

EFFICACY OF SILODOSIN VERSUS TAMSULOSIN IN MEDICAL EXPULSIVE TREATMENT FOR URETERAL STONES - A SYSTEMATIC REVIEW

N. Dhinakarbabu¹, D. Mohan Kumar²

¹Assistant Professor, Department of Urology, Coimbatore Medical College, Tamilnadu, India.

²Senior Resident, Department of Urology, Coimbatore Medical College, Tamilnadu, India.

Received : 18/12/2023
Received in revised form : 16/02/2024
Accepted : 01/03/2024

Keywords:

Ureteral stones, Silodosin, Tamsulosin, Medical Expulsive Treatment, Systematic Review, efficacy.

Corresponding Author:

Dr. N. Dhinakarbabu,
Email: drdhinakar@yahoo.com.

DOI: 10.47009/jamp.2024.6.2.9

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (2); 43-48



Abstract

Background: Ureteral stones are a prevalent challenge in primary healthcare, affecting up to 18% of individuals. The associated decrease in quality of life and socioeconomic burden necessitates effective management strategies. While various interventions exist, Medical Expulsive Therapy (MET) with alpha-blockers has gained prominence. Tamsulosin is the standard choice, but the comparative efficacy of silodosin remains underexplored. **Objectives:** This systematic review aimed to assess the success rates of silodosin compared with tamsulosin in the MET of ureteral stones. This study addresses the scarcity of research comparing these alpha-blockers, seeking to contribute valuable insights for informed decision making in ureteral stone management. **Material and Methods:** A systematic search of PubMed and Google Scholar databases from January 2014 to February 2024 was conducted. Studies comparing the efficacy of silodosin and tamsulosin in the treatment of ureteral stones were included. Data synthesis included a narrative summary of the study characteristics, methodologies, and key findings, emphasising the unique contributions of each study. **Results:** The review incorporated 11 studies, revealing that silodosin consistently outperforms tamsulosin in terms of stone expulsion rate and expulsion time. Meta-analyses emphasize silodosin's efficacy, especially for stones under 1 cm. Adverse events, primarily abnormal ejaculation, were noted with both medications, with silodosin exhibiting a higher incidence. **Conclusion:** Silodosin is a more potent and efficient choice than tamsulosin for ureteral stone treatment. The consistent superiority in stone expulsion rates, shorter expulsion times, and reduced colic episodes position silodosin as a favourable alternative.

INTRODUCTION

Ureteral stones pose a prevalent challenge in primary healthcare settings, with a reported prevalence ranging from 3% to 18% across different regions.^[1] Individuals afflicted with ureteral stones experience diminished quality of life, given that this condition ranks among the most agonising urological ailments.^[2] Urolithiasis leads to deterioration in the quality of life of individuals experiencing recurrent stone formation, and the management of urolithiasis is accompanied by a growing socioeconomic burden.^[3] Urolithiasis leads to deterioration in the quality of life of individuals experiencing recurrent stone formation, and the management of urolithiasis is accompanied by a growing socioeconomic burden.

Approaches to managing ureteral stones include conservative, pharmacological, and minimally invasive interventions, such as extracorporeal shock wave lithotripsy and ureterolithotripsy, which are

effective treatment options in nearly all cases. However, these procedures involve substantial expense and are not devoid of risks. Consequently, urologists must discern and choose a suitable treatment for each patient to determine whether it should be nonsurgical or surgical.^[4] Vigilant observation, linked with the spontaneous expulsion of stones in approximately 50% of cases, can result in complications such as urinary tract infections, hydronephrosis, and colic events. The sustained use of this approach is driven by progress in pharmacological therapy, alleviation of symptoms, and assistance in stone expulsion.

According to the urolithiasis guidelines outlined by the European Association of Urology (EAU), Medical Expulsive Therapy (MET) is recommended for the treatment of (distal) ureteral stones > 5 mm, aiming to reduce episodes of renal colic, and has emerged as a well-established treatment that employs a range of medications that act on the ureter through diverse mechanisms.^[5] The

medications used in MET include alpha blockers, calcium channel inhibitors, and phosphodiesterase-5 inhibitors. Among these, alpha-blockers are considered the standard medication for MET in ureteral stones, and variations in efficacy among alpha-blockers have been observed.^[6] The ureter is coated with α 1-adrenergic receptors, specifically the α 1D subtype, which is predominantly located in the terminal third. These receptors exert a significant influence on the physiology of the lower ureter by affecting the contraction of the detrusor and ureteric smooth muscles.

