Al-Azhar International Medical Journal

Volume 4 | Issue 6 Article 8

2023
Section: Urology

Efficacy and Safety of Silodosin, Mirabegron, and Tadalafil as Medical Expulsive Therapy for Lower Ureteric Stones: A Prospective, Randomized, Comparative Study

Ahmed O. Ahmed
Urology Department, Faculty of Medicine, Al-Azhar University hospitals, Cairo, Egypt.,
dr.ahmedfaseeh@gmail.com

Mohammed A. Elsalhy
Urology Department, Faculty of Medicine, Al-Azhar University hospitals, Cairo, Egypt.

Yasser A. Ahmed
: Urology Department, Faculty of Medicine, Al-Azhar University hospitals, Cairo, Egypt.

How to Cite This Article

Ahmed, Ahmed O.; Elsalhy, Mohammed A.; and Ahmed, Yasser A. (2023) "Efficacy and Safety of Silodosin, Mirabegron, and Tadalafil as Medical Expulsive Therapy for Lower Ureteric Stones: A Prospective, Randomized, Comparative Study," *Al-Azhar International Medical Journal*: Vol. 4: Iss. 6, Article 8.
DOI: https://doi.org/10.58675/2682-339X.1838

ORIGINAL ARTICLE

Efficacy and Safety of Silodosin, Mirabegron, and Tadalafil as a Medical Expulsive Therapy for Lower Ureteric Stones: A Prospective, Randomized, Comparative Study

Ahmed Osama Fasseh*, Mohamed Abdelrahim Elsalhy, Yasser Ali Ahmed

Urology Department, Faculty of Medicine, Al-Azhar University Hospitals, Cairo, Egypt

Abstract

Purpose: **We aim to evaluate and compare the efficacy and safety of silodosin, mirabegron, and tadalafil as a medical expulsive therapy (MET) for lower ureteric stones in adults.**

Material and methods: **A total of 150 cases who had unilateral, single, lower ureteric stone between December 2021 and August 2022 were incorporated in this prospective, randomized comparative study. The patients were randomly divided into three equal groups. The first group received Silodosin, the second group received mirabegron, and the third group received tadalafil. The medications would be continued until expulsion of the stone, for a maximum of 3 weeks. The duration of medical therapy for each patient was no longer than 3 weeks. The treatment duration was until stone expulsion or 3 weeks, whichever came first. The success was considered if the stone passed during 3 weeks of the treatment, if the stone did not pass during the 3 weeks that was considered as a failure, and the patient underwent ureteroscopic intervention for stone removal.**

Results: **Altogether 150 patients 50 (33.3%) in group 1 (Silodosin group), 50 (33.3%) in group 2 (mirabegron group), and 50 (33.3%) in group 3 (Tadalafil group) were enrolled in the study. Expulsion rates for groups 1, 2, and 3 were 86%, 72%, and 78%, respectively; however, no significant difference (P value > 0.05) was determined.**

Conclusion: **While none was noticeably better than the others, silodosin, mirabegron, and tadalafil showed increased expulsion rates for distal ureteral stones.**

Keywords: Mirabegron, Silodosin, Tadalafil

1. Introduction

Urolithiasis prevalence is about 2–3% in all population.[1] About 20% of all urinary tract stones are located in the ureter, and 70% of these stones are discovered in the distal portion of the ureter when they first manifest.[2] As the ureteral orifice is located close to the bladder, patients who have stones in this area frequently experience pain, and the most noticeable symptoms are frequent urination and urgency, which are signs of overactive bladder (OAB) syndrome.[3] Mirabegron is a beta-3 adrenergic agonist that relaxes the smooth muscle by binding to beta-adrenergic receptors found in the urothelium and smooth muscles.[4] A highly selective alpha-1a adrenoceptor blocker with the ability to reduce ureteric smooth muscle spasms, silodosin is widely used for symptoms of the lower urinary tract.[5] In individuals with ureteral stones, alpha-1a adrenergic inhibition and beta-3 adrenergic stimulation can relax the ureter, which may speed up stone expulsion and reduce the analgesic need.[6] Tadalafil, a phosphodiesterase 5 (PDE-5) inhibitor, works by inhibiting the smooth muscle nitric oxide/cGMP signaling pathway, which raises cyclic guanosine monophosphate (cGMP) levels and relaxes

Accepted 27 December 2022.
Available online 5 September 2023

* Corresponding author. Abu Hammad, Sharqia, 44661, Egypt.
E-mail address: dr.ahmedfaseeh@gmail.com (A.O. Fasseh).

https://doi.org/10.58675/2682-339X.1838

the ureteral muscle. Of the available PDE-5 inhibitors, tadalafil's duration of action is the longest. Tadalafil has just recently been utilized to treat ureteral stones in adults as medical expulsive therapy (MET).[7] We aimed to evaluate and compare the efficacy and safety of silodosin, mirabegron, and tadalafil as an MET for lower ureteric stones in adults.

