

Lower Ureteric Calculus—An Evaluation of Medical Management

Varun Rajan

Assistant Professor, Department of General Surgery, Karpagam Faculty of Medical Sciences and Research, Coimbatore, Tamil Nadu, India.

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Corresponding Author: Dr. Varun Rajan

Conflict of interest: Nil

Abstract:

Background: A multitude of clinical trials have been conducted to examine the effectiveness of MET, both in isolation and in conjunction with other medications such as corticosteroids and antibiotics, utilising the selective α -blocker tamsulosin. Tamsulosin treatment considerably increases the evacuation rate of medium-sized (4–10 mm) distal ureteral stones, according to the majority of these randomised investigations. The objective of this study was to evaluate the efficacy of medical management (tamsulosin 0.4 mg) in aiding stone expulsion in adult patients with solitary lower ureteric calculus of sizes between 4 and 10 mm.

Materials and Methods: This was a prospective study conducted over a period of 4 years from 2018 to 2022, involving 324 adult patients with a solitary unilateral lower ureteric calculus between 4 and 10 mm with symptoms of less than 2 weeks duration. Patients enrolled were given a dose of tablet tamsulosin 0.4 mg once at night for two weeks.

Results: The overall calculus clearance rate with tamsulosin was 78.6%. The highest expulsion rate (92.5%) was found among the calculus of size 6 mm. The lowest expulsion rate (40.4%) was found among the calculus of size 10 mm. Among the 63 patients who needed URS, 40 retained the calculus in the same position after a 2-week course of tablet tamsulosin. 12 had developed UTI and 11 had developed an elevated serum creatinine level while on tamsulosin.

Conclusion: The study shows that a two-week course of Tamsulosin is effective in causing spontaneous calculus expulsion in adult patients with a solitary lower ureteric calculus of size between 4 mm and 9 mm but has a lower efficacy for the calculus of size 10 mm without causing any serious side effects.

Key words: Tamsulosin, Lower Ureteric Calculus, α -Blocker.

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Introduction

The most significant parameters to predict spontaneous stone expulsion are stone size, location, and duration of symptoms. Patient-dependent factors like pain threshold and infection development also play a role in determining whether active stone removal or decompression of the renal collecting system is necessary. [1] While endoscopic treatment of ureteral stones is highly successful and consistently yields rapid stone removal, there are some risks associated with the procedure, both surgical and anaesthetic. Serious consequences are rare but can occur. Thus, a conservative course of treatment without intrusive procedures is a desirable choice for a large number of patients. However, cautious waiting may lead to repeated renal colic and does not guarantee stone clearance. Interventional treatment is required if a conservative approach is not successful. However, due to stone impaction and the ureter's ensuing inflammatory response, intervention is either ineffective or carries a higher risk of consequences after a period of conservative treatment. The identification of α receptors in ureteral smooth muscle cells has encour-

aged research into the therapeutic potential of α blockers for ureteral stone disease. The late 1990s saw the first reports of successful MET (Medical Expulsive Therapy) with the nonselective α -blocker doxazosin for patients with distal ureteral stones. Subsequently, a multitude of clinical trials have been conducted to examine the effectiveness of MET, both in isolation and in conjunction with the α 1A/1D selective α -blocker tamsulosin, such as corticosteroids and antibiotics. Tamsulosin treatment considerably increases the evacuation rate of medium-sized (4–10 mm) distal ureteral stones, according to the majority of these randomised investigations. Tamsulosin thus offers an economical and non-invasive substitute for interventional methods. [2]

This study was conducted to evaluate the efficacy of medical management (tamsulosin 0.4 mg) in aiding stone expulsion in adult patients with solitary lower ureteric calculus of sizes between 4 and 10 mm.

Materials and Methods

This was a prospective study conducted over a period of 4 years from 2018 to 2022, involving 324 adult patients with a solitary unilateral lower ureteric calculus between 4 and 10 mm with symptoms of less than 2 weeks duration. Those presenting with features of urinary tract infection were excluded. Those with a past history of diabetes, hypertension and ischemic heart disease were also excluded.

