

Stone Clearance in Patients with Upper Ureteric Stones Using Extracorporeal Shock Wave Lithotripsy Compared with Extracorporeal Shock Wave Lithotripsy Combined with Tamsulosin Therapy

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Abstract

Objective: To assess its role in stone clearance along with ESWL in patients with upper ureteric stones.

Method: This clinical trial was conducted from February 2018 to December 2021 at the Department of Urology, Services Hospital Lahore.. A total of 164 patients (82 in each group) of both sexes between the ages of 18 and 70 years with upper ureteric stone (6mm-15mm) were included in this study. These patients were randomly divided into two groups. Patients in group A received ESWL alone, while patients in group B received ESWL in combination with tamsulosin therapy. Follow-up visits with CT KUB Plain were planned 4 weeks postoperatively to assess stone clearance

Results: The mean age of patients was 44.01±10.88 years. The study included 124 (75.6%) male and 40 (24.4%) female patients. The mean size of stones was 9.59±2.72 mm. Both the groups were comparable in terms of mean age (p=0.539), mean stone size (p=0.936), age groups (p=0.507), stone size groups (p=0.817), and gender distribution (p=0.631). The stone clearance rate was significantly higher in patients treated with ESWL in combination with tamsulosin therapy (92.7% vs. 65.9%; p=0.003) compared to ESWL alone.

Conclusion: The clearance rate was significantly higher in patients treated with ESWL in combination with tamsulosin therapy compared to ESWL alone.

Keywords: ESWL, Tamsulosin therapy, Ureteric stones, Stone clearance

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Introduction

In the early 1980's, the advent of extracorporeal shock-wave lithotripsy (ESWL) revolutionized the treatment of ureteric stones. It has been recommended as first-line therapy for upper ureteric stones up to 20mm in size

with a stone clearance rate of 60-90%.¹ A number of factors determine the success of ESWL, including stone size, shape, composition, and subsequent narrowing of the ureteric lumen, which impedes the removal of stone fragments after an ESWL session.² Tamsulosin is an α -blocker which is widely used in urological practice to relax the smooth muscles in prostate and bladder neck. Over the past decade, the role of tamsulosin as part of medical expulsion therapy for the treatment of patients with kidney and ureteric stones has been extensively researched with notable success.³ A possible mechanism underlying this effect may be ureteric smooth muscle relaxation, alleviation of muscle spasms, resulting in easy and accelerated passage of stones.⁴ Recently, tamsulosin has been used in a number of randomized controlled trials along with ESWL for the management of

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lower ureteric stone, and all of these studies report a significantly increased frequency of stone removal with ESWL and tamsulosin combination therapy, likely due to increased and accelerated passage of stone fragments with tamsulosin.⁵ However, the results need further confirmation as there are some studies that do not support the role of tamsulosin therapy in removing ureteral stones after ESWL.⁶ Taking into account the controversies in the available literature and the absence of locally published studies, the intent of this study is to replicate this trial and confirm the results. Thus, if the results of this study show a significantly increased frequency of stone clearance with the addition of tamsulosin, this study may represent a useful treatment option for future patients presenting with upper ureteric stones.

Materials & Methods

This clinical trial was conducted from February 2018 to December 2021 at the Department of Urology, Services Hospital Lahore. The sample size of 144 patients was computed with a power of 90% and a confidence level of 95%, while the expected stone clearance rate was assumed to be 79.3% in the ESWL group and 96.6% in the ESWL in combination with tamsulosin group.⁷ However, for more accurate results, a larger sample of 164 patients (82 patients in each group) was adopted. The study enrolled patients of both sexes, aged between 18 and 70 years, presenting with a single upper ureteric stone between 6 and 15 mm in the largest diameter. Patients with urinary tract infection (more than 10 pus cells/HPF on complete urine examination), distal ureteric stricture, prior unsuccessful ESWL, concomitant use of alpha-adrenergic antagonists or calcium channel blockers, patients with coagulopathy (INR greater than 1.5), obesity (BMI over 30 kg/m²) and deranged renal function tests (serum creatinine over 2 mg/dl) were excluded from the study. Upon approval by the hospital ethics committee, patients who met the inclusion criteria were admitted through the emergency department and outpatient department. All patients provided informed consent. The patients were randomly divided into two groups. Group A received ESWL, while group B received ESWL along with tamsulosin therapy. Patients in both groups received an ESWL session with an electromagnetic lithotripter at 12 to 15 KV. The stone was located with a C-arm. Patients in Group-B were also advised to take tamsulosin tablet (0.4 mg) once daily for 4 weeks. All patients were assessed for stone clearance after 4 weeks with CT KUB. Patient demographic details along

