Tropical Journal of Pharmaceutical Research June 2026; 25 (6): 865-870
ISSN: 1596-5996 (print); 1596-9827 (electronic)

Available online at http://www.tjpr.org
https://dx.doi.org/10.4314/tjpr.v25i6.12

Original Research Article

Clinical efficacy of tamsulosin and tadalafil in distal urethral stone passage: A randomized clinical trial

Zahraa Nasser Abdul Ghani[1]*, Hayder Abdulhafedh Kurji[2], Inas Sami Ali[3], Wisam Ghazi Sanad[4]

[1]Department of Pharmacology & Physiology, College of Pharmacy, University of Al Mashreq, Baghdad, [2]Department of Clinical Pharmacy, [3]Department of Pharmaceutical Chemistry, College of Pharmacy, University of Bilad Alrafidain, Diyala, [4]Department of Pharmaceutics, College of Pharmacy, Al-Zahraa University for Women, Karbala, Iraq

For correspondence:* ***Email:* *zahraa.naaser.a@uom.edu.iq*

Sent for review: 24 March 2026 *Revised accepted: 18 June 2026*

Abstract

Purpose: *To investigate the efficacy of tamsulosin in combination with tadalafil compared to tamsulosin alone in distal ureteral stones.*
Methods: *A total of 80 adult patients with single distal ureteral stones (5–12 mm) were included in this randomized open-label study. The patients were randomly and equally assigned into study and control groups. Study group (n = 40) received tamsulosin (0.4 mg) plus tadalafil (5 mg) daily, and control group received (n = 40) received tamsulosin (0.4 mg) alone. Follow-up was done for 20 days, and clinical parameters such as stone expulsion rate, time of expulsion, frequency of pain episodes, analgesic requirements, and side effects were compared between both groups. Categorical data were compared using chi-square test. Measurement data were compared using the independent sample t-test. P < 0.05 was considered statistically significant*
Results: *Stone expulsion rate was significantly higher, and mean stone expulsion time was significantly shorter in study group compared to control (p < 0.05). Furthermore, patients in study group experienced significantly fewer pain episodes and required analgesics less frequently (p < 0.05). Adverse effects were milder with no significant difference between the groups (p > 0.05), with no major complications.*
Conclusion: *Tadalafil in combination with tamsulosin significantly increases expulsion rate, accelerates stone expulsion, reduces pain and analgesic use in patients with distal ureteral calculi without any significant increase in side effects.*

Keywords: *Distal ureteral stones, Medical expulsive therapy, Tadalafil, Tamsulosin, Urolithiasis*

Tropical Journal of Pharmaceutical Research is indexed by Scopus, Chemical Abstracts, Embase, Index Copernicus, EBSCO, African Index Medicus, JournalSeek, Directory of Open Access Journals (DOAJ), African Journal Online, Bioline International, Open-J-Gate and Pharmacy Abstracts

INTRODUCTION

Ureteral stones develop when there is progressively large accumulation of crystalline material in the collecting system [1]. While a few stones may reside in the kidney, most commonly grew and rapidly become symptomatic by entering the ureter. Passage is determined by the size of calculi, stone morphology, and the natural dimensions of ureteric segments [2]. Acute obstruction and impaired flow result when stones get stuck in any of the natural constrictions within the ureter, such as the pelviureteric junction (PUJ), junction of the iliac vessels, or vesicoureteric junction (VUJ) [3]. A typical ureteric stone presents as ureteric colic, which is an acute, intense flank pain that irritates the groin due to high pressure and overstretching

of the ureter wall. Other factors that may contribute to the severity of symptoms include local inflammation, edema, hyperperistalsis, and mucosal irritants [4]. Different clinical presentations are due to differences in stone size, anatomic site, and extent of obstruction [5]. Ultrasonography (USG) is the most common initial imaging modality due to its sensitivity for stones at the PUJ and VUJ as well as high sensitivity for hydronephrosis [6]. Diagnostic efficiency is moderate in mid-ureteric stones, but non-contrast computed tomography (NCCT) continues to be the gold standard due to better sensitivity and specificity compared to USG [7].

Conservative therapy of ureter stones includes both hydration and medical expulsive therapy (MET). Increasing fluid improves urine flow and increases hydrostatic pressure proximal to the obstruction, which may allow for stone passage [8]. Pharmacologic MET is increasingly widespread, and α1-adrenergic antagonists, including tamsulosin, have been demonstrated to lower ureteric smooth muscle tone and peristaltic frequency, improve distal ureteral relaxation and facilitate stone passage [9,10]. Phosphodiesterase (PDE) inhibitors like tadalafil additionally enhance smooth muscle relaxation by elevating intracellular cyclic nucleotide levels. Thus, the combination may decrease ureteral spasm and facilitate spontaneous distal ureteral stone clearance. Therefore, this study investigated the efficacy of tamsulosin in combination with tadalafil compared to tamsulosin alone in distal ureteral stones.

