

## **Efficacy of Tamsulosin for Clearance of Lower Ureteric Stones**

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### **ABSTRACT**

**Aim:** To compare the frequency of clearance of stones with and without the use of tamsulosin in patients having lower ureteric stones.

**Methods:** This was a randomized controlled trial study conducted at the department of Urology, Sheikh Zayed Post Graduate Medical Institute, Lahore during 11<sup>th</sup> March 2011 to 11<sup>th</sup> September 2011. Sixty cases of lower ureteric stones, according to the inclusion criteria, were included in the study from urology outpatient department of Shaikh Zayed Hospital. The demographic information of these cases like name, age, sex was recorded. The patients, satisfying the inclusion criteria were randomly divided in to 2 groups by random number table. Group I (control) was prescribed analgesia (diclofenac sodium 50 mg 12 hourly). Group II (study) was prescribed tamsulosin 0.4mg once daily for 28 days or till spontaneous stone passage (which ever was first).

**Results:** In group I the stone expulsion was seen in 11 out of 30 patients and in group II stone expulsion was present in 23 out of 30 patients. Treatment in group II showing a significant results in term of stone expulsion as compared to group I, i.e.  $p\text{-value} = 0.0026$ . The average stone expulsion time was also significantly less in group II as compared to group I.

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

**Keywords:** Efficacy, Lower ureteric stone, shock wave lithotripsy, ureteroscopy

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### **INTRODUCTION**

Urolithiasis is a health problem of worldwide importance. Ureteral stones account for 20% of urolithiasis, and 70% of ureteral stones are located in the lower third of the ureter. Ureteric stones have great bearing on the health as well as quality of life of the patient<sup>1</sup>. The disease spectrum in a developing country like ours is different from that in developed countries, mainly because of delay in diagnosis, investigations and lack of awareness which tend to modify the outcome in cases of ureteral stone or for that matter any disease. More so, advanced interventional facilities in this part of the world are not easily available<sup>2</sup>. It is generally believed that conservative medical treatment for ureteral stones should be applied first. If conservative treatment is unsuccessful, shock wave lithotripsy (SWL) or ureteroscopy (URS) can then be utilized<sup>3</sup>. The most important factors in predicting the likelihood of spontaneous stone passage are stone location and stone size<sup>4</sup>. The spontaneous passage rate for lower ureteric stones less than 5mm is 73.3% as compared to 23.1% for stones more than 5mm<sup>5</sup>.

Over the recent past selective alpha 1 adrenoreceptor antagonists have proved their worth

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for being 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<sup>6</sup>. 12% of general population are observed to be suffering from urinary system stone disease<sup>7</sup>. Urolithiasis also constitutes 40-50% of urological work load in hospitals with a prevalence of 12% in Pakistan<sup>8</sup>. After the 1<sup>st</sup> 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<sup>9</sup>. 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<sup>10</sup>. 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<sup>11</sup>. The most important aspect of examination in the patients with ureteric stone confirmed on imaging is to measure the temperature. If the patients have stone and fever also along with it means, he may have infection in process.<sup>12</sup>

Significant advances have been made during the last two decades in the management of upper urinary tract stones, with the advent of ESWL, small calibre flexible endoscopes, development of the intracorporeal lithotripters allow access to entire urinary tract with little or no effect on renal functions. Consequently open surgery is rarely performed now-a-days. However these procedures are not risk free and they require expensive instruments. The understanding of pathogenesis of stone disease has also progressed and has led to prophylactic dietary measures and medications to prevent stone recurrence. Most stone formers can now be offered prophylactic measures for recurrent stone disease<sup>13</sup>.

Spontaneous expulsion rate of ureteral stones less than 5mm is almost 85%. Consequently observation as a treatment is recommended for this group of stones<sup>16</sup>. 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<sup>15</sup>. The problem that can emerge during this observation period includes renal and ureteric colic attacks, urinary tract infections, hydrouretero-nephrosis and acute pyelonephritis<sup>16</sup>.

