COMPARISON OF SILODOSIN AND TAMSULOSIN USED AS MEDICAL EXPULSIVE THERAPY FOR URETERAL STONES.

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Supervisor's Certificate

I hereby certify that Dr. Faiza Khan having R & RC Enrolment no PHR- 2022-059-25, has been working under my direct supervision with effect from 1-1-2022 to 1-1-2024 in the department of Pharmacology and therapeutics in training institution, Fatima Jinnah Medical University, Lahore.

The enclosed thesis titled, "**COMPARISON OF SILODOSIN AND TAMSULOSIN USED AS MEDICAL EXPULSIVE THERAPY FOR URETERAL STONES"** is prepared according to the guidelines for thesis writing by CPSP. I have read the thesis and found it satisfactory for the FCPS examination in this subject.

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LIST OF ABBREVIATIONS

AUA	American Urology Association
EAU	European Association of Urology
MET	Medical expulsive therapy
PNL	Percutaneous Nephrolithotomy
RCTs	Randomized controlled clinical trials
SPSS	Statistical Package for the Social Sciences
α-AR	Alpha adrenergic receptor
LUTS	Lower Urinary Tract Symptoms

SWL	Shock wave lithotripsy
ESWL	Extracorporeal Shock Wave Lithotripsy
CKD	Chronic kidney disease
SET	Stone ejection time
USD	Ureteric stone disease
SER	Stone ejection rate

Abstract

Introduction: Ureteric stones is a very common disease world over. Medical Expulsive therapy (MET) for stones is a recognized treatment option practiced. Tamsulosin is used commonly in our population for MET however Silodosin another highly uroselective newer drug, with lesser side effects, is not used frequently for this purpose and is still under research. Both of these drugs lead to relaxation of lower ureteric smooth muscle hence facilitate in stone removal.

The rationale of this study is to compare the efficacy of Tamsulosin and Silodosin in MET (medical expulsive therapy) with regards to stone expulsion rate as well as to compare the side effect profile in our population.

Methodology: This is a prospective randomized control trial in Outpatient department of Sir Ganga Ram hospital, Lahore, on 208 patients with ureteric stone who fulfil the inclusion criterion, divided randomly into two groups with 104 patients in the Tamsulosin group and 104 patients in Silodosin group (1:1 ratio). However, 16 patients were subsequently excluded on account of premature end of study, and 12 due to being lost to follow-up (Figure 1). Out of remaining 180 patients 89 were of Tamsulosin and 93 were in Silodosin group. Demographic data including patients' age and comorbid, stone-related data including size, location, laterality and number of stones and duration of symptoms were recorded. The patients were called for follow up at 4 weeks

with an X-ray KUB without bowel preparation. We noted if the stone had passed or not.

Results: Our results showed that Silodosin turned out to be better in expulsing stone as well as in producing lesser side effects and hence better safety profile than Tamsulosin. Silodosin showed greater stone expulsion rate with about 55 patients expulsing stone in less than 14 days in comparison to just about 5 patients on Tamsulosin. Similarly, patients on Silodosin, showed lesser side effects as compared to Tamsulosin. Nine patients on tamsulosin (60.0%) and six patients on silodosin (40.0%) developed orthostatic hypotension. Only a very tiny percentage of patients reported abnormal ejaculation; two individuals on tamsulosin (66.7%) and one patient on silodosin (33.3%). Another side effect that was identified involved headaches, seen by four patients on silodosin (44.4%) and five patients on tamsulosin (55.6%).

INTRODUCTION

Stone disease is one of the most frequent presentations in the field of urology. A large number of these patients arrive with ureteric stones(1). Globally, occurrence of stone formation is 10-12% for men and 6-8% for women. Its prevalence in Pakistan is approximately 16%. The disease's burden has increased in all age categories and both genders over the past 20 years(2). The incidence of urolithiasis in different age groups is 12.2% in the persons 20-29 year old, 29.6% in those who are 30-39-year-old, and 31.5% in 40–49-year-old patients(3).

Medical management ae well as surgical removal are various options available for treating ureteric stones as per American Urology Association (AUA) and European Association of Urology (EAU) guidelines. However, due to risks of surgical approaches there is always an attempt for treatment by using medical expulsive treatment (MET) for ureteric stones first keeping in view different parameters. According to European Association of Urology Guidelines (EAU), the ureteric stones less than 10 mm can be treated with MET(4).

Medical expulsive therapy (MET) is a well-established treatment option for distal ureteric stones, despite a sharp increase in minimally invasive techniques(5). Stones smaller than 5 mm have passage rates ranging from 71% to 98%, while stones with size more than 5 mm had expulsion rates ranging from 25% to 53%(6).

Many factors affect stone removal and must be considered while selecting MET for stones like ureteric spasm, location, size, and number of stones and duration for which it is present and also the ureteric architecture etc(7).

Distal part of the ureter contains a large number of alpha-1 receptors (8).The physiological effect of blocking these receptors is, reduction in peristalsis and force of contraction of ureter (hence aiding in lessening of ureteric spasm), and increased volume of fluid carried down the ureter. These effects help in removing ureteral stones(9).

Tamsulosin an α1A-receptor and α1D- blocker is used commonly for ureteric stones removal in our population. This drug has its side effects like postural hypotension, retrograde ejaculation, headache, etc.(10).

Another highly uroselective drug silodosin which is α1A-receptor antagonist has also been used for this purpose in many countries and due to its highly selective nature, it is found to have lesser side effects. Both of these drugs lead to relaxation of lower ureteric smooth muscle(11).

A systematic review from various data base of science was undertaken to check the effectiveness of the alpha blockers including tamsulosin and silodosin for urinary tract stones. Silodosin was found to be the most effective drug in treating urinary tract stones followed by tamsulosin (10).

Another systematic review and meta-analysis from 2018, from EMBASE, PubMed, Scopus databases and Cochrane library also compared the same effect and concluded that silodosin had better efficacy in expulsion of the stone and also better pain relief(12).

Tamsulosin is used commonly in our population for MET however Silodosin, a newer drug, is not used frequently for this purpose and is still under research. Also, comparison of Silodosin and Tamsulosin has not been explored in our population earlier.

The rationale of this study is to compare the efficacy of Tamsulosin and Silodosin in MET (medical expulsive therapy) with regards to stone expulsion rate as well as to compare the side effect profile in our population.

LITERATURE REVIEW

Background

Ureteric stone is a very common presentation in urology practice (1). One of the most prevalent genito-urinary tract disorders, urolithiasis affects between 5 and 15% of the global population. Since almost 50% of affected patients will experience a recurrence within five years, the illness is lifelong (13).

Prevelance

Worldwide prevalence

Urolithiasis has been more common in the past few years. Its frequency ranges from 1 to 5% in Asia to 7 to 13% and 5 to 9%, respectively, in North America and Europe.

Another study showed nephrolithiasis prevalence varies greatly across the globe. According to estimates, it is 8,8% in the US, 10% in Spain, 9% in Italy, 15% in Greece, 14,8% in Turkey, 10% in Japan, 5% in South Korea, 2.5–9.6% in China, 20% in Saudi Arabia, and 3.96% in Argentina. Furthermore, there has the prevalence of KS has steadily increased during the past few decades. For example, the estimated prevalence of USD in England increased from 7.14 to

11.62% in the first decade of this century, and therapies linked to this condition increased as well(14).

Worldwide prevalence of stone formation in males is 10- 12% (2). Additionally, however, it is becoming more common in females in recent times and is about 6-8%.

Each country has a particular male to female ratio, which is balanced between males and women or marginally in the countries of Europe, South America, North America, and China, but skewed significantly in favor of men in Iraq, Egypt, Pakistan, and India. This resulted in the confirmation of the tendency toward increased stone formation in women from Western countries (9), and more recently from China. In contrast, the male-to-female ratio in Egypt, Pakistan, India, and Iraq remains unchanged from forty years ago(15).

Prevalence in Pakistan

In Pakistan approximately 16%. Patients are of ureteric stone. Over the past few years there is an increase in the prevalence of disease in all age groups as well as in both genders (2).