METHODS

Study design

This was a prospective randomized open-label parallel-group clinical trial carried out in the Outpatient Urology Clinic in Diyala, Iraq, from August 2024 to February 2025, based on the CONSORT 2025 statement for reporting randomized trials [11]. A total of 80 adult patients with single distal ureteral stones (5–12 mm) were included in the study. The patients were randomly and equally assigned to study (n = 40) and control (n = 40) groups. Study group received tamsulosin (0.4 mg) in combination with tadalafil (5 mg), and control group received tamsulosin (0.4 mg) alone.

Sample size

Sample size was determined according to prior randomized trials of MET in distal ureteral stones, which revealed an expected 20 % difference in stone expulsion rates between combination therapy and monotherapy. With an alpha level set at 0.05 (two-sided) and 80 % power, 36 participants in each group would be the minimum required. Considering the possible incidence of dropout and to obtain a more robust analysis, 40 participants were included in each group, making a total of 80.

Participants

This study included 80 adult participants with unilateral distal ureteral stones during the study. All randomized participants completed the study and were included in the final analysis, with no loss to follow-up.

Inclusion criteria

Participants over 20 years, presence of a single distal ureteral calculus diagnosed by ultrasonography or kidney-ureter-bladder (KUB) image, stone size between 5 – 12 mm (as proposed by the EAU Guidelines on Urolithiasis 2025 [12]). All participants must have normal renal function and be able to understand the protocol and give informed consent.

Exclusion criteria

Participants < 20 years, pregnant, or breastfeeding, presence of bilateral ureteral stones, multiple stones within the same side, active urinary tract infection, moderate or severe hydronephrosis according to the EAU Guidelines on Urolithiasis 2025 [12], presence of a congenital urinary tract anomalies, chronic kidney disease, voiding dysfunction, history of ureteral surgery, previous endoscopic management, participants on α-blockers or PDE-5 inhibitors, any previously known hypersensitivity to the study drugs, and any cardiovascular or cerebrovascular conditions that contraindicated the use of PDE-5 inhibitors.

Treatment

Participants were asked to take the medication once every night with adequate fluid intake. Diclofenac (50 mg) was administered for pain management. Secondary evaluations were performed on days 10 and 20 for stone passage, including patient-reported and ultrasonographic confirmation of an expelled stone. During every visit, frequency of pain attacks, analgesic consumption, and presence of adverse effects were recorded. The stone was considered passed if either the patient saw the stone or the ultrasonography showed a stone-free ureter. If no stone was eliminated within 20 days, it was considered therapeutic failure [13,14] (Figure 1).

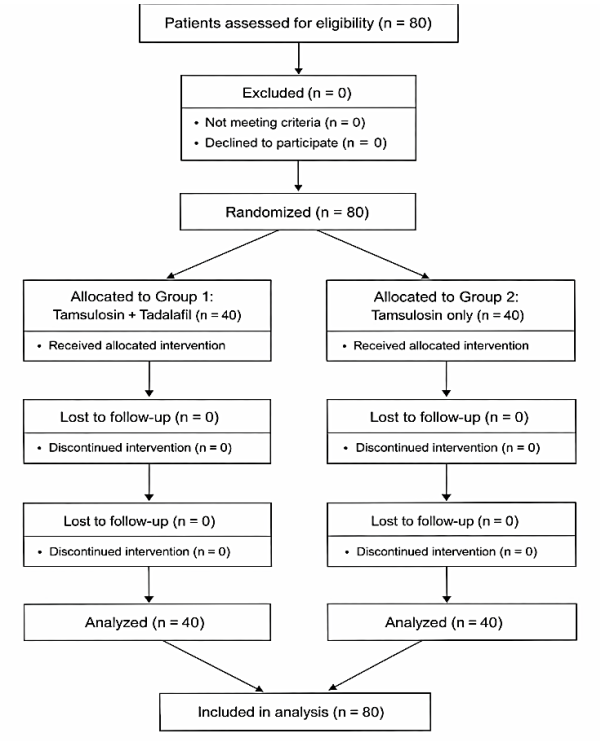

Figure 1: CONSORT flow diagram of patient enrolment, randomization, follow-up, and analysis

Evaluation of parameters/indices

Baseline assessment

All patients underwent a full clinical assessment, including detailed medical history and physical examination, with standard laboratory testing at baseline. Urinalysis, serum creatinine and urea were measured to assess renal function. Imaging assessment included renal US and KUB X-ray. Stone size and location, and pain score were recorded [12,13].

