

REVIEW

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An update on efficacy and safety of alpha-blockers in the treatment of distal ureteric stones: narrative review

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Abstract

Background: Alpha-blockers prescribed as medical expulsion therapy (MET) have replaced minimally invasive procedures as the primary line of treatment for minor ureteric stones. This study aims to investigate the efficacy of MET with alpha-blockers in terms of stone expulsion rate and time and evaluate the safety of several alpha-blockers.

Methodology: Google Scholar, PubMed, and Web of Science databases were searched for relevant publications using keywords published between December 2013 and August 2021. Additional relevant research was found by looking through the references in the articles.

Results: To determine the efficacy and safety of alpha-blockers as a medical expulsive therapy for the management of distal ureteral stones, 15 studies were included, 12 randomized control trials, 2 retrospective observational studies, and 1 prospective study. The most commonly studied primary endpoint was stone expulsion rate and time. According to findings, silodosin appears to be more effective than other alpha-blockers. The data revealed no life-threatening adverse effects were associated with alpha-blockers.

Conclusion: Alpha-blockers are recommended as the first-line therapy for distal ureteral stones. Silodosin was the most efficacious medicine, according to the data. The side effects of alpha-blockers, on the other hand, were minor, consisting primarily of orthostatic hypotension. The alpha-blocker choice differs from urologist to urologist in the management of MET, depending on their experience and the patient's condition.

Keywords: Alpha-blocker, Distal ureteric stones, Medical expulsion therapy, Efficacy, Safety

1 Background

Ureteral stones frequently appear with acute upper urinary system blockage and discomfort, necessitating fast stone clearance [1]. The occurrence varies by geographical region, with greater rates in the Middle East, Western India, and the Southern USA, likely due to the high water and soil content in those places and the hot weather and dehydration [2]. Urinary stones result from various

metabolic, environmental, and nutritional factors. They are typically calcium oxalate with the precipitation of additional calcium salts, uric acid, or other compounds [3]. Ureteral stones account for about 20% of all urolithiasis cases. Roughly 70% of ureteral stones are found in the bottom portion of the ureter and are referred to as distal ureteral stones [4]. Women excrete more citrate and less calcium than males, which may explain why men have a higher rate of stone illness [5]. Colicky pain is the most common symptom of ureteral stones, with nearly half of patients presenting within 5 years of the onset of calculi [2].

The size, location, composition of the stone, degree of obstruction, symptoms, and anatomy of the urinary

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system all play a role in determining the best therapeutic option, and doctors are regularly asked to recommend appropriate therapy [6, 7]. The distal ureteric stone treatment is classified into three categories: observation and medical therapy, shock wave lithotripsy ureteroscopy, and open surgery laparoscopic stone removal [8]. Alpha-blockers, calcium channel antagonists, phosphodiesterase inhibitors, and corticosteroids are some of the medications used for medical expulsive therapy (MET), and they have all been demonstrated to help ureteric stone pass [9]. The goal of MET is to increase fluid intake in order to raise urine volume and hydrostatic pressure, as well as ureteric peristaltic activity [10]. The passage of the stone is aided by relaxation of the ureteric smooth muscle, a decrease in ureteral mucosal oedema, and an increase in the hydrostatic pressure proximal to the stone in MET [11]. In the first line of treatment for small ureteric stones, alpha-blockers administered as MET have replaced minimally invasive methods. Alpha-blockers are recommended by the American Urological Association (AUA) and the European Association of Urology (EAU) to treat ureteric stones [12]. The smooth muscle of the ureter is treated with a variety of medications that work in different ways [13]. The three subtypes of α_1 -adrenergic receptors are 1A, 1B, and 1D, with $\alpha_1D > \alpha_1A > \alpha_1B$ as the distribution of these receptors in the distal ureter [14]. The ureter's wall is made up of smooth muscle. Internally, it is lined with the alpha-1-adrenergic receptor, especially in the lower one-third of the ureter, also known as the distal ureter [15]. Blocking alpha-1-adrenergic receptors, particularly propulsive antegrade peristalsis, aid stone ejection [13]. The most widely prescribed alpha-blockers for medical expulsive therapy are tamsulosin, alfuzosin, silodosin, and naftopidil [16].

This study aims to see how effective MET was with alpha-blockers regarding stone expulsion rate and distal ureteric stone expulsion time. The secondary goal was to assess various alpha-blockers' safety and find the safest alpha-blocker.

