Orginal Article

Effect of Tamsulosin on Stone Clearance after Extra-corporeal Shock Wave Lithotripsy

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Abstract

This prospective study was performed to observe effect of Tamsulosin on stone clearance after Extra-corporeal Shock Wave Lithotripsy (ESWL) for renal stones having size 6-20 mm. According to selection criterion total 80 patients with renal stones were divided into two groups. In group l, 40 patients treated with traditional hydrotherapy after ESWL and in group 2 another 40 patients were treated with additional Tamsulosin. In-group 1, there were 25 male and 15 female patients and in group 2, male and female patients were 30 and 10 respectively. Without considering the stone size within 3 weeks after ESWL stone clearance in group 1 and 2 was 57.50 and 80.00 percent respectively (P<0.05). Considering the stone size, stone clearance in group 1 was 50% and 33.3% among smaller (6-10 mm) and larger (11-20 mm) stones and in group 2 was 50% and 66.7% among smaller and larger stone respectively (P>0.05). In cases of smaller stones, clearance was 100% and 77.8% among group 1 and 2 respectively without any significant difference (P>0.05). But in larger stones, stone clearance was 34.60% and 81.8% among group 1 and 2 respectively and there was a statistically significant difference in clearance between the groups (P<0.05). Morbidity was significantly lower when ESWL was combined with Tamsulosin. Requirement of additional interventional procedures were significantly higher in group 1 (P<0.05). Complications were less common in group 2 than group 1. Haematuria and lower urinary tract symptoms were equally common in both groups.

Keywords: Tamsulosin, Stone clearance, ESWL.

Introduction

Urolithiasis is the third most common disease of the urinary tract, exceeded only by urinary tract infections and pathologic conditions of the prostate .[1]

Urolithiasis affects 4% to 15% of the world population, and the incidence of this is increasing, especially in Europe.[2] Stone fragment expulsion after renal ESWL is probably not dissimilar to spontaneous discharge. Though there is no exact data about its prevalence in Bangladesh but the problem is quite common.

Renal stone disease may be complicated by pyonephrosis, septicaemia, pyelonephritis, hydronephrosis, renal failure and even death. So, early and appropriate treatment is necessary to protect renal function and to avoid some grave complications. Management of urolithiasis ranges from conservative watchful waiting to traditional open surgical procedure. In between these two, there exists a spectrum of procedures, which includes the recently developed non-invasive to minimally invasive procedures. But one option can supplement other for total stone clearance.[3]

ESWL has revolutionized the treatment of urinary stones with the concept of stone fragmentation. The noninvasive nature, requirement of minimal or no anaesthesia and high level of patient acceptance, have made ESWL a preferred treatment for majority of symptomatic renal calculi requiring intervention.[4]

Although ESWL is an effective treatment of urinary calculi, it can cause complications. Stone colic, delayed stone fragment passage or obstructed ureter due to steinstresse (column of stone fragments) may be of different type of clinical situation after ESWL for renal stones may occur.

Several factors are weighed in determining the optimal treatment protocol, including the number, size, location, and composition of the stones and the type of lithotriptor used. The transport of the stones from the kidney and their movement through the ureter is accompanied by the three basic factors: spasm of smooth muscles, submucosal edema and pain.[5] Determining factors are the size and configuration of the stones, their localization as well as their number. Angular stones cause considerable difficulties, mainly after Extracorporeal Shock Wave Lithotripsy (ESWL). The removal and elimination of the calculi from the ureters depends not only on their size and shape but also on the intensity of the contractibility and irritation of the adrenoceptors present in the smooth mucles of the ureters and detrusor. In the transport of stones the greatest obstacle is usually formed by

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the terminal part of the ureters, mainly in its intramural "detrusor tunnel". Based on the molecular and pharmacological diversity of the effect of ?-1 blockers, subtype alpha IID, which has the most pronounced effect on the detrusor relaxation, and the spasm of the lower part of ureters and espacially on its intramural part.[5] Several studies have shown that the density of alpha IID-adrenergic receptors in the ureteral smooth muscle cells is greater than in other adrenergic receptors. In addition, the alpha adrenergic antagonists are able to inhibit basal tone and peristaltic frequency, dilating the ureteral lumen and facilitating stone passage. Some investigators have reported the effectiveness of pharmacologic therapies in increasing ureteral stone expulsion and reducing total analgesic use.[6]

