STATE OF THE ART REVIEWS

The role of Silodosin as a new medical expulsive therapy for ureteral stones: a meta-analysis

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ABSTRACT
To evaluate the efficacy of Silodosin as a medical expulsive therapy of ureteral stones, we searched PubMed, EMBASE, the Cochrane Library, and CBM up to June 2015. All randomized controlled trials (RCTs) were identified in which patients were randomized to receive Silodosin versus placebo or other therapies for ureteral stones. Outcome measures assessed were overall stone expulsion rate (primary) and expulsion time, analgesics times, and the incidence of additional treatment and regarding treatment complications (secondary). Two authors independently assessed study quality and extracted data. All data were analyzed using RevMan 5.3. Seven RCTs with a total of 1035 patients met the inclusion criteria. The pooled meta-analysis showed a significant improvement in stone clearance with Silodosin (Silodosin versus placebo, OR = 1.69, 95% CI [1.19–2.40], p = 0.003; Silodosin versus tamsulosin, OR = 2.82, 95% CI [1.79–4.44], p < 0.00001). According to the size and location of ureteral stone, the pooling effects of Silodosin were analyzed, with a meaningful expulsion rate in distal ureteral stone when the size was 5–10 mm. In addition, a shorter expulsion time, fewer analgesics times, and additional treatments were observed. The common side effect was retrograde ejaculation. In summary, Silodosin appears to be more effective than either placebo or tamsulosin. Within the limits of available data, high-quality multicenter RCTs are needed to thoroughly evaluate the outcome in the future.

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Introduction
Urinary stones are a substantial public health problem. It is the third most common affliction of the urinary tract, exceeded only by urinary tract infections and pathologic conditions of the prostate, with estimated prevalence of 2%–3% and life time recurrence rate of approximately 50%. Urinary stones produced $2.1 billion in healthcare expenditures in the United States, an increase of 50% from 1994 to 2000.4

Ureteral stone is one of the most painful and prevalent urologic disorders. For stones <10 mm, the most common treatment options include medical expulsive therapy (MET), shock wave lithotripsy (SWL), and ureteroscopy (URS). Because of high healthcare expenditures and invasive associated with SWL and URS, MET is preferred by patients that might promote spontaneous expulsion of ureteral stones. The previous meta-analysis has showed that α-blockers, calcium channel antagonists, furosemide, and corticosteroids could promote ureteral stone expulsion. Among these drugs, α-blockers are the most promising stone expulsive agents including tamsulosin, alfuzosin, doxazosin, and terazosin.6–11 Tamsulosin is the most commonly used to facilitating stone passage in clinic, our previous meta-analysis showed a 19% improvement in stone clearance with tamsulosin, especially in distal ureteral stones. However, a recent multicenter randomized controlled trials (RCTs) including 1167 patients reported that current METs such as tamsulosin 0.4 mg and nifedipine 30 mg cannot decrease additional treatments in patients with ureteric colic.12 The ideal goal of management in these patients should be to get a fast complete stone clearance with minimal morbidity. Several recent RCT studies demonstrated that Silodosin, a highly selective alpha 1A-adrenoceptor antagonist, could improve the stone expulsion rate (SER) in patients with ureteral stones and may be superior to the current α-blockers, and patients may benefit from Silodosin treatment. Therefore, it is necessary to conduct a systematic review and meta-analysis of all available evidence from RCTs to assess the efficacy of Silodosin as MET for ureteral stones.
Materials and methods

Publication search

The following databases were searched: PubMed (1966–June 2015), Embase (1974–June 2015), Cochrane Library (2015 issue 6), and Chinese biomedicine literature database (1978–June 2015) using the following search terms: (“Silodosin” OR “KMD-3213”) AND (“Ureteral Calculi” OR “Ureterolithiasis” or “Ureteral Stone*”) to identify all relevant articles on the subject. We also searched the references of included studies to identify additional potentially relevant studies. Hand searching of the reference lists of included studies and reviews was undertaken, and contact was made with experts in the field; unpublished studies were not sought. The search was not restricted by publication year or language.