2 Methodology

The relevant articles published from December 2013 to August 2021 were searched in Google Scholar, PubMed, and Web of Science databases. The articles were limited to the English language. The search keywords were "safety, efficacy alpha-blocker", and "alpha-blocker treatment ureteric calculus". Article references were also checked to find additional relevant studies. The results of the articles were analysed based on the inclusion criteria. All the selected articles were published in peer-reviewed and indexed journals. The included studies were research results that focused on distal urinary stones with a study population of adults that were managed by

alpha-blockers. Studies with pre- or post-lithotripsy were not eligible for review. All the scientific articles meeting the inclusion criteria were critically reviewed by at least two authors and the information is summarized in this narrative review.

3 Results

Fifteen studies, including 12 randomized control trials (RCTs), 2 retrospective observational studies, and 1 prospective study, were included in determining the efficacy and safety of alpha-blockers as MET for managing distal ureteric stones. Agents studied include tamsulosin, silodosin, alfuzosin, and naftopidil.

Studies had similar inclusion criteria including patients above 18 years, and a calculus demonstrated in the distal ureter with the stone size less than 10 mm. Exclusion criteria included patients with fever, urinary tract infection (UTI), hydronephrosis, bilateral ureteric stone, solitary kidney, an extra stone in the upper urinary system, previous surgical history on the ipsilateral ureter, pregnant women, patients with diabetes, renal insufficiency, cardiovascular disease, and hypotension. Study duration varied between seven days to one month.

The most commonly studied primary endpoint was expulsion rate and time, which was successful passing of the stone and the secondary goal was to assess the safety of alpha-blockers.

Four RCTs that compared tamsulosin with placebo or any other drug except alpha-blockers showed that tamsulosin had a better expulsion rate and time. [3, 17–19]. But studies conducted by Puvvada S et al. and Kc HB et al. showed that tadalafil was better when compared to tamsulosin in terms of expulsion rate and time taken for stone expulsion [20, 21].

When monotherapy of tamsulosin was compared with combination therapy of tamsulosin + trosipium chloride, tamsulosin + tadalafil combination therapy proved to be more effective [2, 8].

An RCT conducted by Kohjimoto Y et al. concluded that naftopidil was better than flopropione in terms of expulsion rate and time [22]. Among 2 RCTs, which compared tamsulosin with silodosin, it was found that silodosin was better in expulsion rate and time. [6, 23] but expulsion time contrasted by the studies regulated by Elgalaly H et al. and Imperatore V et al. [12, 24]. The study conducted by Shabana W et al. showed that combination therapy of tamsulosin and methylprednisolone is better than monotherapy with tamsulosin. It was the same as in the case of alfuzosin combination therapy [10].

A retrospective observational study comparing tamsulosin, alfuzosin, and silodosin proved that silodosin was the most effective drug regarding stone expulsion rate and time taken for stone expulsion [5].