Study outcomes

The study outcomes were categorized into primary and secondary.

Primary outcome

Stone expulsion rate was recorded within the 20-day follow-up period [13]. This was confirmed either by direct visualization of the stone by participants or by ultrasound evidence of a stone-free distal ureter [14].

Secondary outcomes

Time to stone expulsion (days), number of painful episodes during follow-up, number of patients requiring rescue analgesics, frequency, and severity of adverse effects were recorded.

Ethical considerations

The study was approved by the Scientific and Ethical Committee, College of Pharmacy, University of Bilad Al-Rafidain (Approval No.: BAUCP2024Aug4) and complied with the Declaration of Helsinki [15]. Written informed consent was obtained from all participants prior to the study.

Statistical analysis

Data were analyzed using SPSS software version 27 (IBM Corp., Armonk, NY, USA). Continuous data were expressed in mean ± standard deviation (SD), and compared using an independent samples t-test. Categorical variables were expressed as frequencies and percentages and compared using the chi-square test. Effect estimates were reported as risk ratios (RR) and mean differences (MD) at 95 % confidence intervals (CI). No missing data were encountered during follow-up. $P < 0.05$ was considered statistically significant.

RESULTS

Baseline characteristics

There was no significant difference in baseline characteristics between study and control groups indicating appropriate randomization and group allocation (Table 1).

Clinical outcomes

Study group achieved significantly higher stone passage, and mean expulsion time was significantly shorter in study group ($p < 0.05$).

Table 1: Baseline characteristics of the study participants (n = 40)

Characteristic	Study group	Control group
Age (years) (mean ± SD)	42.5±14.5	43.2±8.9
Male n (%)	28(70.0)	27(67.5)
BMI (kg/m²) (mean ± SD)	27.2±3.8	26.4±5.1
Stone size (mm) (mean ± SD)	10.1±3.0	9.7±4.5
Stone side (right), n (%)	22(55.0)	21(52.5)
Stone side (left), n (%)	18(45.0)	19(47.5)

Furthermore, number of pain episodes was significantly lower in study group compared to control (Table 2).

Adverse effects

There was no significant difference in incidence of adverse effects between study and control groups ($p > 0.05$). Furthermore, mild adverse effects such as myalgia, headache, and gastric irritation were common. There were no serious adverse effects, hospitalizations, or withdrawals during the study.

DISCUSSION

This study investigated the efficacy of concurrent tadalafil and tamsulosin administration for distal ureteric stones. The results showed that combination therapy demonstrated better results compared to tamsulosin alone, with significantly better expulsion rate, passage time, pain burden, and analgesic consumption, without compromising safety. These findings are in line with increasing number of reports that indicated that PDE-5 inhibitors may have synergistic potential when combined with α-blockers for MET. The higher expulsion rate in the study group is in tandem with previous meta-analyses [4,7], placing tadalafil-based regimens as one of the best treatments for treating distal stones. Such synergistic effect probably occurs due to the combined blockage of α1A/α1D receptors, leading to decreased ureteral peristaltic frequency and PDE-5 inhibitory activity. This enhances intracellular cGMP levels and prolongs relaxation of smooth muscle. This dual effect results in the reduction of intraluminal resistance at the distal ureter, the narrowest part in the tract, and more successful passage of stones. Chronic retention of stone leads to mucosal irritation, episodic obstruction, and recurrent renal colic. Despite a 1-day numerical difference in expulsion time, the rapid clearance observed in study group is of clinical importance. Similar findings were reported by 16. Almaghthawi *et al* [16] and Sun *et al* [6], who demonstrated that PDE-5 inhibitors augment segmental ureteral compliance and reduce intramural pressure. Due to the anatomical limitation of the distal ureter, improved relaxation by tadalafil is probably responsible for earlier passage. Decrease in the number of painful episodes and reduction in use of analgesics in study group is an extra benefit in addition to stone clearance. Renal colic is predominantly the result of forced ureteral contractions with a temporary rise in luminal pressure. Inhibition of PDE-5 blunts the contractile surges and decreases nociceptive signaling. This is consistent with the study of Ramanah *et al* [17], who asserted that PDE-5 inhibitors improve painful hyperperistalsis. From clinical standpoint, pain reduction increases tolerance for conservative therapy and limits emergency department utilization, especially in settings with limited resources.

