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ORIGINAL ARTICLE

EFFICACY OF ALFUZOSIN VERSUS CONTROL GROUP IN UPPER URETERIC STONE EXPULSION IN ADULT POPULATION OF LAHORE, PAKISTAN

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ABSTRACT

Background: Urinary stone disease is one of the commonest urological diseases worldwide. The objective of this study was to compare the efficacy of alfuzosin versus control group in upper ureteric stone expulsion in adult population of district Lahore, Pakistan.

Materials & Methods: This trial was conducted in Department of Urology, Sheikh Zayed Hospital, Lahore, Pakistan form January 2017 to June 2017. All adult patients with upper ureteric stone size 5-10 mm were eligible. Those with multiple stones, having fever, severe pain, history of surgery in past two weeks and growth on urine culture or pyuria were excluded. Experimental and control groups each had 30 patients. Experimental group received Tab. alfuzosin 10 mg daily for four weeks and Tab. diclofenac sodium 50 mg SOS for acute pain. The control group received Tab. diclofenac sodium 50 mg SOS for acute pain. We followed all patients for four weeks for expulsion of ureteric stones by X-ray KUB or CT KUB. Sex, age and stone size were matching variables. Stone expulsion (yes, no) was research variable. We compared count of stone expulsion between two groups by using McNemar chi-square test at alpha 0.5 using GraphPad.

Results: Out of 30 patients in experimental group, 23 (76.67%) were men and seven (23.33%) women and out of 30 in control group, 20 (66.67%) were men and 10 (33.33%) women, almost similar in both groups. Mean age in experimental group was 39.45±10.33 years and in control group it was 37.38±8.28 years, almost similar in both groups. Mean stone size was 7.45±1.47 (5-10) mm in the experimental and 7.28±1.68 (5-10) mm in control group, being comparable in both the groups. In experimental group, stone expulsion was achieved in 23 (76.67%) cases and not in seven (23.33%) cases and in control group, it was achieved in 16 (53.33%) cases and not in 14 (46.67%) cases. There was statistically no significant difference in efficacy of alfuzosin versus control group (p=.1213).

Conclusion: Our study showed no difference in efficacy of alfuzosin versus control group for upper ureteric stone expulsion in adult population of district Lahore, Pakistan.

KEY WORD: Upper Ureteric Stone; Alfuzosin; Experimental Group; Control Group; Adult; Urology; Urological Diseases; Pakistan.

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1. INTRODUCTION

1.1 Background: Urinary stone disease is a common pathological condition globally. The prevalence in Asia is approximately between 1-5% but it is slightly high in Europe approximately 5-9% and still more in USA roughly 13%.[1] Ureteric stones are the commonest presentation in urology outpatients and emergency department and are associated with significant morbidity.

Stones size less than 5 mm passes spontaneously

in up to 98% of the cases.[2] For stones >5 to <10 mm, the estimated spontaneous stone clearance is 47%.[3] The second important factor for stone passage is the location of the calculus in the ureter. Proximal ureteric stones pass spontaneously in 25%, mid ureteric in 45% and distal in 75% of the patients.[2] The time required for spontaneous clearance also depends on the stone size and the location. Small stones <2 mm pass in 8 days while larger one 4 to 6 mm require 22 days to pass spontaneously.[4] Usually a conservative treatment for more than 6 weeks is not recommended due to the risk of kidney damage.[5]

The treatment of ureteric stone has evolved recently due to researches and recent advances from open surgery to medical and minimally invasive techniques. Different less invasive strategies include extracorporeal shock wave lithotripsy and ureterorenoscopic techniques.[6] Although these new techniques are less invasive as compared to open surgeries, but they are more expensive and have known complications. There are known anesthesia and other surgical risks.

