Lower Ureteric Stone Expulsion under the Effect of Alpha Blockers: A Clinical Trial over Alpha Blockers Efficacy

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ABSTRACT

Background: Urolithiasis has become a worldwide health concern. The ureters account for over 20% of urinary tract stones. The lifetime chance of having urinary calculi is between 5-12%, and men are more likely than women to develop them. For the treatment of ureteric calculus, there are a variety of minimally invasive interventional (ESWL and Ureteroscopy) and expectant options. However, the optimum therapy is mostly determined by the type and size of the stone, as well as the stone's location and the patient's demands. We do minimal invasive procedures like ureterostomy and ESWL to remove stone in ureter with some complications. The purpose of this study is to determine the efficacy of alpha blockers in expulsion of lower ureteric stones less than 1cm.

Objective: To determine the efficacy of alpha blockers in expulsion of lower ureteric stones less than 1cm.

Materials and Methods: This descriptive case series From June to December 2020, research was conducted in the Department of Urology, A total of 195 patients were included in this study. All patients were subjected to history taking and examination for suspected ureteric stone. Urine R/E and blood test was performed, which included serum urea and creatinine levels, as well as an x-ray KUB and ultrasound of the pelvis and abdomen by giving alpha blockers 0.4mg at night. Efficacy was measured after four week times.

Results: Our study shows that among 195 patients, 127(65%) patients were in age 15-40 years and 68(35%) patients were in age 41-60 years. 119(61%) patients were male and 76(39%) patients were female. 88(45%) patients had stone size = 10 mm and 107(55%) patients had stone size >10mm. More over alpha blocker was effective in 115(59%) patients and was not effective in 80(41%) patients.

Conclusion: Our study concludes that the efficacy of alpha blockers was 59% in expulsion of lower ureteric stones less than 1cm.

Key Words: efficacy, alpha blockers, expulsion, lowers ureteric stones.

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INTRODUCTION

Urolithiasis has become a worldwide health concern. The ureters account for over 20% of urinary tract stones[1]. The lifetime chance of having urinary calculi is between 5-12%, and men are more likely than women to develop them[2-4]. For the treatment of ureteric calculus, there are a variety of minimally invasive interventional (ESWL and Ureteroscopy) and expectant options. However, the optimum therapy is mostly determined by the type and size of the stone, as well as the stone's location and the patient's demands[5-7]. The stone burden is still the most important consideration when treating a patient with ureteric calculus[8-10]. While deranged renal function or uro-sepsis can worsen a failed prospective treatment, interventional procedures are not always without risk of complications and failure. Recent trials have demonstrated great outcomes for medical expulsive therapy for ureteric calculi in terms of stone expulsion rates and ureteric colic management, using medications (alpha blockers, nifedipine, a stone expulsion drug)53.9%[11].

Stones lodged in the ureter, the tube that transfers urine from the kidney to the bladder, can be painful and necessitate a visit to the doctor. Depending on the region of the ureter the stone is lodged in and the size of the stone, it may pass into the bladder on its own over weeks. People frequently require procedures to remove the stone if it does not come out on its own. To reduce the morbidity in patients having distal ureteric stones alpha drugs are now a days commonly used to reduce the ureteric spasm, dilate and help in ureteric stones expulsion medically and surgical procedure and anesthesia morbidity and mortality. The objective of my study is to determine the efficacy of alpha blockers in expulsion of lower ureteric stones less than 1cm.

MATERIALS AND METHODS

This descriptive case series was conducted in the Department of Urology, from June to December 2020. Patients age 15-60 years with lower ureteric stone size less than 1 cm were included while those having with urinary tract infection, multiple

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ureteric calculi, pregnancy, solitary kidney associated ureteral anomaly, impaired renal functions, previous ureteric surgery or endoscopic procedure, history of drugs intake like steroids and oral contraceptives and those suffering from any inflammatory condition (viral infection, gastroenteritis, respiratory tract infection, hepatitis), active neoplasia, diabetes, obesity, hepatic failure were excluded from the study. Before the patients were enrolled in the trial, they gave their informed written consent. All patients were subjected to history taking and examination for suspected ureteric stone. Urine R/E, blood and investigations includes serum urea and creatinine levels, as well as an x-ray KUB and ultrasound of the pelvis and abdomen were carried out. All above investigations was performed in the same laboratory under supervision of my supervisor, using the same protocol to avoid any conflict by giving alpha-blockers 0.4mg a night. Efficacy was measured after three week times. Efficacy of alpha-blockers was measured by performing CT KUB. The data was entered and analyzed using SPSS 20. Mean ± S.D were calculated for numeric variables like age, stone size and CRP level. Frequency and percentage was calculated for qualitative variables like gender and efficacy of alpha blockers. Efficacy of alpha blocker was stratified among age, gender and stone size. Post stratification was applied using chi-square test. P-value = 0.05 was considered as significant.