To prevent such complications and accelerate spontaneous expulsion various medical treatment methods have been used.<sup>17</sup> The most important advancement in the treatment of distal ureteric calculi in recent year has been the discovery of role of medical expulsive therapy to facilitate spontaneous expulsion of small ureteric calculi<sup>18</sup>. To ease spontaneous expulsion of distal ureteric calculi by adjuvant pharmacological medications like alpha blockers, calcium channel blocker, prostaglandins inhibitors and steroids are being used<sup>19</sup>.

## PATIENTS AND METHODS

This was a randomized controlled trial study conducted at the department of Urology, Sheikh Zayed Post Graduate Medical Institute, Lahore during 11<sup>th</sup> March 2011 to 11<sup>th</sup> September 2011. Sixty cases of lower ureteric stones, according to the inclusion criteria, were included in the study from urology outpatient department of Shaikh Zayed Hospital. The demographic information of these cases like name, age, sex were recorded. The patients, satisfying the inclusion criteria were randomly divided in to 2 groups by random number table. Group I (control) was prescribed analgesia (diclofenac sodium 50 mg 12 hourly). Group II (study) was prescribed tamsulosin 0.4 mg once daily for 28 days or till spontaneous stone passage (which ever was first).

Patients having lower ureteric stone less than 1 cm, sterile urine and symptom free were included. Those patients having obstruction, stone size >1cm and UTI were excluded from the study. The data was analyzed using SPSS-15.

## RESULTS

The average age of all patients was 33.15±8.97 years with the minimum and maximum ages 18-49 years respectively. The average age in group I was 33.87±9.61 years and in group II it was 32.43±8.33 years (Table 1). In group I there were 19(31.67%) male and 11(18.18%) females while in group II the male patients was 18(32%) and female were 12 [18%] (Table 2). The average stone size in group I was 6.63±1.45 mm and in group II it was 6.93±1.39 mm. The range of stone size in group I was 4 -9mm and in group II it was 4 -10mm (Table 3). In group I the stone was discharged in 11 out of 30 patients and in group II stone was discharged in 23 out of 30 patients only. Treatment group II showing a significant results in term of stone discharge as compared to group I [ $P=0.0027$ ] (Table 4). The average expulsion time of stone in group I was 20.93±3.43 days and in group II it was 15.7±3.72 days. The average expulsion time in group II was significantly less than group I [ $P = 0.001$ ] (Table 5).

Table 1: Frequency and percentage of ages

Age (years)	Group I (n = 30)		Group II (n = 30)	
	No.	%	No.	%
18 – 30	15	50.0	14	46.7
31 – 40	10	33.3	12	40.0
41 – 50	5	16.7	4	13.3

$P = 0.3842$  (Not significant)

Table 2: Frequency and percentage of genders

Gender	Group I (n = 30)		Group II (n = 30)	
	No.	%	No.	%
Male	19	63.2	18	60.0
Female	11	36.8	12	40.0

Table 3: Frequency and percentage of stone size

Stone size (mm)	Group I (n = 30)		Group II (n = 30)	
	No.	%	No.	%
4 – 6	10	33.3	8	26.7
7 – 8	12	40.0	14	46.6
9 – 10	8	26.7	8	26.7

$P = 0.4748$  (Not significant)

Table 4: Frequency and percentage of expulsion of stone

Expulsion of stone	Group I (n = 30)		Group II (n = 30)	
	No.	%	No.	%
Yes	11	36.7	23	76.7
No	19	63.3	7	23.3

$P = 0.002687$  (Significant)

Table 5: Frequency and %age of expulsion time (days)

Expulsion time (days)	Group I (n = 30)		Group II (n = 30)	
	No.	%	No.	%
15 – 18	17	56.7	18	60.0
19 – 22	8	26.7	9	30.0
23 – 26	5	16.6	3	10.0

P = 0.001 (Significant)

