mg once a day for 4 weeks Drotaverine 40mg thrice a day for 5 days, and Diclofenac 50mg twice a day for 5 days if creatinine was <1.5 mg/dl. Group B patients received capsule Tamsulosin 0.4mg once a day for 4 weeks Drotaverine 40mg thrice a day, and Diclofenac 50mg twice a day for 5 days if creatinine was <1.5mg/dl. All patients were advised to visit OPD after 4 weeks for the assessment of SE. After 4 weeks, CT KUB was done to evaluate the presence or absence of ureteral stone. All the findings of study variables such as age, gender, hypertension, size of the stone, location of the stone, and effectiveness were noted in predesigned Performa.

Data was analyzed by using SPSS version 27. Mean/median was reported based on normality distribution for quantitative variables such as age, height, weight, BMI, size of stone, and number of stones. Normality was assessed by using the Shapiro-Wilk test. Qualitative variables such as gender, hypertension, stone location, and effectiveness were reported as frequency and percentage. A chi-square test was applied to compare the effectiveness between both groups. Effect modifiers such as age, gender, BMI, hypertension, stone location, and size of stone were stratified. A p-value of ≤0.05 was taken as significant.

RESULTS:

A total of 94 patients were enrolled in this study. The average age of the patients was 31 years. Male patients were more affected (80.9%). While analyzing body composition data, we observed a median weight of 79kg, height of 1.76m, and BMI of 25.18, respectively. A low percentage (21.3%) of hypertensive patients were present. The average stone size was 7mm, and overall, SE was done in 51 (54.3%) of the patients. Details can be observed in Table 1.

Figure 1 displays the prevalence of stone location. The left ureterovesical junction (LUJ) had the highest stone presence (29.8%), followed by the left distal ureter (LDU) (26.6%), the right ureterovesical junction (RUJ) (24.5%), and right distal ureter (RDU) (19.1%).

There was no significant association found between the treatment groups and demographic data (see Table 2). Moreover, no difference was noticed between the Tamsulosin and Mirabegron groups concerning age (32 vs 30 years), weight (78 vs 79 kg), height (1.76 = 1.76 m), and BMI (24.91 vs 25.31). An equal number of hypertensive patients were present in both groups.

Tamsulosin-treated patients mostly had stones in RDU (77.8%), while patients who received mirabegron had stones prominently in RUJ (69.6%). There was no major difference in stone size in both treatment groups (see Table 3).

Table 4 exhibits the difference between both treatment groups on SE. SE was detected in 27 patients (52.9%) who received tamsulosin treatment and 24 patients (47.1%) who received mirabegron treatment. No major effect on SE was seen in either treatment group.

Table 1 Baseline demographic and clinical characteristics

Characteristics	Outcome
Age (years), median (IQR)	31 (24.75 – 39)
Gender, frequency (%)	
Male	76 (80.9%)
Female	18 (19.1%)
Weight (kg), median (IQR)	79 (70 – 85.25)
Height (m), median (IQR)	1.76 (1.73 – 1.78)
Body Mass Index, median (IQR)	25.18 (23.77 – 27.47)
Hypertension, frequency (%)	
No	74 (78.7%)
Yes	20 (21.3%)
Stone Size (mm), median (IQR)	7 (6 – 9)
SE, frequency (%)	
No	43 (45.7%)
Yes	51 (54.3%)
SE: Stone expulsion	

