Does Tamsulosin use before Ureteroscopy Increase the Success of the Operation?

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ABSTRACT:

Objective: To investigate the effect of preoperative tamsulosin use on the success and complications rates of ureteroscopy for ureteral stone removal.

Study Design: A randomised clinical trial.

Place and Duration of Study: Department of Urology, Dursun Odabas Medical Center, Van Yuzuncu Yil University, Turkey, from December 2020 to June 2021.

Methodology: Patients were scheduled for ureteroscopy due to ureteral stones, and were randomly divided into two groups; 67 patients preoperatively were given 0.4 mg tamsulosin for 7 days and 70 patients were not given tamsulosin. Each patient's intraoperative surgical complications, preoperative and postoperative pain, postoperative fever, need for analgesia, stone-free rate, and double J ureteral stent (DJ) insertion rates were recorded and evaluated.

Results: A total of 137 patients, 103 (75.1%) males, and 34 (24.8%) females, were included. In 70 (51.1%) of these patients, the stone was on the right side, while in 67 (48.9%) the stone was on the left side. The stone was in the distal ureter in 47 (34.3%) patients, in the middle in 38 (27.7%) patients, and the proximal in 52 (37.9%) patients. The patients who were given tamsulosin had lower preoperative visual analog scale (p=0.02), operation time (p=0.003), post-ureteroscopic lesion scale (p=0.01), postoperative 24th-hour visual analog scale (p=0.03), fever (p=0.02), and analgesic need (p=0.04), while their rate of accessing the stone (p=0.02); and their stone-free rates (p=0.02) was higher.

Conclusion: Preoperative tamsulosin use increases the success of the operation and reduces complications.

Key Words: *Tamsulosin, Ureteral calculi, Ureteroscopy*.

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INTRODUCTION

Ureteral stones are one of the most common diseases of urology. Twenty per cent of all stones in the urinary system are in the ureter, and these are mostly symptomatic.[1] Ureteral stones can also cause deterioration in ipsilateral kidney function. Therefore, appropriate treatment should not be delayed in ureteral stones.[2] Ureteral stone treatment consists of observation, medical expulsive therapy (MET), ureteroscopy (URS), and ureterolithotomy.[3,4]

Selective alpha-blockers are widely used in MET treatment. In many previously published meta-analyses, European Association of Urology and the American Association of Urology recommend this treatment, because it increases the rate of spontaneous stone passage of ureteral stones.

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Alpha-blockers provide relaxation by blocking alpha receptors in ureteral smooth muscle.[5,6] It also increases the rate of stone clearance after extra-corporeal shock wave therapy (ESWL).[7] While these effects of alpha-blockers are well known, the effect of preoperative (pre-op) alpha-blocker use on URS success and complications in patients undergoing URS has not been adequately studied in the literature.

The aim of this study was to investigate the effect of tamsulosin use before URS on the success (defined as no residual stone larger than 3 mm) of the operation, as well as both intraoperative (intra-op), and postoperative (post-op) complication rates.

METHODOLOGY

This prospective, randomised clinical trial was performed in the Department of Urology, Dursun Odabas Medical Center, Van Yuzuncu Yil University, Van, Turkey. The study was completed between December 2020 and June 2021 after receiving the approval of the local Ethics Committee (Decision No. 2020/09-18, date: 04.12.2020). Group 1 had 67 patients, who were given 0.4 mg tamsulosin for 7 days preoperatively, and Group 2 had 70 patients, who were not given tamsulosin preoperatively. The patients were sequentially divided into groups on a 1:1 basis according to their order of admission. Patients older

than 18 years of age, with a single stone larger than 7 mm and who agreed to participate were included in the study. This study excluded patients with stones smaller than 7 mm, had an active infection or acute azotemia, a DJ stent or nephrostomy, a ureteral operation or known pathology, a solitary kidney, or were pregnant.