with stone size, duration and healing at follow-up were noted on the predesigned proforma. The data collected were entered and analyzed in SPSS version 20. Continuous variables such as age and stone size were presented as means with standard deviation. Categorical variables such as gender and stone clearance were presented as frequencies and percentages. Stone clearance between groups was compared using the chi-square test. Data were stratified by age, sex, and stone size to account for effect modifiers. The post-stratification chi-square test was applied.

Results

In this study, the mean age was 44.01 ± 10.88 years. The mean age in group A was 44.76 ± 10.82 years, while in group B it was 43.27 ± 11.03 years in group B. Of 164 patients, 124 (75.6%) were male and 40 (24.4%) were female. The mean size of stones was 9.59±2.72 mm. Both the groups were comparable in terms of mean age (p=0.539), mean stone size (p=0.936), and age groups (p=0.507), stone size groups (p=0.817), and gender distribution (p=0.631) as elaborated in (Table-1). In this study the stone clearance was found in 54(65.9%) patients after ESWL group, while the stone clearance was found in 76(92.7%) patients in ESWL combined with tamsulosin group. The difference was statistically significant (p=0.003) as illustrated in (Table-2). The stone clearance rate in younger patients (18 to 44 years) was significantly higher in the ESWL combined with

Table 1: Baseline characteristics of patients.

		Group A	Group B	P-value
Age (years)		44.76±10.82	43.27±11.03	0.539
Age groups	18-44 years	40 (48.8%)	46 (56.1%)	0.507
	45-65 years	42 (51.2%)	34 (43.9%)	
Gender	Male	60 (73.2%)	64 (78.1%)	0.631
	Female	22 (26.8%)	18 (21.9%)	
Stone size (mm)		9.61±2.82	9.56±2.65	0.936
Stone size Group	6-10 mm	54 (65.9%)	52 (63.4%)	0.817
	11-15 mm	28 (34.1%)	30 (36.6%)	

Table 2: Comparison of outcome

	Stone Clearance		p-value
	Yes	No	
Group A	54 (65.9%)	28 (34.1%)	0.003
Group B	76 (92.7%)	6 (7.3%)	

Table 3: Stratification of stone clearance with respect to age, gender and size of stone

		Stone clearance in group A	Stone clearance in group B	P-value
Age (years)	18-44	26 (65.0%)	42 (91.3%)	0.034
	45-65	28 (66.7%)	34 (94.4%)	0.032
Gender	Male	41 (68.3%)	59 (92.2%)	0.034
	Female	14 (63.6%)	17 (94.4%)	0.033
Size of stones (mm)	6-10	38 (70.4%)	48 (92.3%)	0.041
	11-15	16 (57.1%)	28 (93.3%)	0.023

tamsulosin group than in the ESWL group. Similarly, it was found that the stone clearance rate was higher in male patients and in patients with smaller stones (6-10 mm) in the ESWL combined with tamsulosin than in the ESWL group.