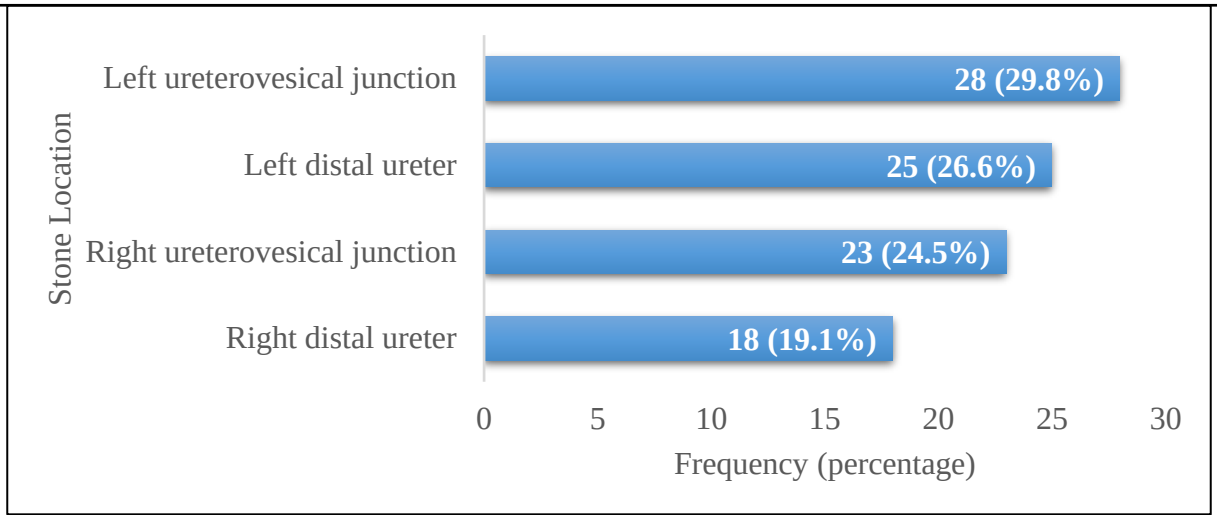

Figure 1 Stone locations in patients

Table 2 Stratification of demographic with treatment groups

Variables	Treatment groups		p-value
	Tamsulosin (N: 47)	Mirabegron (N: 47)	
Age* (years)	32 (25 – 39)	30 (24 – 41)	0.788
Weight* (kg)	78 (70 – 83)	79 (71 – 83)	0.820
Height* (m)	1.76 (1.74 – 1.78)	1.76 (1.72 – 1.78)	0.638
Body mass index*	24.91 (23 – 27)	25.31 (24 – 27)	0.594
Gender			
Male	40 (52.6%)	36 (47.4%)	0.432
Female	7 (38.9%)	11 (61.1%)	
Hypertension			
No	37 (50%)	37 (50%)	1.000
Yes	10 (50%)	10 (50%)	
*Mann-Whitney test applied (median, IQR noted)			

Table 3Stratification of clinical data with treatment groups

Clinical data	Treatment group		p-value
Stone location	Tamsulosin (N: 47)	Mirabegron (N: 47)	
Right distal ureter	14 (77.8%)	4 (22.2%)	0.023¥
Right ureterovesical junction	7 (30.4%)	16 (69.6%)	
Left distal ureter	11 (44%)	14 (56%)	
Left ureterovesical junction	15 (53.6%)	13 (46.4%)	
Stone size* (mm)	8 (6 – 9)	7 (6 – 8)	0.297
*Mann-Whitney test applied (median, IQR noted) ¥ p-value significant, i.e. ≤ 0.05			

Table 4 Effect of Tamsulosin and Mirabegron on stone expulsion

Stone expulsion	Treatment group		p-value*
	Tamsulosin	Mirabegron	
Yes	27 (52.9%)	24 (47.1%)	0.679
No	20 (46.5%)	23 (53.5%)	
*Chi-square test of association applied			

DISCUSSION:

Present research compared the effectiveness of mirabegron and tamsulosin for distal ureteral SE. There was no difference found between both treatments for SE. Morsy et al. also found similar results with no differences in SE rates while comparing mirabegron, tamsulosin, and diclofenac-treated patients for MET (9). Similarly, studies from Egypt and Turkey also concluded that Mirabegron had no effect on stone removal duration and did not improve the rate of SE (10, 11). On the contrary, evidence from China revealed that MET with Mirabegron significantly improved SE in patients with distal UC that are less than 5 mm; for stones that are more than 5 mm, it had little impact (7). Additionally, Mirabegron had a low frequency of side effects and lessened the requirement for painkillers in stones smaller than 10 mm(7). In a retrospective investigation, Solakhan et al. initially documented that mirabegron drastically raised the SE and decreased pain episodes during the removal of distal ureteral stones(12). Though there is still debate, several randomized controlled trials demonstrated that mirabegron is efficacious for expulsion (9, 13). On the other hand, in a study, when used in conjunction with an oral corticosteroid, tamsulosin effectively promoted the spontaneous clearance of distal UC smaller than 10 mm (14). Another research conveyed that compared to tadalafil, tamsulosin was more successful for distal UC, requiring less analgesics and less time to expel the stones(15). Although these results demonstrate tamsulosin's effectiveness, subsequent clinical research has revealed that this medication does not raise the rate of SE above that of a placebo (16, 17).