Table 1 Efficacy and safety of alpha-blockers

References	Type of study	Inclusion criteria	Exclusion criteria	Number of subjects, follow-up period	Treatment	Efficacy	Safety
Jayant K et al. [2]	RCT	Patients aged 18 years or older with a ureteral stone 5–10 mm in size situated below the common iliac vessels, as diagnosed by non-contrast computed tomography	Patients with fever, hydronephrosis, acute or chronic renal insufficiency, multiple ureteral stones, open surgery or endoscopic interventions, diabetes, peptic ulcer or concomitant treatment with β -blockers, calcium antagonists, or nitrates, pregnant or lactating mothers, or requiring immediate intervention	244, 4 weeks	Group A were given tamsulosin 0.4 mg once daily and group B were given tamsulosin 0.4 mg and tadalafil 10 mg once daily	Stone expulsion rate was 65.5% in group A and 83.6% in group B. The mean expulsion time in group A was 16.7 \pm 4.8 days and in group B was 14.9 \pm 4.4 days	Adverse effects-Group A: Headache, dizziness (12.3%), orthostatic hypotension (3.0%) and backache (9.8%) abnormal ejaculation (18.3%). Group B: Headache, dizziness, backache (15.8%), orthostatic hypotension (5.8%), abnormal ejaculation (12.3%)
Gandhi HR et al. [3]	RCT	Patients with a solitary stone in the distal ureter, at the juxtavesical tract (JVT) or vesico-ureteric junction (VUJ) of 5–15 mm	Patients with a UTI, gross hydronephrosis, diabetes, peptic ulcer disease, hypersensitivity to nifedipine or corticosteroid or a history of spontaneous stone expulsion and hypotension, pregnant women, and children	128, 4 weeks	Group 1 received oral nifedipine sustained release 30 mg/day and group B received tamsulosin 0.4 mg/day	Stone expulsion rate in group 1 was 55% and group 2 was 80%. Mean expulsion time for group 1 was 23 days and 9 days for group 2	Adverse effects in group 1- Headache (43%), loose stool (24%), dizziness, fatigue, flushing (5%), palpitation muscle cramps (9%). Group 2- Headache (50%), gastric upset (25%), dizziness (25%)
Sentürk AB et al. [5]	Retrospective observational study	Those patients who had calculi with the size of 4–10 mm which were located under the common iliac arteries and confirmed by computerized tomography, and those responding to the analgesic treatment were included in the study	Those patients who had bilateral ureter calculi, severe urinary tract infection, severe colic attack, fever, severe hydronephrosis, renal impairment, history of endoscopic surgery due to ureter calculi and history of drug which interact with alpha blockers were excluded from the study	143, 4 weeks	Tamsulosin 0.4 mg OD, alfuzosin 10 mg OD, silodosin 8 mg OD	Expulsion rate for tamsulosin group = 70.8%, alfuzosin group = 70.2%, silodosin group = 75%. Expulsion time in tamsulosin group = 10.41 \pm 3.61 days, alfuzosin group = 8.87 \pm 3.54 days, silodosin group = 8.09 \pm 3.66 days	Adverse effects- Hypotension (8.5%) in tamsulosin group, (4.5%) in silodosin group and (6.4%) in alfuzosin group. Retrograde ejaculation was more in silodosin group

Table 1 (continued)

References	Type of study	Inclusion criteria	Exclusion criteria	Number of subjects, follow-up period	Treatment	Efficacy	Safety
Kumar S et al. [6]	RCT	Patients aged 18 years with a ureteral stone of 5–10 mm in size in greatest dimension situated below the common iliac vessels as diagnosed by non-contrast computed tomography or ultrasonography kidney, ureter, and bladder (KUB) were included in this study. Patients were only included if their pain was relieved with diclofenac injection within 1 day	Patients with fever, hydronephrosis, acute or chronic renal insufficiency, multiple ureteral stones, open surgery or endoscopic interventions, diabetes, peptic ulcer or on concomitant treatment with beta-blockers, calcium antagonists, or nitrates; pregnant or lactating mothers or who demand immediate intervention were excluded	285, 4 weeks	Group A-Tamsulosin 0.4 mg OD, group B-sildenafil 8 mg OD, group C=tadalafil 10 mg OD	Expulsion rate in group A was found to be 64.4%, group B = 83.3%, group C = 66.67%. Mean expulsion time in group A was found to be 16.5 ± 4.6 days, group B = 14.8 ± 3.3 days, group C = 16.2 ± 4.2 days	Adverse effects in group A were found to be headache, dizziness (10%), backache (8.8%), orthostatic hypotension (6.6%), abnormal ejaculation (11.2%). Group B = Headache (12.2%), dizziness (8.8%), backache (10%), orthostatic hypotension (3%), abnormal ejaculation (15.6%). Group C = Headache, dizziness, backache (15.5%), orthostatic hypotension (10%), abnormal ejaculation (5.9%)
Abdelaziz AS et al. [8]	RCT	Patients with single lower ureteral stones from 5 to 10 mm	Pregnancy, age below 18 years old, presence of urinary tract infection, renal insufficiency, solitary kidney, multiple stones, a previous history of distal ureter surgery, bilateral ureteral stones, moderate or severe hydronephrosis, current alpha-blocker use and allergic reaction to tamsulosin and trospium chloride	126, follow-up visits were performed on days 7, 14, 21 and 30	Group A received tamsulosin 0.4 mg OD and placebo twice daily. Patient in group B received tamsulosin 0.4 mg OD and trospium chloride 20 mg BID	Stone expulsion rate in group A was 75.8%, group B 90.62%. Mean time to stone expulsion was 17.35 ± 6.21 days in group A and 11.65 ± 5.32 days in group B	Adverse effects- Group A retrograde ejaculation (8.06%), orthostatic hypotension (3.2%), headache, dizziness, fatigue (4.83%), constipation, dry mouth (1.6%) and in group B, retrograde ejaculation (6.25%), orthostatic hypotension, headache, dizziness (3.1%), constipation, dry mouth (7.8%), fatigue (4.68%)