All patients were diagnosed with non-contrast computed tomography. Each patient's age and gender, as well as the stone's lateral location, localisation, and size, were recorded. Each patient's visual analog scale (VAS) score during the pre-op 7-day period was recorded. The VAS is a scale that scores pain severity between 0 and 10, in which 0 indicates no pain, and 10 indicates the most severe pain (Figure 1).

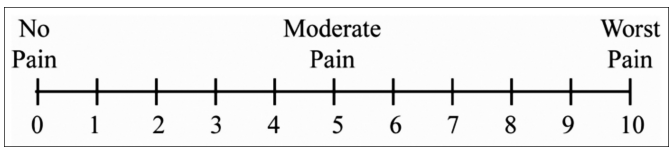

Figure 1: Visual analog scale.

Postureteroscopic Lesion Scale

Grade 0	No lesion	Uncomplicated URS (no grading according to the Dindo-modified Clavien classification of surgical complications)
Grade 1	Superficial mucosal lesion and/or significant mucosal edema/hematoma	
Grade 2	Submucosal lesion	
Grade 3	Perforation with less than 50% partial transsection	Complicated URS (Grade 3a or b according to the Dindo-modified Clavien classification of surgical complications)
Grade 4	More than 50% partial transsection	
Grade 5	Complete transsection	

URS = ureterorenoscopy.

Figure 2: Postureteroscopic lesion scale.

After documenting negative urine cultures in all patients, pre-op single-dose intravenous 2g ceftriaxone was given as prophylaxis. Then the patients were operated on with a ureterorenoscope (distal 8fr and proximal 9.8fr diameter). The cases, where the ureteral orifice could not be passed with the ureterorenoscope, were considered unsuccessful, and the operation was continued after the ureter was dilated with a balloon. Wolf laser device was used for lithotripsy at 1200 mJ and 2000 frequency. Intra-op complication rates were evaluated with the post-ureteroscopic lesion scale (PULS, Figure 2). Intra-op stone access and DJ ureteral stent insertion data was recorded. Patients were given a post-op endoscopic examination, and kidney- ureter- bladder X-rays were taken, and patients with ≤3mm residual stones were considered to be stone-free. Patients' temperatures were taken at a minimum of 4-hour intervals, and patients with a fever of ≥ 38°C in two measurements in the first 24 hours post-op were included in the febrile morbidity group. Patients were asked to fill in the VAS questionnaire at the post-op 24th hour. Alpha-blocker therapy was discontinued in all patients post-op. In addition, on the 21st post-op day, all patients' 21-day pain chart was evaluated with the VAS questionnaire. All this information was recorded by an observer, who did not know the patients that were given alpha-blockers. Nineteen patients with stones smaller than 7 mm, and 10 patients with active infections or acute azotemia, patients with nephrostomy or DJ stents, ureteral pathology or history of operation, and solitary kidney, were excluded from the study because they could affect the success and complication rates of the surgery.

Descriptive statistics for continuous variables, while it is given as mean and standard deviation, it is given as numbers and percentages for categorical variables. Paired t-test was used for the comparison of post-op (24^{th}-hour & 21^{st} day) and pre-op for VAS score. Student t-test was used to compare groups in terms of continuous variables. The Chi-square test was used to determine the relationship between groups and categorical variables. The statistical significance level was taken as 5% in the calculations and the SPSS (version 21) statistical package programme was used for the calculations.

RESULTS

A total of 137 patients, 103 (75.1%) males, and 34 (24.8%) females, were included in this study. The mean age of those patients was 46.58 ± 15.38 (18-91) years. In 70 (51.1%) of these patients, the stone was on the right side, while in 67 (48.9%) patients, the stone was on the left side. The stone was in the distal ureter in 47 (34.3%) patients, in the middle in 38 (27.7%) patients, and the proximal in 52 (37.9%) patients. The mean stone size was 11.45 ± 4.65 mm, and the mean operation time was 52.2 ± 13.47 minutes. Stone-free result was achieved in 110 (80.2%) of these patients, while residual stones were seen in 27 (19.7%) patients. DJ stent was placed in 113 (82.4%) patients.

Table I: Comparison between groups.

