ORIGINAL ARTICLE

Efficacy of Tamsulosin Spontaneous Expulsion in the Treatment of Distal Ureteric Stones

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ABSTRACT

Objective: The objective of study was to determine the efficacy of Tamsulosin (alpha blocker) in spontaneous expulsion of 4-7mm ureteric stones in the distal segment of the ureter.

Subjects and methods: This randomized controlled trial study was conducted in the department of Urology, Shaikh Zayed Hospital between 24th November, 2008 to 24th May, 2009. A total 90 patients with lower ureteric stones equally divided in 2 groups A and B. In Group A tablet Tamsulosin 0.4mg was given at bed time in addition to diclofenic 50mg twice a day and in Group B only diclofenic sodium 50 mg twice-a-days was given. Treatment was continued upto 28 days maximum. All the patients were followed with abdominal ultrasound weekly. It was measured in term of stone expulsion which was confirmed by abdominal ultrasound and X-ray KUB at follow up. The clinical information of all patients was entered into pre designed proforma. The clinical variables were evaluated statistically.

Results: In group A the stone was discharged in 37 out of 45 patients and in group B stone was discharged in 22 out of 45 patients only. Treatment A showing a significant results in term of stone discharge as compared to treatment B i.e. *p-value = 0.001.*The average stone expulsion time was also significantly less in group A as compared to group B.

Conclusion: Alpha 1 antagonist (Tamsulosin) increases spontaneous expulsion of small distal ureteral stones.

Key words: Alpha blocker, Ureteral calculi, Tamsulosin.

INTRODUCTION

Selective alpha 1 adrenoreceptor antagonists have proved to be effective, well tolerated and easy to administer in the management of patients with lower urinary tract symptoms caused by obstruction at bladder neck due to autonomic stimulation.[1] Urinary system stone disease is observed in 12% of the general population[2]. Urolithiasis also constitutes 40-50% of urological work load in hospitals with a prevalance of 12% in Pakistan[3]. After the 1st diagnosis it recurs at mean rate of 75% in 20 years. Of all the urinary system stones, 20% are ureteral stones and almost 70% of these are distal ureteral stones[4]. Symptoms may include hematuria, pain in abdomen, flank or groin. Pain is usually severe and colic in nature. Ureteric calculi originate in the kidney and then due to gravity and peristalsis pass spontaneously down the ureter[5]. Calculi in the lower part of ureter often causes pain that radiates to groin or testicles in males and labia majora in females. Stones in the intramural portion of ureter may mimic cystitis, urethritis or prostatitis by causing suprapubic discomfort, urinary frequency, urgency, dysuria and hematuria. In males diagnosis may be confused with testicular torsion, epididymitis and in females the diagnosis may be confused with menstrual pain, pelvic inflammatory disease, ruptured or twisted ovarian cyst[6]. The most important aspect of examination in the patients with ureteric stone confirmed on managing is to measure the temperature. If the patients has stone and fever also along with it means, he may have infection in process[7].

Spontaneous expulsion rate of ureteral stones less than 5 mm is almost 85% during. Consequently observation as a treatment is recommended for this group of stones[8]. The eventual factors for spontaneous expulsion of ureteral stones are stone size, location, number, spasm in ureteral smooth muscle, mucosal edema, inflammation and ureteral anatomy[9]. The problem that can emerge during this observation period includes renal and ureteric colic attacks, urinary tract infections, hydroureter-onephrosis and acute pyelonephritis[10].

The basis of pharmacotherapy is different for different drug groups. In the case of alpha blockers, the human ureter contains predominantly alpha receptors which are further classified as alpha 1 and alpha 2 receptors. In turn alpha I receptors which are

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divided into subtypes on the bases of their selectivity. Alpha 1a (proximal urethra, prostate, bladder outlet), alpha1b (smooth muscles of vessels) and alpha1d (detrusor, lower ureter)[11]. Specifically those of alpha type, serve an important role in lower urethral physiology. Nor epinephrine is the main alpha-agonist which exerts positive chronotropic effect on the ureter, there by increasing peristaltic frequency. Positive chronotropic effect, increases muscle tone and at high doses may lead to complete ureteral obstruction. In ureter alpha adrenergic receptor antagonists inhibit basal tone and also decrease peristaltic frequency and amplitude. Consequently intraureteral pressure decreases, there is an increase in fluid transport ability which increases the bolus of urine thus exerting pressure above the stone, at the same time peristalsis and intraureteral pressure decrease below the stone. The net effect is an increase in intra ureteral pressure gradient around the stone which ultimately results in stronger expulsive force[12].

