Section: Urology

Research

SILODOSIN AS A MEDICAL EXPULSIVE THERAPY FOR DISTAL URETERAL CALCULI: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Abstract

Background: This systematic review and meta-analysis of randomized controlled trials was performed to determine the therapeutic effects and safety profile of silodosin for medical expulsive therapy (MET) of ureteral stones. **Materials and Methods:** We searched PubMed, EMBASE, the Cochrane library, and Web of science to identify articles published before March 2022 that described randomized controlled trials comparing silodosin and tamsulosin for MET of ureteral stones. Five RCTs with a total of 1145 ureteral stone patients (300 patients in the control group, 287 patients in the tamsulosin group, 558 patients in the silodosin group) were included in this meta-analysis. **Result:** Silodosin showed a significantly improved expulsion rate of distal ureteral stones (RR: 1.42; 95% CI, 1.21–1.67; P < 0.0001), while there was no significant difference between silodosin and the control in expulsion rate of proximal (RR: 0.99; 95% CI, 0.69–1.43; P < 0.97) or mid (RR: 1.13; 95% CI, 0.60– 2.16; P < 0.0001) ureteral stones and in the occurrence of retrograde ejaculation (RR: 1.85; 95% CI, 0.95–3.59; P = 0.07) in MET for distal ureteral stones. However, silodosin provided a significantly higher expulsion (RR: 1.25; 95% CI, 1.13–1.37; P < 0.0001) than tamsulosin for distal ureteral stones. **Conclusion:** Silodosin significantly improved expulsion rate of distal ureteral stones and was clinically superior to tamsulosin.

INTRODUCTION

One of the most prevalent diseases in contemporary culture, stone disease has been found in 5–10% of people worldwide.[1] Ureteral stones account for 14% of urinary tract stones, the majority of which are located at the distal ureter.[2] Additionally, ureteral calculi are becoming more common, which places a greater financial strain on contemporary society.[3] The distal ureteral stone therapy guidelines from the European Association of Urology include alpha -1 receptor blockers.[4] The ureteral smooth muscle can relax and the ureteral lumen can enlarge as a result of inhibiting the alpha -1 adrenergic receptor, which ultimately promotes stone propagation. Tamsulosin has been shown to effectively increase the expulsion rate and decrease the expulsion time since it blocks both alpha -1A and alpha-1D receptors equally. The selective alpha adrenergic receptor blocker silodosin, which was just recently developed, has a substantially higher selectivity for the alpha-1A receptor. Silodosin may be more effective and cause fewer side effects in MET due to its special feature.[5] Studies examining the effectiveness and safety of silodosin and tamsulosin in the treatment of ureteral stones have been published; however, it is debatable whether silodosin is more effective than tamsulosin in MET.[4] This review's goal was to compare the effectiveness and safety of silodosin with tamsulosin in MET for ureteral stones.

MATERIALS AND METHODS

This systematic review is carried out according to the Preferred Reporting Items for Systematic reviews and Meta- Analysis (PRISMA) guidelines.[6]

Literature search and study selection [Figure 1]

To find pertinent papers, we searched electronic databases including PubMed, Embase, Medline, the Cochrane Library, and Google Scholar until March 2022. The keywords "silodosin" or "selective alpha 1 A-adrenoceptor antagonist" and "ureterolithiasis" or "medical expulsive therapy" or "ureteral stone" or

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"stones" or "stones" or "ureteric calculi" or "calculi" were used in conjunction. For each database, we modified our search approach. In order to find more research papers that might be suitable; We also looked at the references in pertinent papers. Studies that satisfy the following selection criteria were included: (1)Study's design, (2) population, (3) intervention, (4) comparison of kidney/ureter/bladder radiography (KUB) and/or computed tomography (CT) in patients aged 18 years and above with ureteral stones of less than 10mm and (5) outcomes: stone expulsion rate, stone expulsion time, analgesic use and retrograde ejaculation rate.

The following information was taken from the studies that were included: features of the studies, characteristics of the patients who were included, and outcomes of the studies. The ejection rate served as the main endpoint. The retrograde ejaculation rate, expulsion time, and nalgesic use served as the secondary objectives.