The above-mentioned search strategy was used to obtain the titles and abstracts of RCTs that were relevant to this review. The titles and abstracts were screened independently by two reviewers, who discarded the studies that were not applicable. The two reviewers independently assessed the titles and abstracts of all identified trials to confirm the fulfillment of the inclusion criteria. Disagreements were resolved in consultation with the third reviewer. The data extraction was performed independently by the same authors using standard data extraction forms. The quality of the included randomized trials was assessed using the Cochrane Collaboration’s tool.

Inclusion criteria

Only RCTs were included by looking at beneficial and harmful effects of the Silodosin for ureteral stone.

Intervention types

The interventions were the Silodosin versus placebo or other therapies.

Outcome measures

Our primary outcome measures were the SER. Secondary outcome measures included expulsion times, analgesics times, the incidence of additional treatment, and regarding treatment complications.

Statistical analysis

We analyzed the data using Review Manager (version 5.3) and Software STATA version 11.0 (Stata Corporation, College Station, TX, USA), and extracted and pooled data for summary estimates. The quality of the included randomized trials was assessed using the Jadad scale score for each study, ranging from 0 to 7 points. According to the Cochrane Collaboration’s guideline, for meta-analysis, we combined data on dichotomous outcomes using the Mantel–Haenszel relative risk method (RR) and 95% confidence intervals (95% CI). We also used the $\chi^2$ statistic and $I^2$ test to assess heterogeneity between trials and the $I^2$ statistic to assess the extent of inconsistency. We used a fixed effect model for calculations of summary estimates and their 95% CI unless there was significant heterogeneity, in which case results were confirmed using a random effects statistical model. When data are available and sufficient, subgroup analysis was performed to explore the influence of the stone size and location. Publication bias was assessed using inverted funnel plots. Funnel plot asymmetry was assessed using Egger’s linear regression test. An asymmetric plot indicated possible publication bias. The significance of asymmetry was determined using the $t$-test, and $p < 0.05$ was considered to indicate a significant publication bias. As a research using systematic review and meta-analysis, ethical approval of this study is not required.

Results

We identified 10 references to potential studies and subsequently excluded 3 articles because these did not meet the previous inclusion criteria. Seven RCTs were included in this systematic review (Figure 1). Seven studies were randomized, but only five studies described the method of randomization. Three studies reported the results of Silodosin compared with placebo for ureteral calculi; four studies compared the efficacy of Silodosin with that of tamsulosin or naftopidil for ureteral calculi and were included the final meta-analysis. In this meta-analysis, two studies reported sample size calculations. The quality and detailed characteristics of included studies are shown in Table 1.

Meta-analysis results

Silodosin versus placebo

Expulsion rate: Three studies reported the SER. Patients who underwent Silodosin treatment demonstrated a significant advantage over placebo in terms of the SER (OR = 1.69, 95% CI [1.19–2.40], $p = 0.003$). The result of the expulsion rate is depicted in Figure 2. An intent to treat sensitivity analysis where dropouts are analyzed as treatment failures showed only minor changes occurred ($I^2 = 0\%$; OR = 1.57; 95% CI: 1.12–2.22).
Expulsion times: Two studies reported the stone expulsion times; the results of meta-analysis were showed in the Figure 3. The results of pooled meta-analysis demonstrated that the expulsion times of Silodosin treatment was significantly shorter than placebo (MD = 4.50 days, 95% CI: 6.08 to 2.92, p < 0.00001).

Analgesics times: Two studies reported the use of analgesics after treatment; the results of meta-analysis were showed in the Figure 4. The pooled results indicated that patients need less analgesics in Silodosin group than placebo group (MD = -1.04 times, 95% CI: -1.69 to -0.39, p = 0.002).

