Original Research Article

Effect of α-adrenergic blockers silodosin in the management of distal ureteric calculus

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ABSTRACT

Background: Urinary calculus disease is one of the 3 most common urological diseases. It affects about 12% of the world population and has become a worldwide health problem. Of all the urinary tract stones 20% are ureteral stones, of which 70% are found in the distal ureter. The objective of the study is to study the effect of silodosin in the passage of calculi in the distal ureter compared to non-steroidal anti-inflammatory drugs (NSAIDs) (diclofenac sodium) and oral fluids.

Methods: This study included a total of 90 patients between the study period from October 2016 to October 2018. 45 patients were chosen randomly and advised to take plenty of oral fluids and treated with NSAIDs and the other 45 patients were treated with silodosin 8 mg HS for one month along with oral fluids and NSAIDs. After 1 month if the stone was passed successfully, it was confirmed with ultrasonography, if failed, advised for surgery.

Results: Majority of the patients were in the age group of 20-45 yrs. The mean size of the calculus was 5.60 cm on the right side and 5.71 cm on the left side. Out of the 45 patients who were on treatment with silodosin 35 patients had passed the calculi and 10 patients had no results with a success rate of 77.7%. In the 45 patients who were not on silodosin, 8 patients passed the calculi and 37 patients did not pass the calculi. 21 patients among the 45 underwent urethrorenoscopy.

Conclusions: Silodosin is an effective and safe drug in the management of calculi in the distal ureter.

Keywords: Alpha blocker, Silodosin, Ureteric stones, Ureteroscopy

INTRODUCTION

Urinary stones have plagued mankind since ages; earliest recorded example being bladder stones detected in Egyptian mummies dated to 4800 B.C.[1] The etiology of the stones however remained obscure. Only in the last two centuries have studies resulted in the identification of composition of urinary stones. Hereditary relationship of urinary stones was shown during the genetic studies performed by Resnik (1968) and McGeown (1960). Familial renal tubular acidosis is associated with nephrolithiasis and nephrocalcinosis in almost 70% of patients.[1] Males are more commonly afflicted than females (Male:female= 3:1). Increased testosterone levels in men causing increased endogenous oxalate production by the liver and protective increased urinary citrate concentrations in women have been postulated as causes for the same.[2] Various studies over time have shown the cause of urinary stones to be multi-factorial.

Stones do not usually form in the ureter but drop down from the pelvi- calyceal system while they are still small. They tend to increase in size as they remain in the urinary passage. Most stones, smaller than 5 mm pass

spontaneously.[3] However some stones may arrest in the ureter producing complications such as obstruction, colic, infection, haematuria and acute renal failure. Therefore, urgent relief is to be given to these patients.

The treatment of ureteral stones has undergone a remarkable evolution in the last 15 yrs. At one time open uretero-lithotomy and blind stone basket manipulation were the mainstay of surgical management, they have now been superseded by an array of superior modalities. Among them ureterorenoscopy (URS) and extracorporeal shock wave lithotripsy are the two most favored methods for the treatment of ureteric stones.[4] The damaging effects of the calculi may result in obstruction with dilatation of the urinary tract, leading to stasis and severe infection, with resultant fibrosis. Ureter is the passage and the ureteric stone is just a passenger on its way from, the kidney, the site of its formation, to the urinary bladder. Many theories have been postulated to explain the aetiology of stone formation, but its exact cause still remains a mystery. The treatment that can be offered to the patient depends on many factors such as the size of the stone, obstruction or infection and site of impaction.

Silodosin is an α1-adrenoceptor antagonist with unequalled selectivity for the α 1A-adrenoceptor subtype. The α1A receptors predominate in mediating prostate contraction and the human urethra contains only α1A receptors whereas α1A, α1B, and α1D all mediate blood vessel dilation.[5] Consequently, the high selectivity of silodosin for the α1A subtype should result in better cardiovascular tolerability without any loss of efficacy on urinary tract symptoms, as compared to less selective α-adrenoceptor blockers. The standard recommended dose is 8mg capsule OD. Administration of silodosin is not recommended in patients with severe renal or liver function impairment.

The most common adverse reaction to the drug are retrograde ejaculation, dizziness, orthostatic hypotension, headache, diarrhoea and nasal congestion. The treatment of α1 blockers decreased the number of ureteral colic episodes and the intensity of pain during spontaneous passage at the lower ureteral calculi, also it will be beneficial to patients quality of life.[6] In the distal ureter alpha 1 adrenergic receptors are expressed with higher density than in the proximal and medial ureter. Blockade of these receptors inhibits ureteral peristaltic amplitude and frequency and decreases intra ureteral pressure thus increasing the rate of urine transport.[7]

Objective of the study was to study the effect of silodosin in the passage of calculi in the distal ureter compared to non-steroidal anti-inflammatory drugs (NSAIDs) (diclofenac sodium) and oral fluids.

