

Effect of Preoperative Alpha-Blocker in Ureterscopy for Ureteral Stones: A Case-Control Study

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ABSTRACT

Background: Urothethiasis is the most common urinary tract disease with a global prevalence rate of 2-20%. Alfa-blocker has a relaxation effect on the smooth muscles of the ureter making the removal of ureteric stone easier during the ureteroscopic procedure.

Objectives: To evaluate the effect of preoperative -adrenoreceptor antagonists therapy (tamsulosin) in the treatment of ureteral stone using a ureteroscope regarding operative time, access to the ureter, and the complication rate.

Materials and methods: A prospective case-control study was conducted at Al-Jamhory Teaching Hospital, Mosul, Iraq. During the period from June 2019 to August 2020. Subjectts with ureteral stones (7-15 mm) scheduled for ureteroscopic intervention were enrolled in the study. The patients were classified into two groups, the first group was received a pre-operative alpha-blocker (tamsulosin 0.4 mg capsule per day for 7 days), and the second group (Control) did not receive further medication. The operative time, uretric access, and intra- and postoperative complications were registered for both groups.

Results: There was a matching between the two groups regarding the age, gender, and side, size, and location of the ureteric stones. There was a statistically significant difference between the two groups regarding the operative time (23.2 ± 4.569 minute in the treated group vs. 25.48 ± 4.904 minute in the control group) (P-value = 0.009). Besides, the ureteroscopic operation was easier (P-value = 0.031) in treated group (n = 51 easy case, 85%) than the control group (n=41, 68.33% easy case). The intraoperative and postoperative complications were mucosal injury, perforation, bleeding, pain, hematuria, and fever. The total number of complicated cases was 14 (23.33%) in the treated group and 25 (41.66%) in the control group, and there was a significant difference between the two groups (P-value = 0.032).

Conclusion: The study revealed that the preoperative alpha-blocker tamsulosin was improved the outcome of ureteroscopy (shorter operative time, easier access to the ureter, and low complication rate).

Keywords: Ureteric stone; Ureterscopy; Alfa-Blocker; Tamsulosin.

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INTRODUCTION

Urolithiasis is a common public health disease. The prevalence rate is 813% in the USA, 58% in Europe, and 15% in Asia [1]. For a long time, there had a debate and controversy among uro-surgeons

for the best treatment of urinary stones useful to the patients. Complicated stones are treated usually by performing an open surgery [2].

Anatomically speaking, both $\alpha 1A$ and $\alpha 1D$ adrenergic receptors are present more densely in the lower third of the ureter (including the intramural part). When they are stimulated, they inhibit the basal tone of the ureteral smooth muscle, peristaltic wave frequency, and the ureteral contractions even in the intramural part of the distal ureter [3]. According to this fact, alpha-blockers can increase the spontaneous pas-

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sage of ureteral stones and enable a reduction in the severity and frequency of pain. This action is more evident in distal ureteral stones [4].

The use of rigid retrograde ureteroscopy had first published by Dr. Perez Castro in 1980 [5]. Ureteroscopy is one of the most commonly performed operations in managing ureteral calculi with a stone-free rate approaching 90%. Over time, there is an improvement in the technical design of the semi-rigid ureteroscope and minimization of the size as well as and the availability of the Holmium: YAG laser. These resulted in a perfect, safe, and powerful fragmentation of the calculus [6]. Access to the ureter is an important step in achieving success ureteroscopy, however, around 40-60% of cases necessitate ureteric orifice dilatation for negotiation by large size ureteroscope (8/9.8 Fr) [7]. However, in some cases, it is not possible to enter the ureter and performing ureteroscopy for various reasons, such as spasms and ureteral stenosis [8]. In such situations, ureteroscopy is postponed after double J (DJ) insertion to dilate the ureter and get access to the stone [9].

As mentioned earlier, the effect of α -adrenoreceptor antagonists on the ureter can be useful theoretically, as it can result in the loosening of the muscles of the prostate, bladder neck, and ureter. Besides, it inhibits the peristaltic movements of these smooth muscles [10]. Based on the role of α -adrenoreceptor antagonists, particularly Tamsulosin, in medical expulsive therapy (MET) for ureteric stone; alpha-blockers can be used before uretroscope for the treatment of ureteric calculi for facilitating ureteral orifice negotiation and accessing ureteral stones [1].