2. Patients and methods

This prospective, randomized comparative study included 150 patients who visited the urology outpatient clinics at Al-Hussein and Sayed Galal, Al-Azhar University Hospitals in Cairo, Egypt, over a 9-month period (from December 2021 to August 2022). The study included adult patients of both Sexs who had a single, unilateral lower ureteric stone (beneath the sacroiliac joint) between 4 and 10 mm in size. Patients included in this study were subjected to the following: complete medical history taking focusing on previous operations and fever, physical examination focusing on temperature and loin tenderness, laboratory investigations including urine analysis, serum creatinine, blood urea, complete blood count, and liver function tests and radiological investigations including plain radiograph for kidneys, ureters and urinary bladder (KUB), abdominopelvic ultrasound scan and noncontrast computed tomography of the urinary tract. Solitary kidney, bilateral ureteric stones, active urinary tract infection, renal insufficiency, moderate or severe hydronephrosis, ureteral obstruction distal to the stone, prior history of ipsilateral ureter surgery, pregnant or lactating women, and comorbidities precluding the use of study medications were excluded from the study.

2.1. Ethical approval

An approval was acquired from the Ethics Research Board (ERB) of the Faculty of Medicine, Al-Azhar University, Cairo, Egypt. Before the study, all patients assigned informed consent after an obvious explanation of the possible adverse events.

Three equal groups of patients were formed by simple randomization based on a single sequence of random assignments:

Group 1 (ilodosin group): 50 patients who received Silodosin 8 mg once daily.

Group 2 (Mirabegron group): 50 patients who received Mirabegron 50 mg once daily.

Group 3 (Tadalafil group): 50 patients who received Tadalafil 5 mg once daily.

Up to a maximum of 3 weeks, patients in our study were guided to receive their medications until the stone was expelled. The medications would be continued until expulsion of the stone, up to a maximum of 3 weeks. The patients were instructed to use a small cloth or net to filter their urine in ordr to check for the expulsion of stones, to notify us as soon as this happened, and to discontinue receiving the prescribed medical treatment. When necessary, patients would receive diclofenac potassium as an analgesic for the control of ureteral colic pain.

Weekly follow-up visits would take place. At the follow-up visit, every patient would undergo complete medical history taking focusing on any stone passage during micturition, frequency and dosage of the analgesic, severity and frequency of renal pain and side effects of the medication, physical examination focusing on temperature and loin tenderness, laboratory investigations including urine analysis and serum creatinine, and radiological investigations including plain radiograph for kidneys, ureters, and urinary bladder (KUB) for patients with radiopaque stones, abdominopelvic ultrasound scan, and noncontrast computed tomography of the urinary tract if the stone was still present at the end of the study for patients with radiolucent stones. The success was considered if the stone passed during 3 weeks of the treatment, if the stone did not pass during 3 weeks that was considered a failure, and the patient underwent ureteroscopic intervention for stone removal. The date of the most recent positive stone status would be noted for individuals whose ureters were clear of stones on the most recent imaging study, but who nevertheless experienced stone expulsion. It would be necessary to visit a urologist and consider surgical intervention if there was an infection, obstruction, resistance or challenge to manage pain, or worsening of renal function.

At the end of the study, we recorded time to stone expulsion, frequency and severity of loin pain, frequency and cumulative dose of analgesics, unplanned hospital admission due to infected hydronephrosis, side effects of the study medications, and the need and type of intervention.

2.2. Statistical analysis

Version 24 of the Statistical Program for the Social Sciences (SPSS) was used to analyze the data. Mean SD was used to present quantitative data. Frequency and percentage were used to express the qualitative data. The sum of values divided by the total number of values yields the mean (average), which is the middle value in a set of discrete

numbers. The standard deviation serves as a gauge for the dispersion of a set of numbers (SD). A low SD suggests that the values often tend to be close to the established mean as opposed to a high SD, which indicates that the values are spread throughout a wider range.