In subgroup analysis (Figures 5–6), Heterogeneity were observed in pooled analysis (p = 0.0003, I² = 84%). We performed meta-analysis by the random-effect model, we found that there was no significant difference in expulsion rate between Silodosin group and placebo group when stone size < 5 mm (OR = 0.49, 95% CI: 0.08–3.04, p = 0.45); however, the expulsion rate of Silodosin group was significantly higher than that of placebo group when the stone size was 5–10 mm (OR = 5.62, 95% CI: 1.01–31.2, p = 0.05). There was a higher SER in distal ureteral stone compared Silodosin with placebo (OR = 2.40, 95% CI: 1.38–4.18, p = 0.002), while no difference was found in upper and middle ureteral stone between Silodosin and placebo (upper: OR = 0.99, 95% CI: 0.49–1.97, p = 0.97; middle: OR = 1.23, 95% CI: 0.43–3.49, p = 0.70).

The incidence of additional treatment: Two available studies’ data reported the incidence of additional SWL (Figure 7). The results of pooled meta-analysis showed that the incidence of additional SWL treatment was significantly lower in Silodosin group than that of placebo group (OR = 0.49, 95% CI: 0.30–0.79, p = 0.004).

The regarding treatment AEs: The commonly reported AEs were retrograde ejaculation and nausea in these studies. The results of pooled meta-analysis...
Figure 2. Pooled results of the expulsion rate between Silodosin and Placebo.

| Study or Subgroup | Experimental | Control | Odds Ratio |
|-------------------|--------------|---------|------------|
|                   | Events       | Total   | Events     | Total   | Weight | M-H. Fixed, 95% CI | M-H. Fixed, 95% CI |
| 1.1.1 Expulsion rate | 59           | 92      | 46         | 92      | 31.6%  | 1.97 [1.08, 3.58] |
| Iloh 2011         | 40           | 55      | 31         | 56      | 17.4%  | 2.15 [0.97, 4.76] |
| Sur 2014          | 60           | 115     | 52         | 117     | 51.1%  | 1.36 [0.81, 2.29] |
| Subtotal (95% CI) | 259          | 265     | 100.0%     |         |        | 1.69 [1.13, 2.49] |
| Total events      | 159          | 129     |            |         |        |                 |

Heterogeneity: Chi² = 1.26, df = 2 (P = 0.53); Ψ² = 0%
Test for overall effect: Z = 2.94 (P = 0.003)

Test for subgroups: Not applicable

Figure 3. Pooled results of the expulsion times between Silodosin and Placebo.

| Study or Subgroup | Experimental | Control | Mean Difference |
|-------------------|--------------|---------|-----------------|
|                   | Mean         | SD      | Total           | Mean         | SD      | Total           | Weight | IV. Fixed, 95% CI | IV. Fixed, 95% CI |
| Iloh 2011         | 10.27        | 8.35    | 89              | 15.19        | 7.14    | 82              | 48.4%  | -4.92 [-7.19, -2.65] |
| Iloh 2013         | 9.29         | 5.01    | 55              | 13.4         | 5.9     | 56              | 51.6%  | -4.11 [-6.31, -1.91] |
| Total (95% CI)    | 144          |         | 148             | 100.0%       | -4.50 [-6.08, -2.92] |

Heterogeneity: Chi² = 0.25, df = 1 (P = 0.62); Ψ² = 0%
Test for overall effect: Z = 3.59 (P < 0.00001)

Figure 4. Pooled results of the analgesics times between Silodosin and Placebo.

| Study or Subgroup | Experimental | Control | Mean Difference |
|-------------------|--------------|---------|-----------------|
|                   | Mean         | SD      | Total           | Mean         | SD      | Total           | Weight | IV. Fixed, 95% CI | IV. Fixed, 95% CI |
| Iloh 2011         | 0.9          | 3.8     | 89              | 1.7          | 3.2     | 82              | 40.5%  | -0.80 [-1.83, 0.23] |
| Iloh 2013         | 0.3          | 0.9     | 55              | 1.5          | 3.1     | 56              | 59.5%  | -1.20 [-2.05, -0.35] |
| Total (95% CI)    | 144          |         | 148             | 100.0%       | -1.04 [-1.69, -0.39] |