Hence, this study aimed to answer the question does preoperative alpha-blocker therapy (tamsulosin) useful in improving quality and convenience, and reduction of the complications of the ureteroscopy?.

MATERIALS AND METHODS

This case-control prospective study was performed at Urology Department in AL-Jamhory Teaching Hospital in Mosul city, Iraq. The study period was between June 2019 to August 2020. A total of 120 patients were involved in the study. Patients with single ureteral stone (7-15 mm) located in the upper or middle or lower ureter that necessitates ureteroscopic intervention were enrolled in the current study. Individuals with ureteral stenosis, abnormal ureteral anatomy, previous history of ureteroscopic intervention, DJ stent, past surgical history in the region, pregnancy, patients who cannot tolerate alpha-blocker side effects, patients younger than 18 years, and those who didn't wish to participate were excluded from the study. Ethical approval was taken from the scientific committee of the hospital. Informed consent was taken from each participant.

The enrolled patients were assigned into two groups: treated group (group A) was received preoperative alpha-blocker (tamsulosin 0.4 mg capsules) single dose at night for 7 days before ureteroscopy and control group (group B) were not received alpha-blocker therapy preoperatively. The enrolled patients were interpreted their age, sex, side, size, number, and location of the stone, medical, and surgical history. All patients were underwent physical examinations, urinalysis, urine culture, serum creatinine measurements, and ultrasonography, KUB (kidneys, ureters, and bladder), excretory urography, or unenhanced CT (computed tomography) scan.

Operative Technique

Patients were underwent either general anesthesia or spinal anesthesia and placed in the lithotomy position. First, cystoscopy was performed to identify the ureteral orifice, then, 0.035 Fr guidewire was inserted into the ureter. The ureteroscope (8/9.5 Fr, Karl Storz, Germany) was introduced to the ureteric orifice. Thereafter, the ureteroscope was advanced into the ureter to access the calculus site and fragmentation was achieved by using pneumatic lithotripsy. Dormia basket and forceps were used to remove the stone fragment. DJ ureteral stent (4.7 Fr) was placed at end of the operation. The operative time was estimated from the insertion of the ureteroscope into the urethra up to the end of the operation. The difficulty level of ureteroscopy (easy or difficult) was recorded based on the judgment of the surgeon. Other factors such as the duration of the procedure, intraoperative (ureteral perforation, mucosal injury, and ureteral avulsion) and postoperative events (ureteral perforation, mucosal injury, ureteral avulsion, hematuria, urinary tract infection, and fever) were recorded and compared between the two groups.

Statistical analysis

Data were presented and statically analyzed using Minitab Statistical software version 19. Results wrer presented as mean standard deviation. Statistical analysis of the data were conducted using an independent T-test and Chi-square test. Significance results were considered as a P-value < 0.05.

RESULTS

A total of 120 patients were included in the study; 60 patients who received preoperative alpha-blockers (tamsulosin 0.4 mg) and 60 patients who not received preoperative alpha-blockers. The demographic data of the patients were shown in Table 1. There were no statistically significant differences between the two groups regarding the age and gender (P-value > 0.05).

The highest age affected in both groups was between 28-49 years, while the least was > 63 years as shown in Figure 1.

Table 1. Demographic data of the 120 patients

Patient Characteristics	Alpha-blocker group	Control group	P-value
Age (mean, SD) years	40.68 ±14.85	40.05 ±12.79	0.803
Gender Male (N*, %)	37, 61.67 %	34, 65.67 %	0.577
Female (N, %)	23, 38.33%	26, 43.33 %	

* Number

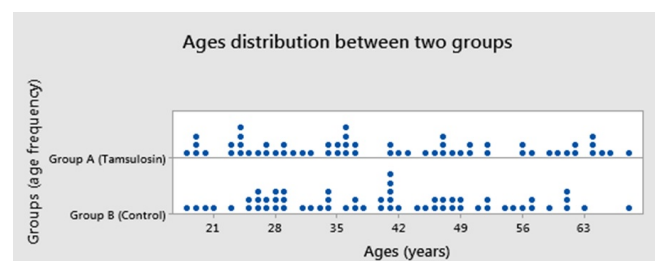


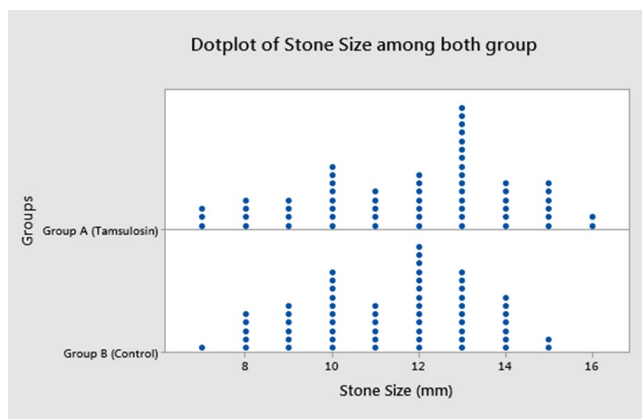
Figure 1. The age distribution of the treated and control groups.