The following tests were done:

Kruskal–Wallis test (KW): whenever more than two means are being compared (for abnormally distributed data).

When comparing nonparametric data, the chi-square test was used.

Probability (*P* value).

P value < 0.05 was regarded as significant.

P value < 0.001 was regarded as highly significant.

P value > 0.05 was regarded as insignificant.

3. Results

Analyses of the study's findings were done once all of the participants are randomized (Table 1).

Regarding both Sex and age, the analyzed groups (Silodosin, Mirabegron, and Tadalafil) do not differ statistically significantly (*P* value > 0.05) (Table 2).

No statistically significant variation between the groups under study (Silodosin, Mirabegron, and Tadalafil) can be seen from this table (*P* value = 0.065) as regards the duration of medication intake (Table 3).

Between the studied groups (silodosin, mirabegron, and tadalafil), this table demonstrates no statistically significant variation (*P*-value >0.05) concerning stone data (stone side, stone size, rate of stone expulsion, and time of stone expulsion) (Table 4).

In terms of clinical data (experience with episodes of renal colic, frequency of pain/3 weeks, and frequency of analgesic intake/3 weeks), there is no statistically significant variation (*P* value > 0.05) between the studied groups (Silodosin, Mirabegron, and Tadalafil) in this table (Table 5).

In terms of the need for intervention due to infected hydronephrosis, the type of intervention, and unexpected hospital admission due to infected hydronephrosis, the study groups (Silodosin, Mirabegron, and Tadalafil) do not differ statistically significantly (*P*-value >0.05) from one another (Table 6).

This table shows the following:

There was no statistically significant variation (*P* value > 0.05) in the incidence of headache, dizziness, backache, myalgia, constipation, or dry eye between the study groups.

When compared with the Silodosin group (0 patients, 0%) and the Tadalafil group (0 patients, 0%), the Mirabegron group had a statistically significant (*P* value = 0.016) higher percentage of nausea (4 patients, 8%).

When compared with the Silodosin group (0 patients, 0%) and the Tadalafil group (0 patients, 0%), the Mirabegron group (4 patients, 8%) had a statistically significant (*P* value = 0.016) higher percentage of tachycardia.

When compared with the Mirabegron group (0 patients, 0%) and the Tadalafil group (0 patients, 0%), the Silodosin group had a significantly higher percentage of retrograde ejaculation (*P* value < 0.001).

Statistically significant (*P* value = 0.008) increased percentage of fainting in the Tadalafil group (8 patients, 16%) when compared with the Silodosin group (3 patients, 6%) and the Mirabegron group (0 patients, 0%).

When compared with the Mirabegron group (0 patients, 0%) and the Tadalafil group (0 patients, 0%), the Silodosin group had an elevated percentage of nasal congestion (8 patients, 16%) that was statistically significantly higher (*P* value < 0.001).

When compared with the Tadalafil group (3 patients, 6%) and the Mirabegron group (0 patients, 0%), the Silodosin group had a statistically significant (*P* value = 0.001) higher percentage of orthostatic hypotension (10 patients, 20%).

When compared with the Mirabegron group (0 patients, 0%) and the Silodosin group (0 patients,

Table 1. Comparison between the groups under study in terms of Sex and age.

	Groups			Stat. test	*P* value
	Silodosin ($n = 50$)	Mirabegron ($n = 50$)	Tadalafil ($n = 50$)		
Sex					
Female	16 (32%)	13 (26%)	15 (30%)	$X^2 = 0.45$	0.798 NS
Male	34 (68%)	37 (74%)	35 (70%)		
Age (years)					
Mean ± SD	38.5 ± 13.3	39.3 ± 14.4	40.5 ± 14.4	KW = 0.45	0.799 NS

KW: Kruskal–Wallis test.

X^2: Chi-square test.

NS: *P* value > 0.05 is considered nonsignificant.

Table 2. Comparison between the groups under study in terms of duration of medication intake.