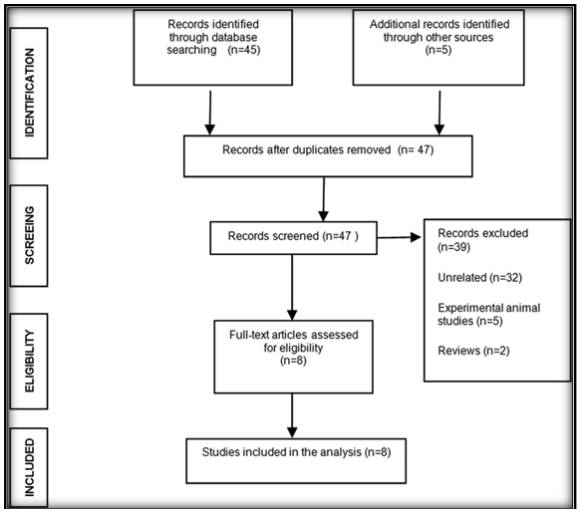

Figure 1: PRISMA and flow of study selection

Statistical Analysis

Utilizing the software Review Manager, statistical analysis was carried out (RevMan v.5.2, Cochrane Collaboration, Oxford, UK). With statistical significance set at(P <0.01), the conventional Chi-squared test was used to evaluate the heterogeneity between trials. The I2 statistic was used to measure heterogeneity; significance was reached when I2 was more than 50%. The random-effects model was employed for statistical analysis due to the trials' large range of clinical and methodological heterogeneity. Funnel plots were used to assess publication bias. In this meta-analysis, statistical significance for other parameters was defined as P <0.05.

RESULTS

As per [Table 1] the main study characteristics of the eight included RCT trials are shown. The dose of silodosin and tamsulosin was the same across the selected studies. Plain X-ray and/or CT scan were used for the evaluation of stone in all RCTs. Follow-up was continued, until the stone has passed or intervention occurred, for a maximum of 4 weeks in all studies methodological quality of included studies was relatively high for two RCTs (Jadadscore : 5 of 5 points) and medium for the rest.

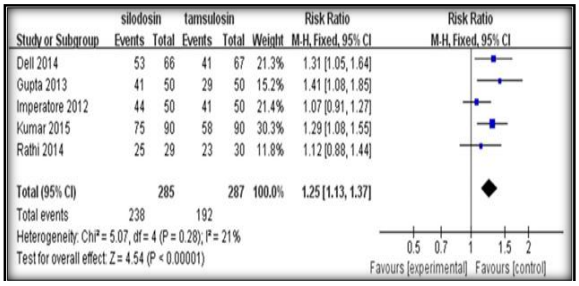

Figure 2: Forest plot representing analysis of expulsion rate between silodosin and tamsulosin

As per [Figure 2] and [Figure 3] five of the selected eight studies compared the efficacy and safety of silodosin and tamsulosin only in MET of distal ureteral stones, which consists of 572 patients. Silodosin provided a significantly higher expulsion rate than tamsulosin (RR: 1.25; 95% CI, 1.13–1.37; P < 0.0001) [Figure 2] in MET for distal ureteral stones, with low heterogeneity among studies (I2 = 21%, P = 0.28) and retrograde ejaculation rate (RR: 1.85; 95% CI, 0.95–3.59; P = 0.07) [Figure 3] in MET for distal ureteral stones.

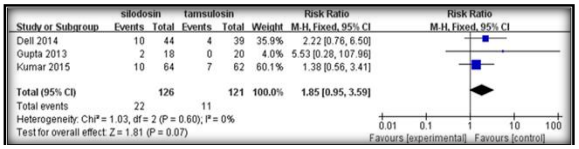

Figure 3: Forrest plot representing analysis of retrograde ejaculation between silodosin tamsulosin