Table 1 (continued)

References	Type of study	Inclusion criteria	Exclusion criteria	Number of subjects, follow-up period	Treatment	Efficacy	Safety
Shabana W et al. [10]	RCT	Patients with a single radiopaque stone of ≤ 10 mm by plain abdominal radiograph of the KUB, stone located below the sacroiliac joint	Patients with UTI, severe hydronephrosis, pregnancy, hypertension, diabetes, ulcer disease, previous pelvic surgery or renal insufficiency	240, 2 weeks	Group 1 patients received tamsulosin 0.4 mg daily, group 2 received tamsulosin 0.4 mg and methylprednisolone 8 mg daily. Group 3 patients received alfuzosin 10 mg daily and those in group 4 received alfuzosin 10 mg and methylprednisolone 8 mg daily	Stone free rate in: Group 1- 54.7%, group 2-71.9%, group 3-52.8% and group 4-73.6%. Median time for stone expulsion: Group 1- 13 days; group 2- 10 days; group 3- 12 days; group 4- 9 days	Adverse effects-Transient hyperglycaemia in group 2 (5.7%), group 4 (3.8%)
Elgalaly H et al. [12]	RCT	Adult patients presented with a symptomatic, unilateral, single, uncomplicated distal ureteric stone of less than 10 mm	Single kidney, bilateral ureteric stones, renal impairment, UTI, high-grade hydronephrosis and any history of previous endoscopic or surgical interventions	115, follow-up was performed every week, for 4 weeks	Group A (58 patients) received a single dose of silodosin (8 mg) daily, and group B (57 patients) received a single dose of tamsulosin (0.4 mg) daily for one month	Stone clearance rate in group A = 83% in Group B = 57%. Mean stone expulsion time in group A = 16.7 days, in group B = 13.3 days	Group A: Orthostatic hypotension (3.8%), abnormal ejaculation (17.3%) Group B: Orthostatic hypotension (7.8%), abnormal ejaculation (5.9%)
Goyal SK et al. [17]	Prospective study	Adult patients > 18 years, presenting with distal ureteric stones sized 6 to 10 mm	Patients with solitary kidney, history of previous surgery on same ureter, UTI, deteriorating renal function, Fever, hydronephrosis, acute or chronic renal failure, multiple ureteral stones, a history of open surgery or endoscopic procedures in the urinary tract, allergy to tamsulosin or tadalafil, concomitant treatment with α -blockers, calcium antagonists or nitrates, pregnant or lactating mothers, patients who demanded urgent stone removal	123, 4 weeks	Group A = tamsulosin 0.4 mg once daily, group B = tadalafil 10 mg once daily	Stone expulsion rate was 73.77% in group A and 69.35% in group B; mean expulsion time for tamsulosin group was found to be 9.38 \pm 6.66 days and for tadalafil group was found to be 9.61 \pm 7.47 days	Adverse effects: Group A-Headache, abnormal ejaculation (9.8%), dizziness (6.6%), backache (4.92%), orthostatic hypotension (3.28%), group B- headache (11.3%), dizziness (9.7%), backache (4.8%), orthostatic hypotension (3.2%), abnormal ejaculation (1.6%)

Table 1 (continued)