	Groups			Stat. test	*P* value
	Silodosin ($n = 50$)	Mirabegron ($n = 50$)	Tadalafil ($n = 50$))		
Duration(days)					
Mean ± SD	9.3 ± 6.3	11.2 ± 6.7	11.2 ± 6.7	KW = 5.5	0.065 NS

KW: Kruskal–Wallis test.
NS: *P*-value >0.05 is considered nonsignificant.

Table 3. Comparison of the groups under study with relation to the stone data.

	Groups			Stat. test	*P* value
	Silodosin ($n = 50$)	Mirabegron ($n = 50$)	Tadalafil ($n = 50$)		
Stone side					
Left	27 (54%)	25 (50%)	27 (54%)	$X^2 = 0.21$	0.899 NS
Right	23 (46%)	25 (50%)	23 (46%)		
Stone size (mm)					
Mean ± SD	7.08 ± 1.8	6.6 ± 1.8	6.8 ± 1.9	KW = 2.12	0.346 NS
Stone expulsion					
No	7 (14%)	14 (28%)	11 (22%)	$X^2 = 2.9$	0.230 NS
Yes	43 (86%)	36 (72%)	39 (78%)		
Time of expulsion (days)					
Mean ± SD	7.7 ± 4.8	8.9 ± 4.2	8.4 ± 4.8	KW = 1.89	0.388 NS

KW: Kruskal–Wallis test.
X^2: Chi-square test.
NS: *P*-value >0.05 is regarded as nonsignificant.

Table 4. Comparison of the studied groups in light of the clinical information.

	Groups			Stat. test	*P* value
	Silodosin ($n = 50$)	Mirabegron ($n = 50$)	Tadalafil ($n = 50$)		
Renal colic episodes					
No	16 (32%)	15 (30%)	17 (34%)	$X^2 = 0.18$	0.912 NS
Yes	34 (68%)	35 (70%)	33 (66%)		
Pain frequency (/3 weeks)					
Mean ± SD	4.6 ± 4.5	4.2 ± 3.7	4.4 ± 4.6	KW = 0.16	0.920 NS
Analgesia intake frequency (/3 weeks)					
Mean ± SD	4.7 ± 4.5	4.2 ± 3.7	4.4 ± 4.6	KW = 0.15	0.924 NS

KW: Kruskal–Wallis test.
X^2: Chi-square test.
NS: *P*-value >0.05 is regarded as nonsignificant.

Table 5. Comparison of the studied groups with regard to intervention and hospital admission.

	Groups			Stat. test	*P* value
	Silodosin ($n = 50$)	Mirabegron ($n = 50$)	Tadalafil ($n = 50$)		
Need for intervention due to infected hydronephrosis					
No	43 (86%)	36 (72%)	39 (78%)	$X^2 = 2.9$	0.230 NS
Yes	7 (14%)	14 (28%)	11 (22%)		
Type of intervention					
JJ fix	1 (14.3%)	2 (14.3%)	2 (18.2%)	$X^2 = 0.08$	0.959 NS
URS	6 (85.7%)	12 (85.7%)	9 (81.8%)		
Unplanned hospital admission due to infected hydronephrosis					
No	49 (98%)	48 (96%)	48 (96%)	$X^2 = 0.41$	0.813 NS
Yes	1 (2%)	2 (4%)	2 (4%)		

X^2: Chi-square test.
NS: *P*-value >0.05 is regarded as nonsignificant.

Table 6. Comparisons between the studied groups as regards the side effects.

	Groups			X^2	*P* value
	Silodosin ($n = 50$)	Mirabegron ($n = 50$)	Tadalafil ($n = 50$)		
Headache	6 (12%)	2 (4%)	6 (12%)	2.5	0.284 NS
Nausea	0 (0%)	4 (8%)	0 (0%)	**8.2**	**0.016 S**
Tachycardia	0 (0%)	4 (8%)	0 (0%)	**8.2**	**0.016 S**
Dizziness	4 (8%)	2 (4%)	5 (10%)	1.37	0.503 NS
Backache	2 (4%)	1 (2%)	6 (12%)	4.9	0.084 NS
Retrograde ejaculation	11 (22%)	0 (0%)	0 (0%)	**23.7**	**<0.001 HS**
Fainting	3 (6%)	0 (0%)	8 (16%)	**9.6**	**0.008 S**
Nasal congestion	8 (16%)	0 (0%)	0 (0%)	**16.9**	**<0.001 HS**
Orthostatic hypotension	10 (20%)	0 (0%)	3 (6%)	**13.3**	**0.001 S**
Myalgia	2 (4%)	2 (4%)	6 (12%)	3.4	0.180 NS
Constipation	0 (0%)	1 (2%)	0 (0%)	2.01	0.365 NS
Dry eye	0 (0%)	1 (2%)	0 (0%)	2.01	0.365 NS
Increased erection	0 (0%)	0 (0%)	13 (26%)	**28.5**	**<0.001 HS**

