COMPARATIVE ANALYSIS OF SILODOSIN AND TAMSULOSIN IN DISTAL URETERIC CALCULUS TREATMENT

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ABSTRACT

BACKGROUND

The urinary stone disease is one of the most common afflictions of the modern society and it has been described since antiquity with the westernisation of global culture. It has led to a lot of distress physically, mentally and financially to the affected individuals. Mini-invasive techniques like ESWL and ureteroscopy have their own negative aspects with discomfort to the patient being the prime in it. Hence, a need for conservative management in the form of pharmacotherapy has arisen in the past years and here we are investigating the same. The aim of the study is to compare the efficacy of silodosin (8 mg) vs. tamsulosin (0.4 mg) both in terms of the stone expulsion rate and the time to stone expulsion.

MATERIALS AND METHODS

A study comprising of 120 patients between the age group of 18-50 years with sonography-proven unilateral, uncomplicated lower ureteric calculus was undertaken from January 2015 to November 2015. Exclusion criteria were calculus more than or equal to 1 cm. Patients were divided in 2 Groups; Group A received silodosin 8 mg once daily for a month while Group B received tamsulosin 0.4 mg once daily. The patients were followed up weekly or biweekly with imaging studies. The endpoint was the stone expulsion rate and time, the rate of the interventions and the side effects.

Settings and Design- With ethical committee clearance, a prospective study was conducted in the Department of Urology, Mahatma Gandhi Medical College and Hospital, Jaipur, India.

Statistical Analysis- The SPSS-16 software was used for the statistical analysis of the data.

RESULTS

Results of our analysis showed that Group A (silodosin) patients were benefited more than Group B (tamsulosin) and it was also backed by the data showing a statistical significance for spontaneous stone expulsion in favour of the silodosin group.

CONCLUSION

Hence, we concluded that silodosin's efficacy in treating patients with distal ureteric calculus was much better when compared to tamsulosin.

KEYWORDS

Efficacy, Expulsion Time, Expulsion Rate.

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BACKGROUND

Urolithiasis is an ingrained disease of mankind, which has enormous public health importance and it accounts for a substantial economic burden on our society. Symptomatic ureteric calculi represent the most common condition encountered by an urologist in an emergency setting after urinary tract infections and pathologic conditions of the prostate.[1] Urolithiasis is the third most common disease of the urinary tract with an estimated prevalence of 2-3% and a lifetime recurrence rate of approximately 50%.[2]

In the presence of normal renal function and absence of infection, observation is generally preferred for ureteric calculi measuring a maximum of 5 mm.[3] However, the spontaneous expulsion rate of distal ureter stone is about 25% if their size is between 4-6 mm, 5% if greater than 6 mm and calculi over 8 mm are very rarely eliminated spontaneously.[4] Therefore, active treatment is recommended for individual with larger stones, especially if their size is greater than 5 mm. Urolithiasis affects 12% of

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the population globally.[5] Ureteric stones represent 20% of urolithiasis cases from which 70% are situated in the lower third of the ureter and termed 'Distal Ureteric Stones' (DUS).[6]

The efficacy of mini-invasive therapies such as Extracorporeal Shock Wave Lithotripsy [ESWL] and ureteroscopy has been proven by several studies. Nevertheless, these procedures are expensive and are not without risk.[4] Recently, the use of watchful waiting approach has been extended by using pharmacotherapy. This can reduce symptoms and facilitate stone expulsion.[7] A conservative approach involving close monitoring can be used in most cases and is becoming more popular as a result of advances in pharmacological therapy, which can reduce symptoms and facilitate stone expulsion. Recent studies have reported excellent results relating to Medical Expulsive Therapy (MET) for distal ureteral calculi in terms of stone expulsion and control of ureteral colic pain using drugs (e.g., nifedipine and prednisolone) that can modulate the function of the ureter obstructed by the stone.[8]

Tamsulosin, an alpha1A adrenoreceptor blocker has been used in several current MET experiments, but the results of studies are variable while silodosin is a novel highly selective α1A-adrenoceptor blocker that has the potential to reduce dynamic neurally mediated smooth muscle relaxation in the ureter while minimising undesirable effects on blood pressure regulation.[9]

OBJECTIVE

With ethical committee clearance, a prospective study was conducted in the Department of Urology, Mahatma Gandhi Medical College and Hospital, Jaipur, India, between January 2015 to November 2015.