Patients enrolled were given a dose of tablet tamsulosin 0.4 mg once at night for two weeks with a precaution to report immediately if they developed any drug allergy or adverse drug reaction. They were also asked to report early if their symptoms became severe, if they developed

fever with chills or if they developed nausea, vomiting and anorexia. They were reviewed after 2 weeks. An ultrasonogram KUB was done during this review and the calculus position was ascertained. Those who had spontaneously passed out the calculus were offered dietary advice and asked to review after 2 months. Those patients who retained the calculus in the same position were advised ureteroscopic calculus removal.

Results

324 patients were enrolled in the study, of which 29 did not turn up for a review 2 weeks after they were given tablet tamsulosin. 232 patients spontaneously passed out the calculus. The remaining 63 underwent ureteroscopic calculus removal. **Figure 1**

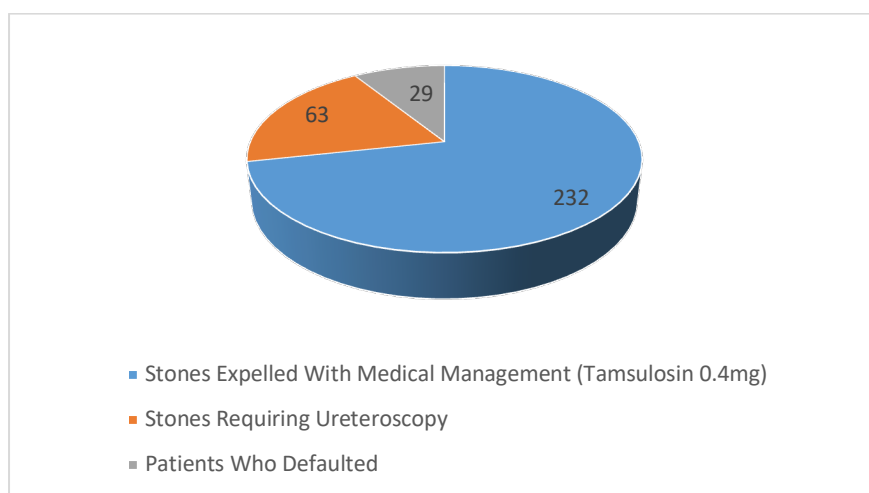


Figure 1: Distribution of Patients Based on Follow-Up

Among these 324 patients, the majority (200) had lower urinary tract symptoms along with lower abdominal discomfort. 114 patients had only lower urinary tract symptoms and 10 had only lower abdominal pain or discomfort. **Figure 2**