Heterogeneity: Chi² = 0.35, df = 1 (P = 0.56); Ψ² = 0%
Test for overall effect: Z = 3.12 (P = 0.002)

Figure 5. Pooled results of the expulsion rate between Silodosin and Placebo according to stone size.

| Study or Subgroup | Experimental | Control | Odds Ratio |
|-------------------|--------------|---------|------------|
|                   | Events       | Total   | Events     | Total   | M-H. Random, 95% CI | M-H. Random, 95% CI |
| 1.4.1 <5mm        | 36           | 45      | 36         | 46      | 26.4%  | 1.11 [0.40, 3.06] |
| Iloh 2011         | 18           | 26      | 28         | 28      | 21.7%  | 0.17 [0.03, 0.91] |
| Subtotal (95% CI) | 71           | 74      | 48.1%      |         |        | 0.49 [0.08, 3.04] |
| Total events      | 54           | 62      |            |         |        |                 |

Heterogeneity: Tau² = 1.25; Chi² = 3.54, df = 1 (P = 0.06); Ψ² = 72%
Test for overall effect: Z = 0.76 (P = 0.45)

1.4.2 ≥5mm
| Study or Subgroup | Experimental | Control | Odds Ratio |
|-------------------|--------------|---------|------------|
|                   | Events       | Total   | Events     | Total   | M-H. Random, 95% CI | M-H. Random, 95% CI |
| Iloh 2011         | 23           | 44      | 14         | 46      | 27.4%  | 2.50 [1.06, 5.93] |
| Iloh 2013         | 22           | 29      | 5          | 28      | 24.5%  | 14.46 [3.99, 52.41] |
| Subtotal (95% CI) | 73           | 74      | 51.9%      |         |        | 5.62 [1.01, 31.20] |
| Total events      | 45           | 19      |            |         |        |                 |

Heterogeneity: Tau² = 1.23; Chi² = 4.92, df = 1 (P = 0.03); Ψ² = 80%
Test for overall effect: Z = 1.97 (P = 0.05)

Total (95% CI)
| Study or Subgroup | Experimental | Control | Odds Ratio |
|-------------------|--------------|---------|------------|
|                   | Events       | Total   | Events     | Total   | M-H. Random, 95% CI | M-H. Random, 95% CI |
| Total events      | 99           | 81      |            |         |        |                 |

Heterogeneity: Tau² = 1.81; Chi² = 18.98, df = 3 (P = 0.0003); Ψ² = 84%
Test for overall effect: Z = 0.75 (P = 0.46)

Test for subgroups: Chi² = 3.64, df = 1 (P = 0.06), Ψ² = 72.6%
showed that there were higher incidence of retrograde ejaculation and nausea in Silodosin group than placebo group (OR = 8.60, 95% CI: 1.96–37.70, p = 0.004; OR = 4.48, 95% CI: 1.11–18.08, p = 0.04). Other AEs such as dizziness, headache, and nasal congestion, no difference was found between Silodosin group and placebo group.

**Silodosin versus tamsulosin**

Expulsion rate: Three studies reported the SER. Patients who underwent Silodosin treatment demonstrated a significant advantage over tamsulosin in terms of the SER (OR = 2.82, 95% CI [1.79–4.44], p < 0.00001). The result of the expulsion rate is depicted in Figure 8. An intent to treat sensitivity analysis where dropouts are analyzed as treatment failures showed only minor changes occurred (I² = 0%; OR = 2.61; 95% CI: 1.69–4.04).

