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]
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 α1-adrenergic receptors, specifically the α1D 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.
Table 1: Characteristics of Included Studies

<table>
<thead>
<tr>
<th>Study Authors</th>
<th>Study Year</th>
<th>Study Type</th>
<th>Participants (n)</th>
<th>Discussion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jung et al.</td>
<td>Dec 2022</td>
<td>Systematic review, meta-analysis, and RCT</td>
<td>14</td>
<td>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.</td>
</tr>
<tr>
<td>Hsu Y-P et al.</td>
<td>August 2018</td>
<td>A Systematic review, and meta-analysis</td>
<td>1812</td>
<td>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.</td>
</tr>
<tr>
<td>Huang et al.</td>
<td>2015</td>
<td>A Systematic review, and meta-analysis</td>
<td>413</td>
<td>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.</td>
</tr>
<tr>
<td>Ozsoy et al.</td>
<td>March 2016</td>
<td>A Systematic review, and meta-analysis</td>
<td>407</td>
<td>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.</td>
</tr>
<tr>
<td>Yu Z-W et al.</td>
<td>August 2021</td>
<td>Meta-analyses</td>
<td>917</td>
<td>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.</td>
</tr>
<tr>
<td>Ramadhani et al.</td>
<td>Dec 2022</td>
<td>Systematic review, and meta-analysis</td>
<td>474</td>
<td>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.</td>
</tr>
<tr>
<td>Sharma et al.</td>
<td>Jun 2020</td>
<td>A Systematic review, and meta-analysis</td>
<td>7077 patients (from 31 RCTs)</td>
<td>Silodosin had the highest Stone Expulsion Rate (SER) with a SU CRA value of 94.8, followed by tamsulosin at 46.2. Silodosin emerged as the most efficacious drug for medical expulsive...</td>
</tr>
<tr>
<td>Study Reference</td>
<td>Date</td>
<td>Study Design</td>
<td>Study Size</td>
<td>Results</td>
</tr>
<tr>
<td>-----------------</td>
<td>------</td>
<td>--------------</td>
<td>------------</td>
<td>---------</td>
</tr>
<tr>
<td>Abdullah et al. [15]</td>
<td>Oct 2023</td>
<td>Comparative study</td>
<td>80</td>
<td>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.</td>
</tr>
<tr>
<td>Elgalaly et al. [16]</td>
<td>Dec 2015</td>
<td>Prospective randomized study</td>
<td>103 (Group A= 52; Group B= 51)</td>
<td>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.</td>
</tr>
<tr>
<td>Imperatore et al. [17]</td>
<td>Jan 2014</td>
<td>Retrospective observational study</td>
<td>100</td>
<td>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 &gt; 5 mm, respectively.</td>
</tr>
<tr>
<td>Gharib et al. [18]</td>
<td>July 2018</td>
<td>Comparative study</td>
<td>150</td>
<td>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.</td>
</tr>
</tbody>
</table>

**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. 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. 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 ± 0.9) and 1.7 (SD ± 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 medical expulsive therapy of ureteral stones: a systematic review and meta-analysis of placebo-controlled trials. A meta-analysis of placebo-controlled trials. Medicine (Baltimore) 2021;100:e27272. https://doi.org/10.1097/MD.0000000000002727.

REFERENCES