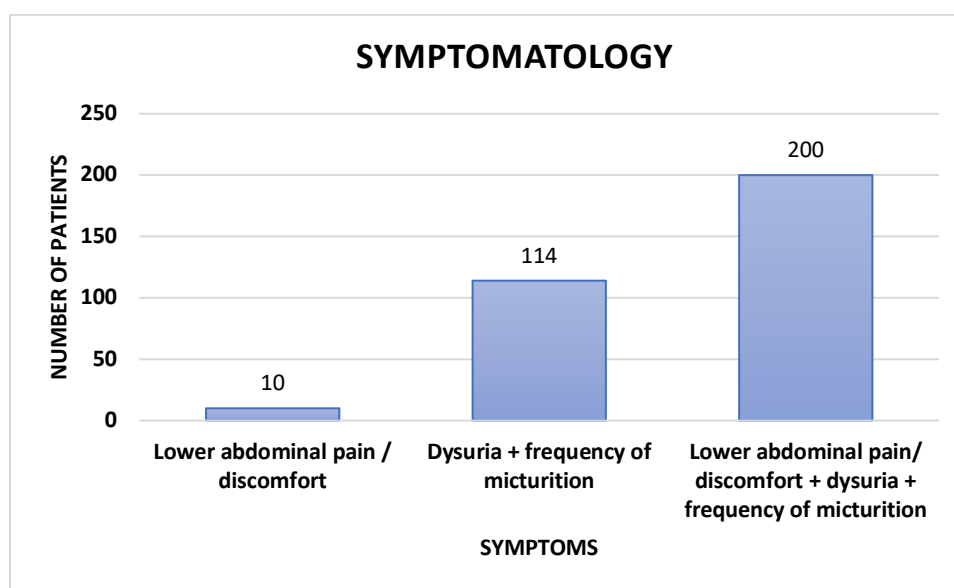


Figure 2: Distribution of Patients Based on Symptoms

The overall calculus clearance rate with tamsulosin was 78.6%. The highest expulsion rate (92.5%) was found among the calculus of size 6 mm. The lowest expulsion rate (40.4%) was found among the calculus of size 10 mm. The data are as shown in Table 1 and Figure 3.

Table 1: Calculus Clearance Rate Based on Size

Calculus Size	Expelled With Tamsulosin (0.4mg)	Needed URS	Total
4 mm	8 (88.9%)	1	9
5 mm	38 (90.5%)	4	42
6 mm	98 (92.5%)	8	106
7 mm	38 (80.9%)	9	47
8 mm	23 (71.9%)	9	32
9 mm	8 (66.7%)	4	12
10 mm	19 (40.4%)	28	47
Total	232 (78.6%)	63	295

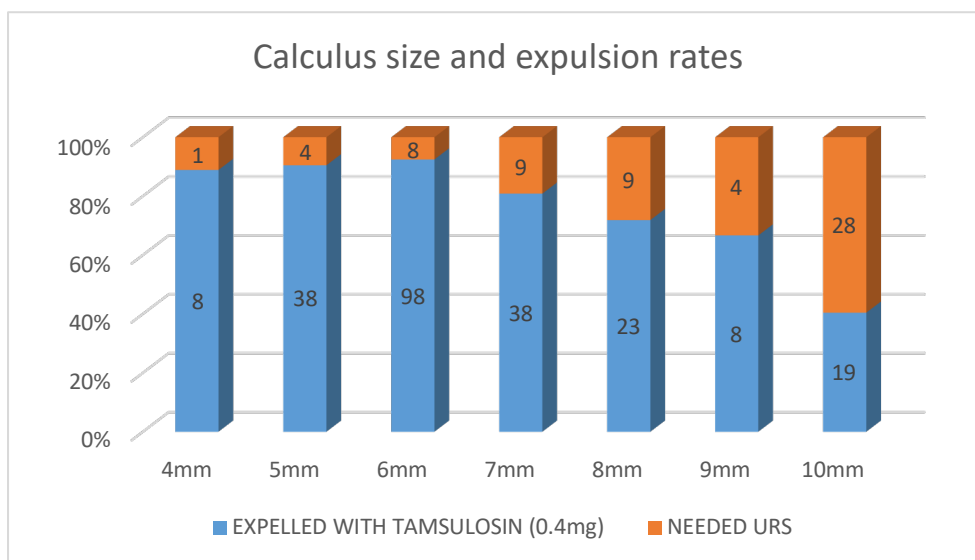


Figure 3: Calculus Clearance Rate Based on Size

Among the 63 patients who needed URS, 40 retained the calculus in the same position after a 2-week course of tablet tamsulosin. 12 had developed UTI and 11 had developed an elevated serum creatinine level while on tamsulosin. **Figure 4**