Table 1: Included Studies for Summary

StudyJadad score	Country Design Participants	Intervention	Outcomes
Itoh 2011[7]	JapanRCT112 male patients: unilateraldistal ureteral calculi of less 10 mm	Silodosin group(n = 56): 8 mg daily; Control group (n = 56): drink 2L of water daily	Expulsion rate;expulsion time;analgesic3use;adverse event
Sur 2014[8]	America RCT246 patients: unilateral Caculus of 4–10mm. Subgroup: proximal ureteral calculus(n = 74);midure- teralcalculus(n = 41); distal ureteral calculus(n = 111)	Sillodosin group (n = 122): 8 mg daily; control group (n = 124): placebo	Expulsion rate;adverse event
Gupta 2013[9]	IndiaRCT100 patients: unilateral non-impacted distal ureteral stones of less	Silodosin group (n = 50): 8 mg daily; tamsu- losin group (n =	Expulsion rate;expulsion time;adverse 3event;

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	10 mm	50): 0.4 mg daily	analgesic use
Kumar 2015,[10]	IndiaRCT180 patients: distal ureteral stone of5–10 mm	Silodosin group (n = 90): 8 mg daily; tamsu- losin group (n = 90): 0.4 mg daily	Expulsion rate;expulsion time;adverse5event;analgesic use
Imperatore 2012,[11]	ItalyRCT100 patients: single unilateral radiopaque distal ureteric stone of less 10 mm	Silodosin group (n = 50): 8 mg daily; tamsu- losin group (n = 50): 0.4 mg daily	Expulsion rate;expulsion time;adverse2event;analgesic use

Table 2: Sensitivity analysis and Publication Bias

Study	RR (95%CI)	I2	P
Dell(2014)	1.23	32	0.21
Gupta (2013)	1.22	14	0.11
Imperatore (2012)	1.20	4	0.34
Kumar (2015)	1.30	32	0.43

As per [Table 2] the findings of expulsion rate in our Meta analysis remained constant despite the exclusion of any single study. [Table 2] shows the outcomes of sensitivity analysis. The quantity of included studies was not sufficient to evaluate publication bias.

DISCUSSION

According to a recent meta-analysis by Huang et al,[12] silodosin was more effective than a placebo or tamsulosin at treating distal ureteral calculi and better at controlling pain. Silodosin's safety profile was similar to that of tamsulosin, though it caused worse retrograde ejaculation when used. They did not, however, conduct a subgroup analysis taking into account the location of ureteral stones (proximal, mid or distal ureteral stones). Consequently, use a fixed-effect model and you will arrive at different conclusions. The studies of Imperatore et al,[11] to examine the expulsion time and analgesic use, as well as Gupta et al,[9] to examine the retrograde ejaculation rate, were not included by Huang et al,[12]though we did. Our meta-analysis suggests that silodosin significantly improves the passage rate of dista ureteral stones and is clinically superior to tamsulosin in MET; silodosin was ineffective in MET for proximal and mid ureteral stones.

Tamsulosin and silodosin are equally successful in MET for distal ureteral stones that are 10 mm or smaller, according to a 2012 study by Imperatoreet al.[18] According to Kumar et al. (2015), silodosin had a substantially greater expulsion rate (83.3%) than tamsulosin (64.4%).[10] Effectiveness of silodosin in MET and the effectiveness of silodosin and tamsulosin in MET for distal ureteral stones must therefore be confirmed through a meta-analysis.

Tamsulosin was found to have a considerably higher stone expulsion rate and shorter expulsion time in proximal ureteral calculi 6 mm when compared to conservative managements alone, according to a study by Lee et al. (2014).[13] According to Sur et al. (2014), there were no appreciable differences in the passing rate of proximal or mid-ureteral stones between the silodosin and placebo groups. Silodosin, however, significantly increased the transit rate of distal ureteral stones compared to placebo (P = 0.01).[11] The effectiveness of alpha-blockers for proximal or mid ureteral stone evacuation requires further RCT research.

In MET for distal ureteral stones, silodosin outperformed tamsulosin clinically. Low heterogeneity was seen among the five trials. The results of our meta-analysis are robust, according to sensitivity analysis. Tsuzaka et al. might therefore put their trust in this finding (2011). In our meta-analysis, we discovered no statistically significant difference between tamsulosin and silodosin in the rate of retrograde ejaculation in MET for distal ureteral stones.[14]

CONCLUSION

In MET for distal ureteral stones, silodosin outperformed tamsulosin clinically. In MET, silodosin had no effect on proximal or mid-ureteral stones. Additionally, randomized controlled trials are required to assess silodosin's function in MET for ureteral stones.

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