A study showed, in Pakistan, urolithiasis affects between 1–5% of people. The prevalence of asymptomatic stones was determined to be 2.8% in that study,

which is in line with the findings of earlier research studies. Stones typically don't say anything at first, but over time, they begin to cause symptoms for the person who has them. Typical symptoms include nausea, vomiting, hematuria, restlessness, urine urgency, and flank discomfort (renal colic). Research indicates that approximately 20% of patients experience symptoms of urinary tract stones over the course of a decade(16).

Additionally, a study conducted in Pakistan found that the general population has a 3% prevalence and a 5% chance of silent stones(16).

In different age groups the incidence of urolithiasis is around 30% in 40-49 year-old persons, around 28-29% in those who are 30-39 year-old, and around 13% in persons of 20-29 year age(3).

According to another study, male patients had greater rates of urolithiasis than female patients. Similar results were obtained by other researchers [18] in their investigation, with male to female ratios of 3.3:1, 1.35:1, and 1.8:1, respectively. The explanation for the increased frequency in male patients may be because androgens, which are more prevalent in men than in women, encourage the production of stones. Estrogens, on the other hand, repress stone formation(17).

Risk Factors

The development of ureteric calculi is influenced by an unknown number of predisposing variables. Dietary practices, hydration levels, and coexisting conditions such as obesity and diabetes mellitus are significant contributors to its etiopathogenesis. Though several hypotheses have been put up to explain the genesis and progression of urologic calculi, none have been able to provide a comprehensive response to the questions surrounding the formation of stones(18).

Urolithiasis development is aided by bacteria. Ammonium urate, magnesium ammonium phosphate, and carbonate apatite are the constituents of infection stones that are formed by urease-producing bacteria infections that persist. However, non-infection stones like calcium phosphate and oxalate may serve as a breeding ground for bacteria. Layers of urine bacteria are incorporated into the growth of urinary stones. According to our univariate analysis, patients with urosepsis were more likely than those in the non-urosepsis group to have infection stones, as well as positive urine and stone cultures. These findings suggest that the urosepsis group in this study had a persistent UTI prior to the bacteria forming ureteral stones(19).

Most Common Presenting Complaint

Most common symptom with which patients of ureteric stone present is colicky pain in lumbar region(20). In addition to incidental findings, urolithiasis can manifest as fever, nausea, vomiting, and loin discomfort. If a patient exhibits symptoms that point to an infection or a single kidney, they ought to be investigated immediately. Urinary tract symptoms (LUTS) are the most common way that bladder stones manifest, although haematuria and suprapubic pain can also be present(4).

Adults frequently complain of macroscopic hematuria, poorly localized pain, and irritability, while younger children are more prone to present with nonspecific symptoms like vomiting and irritation(21).

Treatment Options.

Depending on the size of the stone and how much discomfort it causes, there are several options for treating ureter stones, ranging from careful observation to surgery.

Medical management and various surgical techniques as mentioned below are available for ureteric stones as per American Urology Association (AUA) and European Association of Urology (EAU) guidelines. However, due to risks of surgical approaches there is always an attempt for treatment of ureteric stones

with medical expulsive therapy (MET) first keeping in view different parameters.

Watchful Waiting for the Treatment of Ureter Stones

The most conservative course of therapy for a ureter stone is careful waiting, which entails four to six weeks without receiving any medical attention to remove the stone. Instead, to make sure the stone is not expanding or changing, the doctor periodically takes x-rays or ultrasounds of it. If the stone's diameter is smaller than 7 mm, this method may work well. However, the biggest challenges in waiting for a kidney stone to pass through the body are infection and urinary tract blockage.

Extracorporeal Shock Wave Lithotripsy (ESWL) for the Treatment of Ureter Stones

Using shock waves administered outside to the body, extracorporeal shock wave lithotripsy is a minimally invasive therapy that breaks up the ureter stone into tiny fragments. The fragments of the ureter stone may be better able to naturally flow through the ureter, bladder, and urethra once they have broken down. ESWL is frequently carried out with the use of general or local anesthesia, and it may cause discomfort for the patient. While ureter stones can

be effectively treated with ESWL, more than one session may be required to remove the stone entirely.

Ureteroscopy for the Treatment of Ureter Stones

A ureteroscope is inserted into the ureter during ureteroscopy, a more invasive technique. To see the stone, the thin viewing device is introduced through the bladder and urethra and into the ureter. A flexible basket can be inserted into the ureter by the surgeon to remove the stone once it is visible.

When a stone is too large to pass naturally and is less than 10 mm in diameter, ureteroscopy is often performed to remove it from the lower end of the ureter. For the purpose of removing stone pieces that might not be able to pass through the ureter on their own, this method can be utilized in combination with ESWL.

Percutaneous Nephrolithotomy (PNL) for the Treatment of Ureter Stones

To reach the kidney during a percutaneous nephrolithotomy, or PNL, the surgeon must create an incision in the skin on the back, between the ribs and the hip. The kidney is then slightly incised to allow for the insertion of a tiny guide wire that runs from the kidney to the ureter. To see the guide wire and make sure it is positioned correctly, an x-ray is utilized. The surgeon dilates the guide wire once it enters the ureter to allow a stone-removal tool to be inserted.

Open Surgery for the Treatment of Ureter Stones

Open surgery can be required to remove the ureter stone if less invasive methods prove ineffective. To reach the ureter during open surgery, a lower abdominal incision must be made. In order to remove the stone directly, the ureter is sliced open during this treatment. The patient must recuperate from this invasive and complicated procedure for at least six weeks.

Since its first description, the underlying technology has not seen many developments in comparison to alternative endourological treatments. But in order to produce greater results, SWL (Shock wave lithotripsy) has drawn attention and undergone changes. In a study, a number of potential causes were found for enhanced SFR within the framework of SWL.Thirteen These included boosting lithotripter training, decreasing shock wave rate and ramping energy, improving coupling, reevaluating the present patient and stone selection criteria, and better localizing the stone. Predictive models and nomograms have received attention recently, and new research is emphasizing the importance of novel urine biomarkers in detecting or forecasting infection or bleeding after surgical wound closure(22).

Stone Size For Considering Medical Expulsive Therapy

According to European Association of Urology Guidelines (EAU), the ureteric stones less than 10 mm can be treated with medical expulsive therapy MET (4).

Pharmacological options for stones removal

For medical expulsive therapy, α-blockers are the primary recommendation in the current guidelines. Other drugs Calcium channel inhibitors such as nifedipine, has shown promise in the treatment of renal colic and stone expulsion.

Increasing the rate of stone ejection throughout the ureter to prevent ureteral obstruction and diminish ureteral colic are the main objectives of medical expulsive therapy. In the end, this will help patients avoid the need for more intrusive and potentially problematic surgical procedures. Patients can benefit from effective medical expulsive therapy by lowering the hospital stays and invasive surgical treatments are required to treat the illness. Furthermore, shockwave lithotripsy is a non-invasive process in which shock waves are used to shatter stones. This pharmaceutical therapy can help the fragmented stones travel through the body more easily(23).

As a stone treatment, medical expulsive therapy increases the rate of stone evacuation while lowering the risk of infection, fever, and surgical procedures.

While many research has been conducted to assess MET in adult populations, relatively few of these investigations have focused on paediatric patients. With the exception of one trial where the maximum stone size was 12 mm, the current investigation analysed six RCT studies with 415 patients who had distal ureter stones with a maximum size up to 10 mm. Two trials [12, 14] that assessed doxazosin at a dose of 0.03 mg/kg per day produced conflicting findings. A small rise in SER and a decrease in SET and pain episodes were noted in one study however the results were statistically insignificant ($p > 0.05$)(24).

Also combination of Corticosteroids and Phosphodiesterase 5 inhibitors is used in some patients but because the current results came from studies with small patient numbers, it is not suggested to use combination MET(25).

A wide range of pharmaceutical treatments for ureteral stones, such as antispasmodic drugs, steroids, alpha blocker agents, calcium channel blockers, Phosphodiesterase 5 inhibitors, and their combinations, have been studied in relation to MET(8).

European association of Urology (EAU)Guidelines

. By now, EAU only advises the use of alpha blockers as MET. Patients utilizing alpha blockers had significantly greater success rates (77.3 vs. 54.4%, respectively) in treating distal ureteral stones less than 10 mm, as compared to the ones receiving a placebo or no treatment, (26).