Expulsion times: Two studies reported the stone expulsion times; because heterogeneity was observed in pooled analysis (p < 0.0001, I² = 94%), we performed meta-analysis by the random-effect model. The results of meta-analysis were showed in the Figure 9. The results of pooled meta-analysis demonstrated that there was no statistical difference in the expulsion times between Silodosin group and tamsulosin group (MD = – 4.25 days, 95% CI: – 9.44 to 0.94, p = 0.11).

The incidence of additional treatment: Two available studies’ data reported the incidence of additional treatment including SWL and URS (Figure 10). The results of pooled meta-analysis showed that the incidence of additional treatment was significantly lower in Silodosin.
group than that of tamsulosin group (OR = 0.37, 95% CI: 0.22–0.63, p = 0.0002).

The regarding treatment AEs: The results of pooled meta-analysis showed that AEs such as retrograde ejaculation, dizziness, headache, and orthostatic hypotension, no difference was found between Silodosin group and tamsulosin group.

Silodosin versus naftopidil

Only one RCT compared the efficacy of Silodosin with that of naftopidil for ureteral stones, so we could not perform meta-analysis. Tsuzaka et al. reported that the SER was 61% and 84% in the naftopidil and Silodosin groups, respectively (p = 0.038). There were no significant differences in stone expulsion time or the rate of interventions between the two groups. No serious side effects were found.

Publication bias

Begg’s funnel plot and Egger’s test were performed to assess publication bias. Egger’s test was used to provide statistical evidence for funnel plot symmetry. The shapes of the funnel plots did not reveal any evidence of obvious asymmetry in all comparisons; the Egger’s results did not show any evidence of publication bias.

Discussion

To our knowledge, this is the first the meta-analysis to study the efficacy of Silodosin for ureteral stones and to evaluate the difference between Silodosin and other α-blockers. Our meta-analysis suggests that Silodosin should be the first to be recommended as MET for distal ureteral stones. It significantly improves the SER, shortens the expulsion time, and reduces analgesic requirement and additional treatment (SWL or URS), and except for retrograde ejaculation, side effects were comparable between Silodosin and other α-blockers. In the present meta-analysis, our results also showed that the success rate of Silodosin was superior to placebo for distal
ureter when the stone size was 5–10 mm, while there was no benefit when the stone size <5 mm.

Tamsulosin is a combined alpha 1A- and alpha 1D-selective adrenergic antagonist, and alpha 1A and alpha 1D subtypes are the most common adrenoceptors in smooth-muscle cells of the human ureter. Tamsulosin initially was used to treat benign prostatic hyperplasia; subsequently, it is confirmed that it is an effective MET for ureteral stone. Similarly, Silodosin is a new alpha1A-blocker and has been approved by the US Food and Drug Administration for the treatment of BPH since October 2008. The previous meta-analysis showed that Silodosin is an effective therapy for lower urinary tract symptoms in men with BPH and is not inferior to tamsulosin. It is reported that ureteral contraction was regulated mainly by alpha-1A adrenoceptors in the hamster ureter. Furthermore, Silodosin was demonstrated to have a higher selectivity for the alpha1A-AR subtype than tamsulosin hydrochloride, naftopidil, or prazosin hydrochloride, and the alpha1A-to-alpha1D binding ratio of Silodosin is 56:1. Therefore, Silodosin may be a better MET for ureteral stones.

Seitz et al. performed a meta-analysis and found that there were higher and faster stone expulsion after receiving alpha-Blocker therapy and calcium channel blocker (RR =1.45 vs. 1.49). Another systematic review including 5864 participants showed that alpha-blockers have higher stone-free rates (RR =1.48), shorter stone expulsion time (MD = −2.91), and reduced the need for analgesic drugs (MD = −38.17 mg) compared with control. However, a recent multicenter, randomized, placebo-controlled trial indicated that there was no difference in stone clearance between tamsulosin 0.4 mg or nifedipine 30 mg and placebo (p = 0.78) during 4 weeks. Therefore, new MET therapy is needed for ureteral stones. In this meta-analysis, we found Silodosin had a higher stone clearance (Silodosin versus placebo, OR =1.69, p = 0.003). Because tamsulosin was the most commonly used to promote ureteral stones expulsion, we made a comparison Silodosin with tamsulosin. The results demonstrated that compared with tamsulosin, there was a 20% improvement of stone clearance in Silodosin group. For expulsion time, compared to control, other alpha-blockers could shorten 2.91 days and Silodosin could shorten 4.5 days. These data indicated that Silodosin is an effective MET for ureteral stones and superior to tamsulosin.

