

Effect of perioperative selective alpha-1 blockers in non-stented ureteroscopic laser lithotripsy for ureteric stones: a randomized controlled trial

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Introduction The aim of this study was to assess the efficacy of perioperative alpha-1 blockers on improving the success rate and decreasing complications of non-stented ureteroscopic laser lithotripsy for ureteric stones.

Material and methods A randomized control trial was conducted at two high volume urological centers from September 2017 to December 2018. We enrolled 150 patients with lower ureteric stones. They were randomly divided into two groups. Patients in group A, underwent non-stented ureteroscopy using Ho-YAG laser for stone disintegration and received alpha-1 blockers for one week preoperatively and another two weeks postoperatively. Patients in group B, underwent non-stented ureteroscopy and laser and received a placebo.

Results One hundred and twenty patients were available for analysis at the end of our study. There was no statistically significant difference found between both groups regarding demographic data and stone parameters. The need for intraoperative ureteric dilatation was 32.7% and 51.6% for both groups A and B respectively with a statistically significant difference. The incidence of lower urinary tract symptoms (LUTS) and the need for analgesics were higher in group B with a statistically significant difference.

Conclusions Administration of perioperative tamsulosin seems to not only to significantly decrease the need for intra-operative dilatation and hence operative time, but also leads to a significant decrease in the development of postoperative LUTs, postoperative pain and the need for analgesia and hospital stay.

Key Words: ureteroscopic lithotripsy ↔ non-stented ↔ alpha-1 blocker
↔ lower urinary tract symptoms ↔ postoperative pain

INTRODUCTION

Urolithiasis is a worldwide urological morbidity. Lower ureteric stones represent 70% of all ureteric stones; ureteroscopy and laser (URSL) is considered the first surgical choice for such a condition [1]. Sometimes, surgeons face difficulty in introducing the ureteroscope (URS) into the ureteric orifice to reach the stone. In this case, they employ active ureteric dilatation using balloon or Teflon dilators. Kuntz et al. in their review stated that ureteric balloon dilation before endoscopic treatment of stones was associated with a high success rate, fewer com-

plications and may reduce the need for secondary procedures [2]. Mitchell et al. concluded that serial ureteral dilators represent a safe and effective method to promote ureteral access and allow effective stone treatment in single setting [3].

There are three subtypes of alpha-1 adrenoceptors (ARs) in the ureteric wall: alpha-1A, alpha-1B and alpha-1D. In the proximal ureter, the distribution of ARs was alpha-1D ≥ alpha-1B > alpha-1A. In the distal and middle ureters, the distribution of ARs was alpha-1D > alpha-1A > alpha-1B [4].

Tamsulosin acts on α 1A and α 1D receptors causing the relaxation of the ureteric wall, which conse-

quently increases the urine bolus and intra-ureteral pressure above the stone and lowers intra-ureteral pressure below the stone by decreasing peristalsis in association with the decrease in basal and micturition pressure, even at the bladder neck; thus, it increases the chance of stone expulsion [5, 6, 7].

Preoperative tamsulosin has been evaluated in previous studies to decrease the need for preoperative ureteric dilatation and increase the success rate of surgery. However, its efficacy and duration of intake are not yet clear [4, 5, 8, 9].

We aim through our study to assess the role of tamsulosin in non-stented URSL regarding preoperative ureteric dilatation and its impact on postoperative pain and the need for an analgesic. The regimen of perioperative intake of tamsulosin rather than just preoperative intake for 3 days makes this study unique. The correlation between tamsulosin intake and postoperative pain is another distinctive point of study.

MATERIAL AND METHODS

This randomized controlled clinical trial was conducted on 150 patients with single lower ureteric stones of size ranging between 0.5 and 2 cm. It was conducted at the Urology Departments in Ain Shams University Hospitals and the National Institute of Urology and Nephrology from September 2017 to December 2018. Patients under the age of 18, pregnant women, or those with urinary tract infections (UTI), uncorrected bleeding disorders or coagulopathies, bilateral ureteric stones, single kidney, ureteral stricture, multiple ipsilateral ureteric stones were excluded from our study. Also, any patients who required ureteric stenting were excluded from our study.