Table 2. The stone characteristic in the 120 patients.

Stone Characteristics		Alpha-blocker group	Control group	P-value
Stone Side (n, %)	Right	33, 55	35, 58.33%	0.713
	Left	27, 45	25, 41.67 %	
	Total	60, 100	60, 100	
Stone location (n, %)	Upper ureter	5, 8.33%	5, 8.33%	0.151
	Mid ureter	11, 18.33%	4, 6.67%	
	Lower ureter	44, 73.33%	51, 85	
	Total	60, 100	60, 100	
Stone size (Mean \pm SD) mm	11.817 \pm 2.383	11.350 \pm 1.999	0.248	

Table 3. The operative duration and difficulty level of the two groups.

Operative variables		Alpha-blocker group	Control group	P-value
Operative duration (minutes) mean \pm SD		23.2 \pm 4.569	25.48 \pm 4.904	0.009
Difficulty level (n, %)	Easy	(51, 85%)	(41, 68.33%)	0.031
	Difficult	(9, 15%)	(19, 31.67%)	
	Total	(60, 100%)	(60, 100)	

**Figure 2.** Distribution of the ureteric stone sizes in treated and control groups.

The ureteric stones were located on the right side in 33 (55%) patients of the treated group and 35 (58.33%) patients of the control group. The majority of the stones were located in the lower ureter 73.33% and 85% in the treated and control groups respectively. The mean stone size was 11.817 \pm 2.383 mm in the treated group vs. 11.350 \pm 1.999 mm in the control group. There were no statistically significant differences among these variables between the two groups (P-value > 0.05) as shown in Table 2.

The 13 mm ureteric stones were found with the highest number in the treated group, while the 12 mm was found in the control group as shown in Figure 2.

As shown in Table 3, the operative duration was shorter in the alpha-blocker group (23.2 minute) than the control group (25.48 minute). The difference was statistically significant between the two groups (P-value = 0.009). Besides, the alpha-blocker group was more easy access (85%) to ureter than the control group (68.33%). The difficulty of negotiating ureter was statistically significant between the two groups (p-value < 0.031).

Table 4. Intraoperative and postoperative complications in the patients of both groups*.

Complications	Alpha-blocker group	Control group
Mucosal injury	2 (3.33%)	3 (5%)
Perforation	1 (1.66%)	0
Bleeding	2 (3.33%)	4 (6.66%)
Pain	3 (5%)	7 (11.66%)
Hematuria	2 (3.33%)	4 (6.66%)
Fever	4 (6.66%)	7 (11.66%)
Total	14 (23.33%)	25 (41.66%)

* P-value=0.032

Pain (3 patients in the treated group, and 7 in the control group) and fever (4 patients in the treated group, and 7 in the control group) were the most common complications in both groups. The occurrence of intra and postoperative complications in the alpha-blocker group was in 14 patients (23.33%) and 25 (41.66%) in the control group. It was a statistically significant difference (P-value = 0.032) between the two groups (Table 4). The odds ratio of complication in the intervention group was 0.4261 times more than that in the control group [OR: 0.4261, 95% CI (0.1937 to 0.9372), P=0.0339].

DISCUSSION

There are three types of the alpha-1 adrenergic receptors expressed in the human ureter, the most predominant one is the alpha-1D subtype [11]. While alpha-1A adrenergic receptor has the main role in the ureteral propulsion [10] which is more concentrated in the lower third of the ureter and ureterovesical junction as compared to the proximal and middle ureter [7]. As a result of the inhibition of these receptors, relaxation of the smooth muscles of the ureter leading to dilatation of the uretric lumen [12]. The advantage of adrenoceptor antagonists is established in the literature as medical expulsive drugs for ureteric stones, owing to increase the stone passage rate and minimize expulsion time [13, 14]. Urolithiasis is a common and increasing abnormality with a

prevalence rate across the globe by 2-20% and affecting 15% of males and 5% of females with a total ratio of about 3:1 between males and females [15]. There are various modalities to retrieve the urinary tract stones, one of them is the ureteroscopic removal of the ureteric stones. In the current study, we used (treated group) or not (control) used tamsulosin as an α -adrenoreceptor antagonist before the starting ureteroscopy. The results revealed that the operative time is shorter, easier ureteric access, and low complication rate in the treated group as compared with the control group.