Tamsulosin, an alpha-1 receptor blocker usually used to relax prostatic smooth muscles owing to its inhibitory effect on alpha l-A receptors, but it also can affect on alpha 1-D receptors of ureteric smooth muscles facilitating passage of stone fragments after ESWL. To our knowledge, only a few studies however, has defined the contribution of Tamsulosin in the success of ESWL for renal stones. One such study was performed in our country regarding ureteric stone clearance though not after ESWL. For this reason, we planned to use Tamsulosin, as adjunctive therapy, to verify its role in renal stone fragment expulsion after a single ESWL treatment.

Methodology

This was a randomized controlled trial. This study was carried out in Department of urology, Bangabondhu Sheikh Mujib Medical University (BSMMU), Dhaka, during the period of July 2006 to May 2007. Patients with renal stone came in this hospital were selected according to the selection criteria and included in this study. After successful fragmentation of renal stone by ESWL, patients over 15 years of age were collected randomly for this study. The total number of study population was 80, who were equally divided in two groups.

In group 1, as randomized controlled group all patients were given traditional hydrotherapy after ESWL.

In group 2, as randomized trial group all patients were given additional Tamsulosin 0.4 mg daily orally with traditional therapy.

The inclusion criterions were solitary radioopaque stone in upper or middle calyx or in renal pelvis, stone size- 6-20mm, sterile urine, excreting kidneys etc. On the other hand exclusion criterions were age <15 years, any concomitant renal stone, stone size- <6mm,>20mm, lower calyceal stone, diseased opposite kidney, urinary tract infection, pregnancy, bleeding disorders, severe cardiopulmonary disorders, radioluscent stones, elevated serum creatinine (>2mg/dl), high grade hydronephrosis, diabetes mellitus, concomitant treatment with calcium antagonist or alpha receptor antagonist, congenital anomalies of urinary tract, previous urological surgery causing ureteric stricture, bladder outlet obstruction etc, neuropathic bladder, severe skeletal deformity, morbid obesity. Variables were stone size, location of stone, stone clearance, episodes of colic and other complications after ESWL. Detailed history was taken and clinical examination was done for each patient and recorded in predesigned data entry form.

Before ESWL all patients were investigated with total blood count, serum creatinine, random blood sugar, coagulation profile, urine examination and Electrocardiography. Ultrasonogram and intravenous urography were done in all patients to observe renal excretion and size, location of stone.

Prophylactic antibiotic was given to all the patients 24 hours before the ESWL procedure. ESWL monotherapy with Siemens Lithostar plus (3'a generation) lithotriptor was used to fragment the renal stone. All the patients were given intravenous fluid and analgesic suppository prior to the procedure. In supine position on the ESWL table stone located by fluoroscopy and stones were fragmented. Amount of energy given in each patient was 4Kv to 5.5Kv with an average of 4.7Kv. The patients with successful fragmentation of stone were randomly divided equally into two groups. Patients of group I were allowed to take minimum 2.0 liter water daily and analgesics if required (75 mg diclofenac injection). Patients of group II were instructed to take additional oral Tamsulosin.0.4 mg daily for maximum three weeks. All patients of both groups were asked to compile a diary about postdischarge pain, stone expulsion, episodes of colic, analgesic use and side effects of drug.

All patients were observed weekly for three weeks to see stone clearance. In each follow up, patients were evaluated with X-ray and urine examination was done and data were recorded in data sheet. During follow up period, the patients who developed complications e.g. pain, hematuria, lower urinary tract symptoms (LUTS), ureteral colic has been managed by additional therapies like antibiotics, analgesics, sedatives, etc. Those patients who were refractory to medical management have treated with interventional therapy.

After collection of data, statistical analysis was done using computer SPSS 12.0 version and manual technology. Test of significance was done

by using student's t-test, z-test and χ^2 test. A probability value (p-value) of <0.05 was considered significant. Differences in the success rate between treatments were compared with the chi-square test or Fisher's exact test.