X^2: Chi-square test.
S: *P*-value <0.05 is regarded as significant.
HS: *P*-value <0.001 is regarded as highly significant.
NS: *P*-value >0.05 is regarded as nonsignificant.

0%), the Tadalafil group (13 patients, 26%) had a significantly higher percentage of enhanced erections (*P* value < 0.001).

4. Discussion

Urolithiasis is a chronic condition with significant economic implications and significant public health significance, due to its high recurrence rate—roughly 50% within 5 years and 75% at 10 years—and the fact that it affects young people.[8] Although there are minimally invasive alternatives for treating stones in the lower ureter, such as extracorporeal shock wave lithotripsy (ESWL) and ureteroscopy (URS), are effective and less invasive than conventional open techniques, they are also more expensive, require highly specialized equipment, and require specialized training.[9] Several physiologic and pathophysiologic presumptions led to the development of medical expulsive therapy (MET) as a substitute method for the initial treatment of lower ureteral stones.[10]

Conservative therapy is less likely to be helpful for patients who have persistent partial ureteral obstruction (>4–6 weeks), continuous pain, or a urinary tract infection. Therefore, among informed patients who do not experience difficulties, observation is possible (infection, refractory pain, deterioration of renal function).[11] Tamsulosin is a less effective α1A-adrenergic receptor antagonist than silodosin, which also has a higher rate of stone ejection.[12] The tension of smooth muscle is influenced by the regulation of intracellular cyclic nucleotide turnover by phosphodiesterases (PDEs). Increased levels of cGMP cause the ureteric smooth muscle to relax as a result of PDE-5 inhibitors like sildenafil and tadalafil.[13]

For patients with stones at the lower ureter that were smaller than 5 mm in size, mirabegron significantly improved stone-free rate; however, it had no effect on stones that were larger than 5 mm. In addition, mirabegron minimized the requirement for analgesics in stones smaller than 10 mm with a low rate of side effects.[3]

All data so far indicate that for the first 4 weeks after an incomplete obstruction, irreversible kidney damage does not usually occur without an exacerbating condition, such as a urinary tract infection. Therefore, it only makes sense to provide MET after 4 weeks have passed in the absence of aggravating variables.[14,15] We gave MET after 3 weeks had passed in our study to reduce the safety margin.

In our study, we found that the mean time for stone expulsion was 7.7 ± 4.8 days, 8.9 ± 4.2 days, and 8.4 ± 4.8 days for silodosin, mirabegron, and tadalafil, respectively. According to Wang *et al.*[16] the silodosin group's average time for stone expulsion was 6.31 ± 2.13 days, while the control group's was 9.73 ± 2.76 days ($P < 0.001$). Parikh et al.[17] reported that the mean expulsion time of calculi managed by tadalafil was 13.1 days. According to Bayer *et al.*[6] the silodosin group's stone ejection interval was less (7.1 ± 4.5 days) than the mirabegron group's (12 ± 8.7) ($P = 0.034$). In addition, among patients with stones less than 6 mm, the silodosin group's stone expulsion interval was shorter (5.8 ± 4) than the mirabegron group's (12.2 ± 2.8) ($P = 0.004$).

In our study, we found the pain frequency per 3 weeks for silodosin, mirabegron, and tadalafil was 4.6 ± 4.5, 4.2 ± 3.7, and 4.4 ± 4.6, respectively (*P*

value > 0.05), which was considered nonsignificant. Also, the mean requirement of analgesia was less in the mirabegron group (4.2 ± 3.7) than in the tadalafil group (4.4 ± 4.6) and the silodosin group (4.7 ± 4.5) but not statistically significant.