It is reported that stone size and location are important parameters for predicting MET-success. The definitive management of stones in these patients is usually deferred because approximately 68%–98% of stones <5 mm are expected to pass spontaneously. As stone size increases, however, spontaneous passage becomes less likely; the estimated spontaneous passage rate is 47% for stones >5 mm and <10 mm. There were 60.3% stone-free rate (SFR) in distal ureteral stone and 39.3% SFR in upper ureteral stone, respectively. In this meta-analysis, we found that the SFR of upper, middle, and distal ureteral stone were 45%, 43%, and 71%, respectively. Moreover, when the stone size was 5–10 mm, the SFR was 62% versus 26% (Silodosin versus water); while when the stone size <5 mm, the SFR was 76% versus 84% (Silodosin versus water). These findings demonstrated the meaningful effect of Silodosin for stone expulsion in distal ureteral stone when the size was 5–10 mm.

However, we also found the odds ratios were higher for Silodosin over tamsulosin when one would thought that it would be greater for Silodosin over placebo (OR =2.82 vs. 1.69); the cause may be that stones were mainly located at distal ureter in Silodosin over tamsulosin group, while stones were located at proximal, middle, and distal ureter in Silodosin over placebo group. Two studies reported the mean stone expulsion time was shorter in Silodosin than tamsulosin group, but the pooled results showed there was no difference because of different stone locations between the two studies, and the result should be carefully interpreted.

In the Tsuzaka et al.’s study, the mean stone size was 4.6 mm and 4.2 mm in naftopidil group and Silodosin group, respectively. And spontaneous stone expulsion was 61% (20/33) in naftopidil group and 84% (26/31) in Silodosin group. According to EAU Guideline, the spontaneous passage rate should be 68–98% for the stone size was less than 5 mm; however, the spontaneous passage rate of naftopidil group was lower than the patients who received no treatment, and there was no placebo control group, so whether Silodosin is superior to naftopidil or not should be further studied.

Seven trials reported adverse effects of Silodosin for ureteral stone, mainly including retrograde ejaculation (n = 6), dizziness (n = 3), orthostatic hypotension (n = 5), nausea (n = 2), and headache (n = 3). Overall, Silodosin was well tolerated and just mild adverse effects in most patients. In these trials, retrograde ejaculation was the most commonly reported adverse effects for Silodosin. From current meta-analysis, the incidence of retrograde ejaculation in Silodosin is obviously higher than that of placebo and it is equal to tamsulosin. As well as known, retrograde ejaculation is attributed to smooth muscle relaxation in the vas deferens, bladder neck, prostate, and urethra. It is reported that alpha1A-AR is mainly expressed in the bladder neck, vas deferens, and seminal vesicles, and mediates human vas deferens contraction. Therefore, this adverse effect may be...
explained by the high alpha1A-AR subtype selectivity of Silodosin.

Our systematic review has several limitations. First, these selected studies had a certain clinical heterogeneity which might bring a risk of bias and statistically moderate heterogeneity, and further affect the outcomes. These heterogeneities mainly resulted from the following factors: the difference in stone size and race, using different kinds of standard therapies and different doses or duration of treatment with Silodosin, different follow-up periods and measurement of the final outcomes, unclear or insufficient allocation concealment and blinding, variability in trial design and quality, and the existence of dropout patients. Second, except Sur et al.’s study, only studies with small numbers of patients with ureteral stones were available, and therefore the positive effects of Silodosin in ureteral stones need more large, multicenter RCTs to confirm. Third, we only included the data of published studies and the data of some studies were incomplete, such as some studies did not report the expulsion rate or expulsion time. In addition, we could not obtain relevant data, which may have introduced bias, which might have introduced bias in the interpretation of the results.