RESULTS

In the present study age distribution was analyzed as 127(65%) patients were in age 15-40 years and 68(35%) patients were in age 41-60 years. 119 patients (61%) were male and 76 (39%) were female, according to an analysis of patient gender. In terms of stone size, 107 patients (55%) had stones larger than 10 mm, compared to 88 patients (45%) who had stones smaller than 10 mm. Mean stone size was 8 mm with SD ±2.94. Efficacy of alpha blockers were compared in different age groups and shows 57% efficacy in 5-40 years old patients and 62% in 41-60 years with a p-value(0.5621) (Table -1). Alpha blocker were 595 effective in both male and female gender and 41% no effective with a p-value (0.9572) (Table-2). 58% of <10mm and 60% 10mm of renal stones pass while 41% of the renal stones didn't pass with a p-value (0.7928) (Table-3).

Table 1. Efficacy of Alpha Blockers with Respect to Age

Efficacy	5-40 Years	41-60 Years	Total (%)	P value
Effective	73(57%)	42(62%)	115(59)	0.5621
Not effective	54(43%)	26(38%)	80(41)	
Total	**127(100%)**	**68(100%)**	**195(100)**	

Table 2. Efficacy of Alpha Blockers with Respect to Gender

Efficacy	Male	Female	Total (%)	P value
Effective	70(59%)	45(59%)	115(59)	0.9572
Not effective	49(41%)	31(41%)	80(41)	
Total	**119(100%)**	**76(100%)**	**195(100)**	

Table 3. Efficacy of Alpha Blockers with Respect to Stone Size

Efficacy	≤ 10 mm	> 10 mm	Total (%)	P value
Effective	51(58%)	64(60%)	115(59)	0.7928
Not effective	37(42%)	43(40%)	80(41)	
Total	**88(100%)**	**107(100%)**	**195(100)**	

DISCUSSION

Patients receiving tamsulosin had a stone expulsion rate of 86.2%, compared to 76.6% for patients taking alfuzosine, in a research done in Saudi Arabia[1].While deranged renal function or uro-sepsis can worsen a failed prospective treatment, interventional procedures are not always without risk of complications and failure.

Similar findings were found in another study by Aldaqadossi HA et al[12], who found outstanding outcomes in terms of stone expulsion rates(54.9%) and ureteric colic control sing medicines (alpha blockers, nifedipine (which was stone expulsion 54.9%). While in our study alpha blockers were effective in 64(60%) in patients having distal ureteric calculi $\geq$ 10mm.

Ureteral stones are treated with diameter of less than 10 mm, Without lithotripsy, alpha-blockers were compared to placebo or alternative pharmacologic therapies in four meta-analyses and two randomised controlled trials (RCTs)[13]. The clearance rates of tamsulosin 0.2 mg daily and conservative treatment were same in a Japanese trial. The authors noted that the standard tamsulosin MET dose is 0.4 mg, but the Japanese health insurance system only covers 0.2 mg for benign prostatic hyperplasia[13]. In a Chinese study, both tamsulosin 0.4 mg (82.2%) and naftopidil (72.1%) were shown to be more successful than placebo (30.2%) in eliminating stones[14]. Meta-analyses have been published for each of the selective alpha-blockers (alfuzosin, silodosin, and tamsulosin), as well as one that looked at all alpha-blockers (selective and nonselective)[15]. The meta-analysis of tamsulosin covered over 2700 people were enrolled in 29 trials and concluded that tamsulosin (0.2 mg and 0.4 mg daily) improved clearance rate by 33% when compared to placebo. Tamsulosin was found to be more effective than calcium channel blockers at removing stones (6 studies). Tamsulosin 0.4 mg per day was shown to be as effective as tamsulosin 0.2 mg per day (small study). There was no difference in expulsion rate between tamsulosin and lithotripsy for stones 4-8 mm in diameter, however >8 mm stones removed faster with lithotripsy than with tamsulosin[15]. Meta-analysis of alfuzosin covered over 700 patients were enrolled in seven trials and revealed that alfuzosin 10 mg daily improved clearance rate by 85% when compared to placebo[16]. The silodosin meta-analysis covered over 1000 patients from seven trials and concluded that silodosin 8 mg daily improved clearance rate by 69% when compared to placebo[17]. The alpha-blocker meta-analysis covered nearly 6000 patients from 55 trials and revealed that alpha-blockers improved clearance rate by 49% compared to placebo. The findings were not stratified by medicine or dose[18].