Alpha adrenergic (AR) receptor's location and distribution.

There are three subtypes of alpha-adrenergic receptors: α-1A, α-1B, and α-1D. The urogenital region, which includes the prostate, bladder base, bladder neck, and ureter, is primarily home to α-1A and α-1D adrenergic receptors.

Specifically, α1D receptors are concentrated in the distal portion of the ureter

and influence the contraction of the ureter's smooth muscles, and the detrusor m uscle.

In terms of decreasing abundance, the distribution of αAR in the human ureter is as follows: α-1D > α-1A > α-1B.

Most Common Alpha Blockers Used for MET

The Alpha blocker most commonly prescribed for MET is Tamsulosin which is an α1D- and α1A-receptor blocker.

Another alpha blocker Silodosin that is highly uroselective and is α1A-receptor antagonist has also been used for this purpose in many countries and due to its highly selective nature, it is found to have lesser side effects.

Both of these drugs lead to relaxation of lower ureteric smooth muscle(5).

Mechanism of action of α1A receptor blockers.

Inhibiting the alpha-1 adrenergic receptor causes the ureteral smooth muscle to relax and the ureteral lumen to widen, which ultimately aids in the propagation of stones. By increasing the urine volume above the position of stone and lowering the pressure below this level, these drugs promote anterograde stone propagation. Additionally, α1-adrenoceptor blockers also lessen the requirement for analgesics by reducing ureteric contractions and colic episodes (27).

Studies on Alpha Blockers for Ureteral Stone Removal

A meta-analysis on the clinical efficacy of α-blockers for treating distal ureteral stones stated that patients who received α-blockers had a 44% higher rate of spontaneous stone passage than those who did not (28).

Thus, an RCT of use of silodosin for MET of ureteral stones which are <10 mm size was carried out by Itoh et al. Patients who administered 8 mg of silodosin daily showed a higher rate of stone expulsion and a shorter mean stone expulsion time when compared to those who were encouraged to drink 2 L of water daily. Meta-analyses conducted since the silodosin RCT have demonstrated that silodosin is more effective than tamsulosin for the MET of ureteral stones (29).

A systematic review was undertaken to check the effectiveness of the alpha blockers including Tamsulosin and Silodosin for urinary tract stones. Silodosin was found to be the most effective drug in treating urinary tract stones followed by tamsulosin (6).

A systematic review and meta-analysis from 2018, from EMBASE, PubMed, Scopus databases and Cochrane library also compared the same effect and concluded that silodosin had better efficacy in expulsion of the stone and also better pain relief (7).

One other prospective, an RCT, at outpatient department of Urology, in Bangladesh from 2017-2019 on 220 patients to evaluate the effectiveness of both the drugs. The results showed not much significant difference in the efficacy of both the drugs for the treatment of urinary tract calculi(8). A similar study was conducted in Egypt in children to see the efficacy of both drugs. It was a single blind randomized control trial on 167 patients(9).

Side effects:

A meta-analysis involving five RCTs stated and discovered that while there was no significant difference between the treatments in terms of retrograde ejaculation rate or stone expulsion time, silodosin significantly increased the distal ureteral stones expulsion ratein comparison to Tamsulosin. In a meta-analysis, 13 RCTs are included, including 2 RCTs that are only accessible in abstract form) and three observational research. They discovered that silodosin produced a greater rate of stone ejection and a shorter expulsion duration when compared to tamsulosin; nevertheless, silodosin also increased the incidence of retrograde ejaculation (12).

In addition, the results of four different trials were reviewed as part of the pooled analysis; each study described particular adverse effects that were seen in the treatment arms. Nasal congestion, headaches, lightheadedness, nausea, and orthostatic hypotension—a decrease in blood pressure—were among these adverse effects. These side effects, which represented the variety of possible consequences connected to the therapies under review, were tracked and recorded as part of the safety evaluations conducted for the trials.

All things considered, the thorough examination of the exclusions, withdrawals, and reported adverse effects in the pooled analysis sheds light on the difficulties and conclusions that have been found in a number of research. It emphasizes how crucial it is to closely monitor participant outcomes and unfavorable occurrences in clinical research in order to guarantee the efficacy and safety of the medicines being studied(30).

The treatment for distal ureteral stones with size less than 10 mm with tamsulosin and silodosin has resulted in a high output rates of 57-64% and 80 - 84%, respectively, according to randomized controlled studies. Nonetheless, compared to other trials, the tamsulosin success rate in those investigations is somewhat lower (31). However, tamsulosin demonstrated an 86% success rate in a randomized controlled study with almost 3000 patients(32). Tamsulosin has a 67–90.7% success rate in treating distal ureteral stones, according to Tao

et al.'s meta-analysis.20 The current study's tamsulosin success rates align with some studies (33).

Similar to the current investigation, the comparable rates in the Imperatore et al. study were 82% and 88%, and in the Arda et al. study they were 72.4% and 78.6%. These investigations also revealed no discernible difference between tamsulosin and silodosin. However, only young/middle-aged men were included in this study, whereas both of other investigations included both men and women. This sums up the main distinction between prior studies and the present investigation (34).

Tamsulosin is used commonly in our population for MET however Silodosin, a newer drug, is not used frequently for this purpose and is still under research. Also, comparison of Silodosin and Tamsulosin has not been explored in our population earlier.

Rationale

The purpose of this study is to examine and compare the effectiveness of silodosin and tamsulosin in medical expulsive therapy (MET) in terms of the rate at which stones are expelled from the body, as well as the adverse effect profiles in our patient group.

OBJECTIVES:

To evaluate and compare the efficacy and safety of medical expulsive therapy containing tamsulosin and silodosin, specifically.

To compare the side effect profile of tamsulosin and silodosin when given for medical expulsive therapy.

HYPOTHESIS:

Null Hypothesis:

It is hypothesized that efficacy and safety of medical expulsive therapy, containing tamsulosin and silodosin, is almost the same and silodosin can be used with the same efficacy for the treatment of lower urinary tract calculi.

Alternative Hypothesis:

Silodosin is better than Tamsulosin in efficacy and safety.

OPERATIONAL DEFINITIONS:

STONE CLEARANCE:

Stone clearance will be defined as no evidence of stone on follow up X-ray KUB imaging at 4 weeks .

ANCILLARY PROCEDURES:

Additional urological procedures needed to remove the same stone for which medical expulsive therapy was given if it fails to remove the stone completely.

SIDE EFFECTS:

Any undesirable effect noticed after prescription of the drug including but not limited to abnormal ejaculation, headache, orthostatic hypotension, backache and gastritis etc.

MATERIALS AND METHODS:

STUDY DESIGN:

Prospective randomized control trial.

STUDY SETTING:

Outpatient department of Sir Ganga Ram hospital, Lahore.

DURATION OF STUDY:

18 months.

DURATION OF TREATMENT:

Four weeks.

SAMPLE SIZE:

Using the open-epic software, the sample size was estimated. The minimum sample size that we require is 208 patients with ureteric stone who fulfil the inclusion criterion with 104 in one group receiving tamsulosin and 104 in silodosin group (1:1 ratio) with an inflation of 10 percent for estimated loss to follow up, with an anticipated expulsion rate ranging from 58-64 percent in tamsulosin group and 78-83 percent in silodosin group with a risk difference of 19 to achieve a power of 80 percent and a level of significance of 5 percent.

SAMPLING TECHNIQUE:

Patients visiting the outpatient department of Sir Ganga Ram hospital will be selected by simple random sampling, fulfilling the inclusion criteria.

SAMPLE SELECTION:

Adult male and female patients fulfilling the inclusion criteria will be assigned into two groups by random allotment, 1st group will be given Tamsulosin and 2nd group will be given Silodosin for four weeks.

INCLUSION CRITERIA:

Following factors make up the inclusion criteria for this study.

