

To Compare the Efficacy of Nifedipine and Tamsulosin 0.4 mg in Expulsion of Lower Ureteric Stones

MHAMMAD ZAHID AHMED¹, NAUMAN AHMED², MUHAMMAD ASIF³, MUHAMMAD WAQAR SHAHID⁴, AFTAB AHMED CHANNA⁵, NAEEM AHMED CHEEMA⁶

¹Assistant Professor Urology Department Unit 2, King Edward Medical College / Mayo Hospital Lahore

²Consultant Urologist, Govt Kot Khawaja Saeed Teaching Hospital Lahore

³Assistant Professor Urology, Unit 2, Department of Urology, King Edward Medical College / Mayo Hospital Lahore

⁴Consultant Urologist, Hassan Gazanvi Hospital Jeddah Kingdom of Saudi Arabia

⁵Assistant Professor Urology, Islam Medical College Sialkot

⁶Assistant Professor Urology, Islam Medical College/ Teaching Hospital Sialkot

Corresponding author: Mhammad Zahid Ahmed, Email: zahid.urologist@gmail.com Mobile

ABSTRACT

Objective: To compare the effectiveness of nifedipine and tamsulosin for expulsion lower ureteral stones with size ranging from 4mm-11mm.

Study Design: A Randomized controlled trial.

Methods: The study was held over a 2-year duration from January 2018 to December 2019 in the Urology department of Islam Medical College/ Teaching hospital Sialkot and Govt. Kot Khawaja Saeed Teaching Hospital Lahore. 72 total patients, 37 patients in each group, were selected for the study. The patients in A group were treated with alpha-1-blocker alone (tamsulosin), patients in B group were treated with calcium channel blockers (nifedipine 30-mg). Data on stone size, transit time, stone removal rate and control of pain were analyzed and collected. The mean \pm SD of continuous variables was used to determine the percentage and frequency of categorical variables. The student's t-test and Chi-square test were applied to compare numerical and categorical variables, correspondingly.

Results: 72 total patients were involved and 36 patients in each group were analyzed after randomization. The patients mean age in A group was 36.40 ± 6.98 years, and in B group it was 38.01 ± 9.40 years correspondingly ($p = 0.76$). The mean size of stone was 6.40 ± 1.82 mm in group A and in group B it was 6.51 ± 1.69 mm ($p = 0.80$). Mean time of expulsion in A group was 8.40 ± 2.41 days and for group B; it was 6.71 ± 2.33 days ($p < 0.001$). Patients receiving tamsulosin endured suggestively fewer attacks of pain related with patients receiving nifedipine treatment ($p = 0.017$).

Conclusion: The tamsulosin is safe treatment for appropriately sized lower ureteral stones as compared to nifedipine. The tamsulosin monotherapy have clear advantage over nifedipine but more detailed school studies are needed for efficacy and safety.

Keywords: Tamsulosin, ureter, nifedipine.

INTRODUCTION

Kidney stones are very communal in the Pakistan. The lifetime danger of urinary stones development ranges from 6% to 14% and affects more males than females¹⁻². About 21% of stones in the urinary system are located in the ureters and the most common (70%) are in the lower ureter in the distal third part³⁻⁴. Current developments in endoscopic therapy of stone removal have made it possible to treat kidney stones by means of minimal invasive methods and have a higher success rate and reduce morbidity related with treatment⁵⁻⁶. These developments include ureteroscopy, percutaneous nephrostolithotomy and shock wave lithotripsy (SWL)⁷⁻⁸. The small ureteral stones observation with a high probability of patency was recommended without absolute indication for surgical intervention. For calculus 5 mm or less in diameter in the ureter at the proximal part, the incidence of spontaneous removal without medical intervention is assessed to be 30% to 99%, and 71% to 98% for the the distal ureter⁹. The utmost significant factors in approximating the probability of passage of stones spontaneously are the size and location of the stone. Choosing the utmost suitable management be contingent on a number of factors, including the size and location of the calculi, available knowledge and patient preferences¹⁰. Typical problems associated with minimally invasive treatment are compensated for by difficulties of predictable ineffective treatment, such as urinary tract infections, renal failure and hydronephrosis. The spectrum of diseases and their effects differ in our world for a variety of reasons, including the delayed diagnosis, absence of innovative minimally invasive treatments, less awareness and research¹¹. This exacerbates the problem when added to some local surveys. This study was conducted taking into account these questions and the socioeconomic status of most of our patients. This review will provide other methods of treatment for the appropriate group of patients with distal ureterolithiasis while providing a local perspective on the problem.