		Group 1 (n:67)	Group 2 (n:70)	p-value
Age		47.44 ±16,79	45.75 ±13,96	0.522
Stone size		10.94 ±4,53	11.95 ±4,74	0.202
Reaching the stone		63 (94%)	57 (81%)	0.02*
Operation duration (minutes)		48.80±14,19	55.50± 11.95	0.003*
Stone free		59 (88%)	51 (72.85%)	0.02*
DJ		51 (76.11%)	62 (88.57%)	0.055
Fever		6 (8.95%)	16 (22.85%)	0.02*
Analgesia		15 (22.38%)	52 (74.28%)	0.04*
VAS	Pre-op	4.52 ±0.65	4.82 ±0.90	0.02*
	Post-op 24^{th} hour	2.22 ±0.64	2.44 ±0.58	0.03*
	Post-op 21^{st} day	1.52 ±0.56	1.57 ±0.55	0.6
PULS	Grade 1 Grade 2 Grade 3	51 (76.11%) 13 (19.4%) 3 (4.47%)	38 (54.28%) 28 (4%) 3 (4.28%)	0.019*

**In Group 1, the rate of reaching the stone and the stone-free rate was significantly higher, while the operation time, preoperative and post-operative 24th hour VAS were significantly lower (Paired t-test). *Fever, analgesic requirement and PULS values were significantly lower in Group 1 (Chi-square test). *DJ: Double J, *VAS: Visual Analog Scale, *PULS: Post ureteroscopic lesion scale.*

Forty-two patients (30.6%) needed post-op analgesia. Fever developed in 22 (16%) patients. The operation time of the patients with a fever was 63.18 ± 10.63 minutes, while the duration of the operation for patients without fever was 50.13 ± 12.96 minutes (p = 0.001). No significant difference was observed between the groups in terms of age and stone size. A statistically significant difference was observed in the alpha-blocker group compared to the non-user group in terms of reaching the stone, pre-op VAS, post-op 24th-hour VAS, operation time, stone-free rate, PULS, post-op fever, and need for analgesia (Table I).

DISCUSSION

Appropriate treatment selection is important after the diagnosis of ureteral stones. Stone size is one of the most important factors in choosing a treatment. While stones smaller than 3mm are clinically insignificant, stones larger than 7-10 mm are not expected to spontaneously pass. For stones between 3-10 mm, alpha-blockers are given to provide spontaneous stone passage. Alpha-blockers provide relaxation of the ureter by blocking alpha receptors in the ureteral smooth muscles. This treatment is called MET; and with this treatment, 65% of stones are able to pass spontaneously. Studies suggest using URS for stones larger than 10mm or for stones that do not spontaneously pass with the MET treatment.[8-11]

Since URS is a minimally invasive method, recently it has become the primary treatment for ureteral stones. However, URS has complications such as hematuria, ureteral avulsion, fever, sepsis, and pain that may develop.[12] In some studies, it has been reported that pre-op alpha-blocker treatment facilitates URS and shortens the operation time.[13,14] In this study, it was shown that alpha-blocker treatment shortened the operation time, increased the success rate, decreased intra-op and post-op complications, as well as pre-op and post-op pain.

One of the most important problems in the application of the URS treatment is the difficulty in inserting the URS into the ureteral orifice. Due to the narrow diameter of the orifice, entry into the ureter may be unsuccessful. One of the reasons for this is that alpha-receptors, which are densely located in the distal ureteral smooth muscles, provide smooth muscle contraction. With the effect of alpha-blockers, this contraction is prevented and passive dilatation is provided. Studies have reported that the ureteral orifice of patients using alpha-blockers before ureteroscopy is more open, more visible, and easier to pass. This means less time is needed to pass the orifice, less mucosal damage, and a lower complication rate.[14-16] In this study, ureteral access was easier in the group using alpha-blockers, and the results were in accordance with the literature.