The new development in the endourology methods and recent devices and instruments have greatly changed the management of ureteric calculi away from conventional open procedures to either minimally invasive methods (e.g. extracorporeal shock wave lithotripsy and ureteroscopy) or watchful waiting [13, 16]. Ureterscopy is considered the best way for lower 1/3rd ureteric stone removal, however, it is not without risks [17]. Sometimes ureteral access can be difficult and ureteral dilatation can result in serious ureteral injury [17]. Accordingly and based on this fact, an α -blocker agent by relaxing smooth muscle at the lower ureter could facilitate ureteroscopy negotiation and/or decrease the complications associated with ureteroscopy.

From our work in endourology and the use of semirigid ureteroscope, we noted difficulties in introducing the ureteroscope through the ureter to reach the site of stone and based on the relaxation effect of tamsulosin on smooth ureteral muscle, we adopted our study. The rapid development of ureteroscopes has allowed treatment of most ureteric stones, however, in many investigations, ureteroscopy carries a better success rate for retrieval distal ureteric calculi [18, 19].

In our study, the number of involved males was more prevalent than females. The majority of the patients age was 28-49 years. Similar findings were reported by the previous investigations [1, 2, 7]. The higher incidence of ureteric stones in the male may be attributed to the lifestyle or small sample size included in the study.

Ureteral calculi in the present study were mostly on the right side, lower ureter, and of a mean stone size in α -blocker and control group 11.817 and 11.350 mm respectively. Similar findings regarding the location of the ureteric stones (lower third) were reported by other studies [1, 2, 7, 9]. The highest number of cases with lower ureteric stones may be attributed to that the ureteroscopy has better results in managing distal ureteral stones and distal calculi comprise 70% of the ureteral calculi, which are usually associated with pain [15, 20]. Ureterscopy carries a better success rate for managing distal ureteric calculi in many investigations [18, 19].

Many studies agree with our finding that the right side is more involved than the left side [2, 7, 9]. Our study and these studies failed to find an explanation of the right favorable side of the ureteric stones. While our finding was in contrast with Sokhal et al. study [1]. Concerning the size of the stones, the mean size in our study approaching the upper limit stone size of other studies (8.2-12.9 mm) [[1, 2, 7, 9]. The difference among various studies may be attributed to the ethnic difference and the lifestyle regarding the types of food eating.

In the current study, the operative time in the treated group was significantly shorter than in the control group (P-value = 0.009). This observation was similar to other investigations [2, 7, 9, 21]. As a result of this observation, we recommend the usage of the α -blocker before the ureteroscopy to reduce the risk of general anesthesia and to save the time of the urologists. Besides, the present study was found that the α -blocker serves another purpose of the easier insertion of the ureteroscope in an attempt to remove the ureteric stone than in the control group (P-value = 0.031). Similar results have been reported by the previous studies [2, 7, 9]. Of course, this benefit reduces the complication rate of the ureteroscopic retrieval of the ureteric stone.

Ureterscopy is a safe and valuable operation. As reported in the literature, the complication rate was ranged from 3% to 30% [22]. In our study, the complications were mucosal injury, perforation, bleeding, pain, hematuria, and fever. Fever and pain were the two most complications among both the treated and control group. The current study was showed that the complications were significantly lower in the treated than in the control group (P-value = 0.032). This finding was comparable with previous investigations [1, 2, 7, 14, 23]. This reflects the easy negotiation of the ureteroscope with the ureter in the treated group than in the control group.

Finally, our study has two limitations, a relatively small sample size included in studied groups and the subjective assessment by the surgeons rating the difficulty level of the access by the ureteroscope that could result in bias.

In conclusion, ureteroscopy is an effective modality to manage ureteral stones, mainly lower ureteral stones. The use of the α -blockers before semi-rigid ureteroscopy had a significant effect on the operative time, access to the ureter, and complication rate. We recommend further studies to understand the crucial role of α -blockers before ureteroscopy.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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