Therefore, the medical expulsion therapy (MET) to promote stone expulsion became attractive in recent era. Different drugs e.g. furosemide, calcium channel antagonists and corticosteroids are evaluated as treatment options to facilitate ureteric stone expulsion with inconsistent results.[7] Now the alpha blockers are considered very effective drugs for stone expulsion through the ureter based on various studies.[8-11]

The ureter is supplied by 3 main types of alpha adrenoceptors i.e. α1a, α1b and α1d.[12] The proportion of α1d is greatest in lower ureter and alpha 1a receptors are commonest in upper part of the ureter. Various studies have been conducted on the efficacy of the alpha blockers in expulsion of ureteric stones. The proposed data suggests that blockade of these receptors results in dilatation of ureter that facilitate the expulsion of stones. Spontaneous passage of ureteric stones increases with administration of alpha blockers. Tamsulosin is alpha blocker with alpha 1d selectivity and has impressive results in lower ureteric stones expulsion. Alfuzosin is more selective for alpha 1a and as expected its results in lower ureteric stone expulsion are not as impressive as tamsulosin but still comparable.[13] Most of the studies conducted are done for the lower ureteric stone.[14,15]

Indicating promising results but the data for upper ureteric stones is scarce. Alfuzosin has shown promising results in expulsion of upper ureteric stones. In a study conducted in 67 patients, demonstrated the overall stone clearance rate in the treatment group was 81.8% (27 out of 33 patients) and in the control group 50% (17 out of 34 patients). The increase in the stone clearance was 31.8% (p=.006). In the same study, while considering the upper ureteric stones, the rate of stone expulsion was 72.7% (8/11) in treatment group and 21.4% (3/14) in control group. The increase in the stone clearance was 51.3% (p=.01). in the same study, when considering the lower ureteric stones, the stone expulsion was 86.4% (19 out of 22 patients) in MET group while 70% (14 out of 20 patients) in control group. Here increase in rate was 16.4%, but insignificant statistically. This is because alfuzosin is more selective for alpha 1a receptors which are more abundant in upper ureter as compared to lower ureter.[16]

1.2 Research Objective: The objective of this study was to compare the efficacy of alfuzosin versus control group in upper ureteric stone expulsion in adult population of district Lahore, Pakistan.

1.3 Research (Null) Hypothesis: There is no significant difference in the efficacy of alfuzosin versus control group in upper ureteric stone expulsion in adult population of district Lahore, Pakistan.

1.4 Significance of study: This study will help us in the management of upper ureteric stones as medical treatment has decreased morbidity and is cost effective. This will decrease unnecessary surgical interventions in patients with upper ureteric stones.

2. MATERIAL AND METHODS

2.1 Design, Setting, Duration, Population & Sampling: This non-randomized controlled trial was conducted in the Department of Urology, Sheikh Zayed Hospital, Lahore, Pakistan from January 2017 to June 2017. The sample size was calculated by an online calculator available at www.openepi.com and was equal to 60 cases (30 in each group) by considering the expected percentages of efficacy in the two groups approximately 83.8% in alfuzosin group and 50% in the control group. Sampling was done by nonprobability consecutive sampling

All adult (18-65 years) patients with upper ureteric stone size 5-10 mm were eligible. All patients with multiple stones, having fever, severe pain uncontrolled with oral analgesics, history of surgical intervention in past two weeks and growth on urine culture or pyuria were excluded. If complications developed that warranted some surgical interventions like PCN or URS+DJ-Stenting, those cases were dropped.

2.2 Conduct of Procedure: We took the consent from the patients. The patients were divided in to two groups; group 1 experimental and group 2 control group by lottery method. Experimental group received Tab. alfuzosin 10 mg daily for four weeks and Tab. diclofenac sodium 50 mg SOS for acute pain. The control group received Tab. diclofenac sodium 50 mg SOS for acute pain. We followed all patients for four weeks for expulsion of ureteric stones by X-ray KUB or CT KUB.

2.3 Data Collection and Analysis Plan: Sex (men, women), age in years and stone size were three

matching variables. Stone expulsion (yes, no) was a research variable. Age was a numeric variable and was analyzed by mean and SD. Sex and stone expulsion were two nominal variables and were analyzed by count and percentage.

As we had no pretest data, so we performed the hypothesis testing by posttest only analysis as advised for the experimental studies. We compared frequency/ count of stone expulsion between the two groups by using McNemar chi-square test[17-19] at alpha 0.5 using online statistical calculator GraphPad.[20] Yates correction for continuity was applied.