The predominant α -blocker utilised for medical expulsive therapy (MET) is tamsulosin, although comparable outcomes have been demonstrated with other α -blockers, such as terazosin and doxazosin, suggesting a potential class-wide effect. Silodosin has also been suggested as an alternative to tamsulosin for MET; however, few studies have compared the efficacies of these substances.^[7] In this systematic review, our objective was to examine the existing literature and assess the success rates of silodosin in comparison with tamsulosin for the MET of ureteral stones.

MATERIALS AND METHODS

The overall quality of evidence for each outcome was assessed using the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) methodology. We systematically searched two online databases, PubMed and Google Scholar, to identify all randomised clinical trials involving methotrexate in treating chronic urticaria. This report conforms to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

1. Literature Search Strategy.

A systematic and exhaustive search of major scientific databases, including PubMed and Google Scholar, was conducted to identify pertinent studies related to the efficacy of silodosin versus tamsulosin in the medical expulsive treatment of ureteral stones. The search included studies published between January 2014 and February 2024. Keywords employed in the search strategy included variations of "Ureteral Stones" or "ureteral calculi" and "Silodosin" or "silodosin" and "Tamsulosin" or "tamsulosin," in conjunction with terms such as "Treatment Outcome," "expulsive treatment," "stone expulsion," or "efficacy." Boolean operators (AND OR) were used to refine the search and capture the intersection of these terms.

2. Inclusion and Exclusion Criteria:

Studies were included if they met the following criteria.

- Individuals diagnosed with ureteral stones.
- Studies comparing the efficacy of silodosin and tamsulosin in the treatment of ureteral stones.
- Studies have reported relevant outcome measures, such as stone expulsion rates, time to expulsion, and other efficacy indicators.

- The studies were published between January 2014 and February 2024.
- Included Human Subjects.
- The peer-reviewed articles were published in English between January 2014 and February 2024.

Studies were excluded if they met the following criteria.

- Studies published before January 2014.
- Studies not comparing silodosin and tamsulosin in medical expulsive treatment of ureteral stones.
- Case reports, reviews, letters, editorials, and conference abstracts.
- Studies lacking sufficient methodological details.
- Published in languages other than English.

3. Synthesis of Findings:

Data synthesis involved a narrative summary of the pertinent study characteristics, methodologies employed, and key findings related to the efficacy of silodosin versus tamsulosin in the context of ureteral stones. Owing to the anticipated heterogeneity in study designs, a qualitative approach was adopted, emphasising the unique contributions of each study to the overarching understanding of the comparative effectiveness of Silodosin and Tamsulosin in treating ureteral stones.

4. Ethical Considerations:

As this review was based on an analysis of previously published studies, ethical approval was not required. All the included studies adhered to ethical standards, as outlined in their respective publications.

RESULTS

We incorporated randomised controlled trials that compared the effectiveness of silodosin with either placebo or tamsulosin specifically for the treatment of ureteral calculi. The study cohort was limited to individuals diagnosed with a singular, unilateral, and symptomatic ureteric stone confirmed through visual examination. Diagnostic evaluations included plain radiography, ultrasonography, and unenhanced computed tomography (CT) scans when deemed necessary. Stone size was measured on the initial plain radiograph or CT scan using a digital ruler, with the largest dimension considered as the stone size. The primary endpoints of the study were the rate of stone expulsion and the occurrence of complications, while the secondary outcomes included the time taken for stone expulsion (in days), episodes of pain, and instances of abnormal ejaculation.