- Patients between ages 18 years - 55 years.
- Solitary unilateral ureteral stone
- Stone sizes less than 10 mm measured on non-contrast computed tomography of kidney, ureter and bladder.
- Stones being treated primarily with medical expulsive therapy
- Radio opaque Stone

EXCLUSION CRITERIA:

The presence of following factors will exclude the patients from our study:

- Pregnancy
- Untreated UTI
- Bleeding disorders
- Obstruction distal to stone
- Serum Creatinine > 1.3 mg/dl in males and > 1.2 mg/dl in females.
- Congenital renal anomaly/ skeletal malformation
- Previous treatment for the same stone (PCNL/ URS / push back)
- Solitary Kidney
- Prior JJ stent insertion
- Bilateral ureteral stone

DATA COLLECTION AND PROCEDURE:

The protocol will be submitted to Ethical review committee for review and only once the permission is granted, the study will be started. Patients will undergo standard procedure like detailed history taking, examination and routine investigations. Once decided that the patient will undergo MET, the patient will be explained in detail about medications, their potential side effects, follow up and the potential indications for early follow up. Our study will not change any standard process in place except the randomization between Tamsulosin and Silodosin. The data will be kept confidential as a top priority. Only principal investigator and co-principal investigator will have access to the data.

All patients as per inclusion and exclusion criteria as described above will be included in the study. The CT scan (non contrast computed tomography) will be done on (machine parameters at Ganga ram). Only patients with radio-opaque stones will be included. Patients falling into the inclusion criteria will be explained about the study and once they agree to participate in study, randomization will be done. Demographic data including patients' age and comorbid, stone-related data including size, location, laterality and number of stones and duration of symptoms will be recorded. The patient will be given either Capsule Tamsulosin 0.4 mg once daily at night or Tablet Silodosin 8 mg once daily at night based on the group assigned. The patient will also be

explained about the reasons for follow up earlier than four weeks including fever, persistent pain or gross hematuria. The patients will be called for follow up at 4 weeks with an X-ray KUB without bowel preparation. We will note if the stone has passed or not.

ETHICAL CONSIDERATION:

The funds for supporting this research will be provided by department of pharmacology and therapeutic FJMU, Lahore. Informed consent will be taken from patients prior to research.

DATA ANALYSIS PROCEDURE:

Data will be entered and analyzed on SPSS version 22. Percentages and frequencies will be calculated for the demographic variables of the patients. The comparison of the two groups will be made by using T- test. P-value of less than 0.05 will be considered significant and the power used will be 0.80.

RESULTS

Frequency and percentage of demographic data

Variables		Frequency	Percentage
Gender	**Male**	105	58.7
	Female	74	41.3
Income status	**Less than 50000**	108	60.3
	50000 -150000	69	38.5
	Greater than 150000	2	1.1
BMI	**Normal**	166	92.7
	Obese	13	7.3
Comorbidity	**None**	136	76.0
	HTN	33	18.4
	Diabetes	10	5.6

This information sheds light on the sample population's health and demographic distribution, showing a preponderance of people with normal BMIs and lower income levels, as well as a significant percentage of people without comorbid diseases.

In our study there are total 179 patients out of which 74 are females (41.3%) and 105 males (58.7%).

The income, 108 people, or 60.3% of the total, make less than 50,000Rs in month. Just 2 members, or 1.1 percent, make more than 150,000 monthly, while 69 participants (38.5%) have monthly salaries between 50,000 and 150,000.

13 persons (7.3%) are classed as obese, while 166 people (92.7%) have a normal BMI. These numbers represent a sizable fraction of the sample. In terms of comorbidities, 136 individuals (76.0%) state they have no comorbid conditions. Of the people with comorbidities, 10 (5.6%) had diabetes, and 33 (18.4%) had hypertension (HTN).

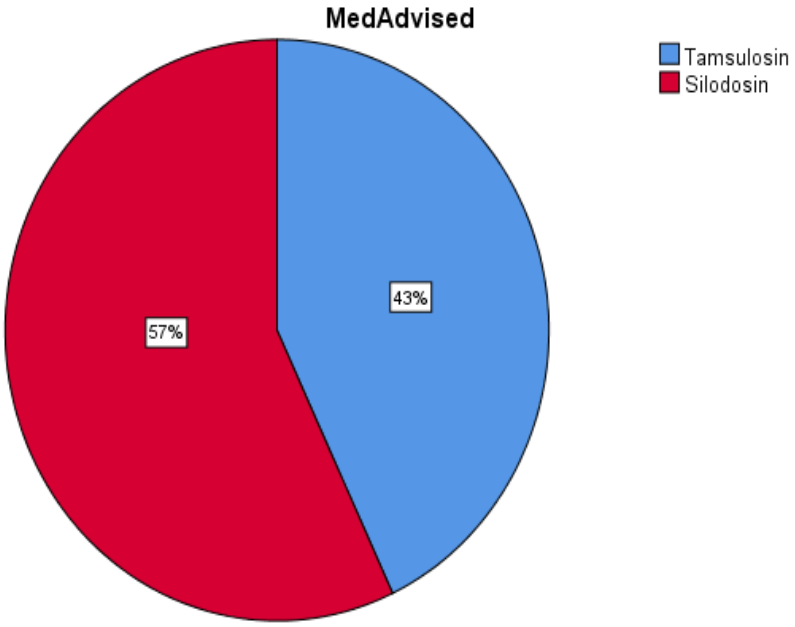


Figure 1: Pie chart of patients using Silodosin and Tamsulosin (Medicine Advised)

Use of medicine (Figure 1)

Tamsulosin and Silodosin, the two drugs prescribed to a group of patients, are distributed as shown in the pie chart. Of the patients, 43% were advised to take Tamsulosin, which is shown as the blue section on the chart. And (57%) of the patients were advised to take silodosin, as shown by the red segment.

Table2: Patient demographic characteristics and study variables are presented as frequency and percentage with association

Varibales		Tamsulosin	Silodosin	p-value
Body Mass index	Normal	72(43.4%)	94(56.6%)	0.730
	obese	5 (38.5%)	08(61.5%)	
Laterality	Right	65(55.6%)	52(44.4%)	0.001
	Left	12(19.4%)	50(80.6%)	
Symp To CT	Less than 1 week	67(64.4%)	37(35.6%)	
	More than 1 week	10(15.2%)	56(84.8%)	0.001
	More than 2 week	0 (0.0%)	09(100%)	
Posl n Ureler	Proximal	28(51.9%)	26(48.1%)	
	Mid	08(17.4%)	38(82.6%)	0.001
	Distal	41(51.9%)	38(48.1%)	
Water intake	Less than 1 litre	59(54.6%)	49(45.4%)	
	More than 1 litre	18(25.4%)	53(74.6%)	0.001
Analgesic requirement	Yes	26(61.9%)	16(38.1%)	0.005
	No	51(37.2%)	86(62.8%)	
Time for removal	Less than 14 days	6(10.3%)	52(89.7%)	
	14-21	14(27.5%)	37(72.5%)	0.001
	22-28	57(81.4%)	13(18.6%)	

The table compares several factors along with the corresponding p-values to assess statistical significance between two drugs tamsulosin and silodosin.

First, based on Body Mass Index (BMI), 43.4% of those with a normal BMI were prescribed Tamsulosin, while 56.6% were recommended Silodosin. On the other hand, among those who were obese, 38.5% were given Tamsulosin and 61.5% were given Silodosin; p-value came out to be 0.730, which meant that there was no statistically significant variation in the medication preferences according to BMI.

15.2% of patients who had pain for more than a week prior to CT scan, received Tamsulosin while 84.8% received silodosin.

51.9% of the patients with proximal ureteric stone were given Tamsulosin and 48.1% received Silodosin.

82.6 percent of patients with mid-ureteric stone problems received Silodosin, while 17.4% received Tamsulosin.

51.9% of patients with distal ureteric stones received Tamsulosin and 48.1% on Silodosin.

Only 38.1% of patients on Silodosin required analgesics, whereas 61.9% of patients on Tamsulosin used analgesics.

89.7% of patients on silodosin had their stone removed in less than 14 days, while only 10.3% of the patients on Tamsulosin had their stone removed in aforementioned duration.

72.5% of patients on Silodosin had their stone removed in 14-21 days, while only 27.5% of the patients on Tamsulosin had their stone removed in same duration.

Moreover, 81.4% on Tamsulosin had their stone removed in 22-28 days and 18.6% patients on Silodosin had it removed in same duration.