Preoperative assessment was done to document the site and size of the stone. An informed consent was obtained from all patients including counseling on treatment options, procedure potential complications and the need for follow-up.

Patients were randomized using computer generated simple randomization into study and control groups. Group A (the study group) contained 75 patients who underwent non-stented ureteroscopy using Ho-YAG laser for stone disintegration. These patients received an alpha-1 blocker 'one tablet tamsulosin 0.4 mg per day' for one week preoperatively, and for another two weeks postoperatively. Group B (the control group) numbered 75 patients and underwent non-stented ureteroscopy using Ho-YAG laser for stone disintegration. These patients received placebo. All patients were blind to the medication received.

Seven surgeons from two centers performed all surgical procedures. Ureteroscopy was performed using a 6.5/9.5 Fr. semi-rigid ureteroscope (Wolf, Richard

Wolf Medical Instruments Corporation, Illinois, USA) without dilatation if feasible. In some cases, we needed to use ureteric Teflon dilators up to 10 Fr in size. A 365-microns laser fiber was used to disintegrate the stone using the dusting mechanism (high frequency 25 Hz and low energy 0.5 J) and the popcorn was used for tiny stone fragments. No ureteric stent was fixed at the end of operation.

In the case of a complication (avulsion, perforation, mucosal tear, bleeding, proximal calculus migration and thermal injury), a double J stent was fixed for 2 weeks and the patient was excluded from the study. Our primary end point was the need for intra-operative ureteric dilatation while other parameters including operative time, residual stones, hospital stay, the presence of postoperative pain according to the Mankoski pain scale, need for analgesics, dysuria, hematuria and fever are considered as a secondary endpoint. Non-contrast computed tomography (CT) was used to evaluate our patients after 1 month regarding any residual stones or backpressure change.

Statistical analysis

Data were collected and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations and ranges when their distribution was found to be parametric and median with interquartile range (IQR) when their distribution was found to be non-parametric. Qualitative data were presented as numbers and percentages.

The comparison between the two independent groups with qualitative data was done by using the Chi-square test and/or Fisher exact test only when the expected count in any cell was found to be less than 5. The comparison between two independent groups with quantitative data and parametric distribution was done by using Independent t-test while with non-parametric data were done by using Mann-Whitney test.

The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant in accordance with the following: $p > 0.05$: Non-significant. $p < 0.05$: Significant. $P < 0.01$: Highly significant.

RESULTS

From the 200 patients initially recruited for the study, 150 were randomized into 2 groups and only 120 patients were available for final analysis as shown in Figure 1. The mean age in group A and B was 39.17 ± 9.96 (22–59) and 37.87 ± 10.91 (19–60) respectively (P -value = 0.56) with 44 (36.7%) fe-

males and 76 (63.3%) males. Patients with previous endourological surgeries in both groups numbered 44 patients (36.7%) while 76 patients (63.3%) had non-urolological operative history. There was no statistically significant difference was found between group A and group B regarding stone parameters as shown in Table 1.

There was a statistically significant increase in the need for dilatation in group B compared to group A with (p-value = 0.03), and also in the operation time in group B compared to group A with p-value = 0.04 as shown in (Table 2)

Regarding postoperative complications as shown in Table 3, patients with lower urinary tract symptoms (frequency, urgency and dysuria) were 14 patients (24.13%) in group A while in group B, they were 27 patients (43.54%) this difference showed a statistically significant difference (P-value = 0.025). Twenty-five patients (43.1%) in group A had loin pain that needed pain medications using (Mankoski pain scale), compared to 39 patients (62.9%) in group B, the lower need for analgesics in group A showed a highly statistically significant difference (P-value = 0.030).