SUBJECTS AND METHODS

A Randomized controlled trial was conducted in urology department in Shaikh Zayed Hospital from 24th November to 23rd May 2009 for 6month period. Total 90 patients with 4-7mm stones in the distal segment of ureter were included in the study. Patients of any age who were presented in our department for the management of 4 to 7 mm stones confirmed on ultrasound in the distal segment of the ureter were included in the study. Presence of UTI, severe hydronephrosis, pregnancy, ulcer disease, hypotension, patients on calcium channel blockers, serum creatinine more than 2mg/dl, multiple ureteral stones, bilateral distal ureteric stones, solitary kidney, ureteral stricture and patient desiring for immediate stone retrieval were excluded in the study Patients were divided into two groups using random number table. In treatment group (A) tablet Terazosin 2mg at bed time was given in addition to regular analgesic tablet Diclofenic sodium 50mg 1 tablet twice a day. To the other control group (B) patients, only analgesics tablet Diclofenic sodium 50mg twice a day was given. Treatment continued up till stone expulsion or 28 days maximum. Patients were followed up in out patient clinic weekly. Patient`s abdominal ultrasound was done on each visit. The criteria for treatment discontinuation was uncontrollable pain, infection, raising serum creatinine. Patient data was collected on attached pre-designed proforma. Data analysis was performed with the program statistical package for social sciences (SPSS version11.0). Numerical variables age, duration of stone expulsion were presented as mean±S.D. The qualitative variables like gender, stone expulsion (Yes/No) and number of analgesic tablets were presented as frequency and percentage. The outcome variable i.e. stone expulsion (Yes/No) was compared between the groups using Chi-square test. P≤0.05 was considered significant.

RESULTS

In group A there were 32(35.55%) male and 13(14.44%) females while in group B the number of male patients was 31(34.44%) and female patients were 14(15.55%) (Fig.1). Average age of all patients was 33.12±11.20 years with the minimum and maximum ages 16-63 years respectively. The average age in treatment group (group A) was 32.40±10.28 years and in control group (group B) it was 33.84±12.13 years. The mean age in both treatment groups was statistically no significant (P=*0.544).* The average stone size in group A was 6.21±0.70 mm and in group B it was 6.00±0.53 mm. The range of stone size in group A was 4-7 mm and in group B it was 4-7mm. The average expulsion time of stone in group A was 13.30±6.31 days and in group B it was 19.18±4.66 days. The average expulsion time in group A was significantly less than group B (P=*0.000)* (Table 1) In group A the stone was discharged in 37 out of 45 patients and in group B stone was discharged in 22 out of 45 patients only. Treatment A showing a significant results in term of stone discharge as compared to treatment B i.e., p-value=0.001 (Table 2).

Fig. 1

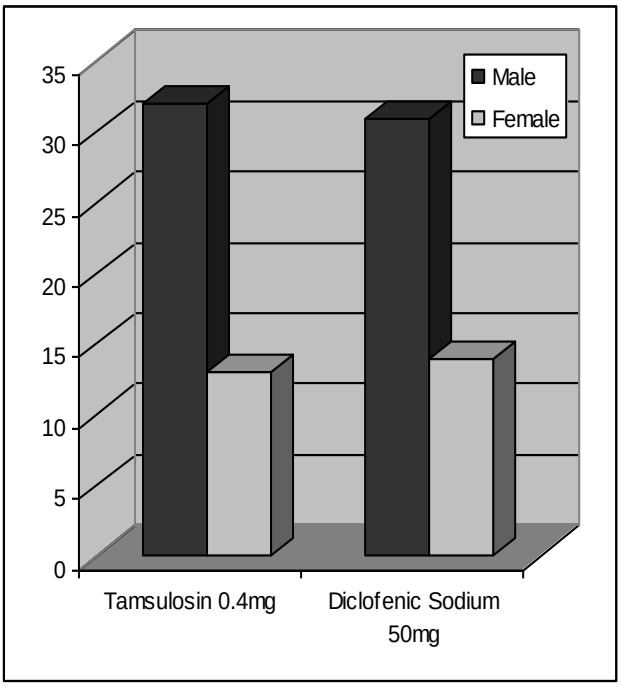

Table 1: Mean±standard deviation of age, stone size and expulsion time in both groups

Parameters	Treatment Groups		P value
	Tamsulosin 0.4mg (n=45)	Diclofenic Sodium 50mg (n=45)	
Age (years)	32.40±10.28	33.84±12.13	*0.544 (NS)*
Stone size (cm)	6.21±0.70	6.0±0.53	
Expulsion time (days)	13.30±6.31	19.18±4.66	*0.000 (S)*