Table 2 Association between Tamsulosin and Silodosin with side effects

		Tamsulosin	Silodosin	p- value
Side effect	None	61 (40.1%)	91(59.9%)	0.3.15
	Othostatic hypotension	09 (60.0%)	06(40.0%)	
	Abnormal ejaculation	2(66.7%)	1(33.3%)	
	Headache	5(55.6%)	4 (44.4%)	

The side effects that patients using silodosin and tamsulosin experienced are analyzed in the table, and the p-value denotes the statistical significance of these data. Patients on Silodosin, with no side effects were 59.9% while 40.1% on Tamsulosin did not report any side effects. This implies that, in comparison to Tamsulosin, Silodosin may have a marginally higher correlation with patients reporting no adverse effects.

Examining particular side effects reveals various themes. Nine patients on tamsulosin (60.0%) and six patients on silodosin (40.0%) developed orthostatic hypotension, a condition marked by a considerable drop in blood pressure upon

standing. It suggested that Tamsulosin users are more likely to have orthostatic hypotension than Silodosin users.

Only a very tiny percentage of patients reported abnormal ejaculation; 2 individuals on tamsulosin (66.7%) and 1 patient on silodosin (33.3%). Again, this points to an increased chance of this specific adverse effect in Tamsulosin users.

Another side effect that was identified involved headaches, which were seen by 4 individuals on silodosin (44.4%) and 5 patients on tamsulosin (55.6%). Headaches were marginally more common among Tamsulosin users compared to Silodosin users, similar to orthostatic hypotension.

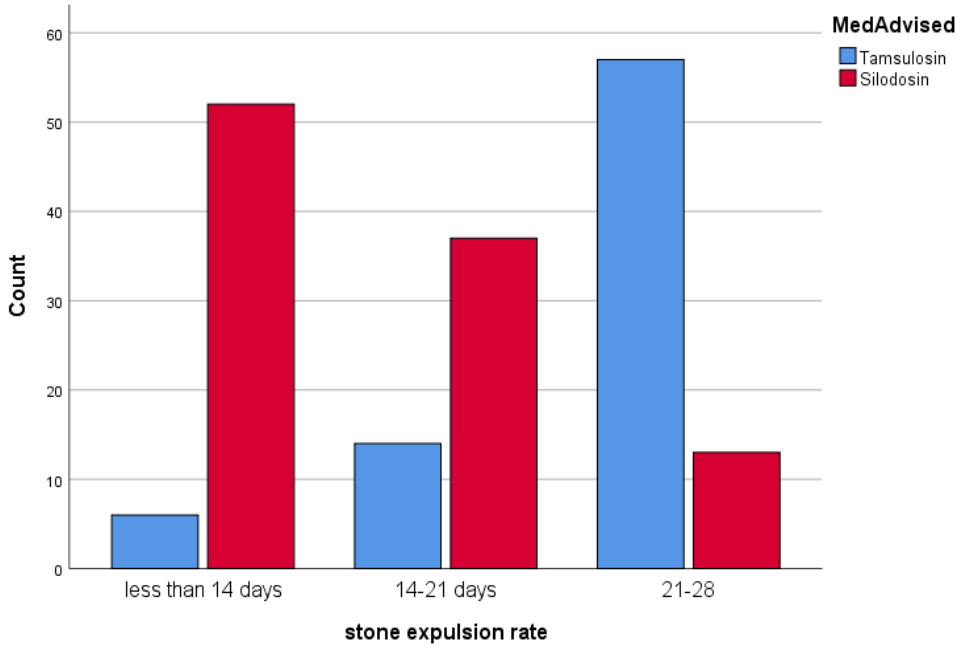
None of the detected differences in side effect distribution between Tamsulosin and Silodosin is statistically significant, according to the p-value of 0.315. This implies that even if there are discernible variations in the frequency of particular adverse effects between the two drugs, these variations might just be the result of random variation rather than an actual distinction in the side effect profiles of tamsulosin and silodosin.

In conclusion, the analysis of side effects reveals that patients taking silodosin have a tendency to report no side effects more often than individuals taking tamsulosin.

On the other hand, it seems that tamsulosin users are more likely to experience certain adverse effects, like headache, orthostatic hypotension, and abnormal ejaculation. Even with these findings, the absence of statistical significance suggests that more investigation using larger sample sizes would be necessary to conclusively identify any significant variations in the side effect profiles of Tamsulosin and Silodosin.

Figure 2

Bar Chart showing comparison of stone expulsion rate in Tamsulosin and Silodosin groups



This bar chart presents a comparative examination of the rates of stone expulsion for patients who were suggested to take Tamsulosin or Silodosin during three distinct time periods—less than 14 days, 14–21 days, and 21–28 days.

The results are color-coded, with red bars denoting silodosin and blue bars denoting tamsulosin.

Silodosin shows a markedly greater efficacy in stone expulsion, with about 55 patients expulsing stone in less than 14 days in comparison to just about 5 patients on Tamsulosin.

This suggests that Silodosin is far more successful at facilitating stone removal in less time than Tamsulosin.

While in 14–21days duration, Silodosin continues to work better than Tamsulosin in removing stones. About 20 patients on Tamsulosin were able to successfully remove stone, compared to about 30 people on Silodosin. This implies that while tamsulosin is also beneficial, silodosin retains greater efficacy.

In the span of 21–28 days, 57 patients on Tamsulosin while 13 on Silodosin were able to eliminate stones. In general, Silodosin is quite successful for rapid stone ejection during the first two weeks. Using the intended period for stone

ejection to guide medicine selection, this time-dependent efficacy analysis offers clinicians important information.

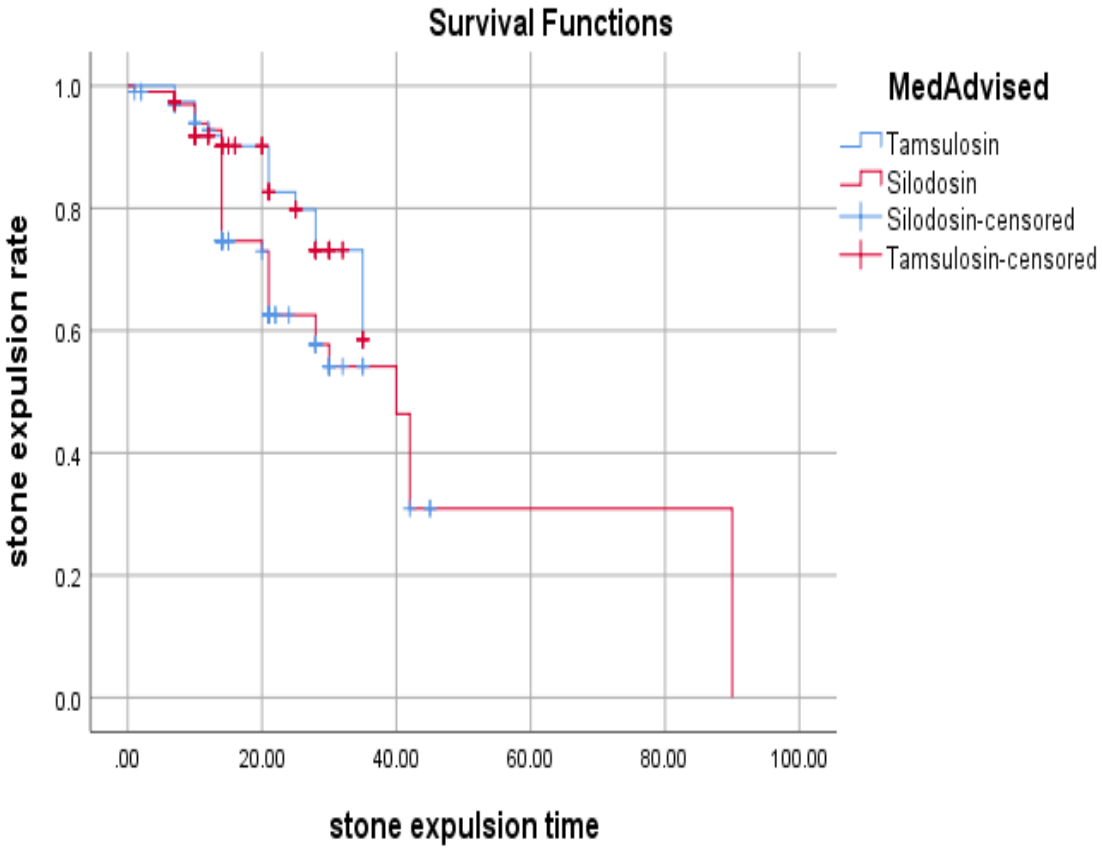


Figure 3 Survival function

This statistical method is commonly used to estimate the time until an event occurs and to compare the survival curves of different groups. In this case, Kaplan–Meier analysis was performed to assess the duration that patients required to expel kidney stones while receiving either silodosin or tamsulosin treatment. The rate of the expulsion of stone and the time for it, for both groups, was evaluated using this method, as can be seen in Figure 2.