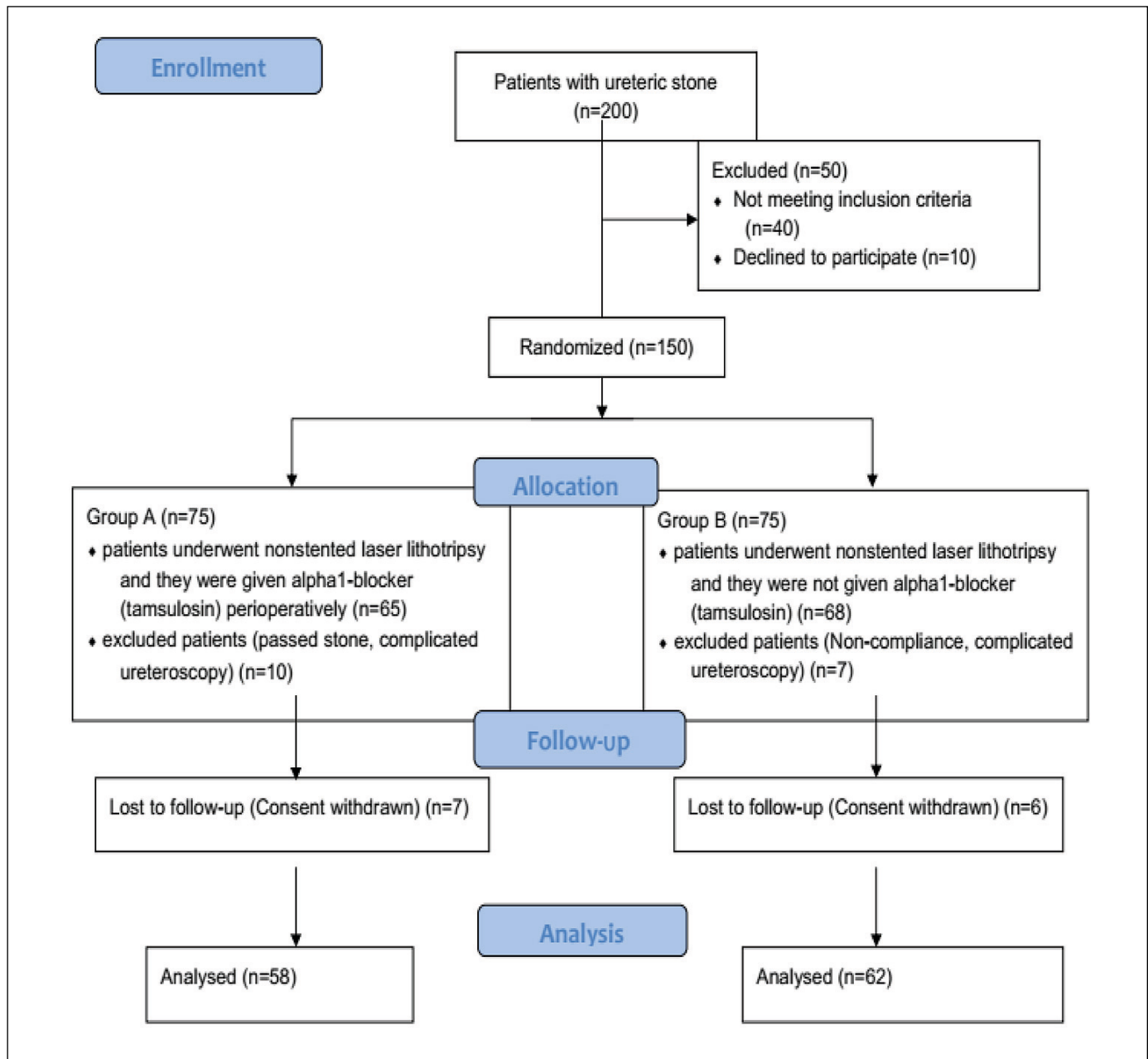


Figure 1. Consort flow chart.