MATERIALS AND METHODS

The study group comprised of 120 patients who presented to the Urology Outpatient Department with distressing lower ureteric calculus. Inclusion criteria were age between 18-60 years, calculus less than 1 cm and uncomplicated calculus; while exclusion criteria were age <18 years and >60 years, calculus more than 1 cm and calculus associated with complications. All patients who fit the criteria in the given time period were included in the study. Patients were treated on Outpatient Department Basis and admission was advised as and when required. Thorough history was taken and diagnosis was made with the help of ultrasonography, x-ray, KUB, noncontrast computed tomography as and when indicated.

Informed written consent was obtained. Patients were here after randomly divided into two groups with Group A receiving Tab. Silodosin 8 mg once daily and Group B receiving Tab. Tamsulosin 0.4 mg once daily. Analgesia in the form of Tab. Diclofenac was advised to the patients. A strict followup was kept where patients were advised to visit once every weak and pain relief of charted as per the visual analogue scale. If during the follow up period, patient gave history of passage of calculus in urine, then it was termed as the endpoint of the study.

RESULTS

The patients' ages in both groups ranged between 21 and 55 years. There was no significant difference between the groups with respect to the patients' ages, the stone sizes and their location. The followup consisted of 52 patients in group A and 54 patients in group B i.e. 14 patients in all were lost in follow up (8 in group A and 6 in group B). Comparing the results, Group A proved to be superior with a significant statistical difference for both stone expulsion time and stone expulsion rate as depicted in the table. This was further augmented by a lesser requirement for analgesics in Group A. Results according to the treatment.

Endpoint	Group 1 (Silodosin)	Group 2 (Tamsulosin)	p-value
Primary Endpoint: Stone Expulsion Rate	43/52 patients (83%)	31/54 patients (57%)	0.008
Secondary Endpoint: Mean±2SD time to Expulsion (Days)	11.3 (4.1)	17.8 (5.4)	0.01
The Difference in Both was Statistically Significant			

Table 1

DISCUSSION

Ureteroscopy and SWL remain the most effective treatments for DUS; 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.[10] There has been a significant improvement in the medical management of the ureteral calculi with the introduction of effective medical therapeutic agents in the market. The likelihood of a ureteral stone passage is dependent on several factors, which include the stone size and the location and the ureteral conditions. Studies have shown stone passage rates between 71-98% for the distal ureteral stones, which are less than 5 mm and from 25-53% for those, which are between 5 and 10 mm.[11] The role of adrenergic receptors in the human ureter was first described in 1970.[12]

It was shown later that the alpha-adrenergic receptors were classified into three different subtypes of α1A, α1B and α1D.[13] The α1A- and α1D-adrenoceptors are the most abundant subtypes in the distal ureter. Stimulation of these α1-adrenoceptors leads to increases in both the frequency of ureteric peristalsis and the force of ureteric contractions. However, blockade of these receptors decreases basal ureteric tone, decreases peristaltic frequency and amplitude leading to a decrease in intraluminal pressure while the rate of urine transport increases and thus increasing the chance of stone passage.[14]

Tamsulosin is a selective α1-blocker with a 10-fold greater affinity for the α1A- and α1D-adrenoceptor subtypes than for the α1B-adrenoceptor subtype, while the affinity of silodosin for the α1A-adrenoceptor subtype is ≈162- and 50-fold greater than its affinity for the α1B- and α1D-adrenoceptor subtypes respectively, which explain the weak cardiovascular adverse effects of silodosin.[9]

For safety issues and adverse effects, both drugs are safe and well tolerated and the most frequently encountered side effect in the present study was retrograde ejaculation, which was reported in three patients (5.8%) in the silodosin group. However, no patient discontinued the treatment because of retrograde ejaculation and the condition was reversible, resolving within a few days of cessation of treatment. The results from the present study show a low mean (SD) number of pain episodes in both groups of 1.3 (0.4) and 1.4 (0.3) in the silodosin and tamsulosin groups, respectively, which was not statistically significantly different (P = 0.15). These results were in agreement with Kumar et al who reported a mean (SD) number of pain episodes of 0.8 (0.9) and 1.70 (1.2) in the silodosin and tamsulosin groups, respectively. The pain relieving effects of the α-blockers may be explained by the blocking of C-fibres responsible for mediating pain.[15]

CONCLUSION

Hence, while concluding, we can effectively say medical expulsive therapy should be offered as a cost-effective treatment for the patients with distal ureteral calculi who are amenable to a waiting management, and if we may add, then, silodosin is more effective than tamsulosin in the management of lower ureteric calculus for the stone clearance rate and stone expulsion time. However, a multicentre study on a larger scale is needed to confirm its efficacy and safety.

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