The log-rank test was applied to compare the rate and time for stone expulsion between the two groups. It is a hypothesis test for comparing the survival distributions of two samples. It was used in this study to see if patients treated with silodosin and those treated with tamsulosin had significantly different times for stones to be expelled. With a p-value of 0.05, the log-rank test findings showed that there was statistically significant difference between the two groups. This indicates that both groups' times to stone expulsion were statistically comparable.

The data showed that patients treated with silodosin demonstrated a higher rate of stone expulsion and faster stone expulsion compared to those treated with Tamsulosin. Though the difference did not achieve statistical significance in this trial, it shows that silodosin may be more beneficial in aiding kidney stone removal. The evaluation of rate and time of stone expulsion for both groups was conducted using Kaplan–Meier analysis, as depicted in Figure 2. This

statistical method is commonly used to estimate the time until an event occurs and to compare the survival curves of different groups. In this context, the Kaplan–Meier analysis was utilized to assess the duration it took for patients to expel kidney stones while being treated with either silodosin or tamsulosin.

DISCUSSION

After prostate pathology and urinary tract infections, renal stones are the third most frequent urinary tract disorder. Ureteral stones account for 14% of stones in the urinary system, most of which are in the distal ureter. Five to ten percent of people have urolithiasis. Their rising incidence is a serious cause for concern(35).

Stones can be treated medically or surgically according to European and American urology associations. The medical management (MET) has its own advantages and is preferred over surgical approach as it is has less risks involved than the surgical procedures. For (MET) medical expulsive therapy we need to keep in view various parameters including the stone's size, position, and ureteric characteristics. The medical care of ureteral calculi has significantly improved since the market saw the release of efficient medicinal therapeutic agents. The results of multiple investigations suggest that alpha blockers aid in the transit of ureteral stones. These have shown that this strategy may speed up and ease the ureteral stones' natural passage. α-AR blockers have been suggested by recent worldwide standard guidelines as a treatment for ureteral stones in adults and adolescents.

In 1970, it was initially reported on how adrenergic receptors function in the human ureter. Alph adrenergic receptor agonists preserve ureteral peristalsis,

which may aid in a spontaneous stone passage, while also preventing the uncoordinated muscular activity associated with renal colic. Instead of totally stopping the action of the ureteric smooth muscle, alpha blockers primarily cause relaxation of the human ureter's distal portion.

There are three different types of alpha receptors. α1A-receptor α-1B, and α1D. Older alpha blockers had interactions with all subtypes of alpha receptors and therefore had more incidence of adverse effects like postural hypotension and retrograde ejaculation etc.

Tamsulosin is highly selective for α1A and α1D receptors and has lesser incidence of side effects like postural hypotension, retrograde ejaculation, headache and gastritis as compared to aforementioned drugs with receptor non selectivity () Silodosin is a selective alpha 1 blocker and is also used recently as medical expulsive therapy.

After being approved in Japan in 2006, the recently introduced selective α-1A AR antagonist silodosin is currently licensed in over 50 countries, including the US and Europe, for the treatment of lower urinary tract symptoms (LUTS).

Given the growing body of evidence supporting the efficacy of medical expulsive therapy (MET) with selective α-blockers, MET treatment for ureteral stones is a financially prudent approach (36).

In our study, we wanted to compare the efficacy of two drugs in MET (medical expulsive therapy) with regards to stone expulsion rate as well as to compare the side effect profile in our population.

Patients with distal ureteral calculi who received alpha blocker drugs had almost 40-50% higher chances of expulsion of stone than those who did not receive this treatment, according to two meta-analyses that offered strong evidence for the clinical benefit of this treatment [29, 34]. Hollingsworth and colleagues recently conducted a meta analysis of trials utilizing alpha blockers in individuals with ureteral stones, and they obtained similar results.
According to a study, an alpha-1A receptor antagonist may not be as helpful for stone ejection as a specialized α-1D receptor antagonist.

According to a different study, using α-1A adrenoceptor blockers instead of α-1D adrenoceptor blockers can result in more successful stone expulsions. Tamsulosin and silodosin exhibit comparable α-1D receptor subtype affinity when taken at a dose of 8 mg once day. However, silodosin has about 38 times greater affinity for α-1A receptors than tamsulosin does(37).

Approximately 95% of stones with a diameter of less than 4 mm passed after 40 days of conservative treatment alone, according to a research. On the other hand, silodosin exhibited a greater stone expulsion rate of 14% in comparison to tamsulosin for larger stones, measuring 5-10 mm in diameter. For distal ureteral stones treated with silodosin, the mean ET (in days) ranged from 6.5 to 16.7 days. Those with symptomatic unilateral ureteral calculi less than 10 mm in diameter were assigned to receive silodosin (8 mg/day) and instructed to consume two liters of water per day for a maximum of eight weeks in a prospective randomized research. The average ET was 10.27 ± 8.35 days overall. The mean ET for distal ureteral stones was 9.29 ± 5.91 days. The mean ET was 9.56 ± 8.45 days for stones with a diameter of 1–5 mm and 11.33 ± 8.31 days for stones with a diameter of less than 10 mm(38).

Our study showed the that 51.9% of the patients with proximal ureteric stone were given Tamsulosin and 48.1% received Silodosin. 82.6 percent of patients with mid-ureteric stone problems received Silodosin, while 17.4% received Tamsulosin. While 51.9% of patients with distal ureteric stones received Tamsulosin and 48.1% Silodosin.

Numerous meta-analyses have investigated how different medication combinations affect ureteric stone treatment. However, there aren't many studies that specifically compare how well different alpha-blockers work to

cure distal ureteric calculi. For distal ureteric stones, the use of supplementary drugs such Tamsulosin has been shown to be beneficial in easing discomfort, lowering risks, and quickening the removal of the stone. According to recent studies, silodosin might be a suitable and effective replacement(39).

In treating distal ureteral calculi silodosin performed better than a placebo or tamsulosin, per a recent meta-analysis. However Silodosin's safety profile was comparable to that of tamsulosin (40).

In another study involving 167 paediatric patients with distal ureteric stones (DUS) less than 1 cm were enrolled in this prospective single-blind placebo-controlled randomized research. The patients were randomly assigned to three groups: 1st group was given 4 mg of Silodosin once a day, 2nd group was given 0.4 mg of Tamsulosin, and 3rd group received neither medication. For a maximum of four weeks, the study groups' adverse medication reactions, the frequency and duration of expulsion of stone, an pain episodes frequency were compared.

In groups I, II, and III, the rates of stone expulsion were 89.3% (50 out of 56 patients), 74.5% (41 out of 55 patients), and 51.8% (29 out of 56 patients), respectively. Group I had a significantly greater stone expulsion rate than groups II and III ($p = 0.04$ and $p < 0.001$, respectively). The stone ejection rate was higher in group II than in group III, with a statistically significant difference ($p = 0.01$). In groups I, II, and III, the corresponding expulsion times in days were 12.4 ± 2.3, 16.2 ± 4.2, and 21.2 ± 5.6. Group I experienced a considerably shorter time to expulsion compared to groups II and III ($p < 0.001$). Additionally, Table 2 shows that group II's expulsion time was much lower than group III's ($p < 0.001$). There was no significant difference between groups I and II ($p = 0.8$), although group I and II had considerably fewer mean daily pain episodes requiring analgesia than group III ($p < 0.001$).

The size, location, and makeup of the stone, the degree of the blockage, and the symptoms all influence the best course of action. The therapy of ureteral stones has undergone a paradigm change in the last ten years due to the advent of less intrusive techniques and the availability of more advanced pharmaceutical agents.(32)

Comparably, silodosin demonstrated a statistically significant greater efficacy in terms of stone ejection rate and time compared to tamsulosin (82.4 vs. 61.5%) in another study involving adult patients.(41).