References	Type of study	Inclusion criteria	Exclusion criteria	Number of subjects, follow-up period	Treatment	Efficacy	Safety
Falahatkar S et al. [18]	RCT	Adult aged 18–64 years who suffered from renal colic and single distal ureteral stone smaller than 10 mm	Patient with fever more than 37.8°C, GFR ≤ 30, single kidney, multiple ureteric stones, history of ureteral surgery, diabetes, gastric ulcer, usage of alpha-blocker drugs, calcium channel blocker and nitrate, pregnancy or any kind of allergy to the drugs	132, 4 weeks	Patients in group A received tamsulosin 0.4 mg, in group B received tadalafil 10 mg, and in group C received placebo	The stone expulsion rate was 72.7% in group A, 63.6% in group B and 56.8% in group C The mean time of stone expulsion in the group A was 17.75 ± 75 days, group B was 21.13 ± 1.17 days and 22.25 ± 1.18 days in group C	Adverse effects-Group A- Headache (4.5%), orthostatic hypotension (4.5%) and retrograde ejaculation Group B- Headache (11.4%), dizziness (15.9%), back pain (9.1%), dizziness (4.5%). Group C-No complications
Furyk JS et al. [19]	RCT	Patients older than 18 years and with symptoms suggestive of ureteric colic and a calculus demonstrated in the distal ureter on computed tomography (CT) scan with a CT kidney, ureter, and bladder protocol	Temperature greater than 38° C (100.4° F), an estimated glomerular filtration rate less than 60 mL/minute per 1.73 m ² , a calculus greater than 10 mm, solitary kidney, transplanted kidney, history of ureteral structure, known allergic reaction to the study medication, or current calcium channel blocker or a-blocker use or hypotension, or if they were pregnant or planning pregnancy	403, 28 days	Patients were allocated to 0.4 mg of tamsulosin and placebo daily for 28 days	Stone passage occurred in 87.0% of the tamsulosin patients and 81.9% of the placebo patients. The median time to stone passage was 7 days for tamsulosin and 11 days for placebo	Patients who received tamsulosin had dizziness (2%), palpitations (6%), sexual dysfunction (5.4%), headache (21.6%), fatigue (28.7%), nausea (30.3%), vomiting (9.2%), diarrhoea (10.3%), constipation (17.8%) Placebo group patients had dizziness (18.9%), palpitations (4.9%), sexual collapse (1.1%), sexual dysfunction (2.2%), headache (29.2%), fatigue (23.8%), nausea (30.3%), vomiting, diarrhoea (10.3%), constipation (17.3%)

Table 1 (continued)

References	Type of study	Inclusion criteria	Exclusion criteria	Number of subjects, follow-up period	Treatment	Efficacy	Safety
Puwada S et al. [20]	RCT	Patients aged \geq 18 years with a ureteral stone size of 5–10 mm in its greatest dimension and situated below the common iliac vessels, as diagnosed by non-contrast computed tomography of the KUB	Patients with fever, hydronephrosis, acute or chronic renal insufficiency, multiple ureteral stones, open surgery or endoscopic interventions, diabetes, peptic ulcer or on concomitant treatment with β -blockers, calcium antagonists, or nitrates, pregnant or lactating mothers or patients who demanded immediate intervention	207, 4 weeks	Group A were given tadalafil 10 mg once daily, and group B received tamsulosin 0.4 mg (prolonged release capsule) once daily	The stone expulsion rate was 84.0% in group A and 68.0% in group B. The mean time for stone expulsion in group A was 14.7 ± 3.8 days and in group B was 16.8 ± 4.5 days	Adverse effects in group A- Headache (14%), dizziness (12%), backache (9%), orthostatic hypotension (8%), abnormal ejaculation (6%), Group B: Headache, backache (11%), dizziness, orthostatic hypotension (10%), abnormal ejaculation (12%)

Table 1 (continued)

References	Type of study	Inclusion criteria	Exclusion criteria	Number of subjects, follow-up period	Treatment	Efficacy	Safety
Kc HB et al. [21]	RCT	Patients with ureteral stones 5–10 mm in size and located in the distal ureter	Patients with urinary tract infection, severe refractory pain, severe hydronephrosis, acute or chronic renal failure, multiple ureteral stones, bilateral ureteral calculus or a single functioning kidney, any history of ureteral surgery or procedure, or urinary tract anomalies, patients receiving concomitant treatment with alpha-blockers, calcium channel blockers, nitrates, steroids, PDES inhibitors; patients having ischemic heart disease, congestive cardiac failure or complicated hypertension, pregnant or lactating mothers and patients who demanded urgent stone removal	85, 2 weeks	Group A received tamsulosin 0.4 mg and group B received tadalafil 10 mg at bedtime for 2 weeks	Stone expulsion rate in the group A was (61%) and in group B was 84.01% The mean stone expulsion time was lower in group B (8.08 ± 3.3 days) than in group A (9.64 ± 3.8 days)	Adverse effects in group 1: Headache (14.6%), dizziness (12.2%), postural hypotension (9.8%), gastritis (7.3%), backache (9.8%), runny nose (2.4%), hearing problem (9.1%) Group B: Headache (27.3%), dizziness (18.2%), postural hypotension (15.9%), gastritis (22.7%), backache (25%), runny nose (4.5%), hearing problem (9.1%)

Table 1 (continued)