Expulsion of stone	Treatment Groups		Total
	Tamsulosin 0.4mg	Diclofenic Sodium 50mg	
Yes	37 (33.3)	22(19.8%)	59(53.1%)
No	8 (7.2%)	23 (20.7%)	31 (27.9)

Chi-Square: 11.07, p-value=0.001

DISCUSSION

In recent years, significant advances have been made in every medical field, ESWL and ureterorenscopy have been widely used for the treatment of ureteric stones. However these procedures are not risk free[13]. Simple watchful waiting for long period of time can also lead to deterioration of renal function. According to literature the expulsion rate of distal ureteral stones by watchful waiting approach is 25% to 54% with mean expulsion time more than 10 days and considerable analgesic use[14]. Ureteric stones usually presents with ureteric colic and microscopic hematuria. The inability to control the pain is usually the indication of treatment. The cause of colicky pain is usually the strain on muscular nerve endings and mucosa. Which is caused by increase in intraluminal pressure secondary to inability of ureteral peristalsis to move the urine distal to the obstructing stone.

The main factors associated with obstruction by stones are ureteral smooth muscle spasm, mucosal edema, pain and infection. It seems that medical therapy addresses these factors. Various drug combinations have described. Calcium channel blockers and steroids have widely been used to reduce muscular spasm and to decrease inflammation. Borghi and colleagues[15] used an expulsive therapy consisting of methyl prednisolone and nifidipine in randomized double blind study, treating patients with ureteral stones as large as 5cm. They demonstrated beneficial effect in reducing the time to stone passage and improving the expulsion rate. Their results were confirmed by Porpiglia et al who used nifidepine, deflazacort.[16] Cooper and associates treated 70 patients having ureteral calculi and found that addition of nifedipine prednisone cetaminophen and antibiotics to standard medical therapy resulted in higher stone passage rate and fewer workday lost, emergency visits and surgical interventions[17]Those investigators came to the conclusion that it is difficult to quantify the result of each of the drug. These drugs also have many adverse effects like asthenia headache, palpitations which may result in discontinuation of treatment. Because alpha 1 receptors are predominant in ureteral smooth muscle, it has been suggested the blockade of such receptors by specific receptors antagonists will decrease ureteral peristaltic activity and consequent loss of intraluminal pressure of ureter leading to increase in urine transport ability. Ukhal and coworkers were the first to report positive result in accelerating the lower ureteral stone passage using alpha blocker agent[18].

They found the rate of spontaneous passage of distal ureteral stones during treatment with Doxazosin was 71.1% and he also observed treatment decreased the frequency of renal colic. More recently it has been demonstrated that specific adrenoreceptor subtypes (α1a/α1d) are prevalent in distal part of ureter.[19] Cervenakov and colleagues performed a randomized study and registered a significant advantage in stone expulsion rates when adding Tamsulosin (alpha blocker) added to standard therapy[20].Dellabela et al found greater efficacy with Tamsulosin which was compared with phloroglucinol, a antispasmodic drug very popular in Italy. More recently the same group published their data on 210 patients in order to compare the efficacy of three drugs (nifedipine, tamsulosin and phloroglucinol) for the spontaneous expulsion of distal ureteral stones[21]. They noted higher expulsion rate in Tamsulosin group that is 97.1% as compared to 77.1% in Nifedipine group and 64.3% in phloroglucinol group. It is also observed in the study that Tamsulosin achieved stone expulsion in significantly shorter time and with fewer hospitalizations, fewer pain episodes and with decrease in need for endoscopic procedures. These investigators then advocated the use of Tamsulosin as a first line agent in treatment of distal ureteral stones[22].

In the present study, total patients were 90. They were divided into two groups, Group A and Group B each with 45 patients. Group A received Tamsulosin 0.4mg 1hr before bedtime in addition to regular analgesic tablet diclofenic sodium 50mg 1 tablet twice a day. Group B patients received only diclofenic sodium 50mg tablet twice a day. Our specific aim was to evaluate the role of alpha 1 receptor antagonist's terazosin in our standard medical approach for the conservative treatment of distal ureteric stones. So stone expulsion rate was

significantly high in group A (alpha blocker group). Stone expulsion time was also significantly less in group A. Pain episodes were also significantly less in terazosin group (group A).

CONCLUSION

A conservative approach should be considered as an option in the management of small uncomplicated distal ureteral stones. We have observed the treatment with Tamsulosin (alpha 1 blocker) improved the rate of spontaneous stone expulsion as well as time of distal ureteral stone expulsion from start of therapy as compared to control group. It also decreased the pain episodes, so the use of alpha 1 blocker is recommended in treatment of small distal ureteral stones because of its high efficacy, excellent patient satisfaction and cost effectiveness.

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