PRISMA flow diagram

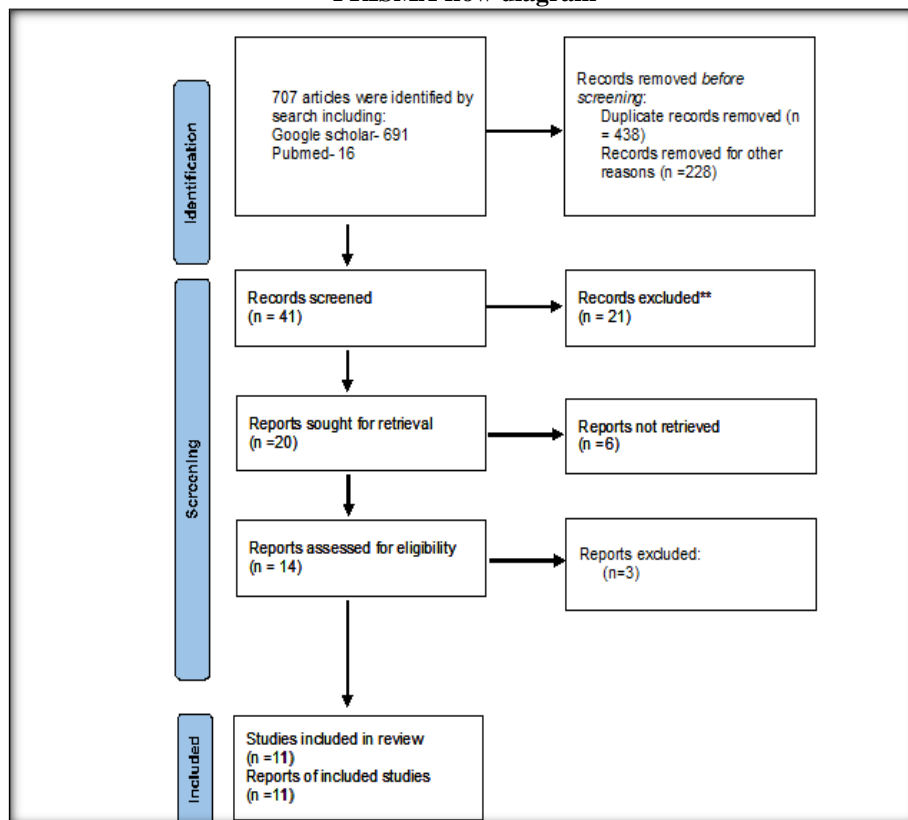


Table 1: Characteristics of Included Studies

Study Authors	Study Year	Study Type	Participants (n)	Discussion
Jung et al. ^[8]	Dec 2022	Systematic review, meta-analysis, and RCT	14	In the expulsion of ureteral stones measuring less than 1 cm, silodosin demonstrated significantly superior performance compared to tamsulosin. For the medical expulsive treatment of ureteral stones measuring less than 1 cm, silodosin might be considered a more favourable option than tamsulosin.
Hsu Y-P et al. ^[9]	August 2018	A Systematic review, and meta-analysis	1812	This study revealed that the average expulsion times with tamsulosin varied between 6.4 to 21 days, while the mean expulsion times with silodosin ranged from 6.5 to 16.7 days. Silodosin likely resulted in shorter expulsion times, approximately 3 days less than tamsulosin. However, it's essential to note that a considerable degree of heterogeneity was observed.
Huang et al. ^[10]	2015	A Systematic review, and meta-analysis	413	The expulsion rate of silodosin was 74.3% in the distal ureter, which was approximately 24% higher with silodosin than placebo. Therefore, the safety characteristics of silodosin closely resembled those of tamsulosin, albeit with a more pronounced occurrence of retrograde ejaculation associated with silodosin usage.
Ozsoy et al. ^[11]	March 2016	A Systematic review, and meta-analysis	407	Assessing side effects is a crucial element in the examination of any medical treatment. Concerning silodosin and tamsulosin, abnormal ejaculation emerged as the predominant side effect observed for both medications. The latest meta-analysis revealed notably elevated rates of stone expulsion and quicker expulsion durations favouring silodosin over tamsulosin.
Yu Z-W et al. ^[12]	August 2021	Meta-analyses	917	Tamsulosin exhibited a reduced time to expulsion for distal ureteral stones compared to the placebo. Patients undergoing tamsulosin treatment reported decreased occurrences of recurrent renal colic and necessitated fewer analgesics.
Ramadhani et al. ^[13]	Dec 2022	Systematic review, and meta-analysis	474	Silodosin demonstrates remarkable uroselectivity, leading to high efficacy in the urogenital tract while exhibiting minimal adverse events related to the cardiovascular system. Theoretically, silodosin has displayed favourable tolerability in individuals with ureteral stones who are concurrently using antihypertensive medications.
Sharma et al. ^[14]	Jun 2020	A Systematic review, and meta-analysis	7077 patients (from 31 RCTs)	Silodosin had the highest Stone Expulsion Rate (SER) with a SUCRA value of 94.8, followed by tamsulosin at 46.2. Silodosin emerged as the most efficacious drug for medical expulsive