There was no significant difference in adverse effects between both groups.

Table 2: Stone expulsion outcomes, pain episodes, and analgesic requirement (n = 40)

Outcome	Study group	Control group	Effect estimate (95 % CI)	*P*-value
Stone expulsion n (%)	29(72.5)	21(52.5)	RR 1.38 (1.02–1.87)	0.030
Time to stone expulsion (days) (mean ± SD)	9.0±1.7	10.0±1.3	MD − 1.02 (−1.98 to −0.06)	0.045
Pain episodes during follow-up (mean ± SD)	2.1±0.9	3.0±1.1	MD −0.9 (−1.3 to −0.5)	0.001
Patients requiring analgesics, n (%)	24(60.0)	32(80.0)	RR 0.75 (0.58–0.97)	0.035

Note: Expulsion time was calculated only for patients who passed the stone during follow-up. Risk ratio (RR), confidence interval (CI), mean difference (MD), and standard deviation (SD)

Table 3: Adverse effects reported during the study period; n = 40 (%)

Adverse effect	Study group	Control group	*P*-value
Any adverse event	22(55.0)	18 (45.0)	0.503
Postural hypotension	6 (15.0)	4 (10.0)	0.737
Retrograde ejaculation	3 (7.5)	7 (17.5)	0.311
Muscle pain	8 (20.0)	5 (12.5)	0.546
Back pain	5 (12.5)	3 (7.5)	0.712
Dizziness	7 (17.5)	8 (20.0)	1.000
Gastric upset	6 (15.0)	4 (10.0)	0.737

This result is consistent with a previous safety report, which demonstrated that low-dose tadalafil combined with α-blockers had no significant effect on the incidence of hypotension or ejaculatory dysfunction [8]. General tolerability encourages further clinical development of this combination in selected patients. Studies by Belkovsky *et al* [7] and Jung *et al* [3] clearly demonstrated that combination therapy was superior to monotherapy in both expulsion rate and symptom control. With better efficacy, tamsulosin plus tadalafil would be an excellent MET manoeuvre among patients with distal ureteral stones when non-invasive approaches are considered. Earlier stone clearance resulted in lower pain burden and less analgesic use, which together improved quality of life. Given that both drugs are cheap and widely available, this regimen is particularly beneficial in under-resourced urological settings. This is a randomized, prospective trial with equal numbers of participants in both study and control groups. Furthermore, a composite assessment of expulsion rates, frequency, analgesic requirements for pain, and adverse effects gives a global clinical evaluation. Although time-to-event analysis using survival methods was not performed, comparison of mean expulsion time provided a clinically relevant estimate of treatment effect. Additional outcome measurements may be a better option in addition to survival analysis in future studies.

Limitations of the study

This study has some limitations. It was a single-center study, and generalizability may not be feasible. Ultrasonography rather than CT scans was used for confirmation of stone clearance, which may have over- or underestimated small residual fragments. The follow-up period was short (20 days), which may have limited assessment of recurrence or long-term results. In addition, the study did not classify participants based on stone density, stone composition, or ureteral wall thickness, which are known predictors for MET success. These restrictions should be considered when interpreting the findings.

Also, assessment of subjective parameters such as number of pain episodes and consumption of analgesics may have introduced bias into the results. Prospective multi-centered and large-sample-size randomized studies are needed in the future to confirm the effectiveness of this combined treatment. The addition of CT-based density (HU) stone measurement, ureteral wall thickness, and exact stone site would provide more reliability. Comparative assessment of novel α-blockers like silodosin and dose-response analysis for PDE-5 inhibitors may further improve MET regimens. Long-term follow-up is necessary to assess recurrence rates, patient-reported outcomes, and cost-effectiveness.

CONCLUSION

Tamsulosin in combination with tadalafil increases stone expulsion rate, decreases the time needed for expulsion, the number of pain episodes, frequency of administration of analgesics, with milder side effects.

DECLARATIONS

Acknowledgement/Funding

None.

Ethical approval

It is stated in the method section.