Results

After successful fragmentation of stone by ESWL, separate instructions were given to both groups of patients. Within next 3 weeks significant number of patients became stone free. There was significant difference in clearance of stone between the groups (Table I).

Table I: Stone clearance in study groups. (Within 3 weeks after ESWL)

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	Group -I (n=40)		Group -II (n=40)		P value
	No.	(%)	No.	(%)	
Stone -free	23	(57.5)	32	(80.0)	0.030
Failure	17	(42.5)	8	(20.0)	

Fisher's exact test

* = Significant (P<0.05)

Same number of smaller stones cleared in both groups but in larger stones clearance was not similar, statistically which was not significant. Among total 80 patients 28 & 27 patients became stone free in group I & group II respectively (Table II)

Table II: Effect of stone size on clearance rate in the two study groups

Stone size		Group-I		Group-II		P value
		No.	(%)	No.	(%)	
6-10 mm	28	14	(50.0)	14	(50.0)	1.000^{ns}
11-20 mm	27	9	(33.3)	18	(66.7)	0.124 ^{ns}

Z-test ns = Not significant

In this study, the incidence of stone clearance in patients of group I and II were 100% and 77.8% respectively. In case of smaller stone 100% of group I and 77.85% of group 2 cleared and 22.2% not cleared. In larger stones 34. 6% of group I and 81.8% of group 2 cleared and 65.4% of group I and 18.2% of group II not cleared. So there is statistically significant difference in stone clearance between groups.

Table III: Relation between stone clearance and stone size

Outcome	Stone size		
	6-10 mm	11-20 mm	
Group-I	(n= 14)	(n=26)	***
Stone-free	14 (100.0)	9 (34.6)	
Failure	0	17 (65.4)	

Group-II	(n= 18)	(n=22)	
Stone-free	14 (77.8)	18 (81.8)	
Failure	4 (22.2)	4 (18.2)	

Fisher's exact test □ □ ns = Not significant □ □ *** = Significant (P<0.001)

In this study, gradually increased number of patients became stone free in subsequent week following post ESWL additional Tamsulosin therapy (group II) but this type of increment was not observed in patients who followed post ESWL hydrotherapy alone.