				therapy of lower ureter stones, than Tamsulosin.
Abdullah et al. ^[15]	Oct 2023	Comparative study	80	There were no instances of treatment cessation among patients attributed to adverse drug effects. Orthostatic hypotension was documented in one patient (2.5%) in the silodosin cohort and three patients (7.5%) in the tamsulosin cohort, although this disparity lacked statistical significance.
Elgalaly et al. ^[16]	Dec 2015	Prospective randomized study	103 (Group A= 52; Group B= 51)	Two patients (3.8%) in Group A experienced orthostatic hypotension, leading to treatment discontinuation, while four patients (7.8%) in Group B encountered the same, with two discontinuing treatments. Abnormal ejaculation was documented in nine patients (17.3%) in Group A (silodosin) and three patients (5.9%) in Group B (tamsulosin), with no statistically significant difference.
Imperatore et al. ^[17]	Jan 2014	Retrospective observational study	100	The likelihood of distal ureteric stones passing spontaneously is notably high, ranging from 71-98% for stones measuring ≤ 5 mm, while it diminishes to 25-51% for stones larger than 5 mm. MET studies, incorporating sub-analyses based on stone size, have revealed elevated expulsion rates for stones ≤ 5 mm compared to their larger counterparts. Tamsulosin-treated patients exhibited a stone expulsion rate of 89.5% for stones ≤ 5 mm and 70% for stones > 5 mm, respectively.
Gharib et al. ^[18]	July 2018	Comparative study	150	Regarding the time for stone expulsion, our findings demonstrated superior outcomes in the silodosin group compared to the tamsulosin group, with durations of 9.4 ± 3.8 days and 12.7 ± 5.1 days for silodosin and tamsulosin groups, respectively.

DISCUSSION

Ureteral colic, primarily attributed to ureterolithiasis, accounts for 1%–2% of hospital emergency admissions. Medical expulsive therapy (MET) has recently emerged as an alternative approach to the initial management of patients with distal ureteric stones. Although ureteroscopy and shockwave lithotripsy remain the most efficient treatments for distal ureteric stones, they incur considerable costs and associated risks.^[19] Nonetheless, spontaneous stone evacuation can occur in up to 50% of cases, in addition to potential complications, such as ureteric colic and urinary tract infections.

Several meta-analyses have explored the impact of diverse combinations of drug interventions on the treatment of ureteric stones. Nevertheless, few studies have explicitly compared the effectiveness of various alpha-blockers in the treatment of distal ureteric calculi. The use of adjunctive medications such as tamsulosin for distal ureteric stones has proven effective in alleviating discomfort, reducing complications, and accelerating stone clearance. Recent research has indicated that silodosin may serve as a viable and efficient substitute.

Despite occasional occurrences of adverse events, such as orthostatic hypotension, dizziness, and diarrhoea, patients tend to persist with their treatment due to their notably enhanced efficacy. Another meta-analysis involving 22 randomised controlled trials encompassing over 9000 patients with lower urinary tract symptoms (LUTS) or benign prostatic hyperplasia (BPH) concluded that silodosin and tadalafil were more effective than placebo in ameliorating LUTS. However, these medications are associated with a high incidence of adverse events.^[20] To evaluate the impact of these treatments on response rates using established thresholds for minimal detectable differences,

disease progression, and adverse effects, long-term studies should be conducted to accumulate sufficient evidence.

In the initial prospective RCT of silodosin for MET of ureteral stones measuring less than 10 mm, Itoh et al,^[21] reported that patients receiving 8 mg of silodosin daily exhibited a shorter mean stone expulsion time and a higher stone expulsion rate than those instructed to consume 2 L of water daily. Subsequent meta-analyses have consistently shown that silodosin surpasses tamsulosin in terms of efficacy of MET in ureteral stones. In a meta-analysis involving five RCTs, Liu et al,^[22] demonstrated that silodosin significantly increased the expulsion rate of distal ureteral stones compared to tamsulosin. However, no significant differences were observed between the two treatments in terms of stone expulsion time or retrograde ejaculation rate.

A crucial aspect of Medical Expulsive Therapy (MET) is its ability to reduce colic episodes. In a study conducted by Kumar et al,^[23] patients were instructed to take 50 mg of diclofenac on demand during the MET. The average number of pain episodes in the silodosin group was significantly lower than that in the tamsulosin group, registering at 0.8 (SD \pm 0.9) and 1.7 (SD \pm 1.2), respectively ($p < 0.001$).