Solakhan et al.[18] reported that mirabegron decreased the attacks of renal pain (1.02 ± 0.52 vs. 1.29 ± 0.57, $P = 0.049$). Wang *at al.*[16] reported that silodosin decreased the renal colic episodes (2.39 ± 1.30) versus (2.75 ± 1.38) in the control group. According to Hasan *et al.*[19] the tadalafil group required considerably fewer analgesics than the placebo group, with a pain score of 3.9 versus 7.9 ($P < 0.0001$).

In our study, we found the rate of stone expulsion was 86%, 72%, and 78% in groups silodosin, mirabegron and tadalafil, respectively. According to Kumar *et al.*[20] tamsulosin, silodosin, and tadalafil had stone ejection rates of 64.4, 83.3%, and 66.7%, respectively; nevertheless, there was no statistically significant variation between the two groups ($P = 0.875$). Hassan et al.[19] reported that the medical therapy based on silodosin demonstrated positive results in 77.42% patients, with a significant statistical variation in the control group (54.10%). According to Kc *et al.*[7] the tadalafil group's stone expulsion rate was significantly greater than the tamsulosin group's (61% vs. 84.1%, $P = 0.017$). Solakhan et al.[18] reported that the spontaneous stone expulsion rate was statistically significantly increased with mirabegron than the control group (73.5 vs. 47.1%, $P = 0.026$).

In our study, we found that one patient (2%) underwent JJ fixation due to infected hydronephrosis in the silodosin group, two patients (4%) in the tadalafil group, and two patients (4%) in the mirabegron group with no statistical difference among the three groups.

There were no noticeable differences in any of the outcomes from our study in headache, dizziness, backache, myalgia, constipation, or dry eye symptoms across the analyzed groups. Headache occurred equal in the silodosin group and the tadalafil group. Dizziness, myalgia, and backache occurred more in the tadalafil group. Constipation and dry eye occurred more in the mirabegron group. However, there were significant statistically differences among the studied groups regarding nausea, tachycardia, retrograde ejaculation, fainting, nasal congestion, orthostatic hypotension, and increased erection. Nausea and tachycardia were significant in the mirabegron group ($P = 0.016$). Retrograde ejaculation and nasal congestion were significantly high in the silodosin group ($P < 0.001$). Orthostatic hypotension was significant in the silodosin group ($P = 0.001$). Fainting was significant in the tadalafil group ($P = 0.008$). Increased erection was highly significant in the tadalafil group ($P < 0.001$). All of these adverse effects, nevertheless, were manageable and tolerable.

In the comparison research of tamsulosin, tadalafil, and silodosin, Kumar et al.[20] reported the side effects to be mild to moderate and well tolerated, probably as a result of the younger study participants and the absence of any concomitant conditions, which is similar to our study. Despite the fact that the prevalence of side effects was higher overall in the tadalafil group, Kc et al.[7] stated in 2016 that there were no major adverse events ($P = 0.099$). Puvvada et al.[21] reported in 2016 that no serious adverse effects were noted. Abnormal ejaculation was seen in 6% of patients in the tadalafil group, and 12% in the tamsulosin group, which was not statistically significant ($P = 0.23$). Improvement in erectile dysfunction was seen in 13% of patients in the tadalafil group. The examination of the anomalous ejaculation episodes involved 309 participants in three randomized, controlled clinical trials (158 in the silodosin group and 151 in the tamsulosin group). Silodosin substantially increased the number of anomalous ejaculation episodes when compared with tamsulosin (OR 2.47, 95% CI 1.20, 5.07, $P = 0.01$).

Our study had some limitations. The sample size was modest, and the course of treatment was brief. It is still useful as a pilot research because this was one of the studies that used mirabegron as a treatment for lower ureteric stones. Mirabegron's usefulness as a medical expulsive therapy for stones at the lower ureter would be further established by larger, multicentric prospective studies including a greater number of patients.

4.1. Conclusion

There were increased expulsion rates for distal ureteral stones with silodosin, mirabegron, and tadalafil, but no statistically significant differences between the three groups. All of the examined groups were able to handle the mild to moderate adverse effects.

Disclosure

The authors have no financial interest to declare regarding the content of this article.

Authorship

All authors have a substantial contribution to the article.

Sources of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest

There are no conflicts of interest.