Along with pain episodes and safety outcomes like orthostatic hypotension and retrograde ejaculation, the key outcomes that were taken into consideration were the stone expulsion rate (SER) and stone expulsion time (SET).

For patients with ureteral stones (distal ureteral stones with a diameter of ≥5 mm and ≤10 mm), silodosin is very efficient in promoting stone expulsion with shorter expulsion times and fewer pain episodes. Additionally, it works well after lithotripsy to speed up stone movement and emphasize clearance rate(37). Dell'Atti L. evaluated the effectiveness of Tamsulosin and Silodosin in the ejection of 4–10 mm ureteral stones in distal parts of urethra. The research included 136 patients in total, all of whom were at least 18 years old. For three weeks, group 1 (67 patients) got 0.4 mg of tamsulosin daily, while group 2 (66 patients) received 8 mg of silodosin daily. Compared to Tamsulosin (61.2%, 41 out of 67 patients), patients treated with Silodosin experienced a statistically significant increase in the expulsion rate (80.3%, 53 out of 66); Silodosin also demonstrated a statistically significant advantage in terms of stone expulsion rate (p: 0.003) and expulsion time (weeks) (p: 0.002). There were no reported serious problems(42).

The rate and time of stone expulsion for both groups was evaluated using this method, as can be seen in Figure 2.

One main result of our study was 89.7% of patients on silodosin had their stone removed in less than 14 days, while only 10.3% of the patients on Tamsulosin had their stone removed in aforementioned duration. Also, 72.5% of patients on Silodosin had their stone removed in 14-21 days, while only 27.5% of the patients on Tamsulosin had their stone removed in same duration. Moreover, 81.4% on Tamsulosin had their stone removed in 22-28 days and 18.6% patients on Silodosin had it removed in same duration.

A similar meta analysis matched our results. Every study that was part of the analysis prescribed silodosin for at least two weeks. The results of several researches were compared by observing the effects of silodosin over a standardized period of time thanks to this constant timeframe. The results of this investigation showed that individuals with distal ureteral stones saw significantly higher rates of stone ejection when they received Silodosin for at least two weeks. This implies that silodosin worked well to help stones transit through the body in a short amount of time, which may lessen the need for more intrusive procedures and enhance patient outcomes when treating distal ureteral stones(43).

A meta-analysis was carried out on the similar comparison and it showed that mean stone ejection time was shorter in patients receiving silodosin 8 mg daily compared to those directed to drink 2 L of water daily and a greater rate of stone ejection. Meta-analyses conducted since the silodosin RCT have demonstrated that efficacy of silodosin is more than that of tamsulosin for the Medical expulsive therapy of ureteral stones. The meta analyses discovered that silodosin, as opposed to tamsulosin, dramatically raised the expulsion rate of distal ureteral stones in a meta-analysis involving five RCTs(44).

A positive but weak link was seen when the length of stone ejection was analyzed in relation to the frequency of renal colic episodes, the dosage of analgesics, and the size of the stone (Table 4; $P<0.001$). The number of renal colic episodes and the dose of analgesics were found to be positively and strongly correlated ($P<0.001$), the number of renal colic episodes and stone size was found to be positively and weakly correlated ($P=0.015$), and the analgesic dosage and stone size was found to be positively and weakly correlated ($P<0.05$)(28).

Overall, compared to 30% of patients in the placebo group, 37.5% of patients in the tamsulosin group experienced drug-related side events (p = 0.7). The most often reported side effect was dizziness, which was more common with tamsulosin (25%) than with 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)].

Because both medications are safe and well tolerated, no significant side effects were seen in the trial. In groups A and C, anejaculation was experienced by 17 out of 23 patients (73.9%) and 21 out of 25 patients (84%) respectively; nevertheless, none of the patients stopped receiving treatment. After the treatment was discontinued, the situation rapidly improved. In the study patients, there was no significant change in their blood pressure or pulse rate. A study of the literature supports the findings, showing no correlation between changes in blood pressure or heart rate and a 50 mg dose of mirabegron(45).

Our Patients on tamsulosin accounted for 40.1% of those who did not report any side effects; those on silodosin made for a larger percentage (59.9%). This

implies that, in comparison to Tamsulosin, Silodosin may have a marginally higher correlation with patients reporting no adverse effects.

There was no discernible difference in the reported orthostatic hypotension values of 3.6, 5.5, and 1.8% for the silodosin, tamsulosin, and placebo groups, respectively. Other side effects were noted in the silodosin, tamsulosin, and placebo groups, respectively, and included headache (3.6, 5.5, and 1.8%), dizziness (7.1, 10.9, and 3.6%), nasal congestion (1.8, 3.6, and 0), and nausea (1.8, 3.6, and 1.8%), all without a statistically significant difference. Based on the Common Terminology Criteria for Adverse Events, version 4.0, all cases were rated as grade 1(46).

The groups who took silodosin alone and the group that took silodosin plus tadalafil experienced similar side symptoms, such as headache, dizziness, backache, orthostatic hypotension, and retrograde ejaculation (Table-III). Given that $P > 0.05$, that was not statistically significant(41).

Examining particular side effects reveals various themes. Nine patients on tamsulosin (60.0%) and six patients on silodosin (40.0%) developed orthostatic hypotension, a condition marked by a considerable drop in blood pressure upon standing. Despite the fact that the sample size for this particular side effect is rather modest, it suggests that Tamsulosin users are more likely to have orthostatic hypotension than Silodosin users.

According to a study, the most common adverse event associated with the silodosin group was decreased or absent ejaculation. Of the patients in groups A and B, eight patients (8 were distressed, four were not, and six were distressed but could wait for their improvement) and nineteen patients (10 were distressed, four were not, and five were distressed but could wait for their improvement) experienced this adverse event most frequently(47).

Only a very tiny percentage of patients reported experiencing abnormal ejaculation; 2 individuals on tamsulosin (66.7%) and 1 patient on silodosin (33.3%) reported this side event. Again, this points to an increased chance of this specific adverse effect in Tamsulosin users, but the numbers are too low to make any firm conclusions. Another side effect that was identified involved headaches, which were seen by 4 individuals on silodosin (44.4%) and 5 patients on tamsulosin (55.6%). Headaches were marginally more common among Tamsulosin users compared to Silodosin users, similar to orthostatic hypotension.

Many urologists agree when it comes to the incidence of retrograde ejaculation that it is an indication of therapy efficacy rather than a negative effect. It seems that silodosin relaxes the smooth muscles in the genital and lower urinary tracts sufficiently to cause a retrograde ejaculation. Retrograde ejaculation was more common in the individuals who experienced the most alleviation from lower

urinary tract symptoms, which was consistent with this conclusion. This finding implies that the retrograde ejaculation is, in fact, a passive marker of the smooth muscle relaxation brought on by silodosin(32).

Typically, nonselective α1 adrenoceptor antagonists such doxazosin and terazosin are linked to orthostatic hypotension. Nonetheless, in clinical trials, silodosin was linked to a modest incidence of orthostatic hypotension. According to the combined analysis of the US and European studies, 1.1% of patients receiving a placebo and 1.3% of patients receiving silodosin experienced orthostatic hypotension(48).

When compared to Tamsulosin, Silodosin is linked to a larger incidence of retrograde ejaculation but a reduced incidence of peripheral vasodilation-related adverse effects, such as orthostatic hypotension and dizziness, according to a retrospective review conducted by Imperatore et al(49).

In our study comparing the effects of Tamsulosin and Silodosin on patients, it was discovered that only 38.1% of those receiving Silodosin needed analgesics to ameliorate ureteric pain. On the other hand, 61.9% of patients receiving Tamsulosin required analgesic intervention, which is a far larger percentage. This significant difference raises the possibility that silodosin is more successful in treating ureteric stones and it also lowers their need for extra painkillers.

Similar results were seen in another study showing that, individuals receiving just tamsulosin treatment needed a greater average analgesic dosage of 391.43 ± 165.60 mg with a p-value of 0.005, which denotes substantial significance, the necessary(50).