Assessment of side effects plays a crucial role in any medical treatment. In the context of silodosin and tamsulosin, abnormal ejaculation emerged as the most prevalent side effect of both the medications. Notably, the study by Dell' Atti et al,^[24] revealed a significant difference, indicating a higher incidence of abnormal ejaculation in the silodosin group than in the tamsulosin group. Specifically, 22.7% of the patients in the silodosin group experienced side effects, as opposed to 10.2% in the tamsulosin group ($p < 0.002$).

CONCLUSION

In conclusion, a comprehensive examination of multiple studies and meta-analyses comparing silodosin and tamsulosin for medical expulsive treatment of ureteral stones consistently revealed noteworthy findings. Silodosin consistently outperformed tamsulosin in various aspects, demonstrating higher efficacy in terms of stone expulsion rates and expulsion times. Studies have indicated that silodosin may be a more favourable option, particularly for ureteral stones measuring less than 1 cm. The shift in ureteral stone management has introduced Medical Expulsive Therapy (MET) as a promising alternative, particularly for distal ureteric stones. While traditional approaches such as ureteroscopy and shockwave lithotripsy pose notable costs and risks, the exploration of alpha-blockers, including tamsulosin and silodosin, has revealed the consistent superiority of silodosin in multiple studies and meta-analyses.

Silodosin stands out for its higher efficacy, demonstrated by improved stone expulsion rates, shorter expulsion times, and reduced colic episodes compared to tamsulosin. However, patients tend to endure occasional adverse events such as orthostatic hypotension and diarrhoea for the overall benefit, particularly favouring silodosin in MET. The literature strongly suggests that silodosin is a more potent and efficient choice than tamsulosin for ureteral stone treatment. This insight emphasises the need to prioritise silodosin, recognise its efficacy, and advocate informed, patient-centric decisions in ureteral stone management.