References	Type of study	Inclusion criteria	Exclusion criteria	Number of subjects, follow-up period	Treatment	Efficacy	Safety
Kohjimoto Y et al. [22]	RCT	Adult patients ≥ 20 years old presenting with acute renal colic, patients with a single distal ureteral stone ≤ 10 mm below the common iliac vessels in whom conservative therapy was judged to be appropriate	Presence of multiple ureteral stones, severe hydronephrosis, acute or chronic renal failure, urinary tract infection, pregnancy or breastfeeding, or serious physical disorder. Patients with a history of endoscopic or open surgical procedures for the ureter, hypersensitivity to nifedipil or flopropione, or current treatment with α - or β -blockers, anti-cholinergic drugs, calcium channel antagonists, or phosphodiesterase type 4 inhibitors or those who wished surgical treatment	92, weekly follow-up for 28 days	Group 1 received nifedipil 75 mg once in the morning and placebo twice a day. Group 2 received flopropione 80 mg three times a day	Cumulative stone expulsion rate in nifedipil group = 77.5% and in flopropione group = 59.1%. Median time to stone expulsion was 8 days for the nifedipil group and 18 days for the flopropione group	Minor adverse events were oedema in the flopropione group and nausea, diarrhoea, constipation and pruritus in the nifedipil group
Gharib T et al. [23]	RCT	Patients aged 18 years or more, harbouring unilateral single stone 5–10 mm in largest diameter, located in the lower 1/3rd of the ureter (between the inferior border of the sacroiliac joint and ureterovesical junction) were included in the study	Patients with single kidney, urinary tract infection, bilateral or multiple stones, marked hydronephrosis, and history of previous endoscopic or open ureteral surgery	150, 4 weeks	Group 1 patients received silodosin 8 mg and in group 2 patients received tamsulosin 0.4 mg	Stone expulsion rate in group 1 was 82.4% and in group 2 was 61.5%. Mean stone expulsion time of group 1 was 9.4 ± 3.8 days and in group 2 = 12.7 ± 5.1 days	Adverse effects: Group 1-Dizziness (4.4%), postural hypotension, headache (1.47%), retrograde-ejaculation (23.3%); group 2- Dizziness (6.2%), postural hypotension (3.1%), headache (1.51%), retrograde ejaculation (12.2%)

Table 1 (continued)

References	Type of study	Inclusion criteria	Exclusion criteria	Number of subjects, follow-up period	Treatment	Efficacy	Safety
Imperatore V et al. [24]	Retrospective observational study	Patients aged \geq 18 years with a single, unilateral, symptomatic, radiopaque ureteric stone of 10 mm or smaller in the largest dimension located between the lower border of the sacroiliac joint and the vesico-ureteric junction as assessed on intravenous urography	Renal insufficiency, urinary tract infections, high-grade hydronephrosis, previous therapies for the stone, solitary kidney, history of ureteral surgery or previous endoscopic procedures, concomitant calcium antagonists or corticosteroids medications, ureteric strictures, cardiovascular diseases, and incomplete data	100, weekly follow-up for 28 days	50% of the patients received daily single dose of tamsulosin 0.4 mg for 28 days and 50% received a daily single dose of silodosin 8 mg for 28 days	Stone expulsion rate was 82% in tamsulosin group and 88% in silodosin group. Mean expulsion time for tamsulosin-6.5 days, silodosin-6.7 days	Adverse effects in tamsulosin group- Retrograde ejaculation (2%), dizziness (8%), nasal congestion (6%), postural hypotension (6%), headache (6%) Adverse effects in silodosin- Retrograde ejaculation (16%), dizziness, nasal congestion, postural hypotension, headache (2%)

No serious adverse effects were associated with the use of alpha-blockers. Most commonly reported adverse effects included orthostatic hypotension, palpitation, headache, dizziness, backache, abnormal ejaculation, retrograde ejaculation, gastritis, fatigue, nasal congestion, constipation, nausea, diarrhoea, asthenia, increased erection, dry mouth, flushing, muscle cramps, dyspepsia, sexual dysfunction, collapse, vomiting, and hearing problem [2, 3, 5, 6, 8, 10, 12, 17–24]. The detailed results are described in Table 1.

4 Conclusion

An ideal treatment for distal ureteral stone should help improve stone clearance rate and expulsion time with minimal pain and without significant detrimental adverse effects. The results from the research studies with alpha-blockers look very promising. In the light of the findings, we recommend using alpha-blockers to treat distal ureteral stones as the first-line treatment. The results suggest that silodosin was the most efficacious drug. However, adverse effects associated with alpha-blockers were limited, mainly orthostatic hypotension. The choice of the alpha-blocker varies from urologist to urologist based on their expertise in the field and patient condition. As more alpha-blockers are marketed, more combinations permutations will come into the market. However, to the best of our knowledge, information on the combination therapy of alpha-blockers with other drug classes is minimal.