The average stone size observed in our study was 7 mm. Among the anatomical sites, the LUJ exhibited the highest frequency of stones, whereas the RDU had the lowest. Besides stone size and location, other factors such as ureteral spasm, edema, and the extent of hydronephrosis also play a significant role in influencing stone expulsion (SE). One study found that ureteral dilation led to a reduced expression of all β3-adrenoceptor (β3-AR) subtypes within the mucosal and muscular layers of the human ureter (18). In the early stages of the condition, the use of highly selective β3-AR agonists may help alleviate symptoms by relaxing ureteral smooth muscle. However, these agents become less effective in the later stages of the disease when structural compensation in the ureter has occurred (18). A previous meta-analysis reported that Mirabegron—a potent and selective β3-AR agonist—significantly improved the expulsion rate of small stones, but it showed no statistically significant benefit for larger stones (4). Mirabegron functions by activating β3-adrenoceptors, resulting in the relaxation of the detrusor muscle during the bladder's storage phase, thereby increasing bladder capacity (19, 20). It has a half-life of approximately 50 hours and is approved for the treatment of overactive bladder (21). The ureter and bladder have a large number of adrenoceptors. The distal ureter is rich in alpha-adrenergic receptors, which relax the ureter while simultaneously preserving antegrade peristaltic movement, thus aiding in stone passage (22, 23). According to the meta-analysis, alpha-blockers considerably raise the rate at which distal ureteric stones are expelled (24). The literature suggests that silodosin is superior to tamsulosin in terms of SE rates, time, and pain episodes (25, 26). Research revealed that many more patient-centered patient-reported outcome measure instruments have been created for the assessment of ureteric stone disorders. Using questionnaires, they evaluate the quality of life associated with health (27, 28).

The single center, limited sample size, and average follow-up of four weeks were the study's weaknesses. Thus, a larger, multicentric sample with a longer follow-up period is recommended by this study. Furthermore, the impact of medications on SE based on stone size was not assessed in this study. Therefore, the SE rate could not be calculated. Nevertheless,

according to the author's knowledge, this is the only research from Pakistan investigating these two medications in a randomized controlled trial. The present study could play an immense role as affordability issues for medications and immediate good care are still an issue.

CONCLUSION:

Due to its affordability and favorable side effect profile, mirabegron may be a viable substitute for conventional alpha-blocker medication in treating distal UC. More studies with bigger sample numbers and a wider range of demographics could help confirm these results and investigate Mirabegron's long-term effects on ureteral SE. Ultimately, this study emphasizes how critical it is to keep researching and contrasting different medical treatments to improve patient care for urolithiasis management.

REFERENCES

1. Wang Z, Chi J, Liu Y, Wu J, Cui Y, Yang C. Efficacy of mirabegron for ureteral stones: a systematic review with meta-analysis of randomized controlled trials. Front Pharmacol. 2023;14:1326600.
2. Turk C, Knoll T, Seitz C, Skolarikos A, Chapple C, McClinton S, et al. Medical Expulsive Therapy for Ureterolithiasis: The EAU Recommendations in 2016. Eur Urol. 2017;71(4):504-7.
3. Matsumoto R, Otsuka A, Suzuki T, Shinbo H, Mizuno T, Kurita Y, et al. Expression and functional role of beta3 -adrenoceptors in the human ureter. Int J Urol. 2013;20(10):1007-14.
4. Cai D, Wei G, Wu P, Huang Y, Che X, Zhang Y, et al. The Efficacy of Mirabegron in Medical Expulsive Therapy for Ureteral Stones: A Systematic Review and Meta-Analysis. Int J Clin Pract. 2022;2022(1):2293182.
5. Shalaby MM, Eldardery MA, Elderwy AA, Abdelaziz MA. The use of tamsulosin in the treatment of 10–15 mm lower ureteral stones in adults: a double-blinded randomized controlled trial. African Journal of Urology. 2022;28(1):54.
6. Abdel-Basir Sayed M, Moeen AM, Saada H, Nassir A, Tayib A, Gadelkareem RA. Mirabegron as a Medical Expulsive Therapy for 5-10 mm Distal Ureteral Stones: A Prospective, Randomized, Comparative Study. Turk J Urol. 2022;48(3):209-14.
7. Tang QL, Wang DJ, Zhou S, Tao RZ. Mirabegron in medical expulsive therapy for distal ureteral stones: a prospective, randomized, controlled study. World J Urol. 2021;39(12):4465-70.
8. Dell'Atti LJUJ. Silodosin versus tamsulosin as medical expulsive therapy for distal ureteral stones: a prospective randomized study. 2015;82(1):54-7.
9. Morsy S, Nasser I, Aboulela W, Abdelazim MS, Ali H. Efficacy of Mirabegron as Medical Expulsive Therapy for Distal Ureteral Stones: A Prospective, Randomized, Double-Blinded, Controlled Study. Urologia Internationalis. 2022;106(12):1265-71.
10. Bayar G, Yavuz A, Cakmak S, Ofluoglu Y, Kilinc MF, Kucuk E, et al. Efficacy of silodosin or mirabegron in medical expulsive therapy for ureteral stones: a prospective, randomized-controlled study. Int Urol Nephrol. 2020;52(5):835-40.
11. Samir M, Awad AF, Maged WA. Does mirabegron have a potential role as a medical expulsive therapy in the treatment of distal ureteral stones? A prospective randomized controlled study. Urologia. 2024;91(1):136-40.
12. Solakhan M, Bayrak O, Bulut E. Efficacy of mirabegron in medical expulsive therapy. Urolithiasis. 2019;47(3):303-7.
13. Chatterjee S, Jalan V, Pal DKJUS. An observational study on the efficacy of mirabegron in medical expulsive therapy of the lower ureteric calculus. 2021;32(3):132-6.
14. Kucukpolat S, Kocaaslan R, Kadihasanoglu M, Bagcioglu M, Kocan H, Sarica K. Is Medical Therapy for Distal Ureteral Stones Efficient? Tamsulosin versus Deflazacort: A Prospective Randomised Trial. Aktuelle Urol. 2022;53(5):454-60.