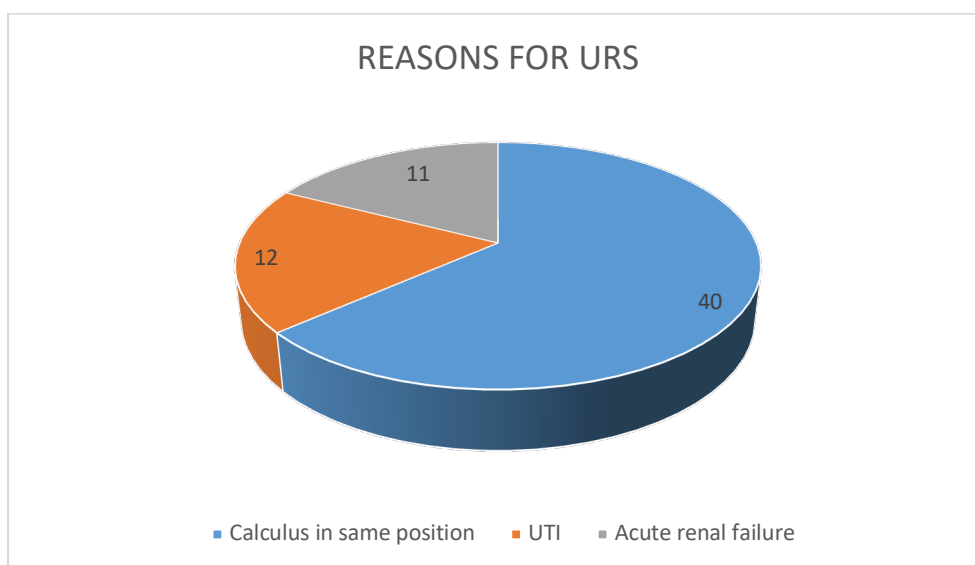


Figure 4: Reason for URS

Discussion

With varying degrees of success, the majority of research on tamsulosin's effectiveness in the ejection of lower ureteral calculi has been conducted in wealthy western nations. Our developing nation's disease spectrum differs from that of developed nations mostly due to factors such as delayed diagnosis, incomplete investigations, and low awareness, all of which can affect the course of any disease, including ureteral stones. Furthermore, it is difficult to access sophisticated interventional facilities in this region of the world. [3] Thanks to advancements in endourological techniques and instrumentation, the management of ureteral stones has shifted from open surgeries to minimally invasive procedures, including ureterorenoscopic stone removal and ESWL, or careful waiting. The current acknowledged gold standards for treating ureteral stones are minimally invasive methods. However, these methods are not without risk, come at a high cost, and are not easily accessible in developing nations [4]. Therefore, the purpose of this study was to assess how well medical therapy with 0.4 mg of tamsulosin can help adult patients expel stones.

324 adult patients with solitary lower ureteric calculus were enrolled in the present study. The majority of the patients presented with lower abdominal discomfort and lower urinary tract symptoms. They were given a dose of tablet Tamsulosin 0.4 mg for two weeks once at night. 29 patients defaulted at the end of two weeks. 23 patients reviewed prior to two weeks on account of development of UTI or renal insufficiency and needed ureteroscopic calculus removal. 40 patients retained the calculus in the same position at the end of two weeks and needed ureteroscopic calculus removal. 232 patients spontaneously passed out the calculus at the end of two weeks. This gives a calculus clearance rate of 78.6%. None of the patients who underwent ureteroscopic calculus removal developed any pre-operative or post-operative complications. Among the 232 patients who had passed out the calculus spontaneously, the calculus of size 6 mm was found to have the highest clearance rate (92.5%) and the lowest clearance rate was for the calculus of size 10 mm (40.4%).

In a related study, Cervenakov et al. (2015) [5] found that 80.4% of patients experienced a significant reduction in LUTS (Lower Urinary Tract Symptoms) and a faster passage of small calculi from the terminal segments of their ureters as a result of α blocker medication. Additionally, they proposed that α blockers enhance the analgesic effects of medications utilised in conventional therapeutic approaches.