Similarly, a study showed statistically significant difference in the amount of analgesics needed by patients treated with Silodosin compared to those treated with tamsulosin only. The robustness of the conclusion was highlighted by the fact that the group receiving Silodosin treatment required considerably fewer analgesics than the groups receiving Tamsulosin, with a p-value of < 0.001(51).

Conclusion

An effective treatment for ureteral stones is medical expulsive therapy. According to our findings, silodosin has a safer profile and is more successful than tamsulosin at ejecting ureteric stones.

Silodosin had an increased rate of stone expulsion and took less time in stone expulsion compared to those treated with Tamsulosin.

In addition, patients treated with silodosin reported fewer side effects, such as a retrograde ejaculation, orthostatic hypotension and headaches as compared to those taking Tamsulosin.

In addition, those who received Silodosin needed less analgesic medication than those who received Tamsulosin.

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INFORMED CONSENT FORM

Research Title: COMPARISON BETWEEN TAMSULOSIN AND SILODOSIN IN MEDICAL EXPULSIVE THERAPY FOR URETERAL STONES.

Researcher Name: Dr Faiza Khan

Email. drfaizakhan@hotmail.com

Introduction: We are conducting research to compare the effects of two drugs for expulsion of ureteral stones. This is based upon two drugs, Tamsulosin and Silodosin which are well known to expel ureteral stones less than 10 mm in size.

Purpose of Research: To have alternate drug Silodosin available after comparing efficacy and side effect profile.

Method:

As per routine, you will be educated about medical expulsive therapy, its dose and mode of administration.

You will be given one of the two drugs and will be told about side effects also. You can contact us anytime during the study period if you face any problem regarding drug. In case the drug therapy does not suit you, you will be given option to change drug or go for surgery.

Possible risks or discomforts

There are no risks or discomforts for you in participating in this study. You can withdraw from the study whenever you want and this will have no adverse effect on your treatment.

Possible benefits

There will be direct benefit to patient in case one drug doesn't suit a patient previously and now he is using the newer drug with lesser side effects. Results of this study will help to make alternate drug treatments available to market

Financial considerations

There is no financial compensation for your participation in this research. There are no additional costs for participation in the study.

Confidentiality

We will not mention your name anywhere in the study and the data will be collected with reference to the Medical Record numbers. All data collected will be strictly confidential and available only to the principal investigator. Your identity in this study will be treated as confidential. A copy of consent form will be given to you. The results of the study, may be published for scientific purposes but your confidentiality will not be compromised. However, any records or data obtained as a result of your participation in this study may be inspected by the Fatima Jinnah Medical University ethical review committee members.

Right of refusal to participate and withdrawal

You are free to choose whether or not to participate in this study. You may refuse to participate or withdraw at any time from the study. There will be no penalty or loss of benefits to which you are otherwise entitled if you choose not to participate.

Authorisation

I have read and understand this consent form, and I volunteer to participate in this research study.

Participants name (Printed or Typed): Date:	Principal investigations signature : Date:
Participants signature : Date:	Signature of person obtaining consent: Date:

باخبر رضامندی کا فارم

تحقیق کا عنوان: پیشاب کی پتھری کے لیے طبی اخراجی علاج میں تمسولوسین اور سیلوڈوسین کے درمیان موازنہ۔

محقق کا نام: ڈاکٹر فائزہ خان

ای میل۔ drfaizakhan@hotmail.com

تعارف: ہم دو دوائیوں کے اثرات کا موازنہ کرنے کے لیے ایک تحقیق کر رہے ہیں جو پیشاب کی پتھری کو خارج کرنے کے دشمن ہیں۔ یہ دو دوائیوں، Tamsulosin اور Silodosin پر مبنی ہے جو 10 ملی میٹر سے کم سائز کی پیشاب کی پتھری کو نکالنے کے لیے مشہور ہیں۔

تحقیق کا مقصد: افادیت اور سائیڈ ایفیکٹ پروفائل کا موازنہ کرنے کے بعد متبادل دوائی Silodosin دستیاب ہونا۔

طریقہ:

معمول کے مطابق، آپ کو طبی خارج کرنے والی تھراپی، اس کی خوراک اور انتظامیہ کے طریقہ کار کے بارے میں تعلیم دی جائے گی۔

آپ کو دو دوائیوں میں سے ایک دی جائے گی اور ضمنی اثرات کے بارے میں بھی بتایا جائے گا۔ مطالعہ کی مدت کے دوران اگر آپ کو منشیات کے حوالے سے کوئی مسئلہ درپیش ہو تو آپ ہم سے کسی بھی وقت رابطہ کر سکتے ہیں۔ اگر ڈرگ تھراپی آپ کے لیے مناسب نہیں ہے، تو آپ کو دوا تبدیل کرنے یا سرجری کے لیے جانے کا اختیار دیا جائے گا۔

ممکنہ خطرات یا تکلیفیں۔

اس مطالعہ میں حصہ لینے میں آپ کے لیے کوئی خطرہ یا تکلیف نہیں ہے۔ آپ جب چاہیں مطالعہ سے دستبردار ہو سکتے ہیں اور اس سے آپ کے علاج پر کوئی منفی اثر نہیں پڑے گا۔

ممکنہ فوائد

مریض کو براہ راست فائدہ ہو گا اگر ایک دوا پہلے مریض کو سوٹ نہیں کرتی تھی اور اب وہ نئی دوائی کو کم سائیڈ ایفیکٹ کے ساتھ استعمال کر رہا ہے۔ اس مطالعہ کے نتائج سے منشیات کے متبادل علاج کو مارکیٹ میں دستیاب کرنے میں مدد ملے گی۔

وہ کم ضمنی اثرات کے ساتھ نئی دوا استعمال کر رہا ہے۔ اس مطالعہ کے نتائج سے منشیات کے متبادل علاج کو مارکیٹ میں دستیاب کرنے میں مدد ملے گی۔

مالی تحفظات

اس تحقیق میں آپ کی شرکت کے لیے کوئی مالی معاوضہ نہیں ہے۔ مطالعہ میں شرکت کے لیے کوئی اضافی اخراجات نہیں ہیں۔

رازداری

ہم مطالعہ میں کہیں بھی آپ کے نام کا ذکر نہیں کریں گے اور ڈیٹا کو میڈیکل ریکارڈ نمبروں کے حوالے سے جمع کیا جائے گا۔ جمع کردہ تمام ڈیٹا سختی سے رازدارانہ اور صرف پرنسپل تفتیش کار کے لیے دستیاب ہوگا۔ اس مطالعہ میں آپ کی شناخت کو خفیہ رکھا جائے گا۔ رضامندی فارم کی ایک کاپی آپ کو دی جائے گی۔ مطالعہ کے نتائج، سائنسی مقاصد کے لیے شائع کیے جا سکتے ہیں لیکن آپ کی رازداری سے سمجھوتہ نہیں کیا جائے گا۔ تاہم، کوئی ریکارڈ یا ڈیٹا حاصل کیا گیا ہے۔

اس مطالعہ میں آپ کی شرکت کے نتیجے میں فاطمہ جناح میڈیکل یونیورسٹی کی اخلاقی جائزہ کمیٹی کے اراکین کی طرف سے معائنہ کیا جا سکتا ہے۔

شرکت سے انکار اور دستبرداری کا حق

آپ اس مطالعہ میں حصہ لینے یا نہ کرنے کا انتخاب کرنے کے لیے آزاد ہیں۔ آپ کسی بھی وقت مطالعہ میں حصہ لینے یا واپس لینے سے انکار کر سکتے ہیں۔ اگر آپ شرکت نہ کرنے کا انتخاب کرتے ہیں تو اس پر کوئی جرمانہ یا فوائد کا نقصان نہیں ہوگا جس کے آپ بصورت دیگر حقدار ہیں۔

اجازت

میں نے رضامندی کے اس فارم کو پڑھ اور سمجھ لیا ہے، اور میں اس تحقیقی مطالعہ میں حصہ لینے کے لیے رضاکارانہ طور پر تیار ہوں۔

پرنسپل تحقیقاتی دستخط تاریخ:	شرکاء کا نام :
رضامندی حاصل کرنے والے شخص کے دستخط: تاریخ:	شرکاء کے دستخط: تاریخ:

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