## DISCUSSION

In recent years, significant advances have been made in every medical field, ESWL and ureterorenoscopy have been widely used for the treatment of ureteric stones. However these procedures are not risk free.<sup>20</sup> 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 been described. Calcium channel blockers and steroids have widely been used to reduce muscular spasm and to decrease inflammation. Borghi and colleagues<sup>21</sup> used an expulsive therapy consisting of methyl prednisolone and nifedipine in randomized double blind study, treating patients with ureteral stones as large as 5 cm. 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 ( $\alpha 1a/\alpha 1d$ ) are prevalent in distal part of ureter.<sup>22</sup> Cervenakov and colleagues<sup>23</sup> performed a randomized study and registered a significant advantage in stone expulsion rates when adding Tamsulosin (alpha blocker) to standard therapy. Dellabela et al<sup>24</sup> found greater efficacy with Tamsulosin which was compared with phloroglucinol, an antispasmodic drug very popular in Italy. They noted higher expulsion rate in Tamsulosin group 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. Dellabella et al<sup>25</sup> also tried to explain the observation why the patient receiving tamsulosin experienced less pain episodes as compared to nifedipine alone. They suppose a double action of tamsulosin on the control of pain associated with ureteric colic, one on smooth muscle, preventing spasm and second on C fibers or sympathetic post ganglionic neurons which also blocks pain conduction to the central nervous system. Propigia

and associates<sup>26</sup> compared the safety and effectiveness of nifedipine and deflazocort with those of tamsulosin and deflazocort for the treatment of distal ureteral stones. They concluded medical therapy particularly with tamsulosin could reduce expulsion times.

Kupeli and coworkers<sup>27</sup> reported their experience with the addition of tamsulosin to medical therapy or to ESWL for lower ureteral stones. They randomized 78 patients into four groups all being reevaluated after 2 weeks. The difference in the stone free rates of tamsulosin and control group was statistically significant. The positive effect of alpha blocker was more evident for larger stones as well. Yilmaz et al<sup>28</sup> were the first to perform randomized comparison of three alpha1 blockers in treatment of distal ureteral stones. They enrolled 114 patients. All patients divided into four groups who received nothing, tamsulosin, terazosin and doxazosin. All patients were observed for 1 month. Expulsion rate in control group was 53.57%, in doxazosin group 75.86%, terazosin group was 78.57%, tamsulosin group was 79.31%. None of the patients in this trial received corticosteroid or antispasmodic agents which permits more accurate assessment of the absolute efficacy of these specific agents. They concluded that all of these agents are equally effective in enhancing spontaneous expulsion of distal ureteral stones and corticosteroid therapy may not be necessary<sup>29</sup>. Actually corticosteroids when given in such patient for prolonged period of time are not risk free because of side effects. Yilmaz et al<sup>28</sup> not used corticosteroids.

In different studies patients with different stone size have been taken, maximum stone size being upto 10mm and observation period was upto 28 day<sup>28,29</sup>. As prolonged period of use may lead to deterioration of renal function. Diclofenic sodium is a non steroidal anti inflammatory drug advocated for use in painful conditions. It possesses potent analgesic properties with fast onset of action and long duration. The patients in group II which is tamsulosin group demonstrated a higher stone passage rate that is 23 out of 30 (76.6%) as compared to group I which was the control group. In the control group stone passage rate was 11 out of 30 patients (36.6%). The average stone expulsion time in group II was 15.69 days and in group I was 20.90 days.

Stone expulsion rate was significantly higher in group II (alpha blocker group). Stone expulsion time was also significantly less in group II. Pain episodes were also significantly less in tamsulosin group (group II). As patients were followed, only 3 cases had side effects in tamsulosin group. The side effects were headache. Regarding retrograde

ejaculation none of the male patients reported any abnormality. So in all aspects our results are comparable to international studies conducted on role of medical therapy in treatment of uncomplicated distal ureteral stones.

## 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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