Dellabella et al. [6] observed an increase in stone expulsion rate and a decrease in stone expulsion time, the need for hospitalisation and endoscopic procedures, and particularly good control of colic pain when using tamsulosin as a spasmolytic drug during episodes of ureteral colic caused by juxtavesical calculi. They believed that the addition of tamsulosin to traditional therapy would help to remove lower ureteral stones. When used with tamsulosin, corticosteroid medication seems to promote faster stone removal. Furthermore, tamsulosin by itself has shown outstanding expulsive efficacy as MET for distal ureteral calculi. [7] At the lower ureteral calculi, α -1 blockers reduced the frequency of ureteral colic episodes and the severity of discomfort during spontaneous passage.[8]

According to Hollingsworth et al., meta-analysis, patients receiving medicinal therapy (with an α -blocker or calcium channel antagonist) had a 65% higher chance of passing stones naturally. [9]

Porpiglia et al. conducted a comparison of analgesics, tamsulosin, deflazocort, and a combination of the two. Age, sex, stone location and size were similar among the groups. The percentages of expulsion for the four groups were, in order, 84.8%, 33.3%, 37.5%, and 60%. Deflazocort alone was surprisingly less effective than tamsulosin or combo therapy. According to the authors' findings, patients benefit most from combination therapy (84.8% expulsion rate); nevertheless, adjuvant α blocker medication will be helpful if steroids are contraindicated (60% expulsion rate). [10]

105 individuals with symptomatic lower ureteric calculi ranging in diameter from 5 to 10 mm were included in the Mayank et al. [11] investigation. Three equal groups of patients were created: group A received only analgesics as a control group; group B received tamsulosin; and group C received a combination of tamsulosin and deflazocort. In groups A, B, and C, the corresponding stone ejection rates were 17/35 (48.30%), 26/35 (74.60%), and 28/35 (80%). Group C's mean expulsion time was noticeably lower than that of groups A and B. According to the authors, MET in combination with deflazocort and tamsulosin had a higher percentage of stone ejection than either treatment alone. Furthermore, a clear difference in the expulsion rates of tamsulosin alone and the control group (74.3% vs. 48.6%) was observed. The combination has also been shown to be safe and effective, with faster stone expulsion.

The trial by Khereddine et al., [12] had 90 patients in total, who were randomised into three equal groups of 30 patients each to receive treatment with 100 mg of ketoprofen once daily (group I), 8 mg of silodosin once daily (group II), and 5 mg of

tadalafil once daily (group III). Overall, the expulsion rate was 22.22%, and the stone clearing rates in group I (20%), group II (23.33%), and group III (23.33%) did not significantly differ from each other ($p = 0.93$). While there were no significant side effects reported, the NSAID group saw a greater incidence of adverse events (26.66% in group I, 13.33% in group II, and 10% in group III; $p = 0.18$). In the group taking ketoprofen, nausea and epigastralgia were the most frequent adverse effects.

Prior to the publication of the SUSPEND (Spontaneous Urinary Stone Passage Enabled by Drugs) experiment, MET was routinely used. In terms of lowering intervention rates to remove ureteral stones, tamsulosin was not found to be more effective than a placebo in this extensive, multicenter, randomised controlled trial conducted by Pickard et al. [13] The primary outcome measure for the experiment was the requirement for urologic intervention. Medical expulsive therapy has been weakened since that study. To clarify the differences between a high-quality randomised controlled trial and some meta-analyses of primarily small studies [14,15] new multicenter, randomised, double blind, placebo-controlled trials were carried out. Tamsulosin-based medical expulsive therapy was not beneficial for individuals with distal ureteral stones, according to a randomised controlled trial conducted by Furyk et al. [16] involving 403 patients. On the other hand, the subgroup of patients whose stones were between 5 and 10 mm had a higher ejection rate. Furthermore, there was no difference in the percentage of patients who passed stones between those treated with tamsulosin and those who received a placebo (52% versus 49%) in Meltzer et al.'s [17] randomised study, which had 512 patients with ureteral stones ranging in size from 1 to 8 mm. Tamsulosin and placebo were compared for 4 to 7 mm distal ureteral stones in a population of 3200 patients in a more recent large prospective randomised trial. [18] Similar to the findings of the

Meltzer et al., experiment, there was no change for stones 5 mm or less and an increase in stone passage (87% vs. 75%) in the group with 5.1 to 7 mm stones, with a slight overall benefit (86% vs. 79%) when all sizes were taken into account.