References

1. Cui Y, Zong H, Yang C, Yan H, Zhang Y. The efficacy and safety of mirabegron in treating OAB: a systematic review and meta-analysis of phase III trials. *Int Urol Nephrol*. 2014;46:275–284.
2. Ahmed AA, Al-Sayed A-YS. Tamsulosin versus alfuzosin in the treatment of patients with distal ureteral stones: prospective, randomized, comparative study. *Korean J Urol*. 2010; 51:193–197.
3. Tang Q, Wang D, Zhou S, Tao R. Mirabegron in medical expulsive therapy for distal ureteral stones: a prospective, randomized, controlled study. *World J Urol*. 2021;39:4465–4470.
4. Matsumoto R, Otsuka A, Suzuki T, et al. Expression and functional role of β3-adrenoceptors in the human ureter. *Int J Urol*. 2013;20:1007–1014.
5. Sakhaee K, Maalouf NM, Sinnott B. Kidney stones 2012: pathogenesis, diagnosis, and management. *J Clin Endocrinol Metab*. 2012;97:1847–1860.
6. Bayar G, Yavuz A, Cakmak S, et al. Efficacy of silodosin or mirabegron in medical expulsive therapy for ureteral stones: a prospective, randomized-controlled study. *Int Urol Nephrol*. 2020;52:835–840.
7. Kc HB, Shrestha A, Acharya GB, Basnet RB, Shah AK, Shrestha PM. Tamsulosin versus tadalafil as a medical expulsive therapy for distal ureteral stones: a prospective randomized study. *Investig Clin Urol*. 2016;57:351–356.
8. Hollingsworth JM, Rogers MAM, Kaufman SR, et al. Medical therapy to facilitate urinary stone passage: a meta-analysis. *Lancet*. 2006;368:1171–1179.
9. Osorio L, Lima E, Soares J, et al. Emergency ureteroscopic management of ureteral stones: why not? *Urology*. 2007;69: 27–31.
10. Tzortzis V, Mamoulakis C, Rioja J, Gravas S, Michel MC, de la Rosette JJMCH. Medical expulsive therapy for distal ureteral stones. *Drugs*. 2009;69:677–692.
11. Türk C, Petřík A, Sarica K, et al. EAU guidelines on interventional treatment for urolithiasis. *Eur Urol*. 2016;69: 475–482.
12. Elgalaly H, Sakr A, Fawzi A, Salem EA, Desoky E, Shahin A. Kamel M Silodosin vs tamsulosin in the management of distal ureteric stones: a prospective randomised study. *Arab J Urol*. 2016;14:12–17.
13. Gratzke C, Ückert S, Reich O, et al. PDE-5-Inhibitoren. *Urologe*. 2007;46:1219–1223.
14. Hübner WA, Irby P, Stoller ML. Natural history and current concepts for the treatment of small ureteral calculi. *Eur Urol*. 1993;24:172–176.
15. Türk C, Knoll T, Seitz C, Skolarikos A, Chapple C, McClinton S, European Association of Urology. Medical expulsive therapy for ureterolithiasis: the EAU recommendation in 2016. *Eur Urol*. 2017;71:504–507.
16. Wang CJ, Tsai PC, Chang CH. Efficacy of silodosin in expulsive therapy for distal ureteral stones: a randomized double-blinded controlled trial. *Urol J*. 2016;13:2666–2671.
17. Parikh C, Gurjar V, Shah S. Tamsulosin versus tadalafil as medical expulsive therapy of distal ureteric stones: a comparative study. *Int Surg J*. 2019;6:982–988.
18. Solakhan M, Bayrak O, Bulut E. Efficacy of mirabegron in medical expulsive therapy. *Urolithiasis*. 2019;47:303–307.
19. Hasan HF, Jaffal WN, Al-Hossona HA. The role of tadalafil in lower ureteric stone expulsion. *Iraqi Postgr Med J*. 2011;10: 24–32.
20. Kumar S, Jayant K, Agrawal MM, Singh SK, Agrawal S, Parmar KM. Role of tamsulosin, tadalafil, and silodosin as the medical expulsive therapy in lower ureteric stone: a randomized trial (a pilot study). *Urology*. 2015;85:59–63.
21. Puvvada S, Mylarappa P, Aggarwal K, Patil A, Joshi P, Desigowda R. Comparative efficacy of tadalafil versus tamsulosin as the medical expulsive therapy in lower ureteric stone: a prospective randomized trial. *Cent Eur J Urol*. 2016;69: 178.