Abbreviations

MET: Medical expulsion therapy; RCT: Randomized controlled trial; AUA: American Urological Association; EAU: European Association of Urology; UTI: Urinary tract infection; JVT: Juxtavesical tract; VUJ: Vesico-ureteric junction; KUB: Kidney, ureter and bladder; GFR: Glomerular filtration rate; CT: Computed tomography; PDE5: Phosphodiesterase type 5.

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Author contributions

This work was carried out in collaboration among all authors. Authors BRKC and SK designed the study and performed the data collection. Authors AL, VS, and UAM managed the data analysis and interpretation of the study. Authors SK, AL, VS, and UAM wrote the article's first draft. Authors BRKC and NP made a critical revision. All authors read and approved the final manuscript.

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Competing interests

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References

- Sen H, Erturhan S, Sadioglu E, Bayrak O, Seckiner I (2017) A comparison of efficacy of doxazosin 4 and 8 mg in medical expulsive therapy of distal ureteral stones: a prospective randomized clinical trial. *Urolithiasis* 45(5):461–464. <https://doi.org/10.1007/s00240-016-0927-0>
- Jayant K, Agrawal R, Agrawal S (2014) Tamsulosin versus tamsulosin plus tadalafil as medical expulsive therapy for lower ureteric stones: a randomized controlled trial. *Int J Urol* 21(10):1012–1015. <https://doi.org/10.1111/iju.12496>
- Gandhi HR, Agrawal C (2013) The efficacy of tamsulosin vs. nifedipine for the medical expulsive therapy of distal ureteric stones: a randomised clinical trial. *Arab J Urol* 11(4):405–410. <https://doi.org/10.1016/j.aju.2013.08.008>
- Cao D, Yang L, Liu L, Yuan H, Qian S, Lv X, Han P, Wei Q (2014) A comparison of nifedipine and tamsulosin as medical expulsive therapy for the management of lower ureteral stones without ESWL. *Sci Rep* 4(1):1–5. <https://doi.org/10.1038/srep05254>
- Sentürk AB, Aydin C, Ekici M, Yaytokgil M, Akkoc A, Baykam MM (2018) Comparison of three most frequently used alpha blocker agents in medical expulsive therapy for distal ureteral calculi, result of a retrospective observational study. *Archivio Italiano di Urologia e Andrologia* 90(1):25–28. <https://doi.org/10.4081/aiua.2018.1.25>
- Kumar S, Jayant K, Agrawal MM, Singh SK, Agrawal S, Parmar KM (2015) Role of tamsulosin, tadalafil, and silodosin as the medical expulsive therapy in lower ureteric stone: a randomized trial (a pilot study). *Urology* 85(1):59–63. <https://doi.org/10.1016/j.urology.2014.09.022>
- Wang CJ, Tsai PC, Chang CH (2016) Efficacy of silodosin in expulsive therapy for distal ureteral stones: a randomized double-blinded controlled trial. *Urol J* 13(3):2666–2671. <https://doi.org/10.22037/uj.v13i3.3266>
- Abdelaziz AS, Badran YA, Aboelsaad AY, Elhilaly H (2017) Preliminary study of the efficacy of the combination of tamsulosin and trospium as a medical expulsive therapy for distal ureteric stones. *Afr J Urol* 23(1):38–42. <https://doi.org/10.1016/j.afju.2016.02.006>
- Yu B, Zheng X, Sun Z, Cao P, Zhang J, Gao Z, Cao H, Zhang F, Wang W (2021) The safety and efficacy of doxazosin in medical expulsion therapy for distal ureteric calculi: a meta-analysis. *PLoS ONE* 16(1):1–12. <https://doi.org/10.1371/journal.pone.0245741>
- Shabana W, Teleb M, Dawod T, Abu Taha H, Abdulla A, Shahin A, Eladi M, Abo-Hashem S (2016) Outcome of α -blockers, with or without methylprednisolone combination, in medical expulsive therapy for lower ureteric stones: a prospective randomised study. *Arab J Urol* 14(1):7–11. <https://doi.org/10.1016/j.aju.2015.11.006>
- Rahman MJ, Faridi MS, Mibang N, Singh RS (2018) Comparing tamsulosin, silodosin versus silodosin plus tadalafil as medical expulsive therapy for lower ureteric stones: a randomised trial. *Arab J Urol* 16(2):245–249. <https://doi.org/10.1016/j.aju.2017.11.012>
- Elgalaly H, Sakr A, Fawzi A, Salem EA, Desoky E, Shahin A, Kamel M (2016) Silodosin vs tamsulosin in the management of distal ureteric stones: a prospective randomised study. *Arab J Urol* 14(1):12–17. <https://doi.org/10.1016/j.aju.2015.11.004>
- Gnyawali D, Pradhan MM, Sigdel PR, Parajuli P, Chudal S, Poudyal S, Chapagain S, Luitel BR, Chalise PR, Sharma U, Gyawali PR (2020) Efficacy of tamsulosin plus tadalafil versus tamsulosin as medical expulsive