3. RESULTS

Out of 30 cases in experimental group, 23 (76.67%) were men and seven (23.33%) women. Out of 30 cases in control group, 20 (66.67%) were men and 10 (33.33%) women, almost similar in both groups.

The mean age of the patients in experimental group was 39.45±10.33 years and in control group it was 37.38±8.28 years, almost similar in both groups.

The mean stone size was 7.45±1.47 (5-10) mm in the experimental group. In the control group it was 7.28±1.68 (5-10) mm, being comparable in both the groups.

In experimental group, stone expulsion was achieved in 23 (76.67%) cases and not in seven (23.33%) cases and in control group, it was achieved in 16 (53.33%) cases and not in 14 (46.67%) cases. There was statistically no significant difference in efficacy of alfuzosin group versus control group for stone expulsion with a p-value of 0.1213. (Table 1)

4. DISCUSSION

In our study the stone expulsion rate was 76.67% in alfuzosin group while in control group it was 53.33%. Our study showed no difference in efficacy of alfuzosin versus control group for upper ureteric stone expulsion in adult population of district Lahore, Pakistan.

From the literature we came across the fact that the alpha blockers e.g. tamsulosin, alfuzosin etc. improve the chances of stone expulsion in the cases of distal ureteric stones. A lot of studies are conducted on lower ureteric stones using tamsulosin and a very few studies described the use of alfuzosin. Alfuzosin is a very uroselective and effective drug for the treatment of BPH.

Similar results are shown by the Wood, et al.[21] They showed in their study having 76 patients divided into the alfuzosin and placebo groups that the rate of passage of the stone was 73.5% in the alfuzosin group, while 77.1% in the control group with no significant difference in both groups. The patients in the alfuzosin group showed less morbidity as demonstrated by pain scales. Similarly they passed stone in short time interval.

Contrary to our study, Reddy, et al.[22] showed that the calculus expulsion rate was higher in the group receiving alfuzosin (74%) as compared to the control group (32%) and the difference was statistically significant (p=.00001). Patients with small calculus had low failure rate as compared to patients having bigger calculus size. The analgesic requirement was more in the placebo group. Also the intervention required was lower in alfuzosin group.

Contrary to our results, Chau, et al.[23] showed in their study from China that alfuzosin was better as compared to the control group for stone expulsion. They demonstrated 51.3% increased upper ureteric stone expulsion rate in the alfuzosin group.

Contrary to our results, Agrawal, et al.[24] compared alfuzosin and control groups in patients with the lower ureteric stones. They showed the stone expulsion in 70.5% of the patients in the alfuzosin group, while 35.2% in controls with p-value significant.

Contrary to our results, Ahmed, et al.[25] showed that 23 out of 30 patients (76.6%) passed lower ureteric stone in the alfuzosin group, while in the control group 14 out of 28 patients (50%) passed the stone. The difference was statistically significant (p=.035).

Contrary to our results, El Said, et al.[26] showed in a study of 54 patients that stone expulsion rate was higher in the alfuzosin arm (53.6%, 15/28) as compared to the control arm (26.9%, 7/26, p=0.04). They recommended that the patients of the lower ureteric stone should be treated by the alfuzosin therapy for early passage of stone.

Table 1: Comparison of efficacy of alfuzosin versus control group for stone expulsion in adult population of district Lahore, Pakistan

Groups	Stone expulsion in experimental group			Columns total	Chi-square value	d.f	p-value
Stone expulsion in control group	Attributes	Yes	No				
	Yes	12	4	16	2.400	1	0.1213
	No	11	3	14			
Rows total		23	7	30 pairs	Null hypothesis was accepted		

5. CONSLUSION

Our study showed no difference in efficacy of alfuzosin versus control group for upper ureteric stone expulsion in adult population of district Lahore, Pakistan.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	FH, GM, MS
Acquisition, Analysis or Interpretation of Data:	FH, GM, MS, GK, NJ, MA
Manuscript Writing & Approval:	FH, GM, MS, GK, NJ, MA

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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