In summary, within the limits of available data, Silodosin appears to be more effective than either placebo or tamsulosin. In the future, high-quality multicenter RCTs are needed to thoroughly evaluate the outcome.

**Disclosure statement**

The authors declare that they have no conflict of interest.

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**References**

1. Papadoukakis S, Stolzenburg J-U, Truss MC. Treatment strategies of ureteral stones. *EAU-EBU Update Series.* 2006;4:184–190.
2. M M, BC P, GW D, et al. Urinary lithiasis: Etiology, diagnosis, diagnosis and management. In: Walsh PC, ed. *Campbell’s Urology.* 7th ed., Philadelphia, PA: Saunders; 1998:2661–2733.
3. Bihl G, Meyers A. Recurrent renal stone disease – Advances in pathogenesis and clinical management. *Lancet.* 2001;358:651–656.
4. Pearle MS, Calhoun EA, Curhan GC. Urologic diseases in America project: Urolithiasis. *J Urol.* 2005;173:848–857.
5. Kumar A, Mohanty NK, Jain M, et al. 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;24:2059–2066.
6. Campscherro T, Zhu Y, Duijves D, et al. Alpha-blockers as medical expulsive therapy for ureteral stones. *Cochrane Database Syst Rev.* 2014;4:CD008509.
7. Hollingsworth JM, Rogers MA, Kaufman SR, et al. Medical therapy to facilitate urinary stone passage: A meta-analysis. *Lancet.* 2006;368:1171–1179.
8. De Sio M, Autorino R, Di Lorenzo G, et al. Medical expulsive treatment of distal-ureteral stones using tamsulosin: A single-center experience. *J Endourol.* 2006;20:12–16.
9. Pedro RN, Hinck B, Hendlin K, et al. Alfuzosin stone expulsion therapy for distal ureteral calculi: A double-blind, placebo controlled study. *J Urol.* 2008;179:2244–2247. discussion 2247.
10. Zehri AA, Ather MH, Abbas F, et al. Preliminary study of efficacy of doxazosin as a medical expulsive therapy of distal ureteric stones in a randomized clinical trial. *Urology.* 2010;75:1285–1288.
11. Wang CJ, Huang SW, Chang CH. Efficacy of an alpha1 blocker in expulsive therapy of lower ureteral stones. *J Endourol.* 2008;22:41–46.
12. Pickard R, Starr K, MacLennan G, et al. Medical expulsive therapy in adults with ureteric colic: A multicentre, randomised, placebo-controlled trial. *Lancet.* 2015;386:341–349.
13. Sur RL, Shore N, L’Esperance J, et al. Silodosin to facilitate passage of ureteral stones: A multi-institutional, randomized, double-blinded, placebo-controlled trial. *Eur Urol.* 2015;67:959–964.
14. Itoh Y, Okada A, Yasui T, et al. Administration of the selective alpha 1A-adrenoceptor antagonist Silodosin facilitates expulsion of size 5-10 mm distal ureteral stones, as compared to control. *Int Urol Nephrol.* 2013;45:675–678.
15. Gupta S, Lodh B, Singh AK, et al. Comparing the efficacy of tamsulosin and silodosin in the medical expulsive therapy for ureteral calculi. *J Clin Diagn Res.* 2013;7:1672–1674.
16. Dell’Atti L. Silodosin versus tamsulosin as medical expulsive therapy for distal ureteral stones: A prospective randomized study. *Urologia.* 2015;82:54–57.
17. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: Is blinding necessary? *Control Clin Trials.* 1996;17:1–12.
18. Higgins J, Green S. Cochrane handbook for systematic reviews of interventions, version 5.0.2, updated September 2009. The Cochrane Collaboration 2009.
19. Kumar S, Jayant K, Agrawal MM, et al. 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.
20. Tuszaka Y, Matsushima H, Kaneko T, et al. Naftopidil vs silodosin in medical expulsive therapy for ureteral stones: A randomized controlled study in Japanese male patients. *Int J Urol.* 2011;18:792–795.
21. Itoh Y, Okada A, Yasui T, et al. Efficacy of selective a1A adrenoceptor antagonist silodosin in the medical expulsive therapy for ureteral stones. *Int J Urol.* 2011;18:672–674.
22. Sigala S, Dellabella M, Milanese G, et al. Evidence for the presence of alpha1 adrenocceptor subtypes in the human ureter. *Neurourol Urodyn.* 2005;24:142–148.