Discussion

The main objective of treating kidney stones is to attain stone clearance with minimum possible morbidity for the patient. The advent of ESWL and continued advances in the field of urology have made it possible to treat most patients with kidney stones in a minimally invasive manner. Today, ESWL is the mainstay of treatment for kidney stones less than 2cm in size. For kidney stones, removal can be affected by many factors, comprising stone size, stone location, stone composition, kidney and ureter anatomy, and distal blockage due to edema, spasm, or stricture. The relaxation of the ureter in the stone area is considered a decisive factor in promoting the passage of the stone. Recently attention has been paid to medical expulsion treatment targeting some of the reversible factors involved in the passage of stones through the ureter. There is evidence of alpha-1 adrenergic receptors in the ureter. Therefore, the rationale for using alpha-1 adrenergic antagonist in clearing upper ureteric stones after ESWL is its ability to reduce tone of ureteric muscles and peristaltic ureteric contractions, dilating the lumen and thereby promoting stone passage through the ureter.⁸⁻¹⁰ Hence, this randomized controlled trial was conducted to assess the role of alpha-1 blockers (tamsulosin) in clearing upper ureteric stone after ESWL.

In this study, stone clearance rate was significantly higher in patients receiving ESWL therapy in combination with tamsulosin therapy than in patients receiving ESWL therapy alone (92.7% vs. 65.9%; $p=0.003$). The evaluation took place 4 weeks after the therapy with CT KUB. In a randomized controlled trial conducted by Bhagat and colleagues in patients with mixed ureteric and renal stones, the stone clearance was significantly higher in the patients receiving ESWL together with tamsulosin therapy than in ESWL therapy alone (96.6% vs 79.3%; $p=0.04$).⁷ These results are consistent with our study. Similarly, Gravina et al. concluded in their study that patients treated with ESWL and tamsulosin had achieved greater clinical success after 3 months than patients treated with ESWL alone (78.5% vs 60.0%; $p=0.03$)¹¹. A meta-analysis of 49 studies including 6436 patients also concluded that use of tamsulosin therapy not only augmented the stone clearance (80.5% vs 70.5%; $p<.00001$) but also shorten the time of stone expulsion.¹² Our study further suggested that smaller stones have a greater clearance rate with tamsulosin therapy. However, in the above studies, larger stones (more than 10mm) had a better stone clearance rate in the patients treated with tamsulosin compared to the controls after ESWL session. Contrary to our results, other authors have described a limited role of alpha-1 blockers (tamsulosin) after ESWL for ureteric stone clearance. A randomized prospective study conducted by Karim and his coworkers indicated that stone clearance rate was not significantly affected by the addition of tamsulosin therapy (92.5% in tamsulosin group vs. 86.9% in placebo; $p=0.2$), however, the tamsulosin therapy was associated with less post-ESWL pain.¹³ De Nunzio et al. showed in their study that there was no statistically significant difference in stone clearance between the patients treated with tamsulosin and controls (58% vs. 47%; $p=0.399$) after a single cycle of ESWL.¹⁴ Similarly, Ahmed et al. also found no significant difference in the stone clearance between tamsulosin-treated patients and controls (78% vs. 69%; $p=0.108$) in a randomized controlled trial lasting up to 12-week study.¹⁵ Such findings were also observed by Zaytoun et al.¹⁶ and Falahatkar et al.¹⁷ in their studies. This work suffers from a number of limita-

tions. First, the results are based on a single-center trial. Second, the vexing problem that patients suffer after ESWL is the excruciating pain due to stones being pushed in and out through the ureter. However, we did not measure post-treatment pain scores between groups, as this may lead to further usefulness of tamsulosin therapy in reducing post-treatment pain symptoms. However, there are some notable strengths of this study such as its prospective controlled randomized design and the inclusion of CT KUB as an evaluation tool, which allowed accurate measurement of stone clearance (outcome) in the patients.

Conclusions

Stone removal in patients receiving ESWL therapy in combination with tamsulosin therapy was significantly greater in patients with a single upper ureteric stone compared to patients treated with ESWL therapy alone. Therefore, we recommend the concomitant use of tamsulosin therapy with ESWL for the treatment of upper ureteric stones.

Conflict of Interest *None*

Funding Source *None*

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OUR, FURH: Data Collection

NAG, MR: Literature Search

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SHC, MSA: Drafting, Revision

SHC: Writing of Manuscript