METHODS

This study includes a total of 90 patients admitted with distal ureteric calculus of diameter 4-7 mm in the Department of General Surgery and Department of Urology, Yenepoya Medical College and Hospital between the study period from October 2016 to October 2018. 45 patients were chosen randomly and advised to take plenty of oral fluids and treated with NSAIDs (diclofenac sodium) and the other 45 patients were treated with Silodosin (alpha blocker) 8 mg HS for one month along with oral fluids and NSAIDs (diclofenac sodium). Follow up of the patients was done on 7th day, 14th day, 21st day and 28th day. Option of URS was advised for the patients who failed to expel the calculus with the above treatment. Statistical analysis done using Student-t test, ANOVA, Chi-square test.

Inclusion criteria

Patient of age group >20 yrs and with distal ureteric calculi with stone size 4 mm-7 mm were included in the study.

Exclusion criteria

Patients with previous history of surgical intervention in the ureter, use of any other anti-hypertensive α-blocker drug, congenital abnormality detected on ultrasonography, bilateral ureteric calculi, altered RFT and LFT and with multiple site calculi were excluded.

RESULTS

In this series majority of the patients were in the age group of 20-30 (22 patients) years followed by 30-40 years (21 patients). 27.7% of patients in this study group were female patients and 72.2 % were male patients (Table 1).

Table 1: Age and sex distribution.

Age (in years)	Female	Male	Total	Percentage (%)
20-30	5	17	22	24.4
30-40	7	14	21	23.3
40-50	5	12	17	18.8
50-60	4	15	19	21.1
60-70	4	6	10	11.1

In our study, 100% of the patients complained of only pain abdomen, 23.3% of the patients had hematuria, 33.3% patients had burning micturition and 57.7% patients had fever (Table 2).

Table 2: Distribution of samples by symptoms.

Symptoms	No. of patients (N)	Percentage (%)
Pain abdomen	90	100
Hematuria	21	23.3
Burning micturition	30	33.3
Fever	52	57.7

In study group, 26.6% of patients passed the ureteric calculus within 7 days, 31.1% of the patients passed the calculus within 14 days, 11.1% of the patients passed the calculus within 21 days and 8.8% of the patients passed the calculus within 28 days of follow up and 22.2% patients did not pass the calculus. P value is less than 0.05, hence statistically significant.

In control group, 6.6% of the patients passed the calculus within 7 days, 4.4% patients passed the calculus within 14 days, 6.6% of the patients passed the calculus within 21 days and 0 patients passed the calculus within 28 days of follow up. 82.2% of the patients did not pass the calculus (Table 3).

Table 3: Days of follow up.

No. of days	Study cases N (%)	Control cases N (%)
7	12 (26.6)	3 (6.6)
14	14 (31.1)	2 (4.4)
21	5 (11.1)	3 (6.6)
28	4 (8.8)	0 (0)
Not passed	10 (22.2)	37 (82.2)

DISCUSSION

Age and sex

Majority of the patients were in the age group of 20-30 years (22 patients) 24.4% followed by 30-40 years (21 patients) 23.3%. The commonest age reported by most of the series for the presentation of ureteric calculi is between 20-40 years (Table 1).[8] In this series 72.2% were male patients and 27.7% of patients in this study group were female patients. Most of the studies have reported a male to female ratio between 3:1 and 2:1. In a study by Porpiglia et al in 2008 reported that in group A the number of males was 17 and females were 29, and in group B males were 23 and females was 22.[9] Males and those with a family history of stone disease are three times more likely to be afflicted than others for urinary stone disease. Men appear to excrete more oxalate in their urine and women more citrate (thus protecting against stone formation).

Location of ureteric calculi

In our study 100 % of calculi were present in distal ureter as our study has excluded calculi at other sites. Puppo series of 378 patients reported an incidence 16.4% of calculi in the upper 1/3rd of the ureter, 25.3% in the middle 1/3rd of the ureter and 58.3% in the lower 1/3rd of the ureter.[10]

Size of calculi

In this series mean size of the calculus was 5.60 cm on the right side and 5.71 cm on the left side. In a study in

by Porpiglia et al showed that the mean size of the calculus was 5.93 mm in group A and 6.03 mm in group B.[9]

Duration of symptoms

In this series, 10% of patients came in the first week after appearance of symptoms, 30 % came in the second week and 60% patients came in the third and fourth week after appearance of symptoms. It is reported that duration of symptoms varies from 3 hours to 5 years. 80% of the patients came within 1 month of onset of symptoms, 4% gave a history of one year or longer.[10]