REFERENCES

- Jung HD, Seo IY, Lee JY. Large database study of urinary stone composition in South Korea: Korean Society of Endourology and Robotics (KSER) Research series. *Investig Clin Urol* 2021; 62:462–9. <https://doi.org/10.4111/icu.20210039>.
- Fwu C-W, Eggers PW, Kimmel PL, Kusek JW, Kirkali Z. Emergency department visits, use of imaging, and drugs for urolithiasis have increased in the United States. *Kidney Int* 2013; 83:479–86. <https://doi.org/10.1038/ki.2012.419>.
- Kumar A, Mohanty NK, Jain M, Prakash S, Arora RP. A prospective randomized comparison between early (<48 hours of onset of colicky pain) versus delayed shockwave lithotripsy for symptomatic upper ureteral calculi: A single center experience. *J Endourol* 2010; 24:2059–66. <https://doi.org/10.1089/end.2010.0066>.
- Yang SY, Jung HD, Kwon SH, Lee EK, Lee JY, Lee SH. Does early retrograde intrarenal surgery improve the cost effectiveness of renal stone management? *Yonsei Med J* 2020; 61:515–23. <https://doi.org/10.3349/ymj.2020.61.6.515>.
- Tiselius HG, Ackermann D, Alken P, Buck C, Conort P, Gallucci M. Guidelines on urolithiasis. *Eur Urol* 2001; 40:362–71. <https://doi.org/10.1159/000049803>.
- Dellabella M, Milanese G, Muzzonigro G. Randomized trial of the efficacy of tamsulosin, nifedipine and phloroglucinol in medical expulsive therapy for distal ureteral calculi. *J Urol* 2005; 174:167–72. <https://doi.org/10.1097/01.ju.0000161600.54732.86>.
- Parsons JK, Hergan LA, Sakamoto K, Lakin C. Efficacy of α -blockers for the treatment of ureteral stones. *J Urol* 2007; 177:983–7. <https://doi.org/10.1016/j.juro.2006.10.023>.
- 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; 58:1794. <https://doi.org/10.3390/medicina58121794>.
- Hsu Y-P, Hsu C-W, Bai C-H, Cheng S-W, Chen K-C, Chen C. Silodosin versus tamsulosin for medical expulsive treatment of ureteral stones: A systematic review and meta-analysis. *PLoS One* 2018;13: e0203035. <https://doi.org/10.1371/journal.pone.0203035>.
- Huang W, Xue P, Zong H, Zhang Y. Efficacy and safety of silodosin in the medical expulsion therapy for distal ureteral calculi: a systematic review and meta-analysis: Efficacy and safety of silodosin for calculi. *Br J Clin Pharmacol* 2016; 81:13–22. <https://doi.org/10.1111/bcp.12737>.
- Ozsoy M, Liatsikos E, Scheffbuch N, Kallidonis P. Comparison of silodosin to tamsulosin for medical expulsive treatment of ureteral stones: a systematic review and meta-analysis. *Urolithiasis* 2016; 44:491–7. <https://doi.org/10.1007/s00240-016-0872-y>.
- Yu Z-W, Wang R-H, Zhang C-C, Gao J-G. The efficacy and safety of alpha-adrenergic blockers for medical expulsion therapy in patients with ureteral calculi: A meta-analysis of placebo-controlled trials: A meta-analysis of placebo-controlled trials. *Medicine (Baltimore)* 2021;100: e27272. <https://doi.org/10.1097/MD.00000000000027272>.
- Ramadhani MZ, Klopung 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; 39:21–6. https://doi.org/10.4103/iju.iju_115_22.
- Sharma G, Pareek T, Kaundal P, Tyagi S, Singh S, Yashaswi T, et al. Comparison of efficacy of three commonly used alpha-blockers as medical expulsive therapy for distal ureter stones: A systematic review and network meta-analysis. *Int Braz J Urol* 2022; 48:742–59. <https://doi.org/10.1590/S1677-5538.IBJU.2020.0548>.
- Abdullah A, Basoo Gupta Y, Selvaraj S, Ganapathy R, Ilangovan AK, Sivalingam S, et al. A comparison between silodosin and tamsulosin for medical expulsive therapy of distal ureteric calculus. *Cureus* 2023;15: e47008. <https://doi.org/10.7759/cureus.47008>.
- Elgalaly H, Sakr A, Fawzi A, Salem EA, Desoky E, Shahin A, et al. Silodosin vs tamsulosin in the management of distal ureteric stones: A prospective randomised study. *Arab J Urol* 2016; 14:12–7. <https://doi.org/10.1016/j.aju.2015.11.004>.
- Imperatore V, Fusco F, Creta M, Di Meo S, Buonopane R, Longo N, et al. Medical expulsive therapy for distal ureteric stones: tamsulosin versus silodosin. *Arch Ital Urol Androl* 2014; 86:103–7. <https://doi.org/10.4081/aiua.2014.2.103>.
- Gharib T, Mohey A, Fathi A, Alhefnawy M, Alazaby H, Eldakhkhny A. Comparative study between Silodosin and Tamsulosin in expectant therapy of distal ureteral stones. *Urol Int* 2018; 101:161–6. <https://doi.org/10.1159/000490623>.
- Tzortzis V, Mamoulakis C, Rioja J, Gravas S, Michel MC, de la Rosette JJMCH. Medical expulsive therapy for distal ureteral stones. *Drugs* 2009; 69:677–92. <https://doi.org/10.2165/00003495-200969060-00003>.
- MacDonald R, Brasure M, Dahm P, Olson CM, Nelson VA, Fink HA, et al. Efficacy of newer medications for lower urinary tract symptoms attributed to benign prostatic hyperplasia: a systematic review. *Aging Male* 2019; 22:1–11. <https://doi.org/10.1080/13685538.2018.1434503>.
- Itoh Y, Okada A, Yasui T, Hamamoto S, Hirose M, Kojima Y, et al. Efficacy of selective α 1A adrenoceptor antagonist silodosin in the medical expulsive therapy for ureteral stones: Silodosin as a medical expulsive therapy. *Int J Urol* 2011; 18:672–4. <https://doi.org/10.1111/j.1442-2042.2011.02810.x>.
- Liu H, Wang S, Zhu W, Lu J, Wang X, Yang W. Comparative efficacy of 22 drug interventions as medical expulsive therapy for ureteral stones: a systematic review and

- network meta-analysis. *Urolithiasis* 2020; 48:447–57. <https://doi.org/10.1007/s00240-019-01159-5>.
23. 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. <https://doi.org/10.1016/j.urology.2014.09.022>.
24. Dell'Atti L. Silodosin versus Tamsulosin as medical expulsive therapy for distal ureteral stones: a prospective randomized study. *Urologia* 2014. <https://doi.org/10.5301/uro.5000083>.