15. Falahatkar S, Akhavan A, Esmaeili S, Amin A, Kazemnezhad E, Jafari A. Efficacy of tamsulosin versus tadalafil as medical expulsive therapy on stone expulsion in patients with distal ureteral stones: A randomized double-blind clinical trial. Int Braz J Urol. 2021;47(5):982-8.
16. Pickard R, Starr K, MacLennan G, Lam T, Thomas R, Burr J, et al. Medical expulsive therapy in adults with ureteric colic: a multicentre, randomised, placebo-controlled trial. Lancet. 2015;386(9991):341-9.
17. Furyk JS, Chu K, Banks C, Greenslade J, Keijzers G, Thom O, et al. Distal Ureteric Stones and Tamsulosin: A Double-Blind, Placebo-Controlled, Randomized, Multicenter Trial. Ann Emerg Med. 2016;67(1):86-95 e2.
18. Shen H, Chen Z, Mokhtar AD, Bi X, Wu G, Gong S, et al. Expression of beta-adrenergic receptor subtypes in human normal and dilated ureter. Int Urol Nephrol. 2017;49(10):1771-8.
19. Faridi MS, Deshpande SJCEJoU. Comparing silodosin and mirabegron as medical expulsive therapy for distal ureteral calculus: a prospective, randomised study. 2024;77(2):286.
20. Takasu T, Ukai M, Sato S, Matsui T, Nagase I, Maruyama T, et al. Effect of (R)-2-(2-aminothiazol-4-yl)-4'-2-[(2-hydroxy-2-phenylethyl)amino]ethyl acetanilide (YM178), a novel selective beta3-adrenoceptor agonist, on bladder function. J Pharmacol Exp Ther. 2007;321(2):642-7.
21. Al Hussein Alawamlh O, Al Hussein Al Awamlh B, Lee U, Lee RKJCBDR. Overactive Bladder in Women: an Update for Primary Care Physicians. 2020;15:44-52.
22. Park HK, Choi EY, Jeong BC, Kim HH, Kim BK. Localizations and expressions of alpha-1A, alpha-1B and alpha-1D adrenoceptors in human ureter. Urol Res. 2007;35(6):325-9.
23. Ahmed AF, Al-Sayed AY. Tamsulosin versus Alfuzosin in the Treatment of Patients with Distal Ureteral Stones: Prospective, Randomized, Comparative Study. Korean J Urol. 2010;51(3):193-7.
24. Amer T, Osman B, Johnstone A, Mariappan M, Gupta A, Brattis N, et al. Medical expulsive therapy for ureteric stones: Analysing the evidence from systematic reviews and meta-analysis of powered double-blinded randomised controlled trials. Arab J Urol. 2017;15(2):83-93.
25. Rahman MJ, Faridi MS, Mibang N, Singh RS. Comparing tamsulosin, silodosin versus silodosin plus tadalafil as medical expulsive therapy for lower ureteric stones: A randomised trial. Arab J Urol. 2018;16(2):245-9.
26. Ramadhani MZ, Kloping YP, Rahman IA, Yogiswara N, Soebadi MA, Renaldo J. Silodosin as a medical expulsive therapy for distal ureteral stones: A systematic review and meta-analysis. Indian J Urol. 2023;39(1):21-6.
27. Mehmi A, Jones P, Somani BK. Current Status and Role of Patient-reported Outcome Measures (PROMs) in Endourology. Urology. 2021;148:26-31.
28. Jones P, Pietropaolo A, Chew BH, Somani BK. Atlas of Scoring Systems, Grading Tools, and Nomograms in Endourology: A Comprehensive Overview from the TOWER Endourological Society Research Group. J Endourol. 2021;35(12):1863-82.