Campshroer et al., [15] conducted a subgroup analysis in a Cochrane database systematic review, splitting lower ureteric stones into two groups based on size (≤ 5 mm and 6–10 mm). According to their findings, alphablockers had little to no influence on stone removal for stones that were 5 mm or smaller and a significant impact on stones that were 6–10 mm. Aboumarzouk et al., meta-analysis, [19] which comprised 60 randomised studies with over 9500 participants, detailed the same conclusions.

In terms of stone expulsion, MET with alphablockers did not prove to be more beneficial than a placebo in eight placebo-controlled trials including 2284 patients, according to a recent meta-analysis by Yu et al. [20] They did not perform the subgroup analysis, which divides the stones into two groups (≤ 5 mm and 6–10 mm). Several research [15,16] have shown that this analysis had an impressive alphablocker effect on the expulsion of the bigger stone group.

Of the 116 individuals who were enrolled in the trial by Shalaby et al.,^[21] had ureteroscopies because they were unable to expel stones after eight weeks. Compared to 85.3% of the tamsulosin group, ureteral dilatation was always necessary in the control group ($p = 0.015$). Following ureteroscopy, the treatment group required fewer ureteral stents (76.5%) than the control group (87.5%) ($p = 0.2$).

Our study showed a clear benefit of tamsulosin with a good expulsion rate, similar to other studies, compared in the table below. However, larger trials involving a larger number of patients are warranted to ascertain its role.

Table 2: Comparison of Expulsion Rates in Various Studies

Study	Expulsion Rate
Porpiglia et al.,[10]	66
Dellabella et al.,[6]	90
Autorino et al.,[22]	88
Mayank et al.,[11]	74.30
Present Study	78.6%.

There is still reason to be concerned about the alpha-blocker side effect profile. Concerns have been raised over their hypotensive effect, particularly in the elderly and those using concurrent vasodilator medications, and especially at the beginning of treatment. Moreover, men find ejaculatory dysfunction to be extremely

uncomfortable. Another significant risk factor for problems during cataract surgery is intraoperative floppy iris syndrome, which is likewise linked to tamsulosin. [19] All of the individuals in this trial did not have any adverse reactions or drug allergies, nevertheless.

Shalaby et al., study found that although 30% of patients in the placebo group experienced drug-related side effects, 37.5% of patients in the tamsulosin group experienced them ($p = 0.7$). The most often reported side effect was dizziness, which happened more often when using tamsulosin (25%) as opposed to a placebo (22.5%) ($p = 0.9$). Other adverse effects (sinus pressure, nosebleed, nausea, tinnitus, hands and feet swelling) that may or may not be related to the medication were recorded in isolated cases. In neither group were there any significant side effects noted. However, men in the tamsulosin group experienced ejaculatory dysfunction more frequently [5 (17.9%) vs. 1 (3.5%), ($p = 0.1$)].

Conclusion

The study shows that a two-week course of tamsulosin is effective in causing spontaneous calculus expulsion in adult patients with less than severe symptoms and a solitary lower ureteric calculus of size between 4 mm and 9 mm but has a lower efficacy for the calculus of size 10 mm, without causing any serious side effects.