23. Schilit S, Benzeroual KE. Silodosin: A selective alpha1A-adrenergic receptor antagonist for the treatment of benign prostatic hyperplasia. *Clin Ther.* 2009;31:2489–2502.

24. Ding H, Du W, Hou ZZ, et al. Silodosin is effective for treatment of LUTS in men with BPH: A systematic review. *Asian J Androl.* 2013;15:121–128.

25. Tatemichi S, Tomiyama Y, Maruyama I, et al. Uroselectivity in male dogs of Silodosin (KMD-3213), a novel drug for the obstructive component of benign prostatic hyperplasia. *Neurourol Urodyn.* 2006;25:792–799. discussion 800–791.

26. Tatemichi S, Kobayashi K, Maezawa A, et al. [Alpha1-adrenocceptor subtype selectivity and organ specificity of Silodosin (KMD-3213)]. *Yakugaku Zasshi.* 2006;126:209–216.

27. Seitz C, Liatsikos E, Porpiglia F, et al. Medical therapy to facilitate the passage of stones: What is the evidence? *Eur Urol.* 2009;56:455–471.

28. Furyk JS, Chu K, Banks C, et al. Distal ureteric stones and tamsulosin: A double-blind, placebo-controlled, randomized, multicenter trial. *Ann Emerg Med.* 2015;67:86–95.

29. Tasian GE, Cost NG, Granberg CF, et al. Tamsulosin and spontaneous passage of ureteral stones in children: A multi-institutional cohort study. *J Urol.* 2014;192:506–511.

30. Fan B, Yang D, Wang J, et al. Can tamsulosin facilitate expulsion of ureteral stones? A meta-analysis of randomized controlled trials. *Int J Urol.* 2013;20:818–830.

31. Sahin C, Eryildirim B, Kafkasli A, et al. Predictive parameters for medical expulsive therapy in ureteral stones: A critical evaluation. *Urolithiasis.* 2015;43:271–275.

32. Phipps S, Tolley DA, Young JG, et al. The management of ureteric stones. *Ann R Coll Surg Engl.* 2010;92:368–372.

33. Preminger GM, Tiselius HG, Assimos DG, et al. 2007 Guideline for the management of ureteral calculi. *Eur Urol.* 2007;52:1610–1631.

34. Francesca F, Bader P, Echtle D, et al. EAU guidelines on pain management. *Eur Urol.* 2003;44:383–389.

35. Cummings JM, Boullier JA, Izenberg SD, et al. Prediction of spontaneous ureteral calculous passage by an artificial neural network. *J Urol.* 2000;164:326–328.

36. Preminger GM, Tiselius HG, Assimos DG, et al. 2007 guideline for the management of ureteral calculi. *J Urol.* 2007;178:2418–2434.

37. Rossi M, Roumeguere T. Silodosin in the treatment of benign prostatic hyperplasia. *Drug Des Devel Ther.* 2010;4:291–297.

38. Moriyama N, Nasu K, Takeuchi T, et al. Quantification and distribution of alpha 1-adrenocceptor subtype mRNAs in human vas deferens: Comparison with those of epididymal and pelvic portions. *Br J Pharmacol.* 1997;122:1009–1014.