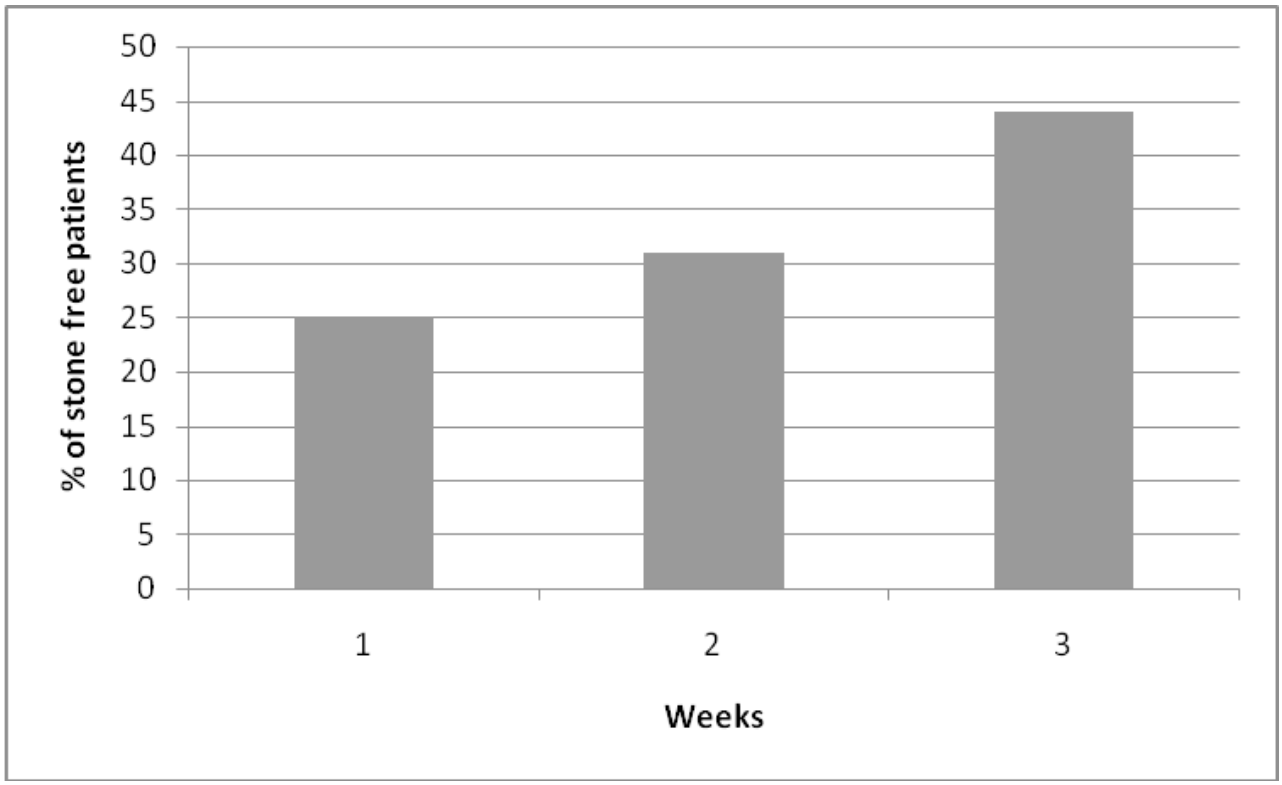

Fig -1 Bar diagram showing stone free patients at different weeks in group-2.

After ESWL complications developed in some patients of both groups. Most of the patients were improved on the same day. Among total 35 patients who developed some sorts of complication after ESWL, 23 patients were from group I and 12 patients were from group 2 which was statistically significant. All patients of Group II had episodes of colic during follow up period but only a few patients of Group I.

Table IV: Post-ESWL complications status in each group

Complication	Group-I (n=40) No.	(%)	Group-II (n=40) No.	(%)	P value
Yes	23	(57.5)	12	(30.0)	0.024*
No	17	(42.5)	28	(70.0)	

Fisher's exact test * - Significant (P<0.05)

During the follow up period some patients of both groups needed additional treatment. Additional treatment required in group I and II was 57.50% and 47.5% respectively which is not significant statistically. In group I, 23 patients were subjected to take additional treatment of whom 12 patients were taken medical therapy and 11 patients were needed additional intervention which is not significant statistically. In group II, 19 patients were subjected to take additional treatment of which 16 patients taken medical therapy but only 3 patients needed additional intervention which is statistically significant.

Table V: Additional treatment required in group-1 and group-II patients

Parameters	Group -I (n=40) No. (%)		Group -II (n=40) No. (%)	
Treatment required				
Yes	23	(57.5)	19	(47.5)
No	17	(42.5)	21	(52.5)
P value	0.429 °ns		0.874 °S	

Z-test ns = Not significant s=significant

Discussion

The present study has been designed to assess the effectiveness of Tamsulosin than traditional therapy (Hydrotherapy) after ESWL for renal stone of 6-20 mm size.

Several variables play a fundamental role for the migration process of stone fragments: stone size, intrinsic areas of narrowing within the ureter, ureteral peristalsis and edema, infection, and spasm of the ureter at the site at which the stone is lodged. Edema, infection, spasm, and ureteral peristalsis could be modified by an appropriate medical therapy. Some investigators have reported the effectiveness of different pharmacologic therapies in increasing ureteral stone expulsion by acting primarily on spasm and ureteral peristalsis. In a study, association of nifedipine and steroids improved the rate of ureteral stone expulsion and reduced the time for stone passage.[7] Furthermore, alpha l-adrenergic antagonist can cause a decrease in ureteral peristaltic frequency, reducing ureteral spasm. These changes are accompanied by an increase in the rate of fluid transport.[8] In this regard, several studies have demonstrated that lower tract ureteral stones can be treated efficiently with different types of alpha l-blockers with a low incidence of side effects. Of the available alpha 1 -blockers, Tamsulosin has been chosen because it is a combined alpha lA and alpha lD-selective adrenergic antagonist. In this study it was observed that 3 weeks of Tamsulosin therapy had a favorable impact on the clearance of residual fragments after ESWL.