Table 1. Stone parameters in both groups

Stone parameters		Group A N = 58	Group B N = 62	P-value	Sig.
Size (cm)	Mean \pm SD	1.16 \pm 0.30	1.12 \pm 0.29	0.491•	NS
	Range	0.8–2	0.7–2		
Laterality	Left	31 (53.4%)	33 (53.2%)	0.981*	NS
	Right	27 (46.5%)	29 (46.7%)		
Radio density	Radiolucent	15 (25.8%)	25 (40.3%)	0.093*	NS
	Radioopaque	43 (74.1%)	37 (59.6%)		

NS – non-significant; * – Chi-square test; • – Independent t-test

Table 2. Need for dilatation and time of operation in both groups

		Group A No. = 58	Group B No. = 58	P-value	Sig.
Need for dilatation	No	39 (67.2%)	30 (48.3%)	0.037*	S
	Yes	19 (32.7%)	32 (51.6%)		
Time of operation (min)	Mean \pm SD	48.19 \pm 11.72	52.9 \pm 13.16	0.04•	S
	Range	30–85	30–100		

S – significant; • – independent t-test; * – Chi-square test

Table 3. Postoperative assessment in both groups

Postoperative assessment		Group A No. (%)	Group B No. (%)	P-value	Sig.
Lower urinary tract symptoms	No	44 (75.86%)	35 (56.45%)	0.025	S
	Yes	14 (24.13%)	27 (43.54%)		
Need for analgesia	No pain medications needed '0, 1 and 2 on the scale'	33 (56.89%)	23 (37.09%)	0.030	S
	Pain relieved by medication '3, 4, 5 and 6 on the scale'	25 (43.1%)	39 (62.9%)		
Gross Hematuria	No	50 (86.2%)	48 (77.41%)	0.214	NS
	Yes	8 (13.79%)	14 (22.58%)		
Fever	No	56 (96.5%)	58 (93.5%)	0.451	NS
	Yes	2 (3.44%)	4 (6.45%)		

NS – non-significant; S – significant

No patients needed any further surgical intervention in both groups.

Postoperative hematuria was seen in 8 patients in group A compared to 14 patients in group B. Two patients (3.44%) developed fever in group A, compared to 4 patients (6.45%) in group B. There were no statistically significant results (p-value = 0.214 and 0.451 respectively).

Postoperative CT did not detect any residual stone or back pressure changes in both groups. There was

a statistically significant difference between group A and group B regarding LUTS and the need for analgesia with p-value = 0.02 and 0.03 respectively while no statistically significant difference was found between the two studied groups regarding hematuria and fever. See (Table 3).

The mean hospital stay in hours was 27.05 \pm 11.63 and 32.58 \pm 15.26 for group A and group B respectively with a statistically significant increase in the postoperative hospital stay for group B (p-value = 0.027).

DISCUSSION

Since the development of ureteroscope by Hopkins in 1956, it has been considered a cornerstone in the management of ureteric stones [10]. Among the different lithotripsy techniques used nowadays, the most used technique is holmium YAG laser. It improves the outcome of ureteroscopy due to its safety, efficacy, and lower morbidity [11].

There is a controversy surrounding post-operative stenting; some authors advocate its use because it may decrease postoperative loin pain and ureteric obstruction resulting from ureteric edema while others do not advice its routine use due to disadvantages associated with it such as dysuria, frequency, hematuria, UTI and encrustations. Therefore, post-operative stenting was reserved for a complicated ureteroscopy [7, 10, 11, 12].

Tamsulosin acts on α -1a- α -1d receptors in the ureter to relax of the ureter and decrease intraluminal pressure. Also, it acts on nerves and neurotransmitters to decrease bladder contraction and pain. Several studies have established its efficacy as medical expulsive therapy, in addition to decreasing stent related symptoms [9, 13, 14, 15].

In our study, tamsulosin reduced the need for ureteric dilatation from 51.6% to 32.7% and that was associated with a decrease in the operative time from 52.9 ± 13.16 minutes to 48.19 ± 11.72 minutes. Abdelaziz and Kidder's study in 2017 reported a statistically significant decrease in the need for ureteric dilatation during URS following tamsulosin. In their study, stone disintegration was performed by pneumatic lithoclast and ureteric stent was routinely fixed which together increased the overall operative time [9].