Alpha-blockers were studied in five RCTs, one case-control research, and two meta-analyses as supplemental therapy (tamsulosin, alpha-blockers) for renal or ureteral stones after lithotripsy[19]. The RCTs used stones with diameters ranging from 4 to 20 mm. Four of the five RCTs looked at tamsulosin 0.4 mg once a day. When compared to control, Its clearance rate was 73% to 86% at 4 weeks, compared to 55% to 69% at 8 weeks, 95% compared to 57% at 8 weeks, and 78% to 91% compared to 46% to 74% at 12 weeks.. All but one of the 12-week trials yielded meaningful effects [20]. Tamsulosin was proven to be effective in lowering renal colic in three RCTs[21]. Tamsulosin was found When compared to smaller stones(less than 10 mm), it appears to be more effective for larger stones (11-20 mm) in one tamsulosin RCT[22]. In one RCT, alfuzosin 10 mg daily had a clearance rate of 76.7 percent against 46.7 percent for renal stones 11 to 15 mm when compared to control. For stones measuring 5 to 10 mm, there was no change [23,24]. The tamsulosin meta-analysis covered over 1300 participants from 15 trials and indicated a 24 percent improvement in clearance rate for upper urinary tract stones with tamsulosin 0.4 mg daily compared to control. The results were not divided into categories based on the size of the stones. It also discovered that 0.4 mg daily provided better benefit than 0.2 mg daily[15]. The alpha-blocker meta-analysis included about 2900 patients from 26 studies and found that both alpha-blockers and nifedipine significantly improved the stone-free rate (odds ratio 2.77) when compared to control for upper urinary tract stones. The size or position of the stone had no effect on the results[25]. Taiwanese patients who took alpha-blockers after lithotripsy were observed for up to 180 days in a case control study, and it was discovered that the longer they took alpha-blockers, the less likely they were to have a recurrence. The recurrence rates per 1000-person years were 45.64 and 18.52 in the first (days 1-45) and fourth (days 135-180) quartiles, respectively[24].

Adverse outcomes were reported seldom in the studies, and no major side effects were linked to the usage of alpha-blockers. Dizziness,

hypotension, headache, and ejaculatory dysfunction were among the side symptoms reported. The uro-selectivity of alpha-blockers had no effect on adverse effects [26]. According to a Cochrane study, Alpha-blockers cause the vasculature to dilate, resulting in a moderate reduction in blood pressure, averaging 8 mm Hg systolic and 5 mm Hg diastolic[27]. The most common side effects of alpha-blockers are dizziness (3%-19%) and headache (0%-21%), which are caused by a drop in blood pressure. Orthostatic hypotension has been recorded in patients starting alpha-blocker therapy (between 0% and 19%), however it is less common with long-term use (0%-4%)[28].

According to a study done in Lahore, Pakistan, patients were only given alpha-1-blockers tamsulosin with (p=0.017), the average expulsion time was 8.40 ± 2.41days[29]. The rate of stone expulsion in distal ureteric calculi was 70.8% in the tamsulosin group, 70.2% in the alfuzosin group, and 75% in the silodosin group, according to a study done in Turkey[30], while in our study it was 51(58%) in patients having = 10 mm and 64(60%) with calculi of >10mm. a study conducted by Sharma G et al, to know the efficacy of different alpha blockers in distal ureteric stone, Stone free rate was highest for silodosin(94.8%) values followed by alfuzosin (58.8%) and tamsulosin (46.2%)[31]. A Turkish study was done to determine the effectiveness of several alpha medications for treating distal ureteric stone. Alfuzosin had a high expulsion rate of 78.1%, doxazosin of 75.7%, tamsulosin of 76.5%, silodosin of 88.6%, and tadalafil of 90% in the distal ureter (p = 0.44)[32]. In a Pakistani study, patients who were given alpha blockers for distal ureteric stones had a stone ejection rate of (61.1%; p=0.019)[33]. According to a study by Palmisano F et al[34], 61% of patients who received tamsulosin treatment for distal ureteric stones spontaneously expelled the stones (p 0.01). Another meta-analysis study was undertaken by Ole for -blockers for ureteric stones with a focus on distal ureteric stones and stones larger than 5 mm, which is related to better stone expulsion[35]. While in our study alpha drugs were effective in 59% of patients.

CONCLUSION

By completing 4 weeks treatment and performing CT-KUB our study conclude that alpha blockers were 59% effective at causing lower ureteric stones expulsion of less than 1 cm in diameter. Medical treatment should be used initially in order to reduce surgical morbidities.

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AUTHOR'S CONTRIBUTION
The following authors full fill authorship criteria as per ICMJE guidelines;

Khan S, Ullah A:	Idea conception, drafting the work, final approval, agreed to be accountable for all the work.
Rehman IU, Bilal M:	Design of the work, data acquisition, critical rivision, final approval, agreed to be accountable for all the work.
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