- therapy for lower ureteric stones: a randomized controlled trial. *Adv Urol* 29(2020):1–5. <https://doi.org/10.1155/2020/4347598>
14. Lv JL, Tang QL (2014) Comparative evaluation of efficacy of use of nifedipil and/or celecoxib for medical treatment of distal ureteral stones. *Urolithiasis* 42(6):541–547. <https://doi.org/10.1007/s00240-014-0708-6>
 15. Shafique MN, Hussain M (2018) Efficacy of Tamsulosin alone versus Tamsulosin Phloroglucinol combination therapy for medical expulsion of lower Ureteral calculi. *Pak J Med Sci* 34(2):393–398
 16. Sridharan K, Sivaramakrishnan G (2018) Efficacy and safety of alpha blockers in medical expulsive therapy for ureteral stones: a mixed treatment network meta-analysis and trial sequential analysis of randomized controlled clinical trials. *Expert Rev Clin Pharmacol* 11(3):291–307. <https://doi.org/10.1080/17512433.2018.1424537>
 17. Goyal SK, Singh V, Pandey H, Chhabra MK, Aggarwal SP, Bhat A (2018) Comparative efficacy of tamsulosin versus tadalafil as medical expulsive therapy for distal ureteric stones. *Urol Ann* 10(1):82–86
 18. Falahatkar S, Akhavan A, Esmaeili S, Amin A, Kazemnezhad E, Jafari A (2021) 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* 47(5):982–988. <https://doi.org/10.1590/S1677-5538.IBJU.2020.1007>
 19. Furryk JS, Chu K, Banks C, Greenslade J, Keijzers G, Thom O, Torpie T, Dux C, Narula R (2016) Distal ureteric stones and tamsulosin: a double-blind, placebo-controlled, randomized, multicenter trial. *Ann Emerg Med* 67(1):86–95. <https://doi.org/10.1016/j.annemergmed.2015.06.001>
 20. Puvvada S, Mylarappa P, Aggarwal K, Patil A, Joshi P, Desigowda R (2016) Comparative efficacy of tadalafil versus tamsulosin as the medical expulsive therapy in lower ureteric stone: a prospective randomized trial. *Central Eur J Urol* 69(2):178–182
 21. Kc HB, Shrestha A, Acharya GB, Basnet RB, Shah AK, Shrestha PM (2016) Tamsulosin versus tadalafil as a medical expulsive therapy for distal ureteral stones: a prospective randomized study. *Invest Clin Urol* 57(5):351–356. <https://doi.org/10.4111/icu.2016.57.5.351>
 22. Kohjimoto Y, Hagino K, Ogawa T, Inagaki T, Kitamura S, Nishihata M, Iba A, Matsumura N, Hara I (2015) Nifedipil versus flopropione as medical expulsive therapy for distal ureteral stones: results of a randomized, multicenter, double-blind, controlled trial. *World J Urol* 33(12):2125–2129. <https://doi.org/10.1007/s00345-015-1556-x>
 23. Gharib T, Mohey A, Fathi A, Alhefnawy M, Alazaby H, Eldakhkhny A (2018) Comparative study between silodosin and tamsulosin in expectant therapy of distal ureteral stones. *Urol Int* 101(2):161–166. <https://doi.org/10.1159/000490623>
 24. Imperatore V, Fusco F, Creta M, Di Meo S, Buonopane R, Longo N, Imbimbo C, Mirone V (2014) Medical expulsive therapy for distal ureteric stones: tamsulosin versus silodosin. *Archivio Italiano di Urologia e Andrologia* 86(2):103–107. <https://doi.org/10.4081/aiua.2014.2.103>

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