www.jmscr.igmpublication.org
Impact Factor 5.84
Index Copernicus Value: 71.58
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v5i12.106

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Comparative Efficacy of Silodosin vs Tamsulosin for Ureteric Calculus: A Single Centre Double Blind Randomised Controlled Trial

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Abstract
Background: *Ureteric calculus is now emerging as a major health concern irrespective of age of the patient due to the lifestyle changes. It can be managed both medically (MET) and surgically depending on various factors like it's size number, site and comorbidities of patient. For Medical expulsion therapy we use α-blockers like tamsulosin, terazosin, doxazosin, silodosinetc but the effectiveness varies with each drug. So in this study we aim to compare the success rates of silodosin to tamsulosin for medical expulsive therapy of ureteral stones.*
Aim: *As per many urological guidelines the patient can be started on MET unless there is absolute indication for intervention. Selective alfa 1 -adrenergic antagonists are now first-line drugs in MET. We conducted a prospective single-blind, parallel group, randomized, controlled trial to compare the effectiveness and safety of the alfa 1 –blocker silodosin versus tamsulosin in the treatment ureteric calculus.*
Materials and Methods: *For this prospective single centre, double blind, randomised, placebo-controlled trial, our study group included adults aged 18-65 years undergoing expectant management for a single ureteric stone identified by CT. Participants were randomly assigned in a 1:1 ratio to tamsulosin 400 µg or silodosin 8 mg taken daily for up to 2 weeks. The primary outcome was the proportion of participants who did not need further intervention for stone clearance within 2 weeks. 173 patients were studied from October 2014 to July 2017 at VIMS, Ballari. This study was done after due clearance from ethical committee.*
Results: *In our present study, the stone clearance rate was significantly higher in the silodosin group compared with the tamsulosin group, at 53% and 34%, respectively (P = 0.009). The status of stones was re assessed after 2 weeks using NCCT-KUB as the diagnostic modality. Those patients who could not expel stones after 2 weeks of MET were subjected to Ureteroscopic removal of stone.*
Conclusions: *In conclusion, silodosin is more effective than tamsulosin as MET (Medical Expulsive Therapy) for ureteric calculus.*
Keywords: *Ureteric calculus, MET (Medical expulsion therapy).*

Introduction

Ureteral stones account for 22 % of all urinary tract stones with 68 % of them being located in the distal ureter[1]. Conservative management strategies such as observation or medical expulsive therapy (MET) using pharmacological agents to facilitate spontaneous passage of ureteral stones have gained popularity in the management of ureteral stones during the recent years[2]. Stones <10 mm can be considered to pass spontaneously [3].

The mechanism of action behind the above effects is associated with the presence of adrenergic receptors (ARs) in the ureteric smooth muscle cells with the α1-adrenergic receptors to be the most abundant [4]. α1A-, α1B- and α1D-ARs are the three types of α1-ARs that are expressed in the human ureter with the following order of abundance α1D > α1A > α1B. The blocking of these receptors results in selective relaxation of the ureteric smooth muscle and, therefore, causes ureteric lumen dilatation. The latter phenomenon results in facilitation of stone expulsion.[5-7].

The most commonly used α-blocker for MET is tamsulosin, but similar effects have been shown by other α-blockers such as terazosin, doxazosin & silodosin, indicating a possible class effect [3]. Silodosin has been also proposed for MET instead of tamsulosin but studies comparing these substances for MET are scarce. In this RCT we aim to compare the success rates of silodosin to tamsulosin for MET of ureteral stones.

Ureteroscopy and SWL remain the most effective treatments for ureteric calculus; however, they are expensive and not risk free. Spontaneous stone expulsion can occur in up to 50% of cases, nevertheless, many complications such as ureteric colic, UTI, and hydronephrosis, may occur. Recently, the use of various adjuvant medications as MET for ureteric calculus has helped to reduce pain, complications, and increase the rate of stone clearance [8], [9].

Highly selective α_{1A}-adrenoceptor blockers have been developed to minimise the cardiovascular adverse effects while maintaining their efficacy on the urinary tract [10]. Tamsulosin is a selective α_1-blocker with a 10-fold greater affinity for the α_{1A}- and α_{1D}-adrenoceptor subtypes than for the α_{1B}-adrenoceptor subtype, while the affinity of silodosin for the α_{1A}-adrenoceptor subtype is ≈162- and 50-fold greater than its affinity for the α_{1B}- and α_{1D}-adrenoceptor subtypes respectively, which explain the weak cardiovascular adverse effects of silodosin [10].

Several factors can affect spontaneous stone clearance of ureteric calculus including: stone size, site, number, and also the presence or absence of ureteric smooth muscle spasm and/or submucosaloedema. Coll et al. [11], found a direct relationship between stone size and spontaneous clearance.

Aims and Objectives

As per many urological guidelines the patient can be started on MET unless there is absolute indication for intervention. Selective alfa $_1$ -adrenergic antagonists are now first-line drugs in MET. We conducted a prospective single-blind, parallel group, randomized, controlled trial to compare the effectiveness and safety of the alfa $_1$ -blocker silodosin versus tamsulosin in the treatment ureteric calculus.

Materials and Methods

This is a single centre, double-blind, placebo-controlled, randomized trial evaluating two MET treatments (silodosin or tamsulosin). 173 patients were studied from October 2014 to July 2017 at VIMS, Ballari.

Inclusion criteria

- Patients presenting acutely with ureteric colic.
- Adults between 18 and 65 years of age (inclusive).
- Presence of stone already confirmed by non-contrast computed tomography of the kidney, ureter and bladder (CTKUB).
- Stone within any segment of the ureter.
- Unilateral ureteric stone.
- Largest dimension of the stone ≤10 mm.