Additionally, Bhattar et al. in 2017 and Aydin et al. in 2018 both evaluated the preoperative alpha-1 blocker using Silodosin on ureteric dilatation in URS. They found a statistically significant decrease in the need for ureteric dilatation during URS and operative time. These results were confirmed in another study by Mohey et al. in 2018 [8, 16, 17].

On the other hand, in 2017, Sokhal et al. reported that there was not a statistically significant decrease in the need for ureteric dilatation during URS when using pre-URS tamsulosin. This may be attributed to the short-term use of pre-operative tamsulosin – for 3 days only [17, 18].

In our study, the operative time was reduced by 5 minutes and the hospital stay was reduced by 5 hours in group A using tamsulosin compared to group B. Despite that both results were statistically significant, it did not reflect a clinically significant difference in both operative time and hospital stay. Abdelaziz and Kidder's study in 2017 showed

no statistically significant difference in hospital stay using days instead of hours [9].

Kaler et al. reported that the usage of 1 week preoperative tamsulosin increased the success rate of application of 16-French ureteric access sheath without preoperative ureteral stenting which represent a similar concept for successful ureteric access instead of preoperative ureteric stenting before ureteroscopy for lower ureteric stones [19]. Ahmed et al. also concluded that preoperative tamsulosin increased the success rate of ureteroscopy in proximal ureteric stones [20].

Our study demonstrated that the use of peri-operative tamsulosin, especially for 2 week postoperatively, reduced postoperative pain in the non-stented group and subsequently the need for pain medications. 43.1% of patients with tamsulosin compared to 62.9% of patients with placebo needed analgesics. The use of perioperative tamsulosin statistically reduced the number of patients who developed postoperative LUTS from 43.54% of patients to 24.13% of patients with tamsulosin. In a study conducted by Zhu and colleagues in 2016, the authors reported that (22/40) 55% of patients in non-stented group were pain-free with the use of post-operative tamsulosin and (26/40) 65% of patients in the same group had no postoperative LUTS [21].

In 2014, Ketabchi and Mehrabi studied the effect of preoperative tamsulosin for one day in non-stented URS on postoperative pain, the need for pain medications and LUTS; they reported that the use of preoperative tamsulosin resulted in a significant reduction in the number of patients who developed LUTS and a decrease in the need for pain medications [1].

In our study, the incidence of hematuria in patients was reduced by using tamsulosin from 22.58% to 13.79%. Moreover, the incidence of postoperative fever was reduced from 6.45% in the patients receiving placebo compared to 3.44% in the tamsulosin group. However, these results regarding fever and hematuria were not statistically significant.

We do recommend conducting more studies about larger stones burden or in the upper and mid ureteric stones, to confirm our results and the efficacy of using perioperative alpha-1 blockers.

CONCLUSIONS

Administration of perioperative tamsulosin seems to not only significantly decrease the need for intra-operative dilatation and hence operative time, but also leads to a significant decrease in the development of post-operative lower urinary tract symptoms, post-operative pain and the need for analgesia and hospital stay.

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

The protocol was approved by the Research Ethics Committee of the Faculty of Medicine of Ain Shams University with approval No. (FMASU MS 100/2018).

CONSENT FOR PARTICIPATION

Written consent was obtained from all patients before participation.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

COMPETING INTEREST

No competing interests to declare.

FUNDING

We received no funding in our study.

AUTHOR'S CONTRIBUTION

A.M. Tawfeek: outline study design, primary surgeon, Data collection, Manuscript writing.

M.S. Abdelwahab: Outline study design, Data collection.

Ahmed Radwan: Methodology section writing and final revision.

Ahmed Higazy (corresponding author): Data collection, Introduction, Discussion writing.

Sh. A. Swar: Primary surgeon, Abstract writing, final revision.

Hassan S. Shaker: Results and discussion writing and final revision.

Ahmed Farouk: Abstract and result writing and final revision.

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