Presenting symptoms and follow up

In this series, 100 % (90 patients) had complaints of pain abdomen, 21 patients (23.3%) had hematuria, 30 patients had fever (33.3%), 52 patients (57.7%) had complaints of burning micturition (Table 2). Pain, nausea/ vomiting, hematuria, burning micturition/urgency/frequency of micturition and oliguria were the most common symptoms. Mouse and Resnick 1991 reported 87% had loin pain, 17% patients had vomiting and 3% presented with fever.[10,11] In this present series of 90 patients diagnosed to be having distal ureteric calculi, 45 patients were started on α blocker drug (silodosin) for 1 month. 45 patients were not given α blocker; they were given only NSAIDS and plenty of fluids. The stimulation of alpha 1 adrenergic receptors increases ureteral peristaltic frequency, smooth muscle tones and contractile force, resulting in ureteral spasm and decreased ureteral flow.[12] In this series, follow up was done every week for a period of 4 weeks. The patients were asked to pass urine in a filter and identify the passage of calculi. In study group 26.6% of patients passed the ureteric calculus within 7 days, 31.1% of the patients passed the calculus within 14 days, 11.1% of the patients passed the calculus within 21 days and 8.8% of the patients passed the calculus within 28 days of follow up and 22.2% patients did not pass the calculus (Table 3) p value is less than 0.05, hence statistically significant. In the control group, 6.6% of the patients passed the calculus within 7 days, 4.4% patients passed the calculus within 14 days, 6.6% of the patients passed the calculus within 21 days. 82.2% of the patients did not pass the calculus after 28 days of follow up. Out of the 45 patients who were on α blocker (Silodosin) 35 patients had passed the calculi and 10 patients had not passed, with a success rate of 77.7%. In the 45 patients who were not on silodosin, 8 patients passed the calculi and 37 patients did not pass the calculi. 21 patients among the 45 underwent URS. Mores et al showed that the rate of spontaneous passage is highly dependent on stone location. Passage rates from the proximal, middle and distal ureter were 22%, 46% and 71% respectively.[11]

CONCLUSION

Silodosin is an effective and safe drug in the management of calculi in the distal ureter with a success rate of 77.7%.

Most patients with ureteric calculi were rendered stone free with endourological procedures if conservative treatment failed.

REFERENCES

1. Sutton RA, Walker VR. Responses to hydrochlorothiazide and acetazolamide in patients with calcium stones: Evidence suggesting a defect in renal tubular function. N Engl J Med. 1980;302(13):709-13.
2. Morse RM, Resnick MI. Ureteral calculi: natural history and treatment in an era of advanced technology. J Urol. 1991;145(2):263-5.
3. Ehreth JT, Drach GW, Arnett ML, Barnett RB, Govan D, Lingeman J, et al. Extracorporeal shock wave lithotripsy: Multicenter study of kidney and upper ureter versus middle and lower ureter treatments. J Urol. 1994;152:1379-85.
4. Segura JW, Preminger GM, Assimos DG, Dretler SP, Kahn RI, Lingeman JE, et al. Ureteral stone s clinical guidelines panel summary report on the management of ureteral calculi. The American Urological Association. J Urol. 1997;158:1915-21.
5. Guimaraes S, Moura D. Vascular adrenoceptors: an update. Pharmacol Rev. 2001;53:319-56.
6. Resim S, Ekerbicer H, Ciftci A. Effect of tamsulosin on the number and intensity of ureteral colic in patients with lower ureteral calculus. Int J Urol. 2005;12(7):615-20.
7. Morita T, Wada I, Saeki H, Tsuchida S, Weiss RM. Ureteral urine transport:changes in bolus volume, peristaltic frequency, intraluminal pressure and volume of flow resulting from autonomic drugs J Urol. 1987;137(1):132-5.
8. Rizvi SAH, Naqvi SAA, Hussain Z, Hashmi A, Hussain M, Zafar MN, et al. The management of stone disease. Br Jr Urol. 2002;89:62.
9. Porpiglia F, Fiori C, Ghignone G, Vaccino D, Billia M, Morra I, et al. A second cycle of tamsulosin in patients with distal ureteric stones: a prospective randomized trial. BJUI. 2009;103(12):1700-3.
10. Puppo P, Ricciotti G, Bozzo W, Introini C. Primary Endoscopic treatment of ureteric calculi: A review of 378 cases. Euro Urol. 1999;36(1):48-52.
11. Morse RM, Resnick MI. Ureteral calculi: natural history and treatment in an era of advanced technology. J Urol. 1991;145(2):263-5.
12. Xizhao Sun, Lei He, Weihong Ge, Jianlin Lv. Efficacy of selective alpha 1D blocker Naftopidil as Medical Expulsive therapy for distal ureteral stones. J Urol. 2009;181:1716-20.