One of the most important factors in the treatment of ureteral stones is pain management, as ureteral stones cause severe colic pain. Many treatment methods and analgesia types have been investigated to prevent renal colic. For this reason, non-steroidal anti-inflammatory agents, like ketorolac and other narcotics have been used, but none of these drugs are without side effects. Therefore, it is important to reduce the severity of renal colic.[8,17] In this study, the pre-op pain score of the alpha-blocker group was lower than in Group 2. Pain management in post-op patients is also important. Even though post-op pain is considered to be a minor complication, many patients suffer from pain after surgery. In a study, it was observed that in 57% of patients, the pain developed after URS.[18] The causes of early post-op pain are not clear. While one of the factors associated with post-op pain is prolonged operation time, the most common factors that are associated with post-op pain are stretching of the renal capsule, extravasation of irrigation fluid, and ureteral obstruction by stone particles and blood clots due to edema in the ureter.[19] In a study by Tanrıverdi *et al*., 8.3% of patients who did not have a DJ stent placed during URS operation, needed stent placement in the post-op period and reported that almost all of the pain in the re-performed URS was caused by diffuse edema in the ureter.[18]

Pain due to ureteral edema occurs in the first 24 hours postoperatively.[19] However, contrary to this study, there is a study stating that patients with stents suffer from more pain than patients without stents.[20] This is due to DJ stent-induced trigone of bladder irritation. In addition, it has been reported that DJ stents can also cause hematuria, sexual dysfunction, suprapubic, and flank pain other than irritative bladder symptoms.[18,20]

Studies have reported that alpha-blockers relieve irritative bladder symptoms and suprapubic pain, and improve sexual symptoms. In addition, it has also been reported that abnormal contractions develop in the ureter after URS and that the resulting reflux causes colic pain. Alpha-blockers have been shown to reduce pain by blocking alpha receptors in the ureter.[20] The most effective analgesics after URS are NSAIDs and narcotics. However, in addition to NSAII-induced nephrotoxicity and liver failure, there is a risk of anaphylaxis with some NSAIDs.[21,22] In narcotic analgesics, there are risks of addiction and death due to overdose, as well as liver and kidney failure.[23,24] Therefore, it is important to reduce the need for analgesics after URS.

This study showed that alpha-blockers reduce both pre-op and post-op pain. In addition, the level of post-op analgesic use was also lower. The reason for this was thought to be the shortened operation time due to the dilated ureter, enabling us to reach the stone in a shorter time, the lower rate of obstruction by blood clots and stone particles, and less irritation of the wall of the ureter by the DJ stent.

Fever develops in 2-15% of patients after a URS operation. Studies have shown that a positive urine culture is the most common cause of fever after ureteroscopy; but when a negative urine culture is documented, the most common cause of fever is the operation time, which is determined by the complexity of the operation. In addition, despite a negative urine culture, postoperative fever and even sepsis can be seen, as urine that cannot drain due to impacted ureteral stones becomes infected. Bacteria in the urine enter the systemic circulation due

to intraoperative mucosal laceration and increased hydrostatic pressure. Therefore, pre-op antibiotic prophylaxis and post-op fever follow-up are recommended even if the urine culture is negative.[16,18,25] In this study, a significantly lower rate of post-op fever was observed in the group using alpha-blockers. It was thought that the rate of post-op fever in patients decreased because alpha-blockers shortened the operation time. In addition, the authors estimate that facilitating urinary drainage due to the relaxation of the ureter by the alpha-blocker may also have contributed to the lower post-op fever rate.

One of the limitations of this study was that there was no preoperative assessment of the ureteral orifice.

CONCLUSION

Preoperative use of alpha-blockers reduces intra-op and post-op complications and increases patient comfort. Therefore, a pre-op alpha-blocker may be beneficial not only for MET but also for all patients scheduled for URS due to ureteral stones.

ETHICAL APPROVAL:

The approval of the local Ethics Committee was received (Decision No. 2020/09-18, date: 04.12.2020).

PATIENTS' CONSENT:

All patients were included in the study after obtaining a written consent form.

CONFLICT OF INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

MD, KE, RA, RE, MS, KT: Collected and analysed data, wrote manuscript, searched literature, and designed study.

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