In this study, stone clearance was 57.5% and 80% among group I (traditional hydrotherapy) and group II (additional Tamsulosin) respectively. Here statistical analysis shows significant difference of clearance ($P<0.05$) which is more or less similar to another study where post ESWL stone clearance rate after 3 months follow up with traditional hydrotherapy and analgesic and with additional Tamsulosin was 60% and 78.5% respectively.[6]

In group I of this study, 35% patients were in stone size between 6-10 mm and 65% were in stone size between 11-20 mm and in group II, 45% had stone size between 6-10 mm and 55% had stone size between 11-20 mm. The above distribution correlates other study having stone size between 4-10 mm and 11-20 mm in each group but does not correlate with the another study having stone size of < 20 mm and 20 or > 20 mm in each group.[6,11]

In this study, stone clearance in group I was 100% and 34.6% for smaller (6 to 10 mm) and larger stones (11-20 mm) respectively and in group II, 77.8% and 81.8% for smaller and larger stones indicates lower clearance rate in larger stones in group I but higher clearance rate in larger stones in group II. This observation may be due to lower spontaneous expulsion rate of fragments of stone of large size and due to more facilitating effect of Tamsulosin in stone clearance preferably in larger size of stone. Again

among 28 cleared small stones, 14 (50%) were of group I and another 14 (50%) were from group- 2 and among 27 cleared larger stones, 9 from group I and 18 from group II. So, statistical analysis shows no significant difference of clearance rate (P>0.05) among smaller and larger stones. Another study showed same finding which included patients with stones 11 to 20 mm in diameter. A relevant difference in the success rate between the two groups, 81% in group II (Tamsulosin group) and 55% in group I (traditional therapy group); P = 0.009) were found.[6]

In this study a similar success rate was obtained in patients with renal pelvi caliceal stones (P-0.523) which is also observed in that study with p value >0.05.[6]

We used ESWL monotherapy with Siemens Lithostar plus (3rd generation) lithotriptor to fragment the renal stone. Amount to energy given in each patient was 4Kv to 5.5Kv with an average of 4.7Kv. In another study using a spark gap second generation lithotriptor (Sonolith 3000) showed stone clearance in ESWL group 75% and 57% for stone size 1-2 cm and 2-3 cm respectively.[9] This clearance rate roughly correlates with the present study.

In another study using HM-3 Dornier lithotriptor found stone clearance in ESWL group 75% and 43% for 1-2 cm and 2-3 cm stone size respectively.[10] This result is roughly comparable with present study for smaller stone but different for larger stones .This difference of results between studies might be due to the fact that their maximum stone size was 3 cm.

In this study, complications were less in group II (30%) than group I (57.5%), which is statistically significant (p value-.024). Colicky pain was less in patients of group II (Mean no. of episodes

1.83+{-2,15) than group I (Mean no. of episodes 4.43+/-2.04) which is statistically significant (p value=.0001). Haematuria and lower urinary tract symptoms were common in both groups. Steinstrasse was present only in group I. Above findings correlates with different other studies.[2,11]

In the current study, additional treatment required in-group I and II were 57.5% and 47.5% respectively and no significant difference in requiring adjuvant treatments was observed (P>0.05). In-group I, among 23 patients, 52.2% received only medical treatment and 47.8% required intervention but in-group II, among 19 patients, only 3 required intervention which is statistically significant (p value .004).

In another study, adjuvant or additional intervention was necessary in 31.5% of all patients and serious complications were not recorded after ESWL.[6] These findings were close to the results of present study.

Conclusion

Considering the findings of the present study and the studies previously done by others, it can be concluded that additional Tamsulosin is more effective than traditional hydrotherapy alone in clearing larger renal stones. To our knowledge, only a few studies however, has defined the contribution of Tamsulosin in the success of ESWL for renal stones. So, use of Tamsulosin, as adjunctive therapy in renal stone fragment expulsion after a single ESWL treatment would be contributory for further research.

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