References

- Carstensen HE, Hensen JS. Stones in ureter; Acta Chir Scand 1973;433:66-71.
- Segura JW, Preminger GM, Assimos DG, et al. Ureteral stones (Clinical Guidelines Panel summary report on the management of ureteral calculi). J Urol 1997;158:1915-21.
- Singal RK, Denstedt JD. Contemporary management of ureteral stones Urol Clin North Am 1997;24:59-70.
- Marberger M, Hofbauer J, Tuerk C, et al. The management of ureteric stones. Eur Urol 1994;25:265-8.
- Cervenakov I, Fillo J, Mardiak J, et al. Speedy elimination of ureterolithiasis in lower part of ureters with the alpha 1-blocker tamsulosin. Int Urol Nephrol 2002;34:25-9.
- Dellabella M, Milanese G, Muzzonigro G; Efficacy of tamsulosin in the medical management of juxtavesical ureteral stones; J Urol 2003;170(6 Pt 1):2002-5.
- O'Leary MP. Tamsulosin (current clinical experience). Urology 2001;58(Suppl 6A):42-8.
- Resim S, Ekerbices H, Cifti A. Effect of tamsulosin on the number and intensity of ureteral colic in patients with lower ureteral calculus; Int J Urol 2005;12:615-20.
- Hollingsworth JM, Rogers MA, Kaufman: Efficacy of alpha-blockers for the treatment of ureteral stones; J Urol 2007;177:83.
- Porpiglia F, Destefanis P, Fiori C, et al. Effectiveness of nifedipine and deflazacort in the management of distal ureteral stones. Urology 2000;56:579-82.
- Saini A, Jain M, Kamath K. Role of medical expulsive therapy in lower ureteral calculus. World Journal of Pharmacy and Pharmaceutical Sciences 2020;9(3).
- Khereddine MD, Tiéoulé TM, Aziz K, Kays C, Rhouma B, Ahmed S, et al. Medical Expulsive Therapy (MET) for Large Distal Ureteral Stones: A Prospective Study Comparing Three Drugs. Open Journal of Urology 2020;10:152-7.
- Pickard JS, Starr K, Banks C, et al. Medical expulsive therapy in adults with ureteric colic: a multicentre, randomised, placebo-controlled trial. The Lancet 2015;386:341-49.
- Hollingsworth JM, Canales BK, Rogers MA, et al. Alpha Blockers for Treatment of Ureteric Stones: Systematic Review and Meta-Analysis. BMJ 2016;355:6112.
- Campschroer T, Zhu Y, Duijvesz D, et al. Alpha-blockers as medical expulsive therapy for ureteral stones. Cochrane Database of Systematic Reviews 2014;4:CD008509.
- Furyk JS, Chu K, Banks C, et al. Distal ureteric stones and tamsulosin: a double-blind, placebo-controlled, randomized, multicenter trial. Annals of Emergency Medicine 2016;67:86-95.
- Meltzer AC, Hollander JE, Wolfson AB, et al. Randomized clinical trial of treatment with tamsulosin begun in the emergency department to promote passage of urinary stones. Journal of Urology 2017;197:604.
- Ye Z, Zeng G, Yang H, et al. Efficacy and safety of tamsulosin in medical expulsive therapy for distal ureteral stones with renal colic: a multicenter, randomized, double-blind, placebo-controlled trial. European Urology 2018; 73:385-91.
- Aboumarzouk OM, Jones P, Amer T, Kotsiris D, Emiliani E, Somani B, et al. What is the role of alpha-blockers for medical expulsive therapy? Results from a meta-analysis of 60 randomized trials and over 9500 patients. Urology 2018;119:5-16.
- Yu ZW, Wang RH, Zhang CC, Gao JG. The efficacy and safety of alpha-adrenergic blockers for medical expulsion therapy in patients with ureteral calculi: a meta-analysis of placebo-controlled trials. Medicine (Baltimore) 2021;100(37):e27272.
- Shalaby MM, Eldardery MA. The use of tamsulosin in the treatment of 10–15 mm lower ureteral stones in adults: a double-blinded randomized controlled trial. African Journal of Urology 2022;28:54.
- Autorino R, De Sio M, Damiano R, et al. The use of tamsulosin in the medical treatment of ureteral calculi: where do we stand? Urol Res 2005;33:460-4.