Use of Artificial intelligence/Large language models

The authors confirm that AI-based tools were used solely for language editing and manuscript polishing purposes (e.g., grammar, phrasing, and clarity). No AI tools were used to generate content, interpret data, or influence study design, results, or conclusions. All intellectual contributions, study analyses, and interpretations reported in the manuscript are the original work of the authors.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the author(s) named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

REFERENCES

1. Abhishek L, Shashikant M, Arvind G, Ravindra S, Desai DM. Comparison of tadalafil and tamsulosin in medical expulsive therapy for ureteric calculus: prospective, randomized, placebo-controlled study. Inn J Med Health Sci 2019; 9(2): 294-298
2. Liu Z, Su J, Yuan D, Zhang Y, Wang W, Jiao K, et al. Efficacy and safety of PDE 5-Is and α1 blockers for treating distal ureteral calculi: a mixed treatment comparison network meta-analysis of randomized controlled clinical trials. Int J Clin Exp Med 2019; 12(5): 4623-4637
3. Jung HD, Cho KS, Jun DY, Jeong JY, Moon YJ, Chung DY, et al. Silodosin versus tamsulosin for medical expulsive therapy of ureteral stones: an updated systematic review and meta-analysis of randomized controlled trials. Medicina (Kaunas) 2022; 58(12)
4. Taheri M, Borumandnia N, Abdi H, Kashi AH, Nourani S, Sheikholeslami S, et al. Which combination of medical expulsive therapy is more effective for treatment of distal ureteral stones in adults? A systematic review and network meta-analysis. BMC Urol 2025; 25(1): 18
5. Abdelaal MA, El-Dydamony EM. Comparative study between Tamsulosin, Silodosin and Tadalafil as a medical expulsive therapy for lower ureteral stones. Arch Ital Urol Androl 2023; 95(1): 10849.
6. Sun F, Liu H, Wu G, Liu M, Liu S, Wang L, et al. Pooled analysis of tadalafil and tamsulosin for ureteral calculi. Front Pharmacol 2024; 15: 1351312.
7. Belkovsky M, Zogaib GV, Passerotti CC, Artifon ELA, Otoch JP, Da Cruz JAS. Tamsulosin vs. Tadalafil as medical expulsive therapy for distal ureteral stones: a systematic review and meta-analysis. Int Braz J Urol 2023; 49(6): 668-676.
8. Ebrahimpour S, Kargar M, Balvardi M, Tabatabaei-Malazy O, Asadi P, Mohammadi M. Comparing efficacy and safety of monotherapy and combination therapy with tadalafil, tamsulosin, and silodosin for distal ureteral stones: A systematic review and meta-analysis. Asian J Urol 2025; 12(2): 189-203.
9. Lee JY, Andonian S, Bhojani N, Bjazevic J, Chew BH, De S, et al. Canadian Urological Association guideline: Management of ureteral calculi - Abridged version. Can Urol Assoc J 2021; 15(12): 383-393.
10. Abbood MK, Abass WA, Fadil A. Effect of Tamsulosin on biomarkers after ureteral stones lithotripsy. Al Mustansiriyah J Pharm Sci 2015; 15(2): 13-20.
11. Hopewell S, Chan AW, Collins GS, Hróbjartsson A, Moher D, Schulz KF, et al. CONSORT 2025 statement: updated guideline for reporting randomised trials. BMJ 2025; 389: e081123.
12. European Association of Urology. EAU Guidelines. EAU Guidelines on Urolithiasis (Edn. presented at the EAU Annual Congress Madrid 2025). EAU Guidelines Office. 2025.
13. Kadırhan Ö, Aydın S, Keskin E, Kantarcı M. Role of ureteral wall thickness and computed tomography imaging in predicting spontaneous passage of ureteral stones. Diagn Interv Radiol 2026; 32(2): 139-148.
14. Erdoğan E, Şimşek G, Aşık A, Yaşar H, Şahin C, Sarıca K. Optimal duration of medical expulsive therapy for lower ureteral stones: a critical evaluation. Urolithiasis 2024; 52(1): 48
15. World Medical Association Declaration of Helsinki: Ethical principles for medical research involving human participants. JAMA 2025; 333(1): 71-74.
16. Almaghthawi MM, Alotaibi EA, Alotaibi MS, Alomari RW, Alsulami YD, Alahamdi MA, et al Efficacy of alpha-blockers in medical expulsive therapy for ureteral stones: A systematic review and meta-analysis of randomized controlled trials between 2010 and 2025. Arab J Urol 2026; 24(1): 1-14.
17. Ramanah M, Banerjee I, Nunkoo S, Robinson J, Krissheeven M, Banerjee I. The comparative effectiveness of PDE5 inhibitors and β3 agonists versus α-Blockers in medical expulsive therapy for distal ureteric stones: A systematic review and meta-analysis of randomized controlled trials. Cureus 2025; 17(11): e96637.