- Capable of giving written informed consent, which includes compliance with the requirements of the trial.

Asymptomatic incidentally found ureteric stone

Exclusion criteria

- Women who have a known or suspected pregnancy (confirmed by a pregnancy test).
- Women who are breastfeeding.
- Stone with any one dimension >10 mm.
- Multiple (that is ≥ 2) stones within ureter.
- Bilateral ureteric stones.
- Stone in a ureter draining a solitary kidney (either anatomically or functionally).
- Patients with abnormal renal tract anatomy (such as a duplex system, horseshoe kidney or ileal conduit).
- Presence of urinary sepsis.
- Chronic kidney disease stage 4 or stage 5 (estimated glomerular filtration rate < 30 ml/min).
- Patients currently taking an α-blocker.
- Patients currently taking a calcium-channel blocker.
- Patients currently taking PDE5 inhibitors.
- Patients who are unable to understand or complete trial documentation.

Randomization and Allocation

Eligible and consenting participants will be randomized to one of the two intervention groups on a 1:1 basis. Upon randomization, the participants were allocated a unique participant study number and assigned a numbered participant pack containing over-encapsulated trial medication to ensure that the participant &investigator remain blind to treatment.

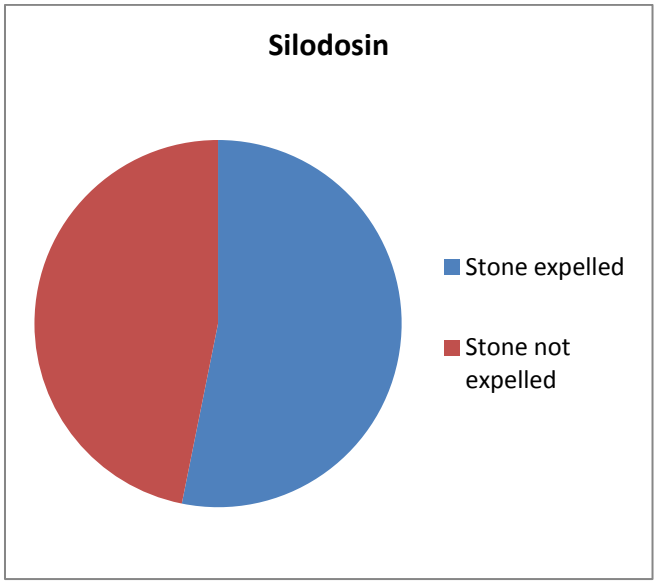
Outcome measures

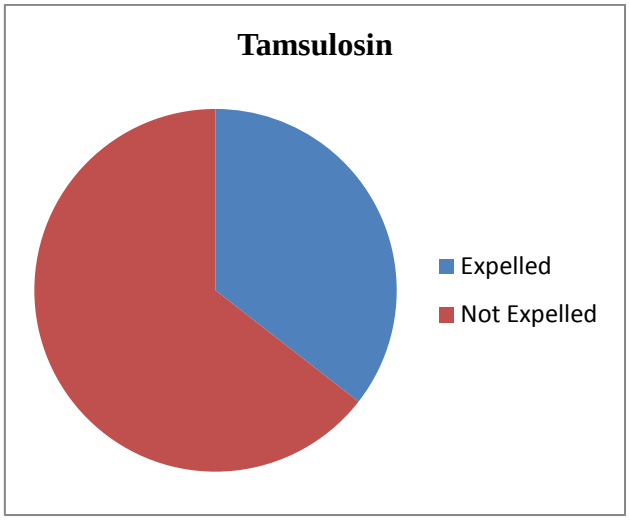
The primary outcome is spontaneous passage of ureteric stones at 2 weeks (defined as no further intervention required to facilitate stone passage).

Observations

Treatment	Silodosin	Tamsulosin	Total
Expelled	42	27	69
Not expelled	37	51	88
Total	79	78	157

As per statistical analysis using Yates Corrected Chi square test the p value was found to be 0.009. p value being less than 0.05 is statistically significant. As per this study Silodosin was found to be much more effective than Tamsulosin as a modality of Medical expulsive Therapy.





Result

173 patients were studied from October 2014 to July 2017 at VIMS, Ballari. 16 patients were excluded from study as per exclusion criteria. Spontaenous stone passage on MET was noted in 42 of the 79 patients on Silodosin. The same

expulsion was not seen with Tamsulosin which showed an expulsion in 27 patients out of a total of 78 patients studied. Patients with non expelled stones after 2 weeks of MET were subjected to intervention in the form of URS (Ureteroscopic Removal of Stone).

Discussion

In our present study, the stone clearance rate was significantly higher in the silodosin group compared with the tamsulosin group, at 53% and 34%, respectively ($P = 0.009$). Our results are in agreement with those of Gupta et al.[12], who reported stone clearance rates of 82% and 58% for their silodosin and tamsulosin groups, respectively; and also in agreement with those of Kumar et al. [13], who reported stone clearance rates of 83.3% and 64.4% for their silodosin and tamsulosin groups, respectively. However, Imperatore et al. [14] reported a nonsignificant difference of stone clearance rates between silodosin (88%) and tamsulosin (84%). While Sur et al. [15] reported a stone clearance rate of 52% with silodosin treatment of all ureteric stones (upper, middle and lower), which may reduce the overall efficacy as α-receptors are more abundant in the distal ureter. But most of the quoted studies have shown an expulsion rate of >80% with Silodosin whereas in our study the rate of stone expulsion was much lower at 53%.

In conclusion from our study SILODOSIN is found to be more effective than TAMSULOSIN as medical expulsive therapy for treatment of ureteric calculus.

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