MATERIAL AND METHODS

The study was conducted over 2-year duration from January 2018 to December 2019 in the Urology department of Islam Medical College/ Teaching hospital Sialkot and Govt. Kot Khawaja Saeed Teaching Hospital Lahore. 72 total patients, 37 patients in each group, were selected for the study. The patients in a group were treated with alpha-1-blocker alone (0.4 mg tamsulosin), patients in group B were treated with calcium channel blockers (nifedipine 30-mg). Data on stone size, transit time, stone removal rate and control of pain were analyzed and collected. The hospital's ethics committee has given approval of the study. The study comprised 72 patients (interview and clinical examination) who came to the outpatient clinic diagnosed with ureteral colic due to ureterolithiasis. The study included patients aged 20 years and above with solitary stone in the lower ureter with size 4mm-11mm. The patients who were pregnant or lactating patients, previous ureter surgery on the same side, urinary tract infection, single kidney, currently using alpha-blockers, moderate or severe hydronephrosis, diagnosed allergy to tamsulosin, kidney failure and contraindications to non-steroidal anti-inflammatory drugs e.g., gastritis not included. The diagnosis was established on the base of renal-ureteral bladder radiography (KUB), intravenous urography (IVU), ultrasound of the abdominal cavity and if necessary, on computed tomography (CT). In adding, tests such as blood count, serum urea, serum creatinine and urine R / E were also performed. All subjects received intravenous injection of tramadol hydrochloride 100 mg if they experienced severe pain. Afterward the ache had subsided, the individual was registered in the analysis. Patients were clarified the benefits and risks of the treatment method and obtained consent in written. Study drugs were withdrawn at the end of the spontaneous stone removal, intervention, or study period. Treatment failure was defined as the inability to remove the stones prior to completion of the study due to uncontrolled pain or side effects. Control visits took place every two weeks. At the follow-up visit, all patients were subjected to

urine tests, serum creatinine determination, simple KUB radiography and abdominal ultrasound. Patients were also asked if they saw stones fragments while urinating. Patients with radiolucent stones underwent abdominal CT scans if the stone was not passed at the culmination of the study. Alternative treatments such as ESWL or ureteroscopy were recommended for patients who were unable to remove calculus on their own or who had complications during the study period. The effectiveness of the management given was assessed in terms of the rate of stone removal and the duration and pain attacks frequency. The data analysis using SPSS version 21.0 was done. The mean \pm SD of continuous variables was used to determine the percentage and frequency of categorical variables. The student's t-test and Chi-square test were applied to compare numerical and categorical variables, correspondingly. The probability less than or equal to 0.05 was measured statistically significant.

RESULTS

72 total patients were included and 36 patients in each group were analyzed after randomization. The patients mean age in A group was 36.40 ± 6.98 years, and in B group it was 38.01 ± 9.40 years correspondingly (p 0.76). The mean size of stone was 6.40 ± 1.82 mm in A group and in group B it was 6.51 ± 1.69 mm (p 0.80). Mean time of expulsion in A group was 8.40 ± 2.41 days and for group B; it was 6.71 ± 2.33 days (p <0.001). Table 1.

Table 1: The patients' tomographic features

Patients	Group A (0.4 mg tamsulosin) (n=36)	Group B (nifedipine 30-mg) (n=36)
Age		
Mean	36.40	38.01
S.D.	6.98	9.40
Gender		
Male	28	25
Female	8	11
Stone Size		
Mean	6.40	6.51
S.D.	1.82	1.69
Stone Side		
Left	14	17
Right	22	19

Table 2: Patients receiving tamsulosin alone experienced significantly fewer attacks of pain compared with patients receiving nifedipine treatment (p 0.017).

Table 2: Primary Outcome Characteristics

Patients	Group A (n=36)	Group B (n=36)
Stone Rate of Expulsion <5 mm size		
N=%	97%	88%
Stone Rate of Expulsion \geq 5 mm size		
N=%	94%	80%
Time of Stone Expulsion (Days)		
Mean	8.40	6.7
S.D.	2.41	2.33
No. of pain Attacks		
Mean	1.33	1.08
S.D.	0.68	0.59

DISCUSSION

Alpha-1- receptors of adrenergic system are found in the human ureter. The physiological response of these receptors to antagonism is a reduction in contractile force, a reduction in peristaltic velocity, and an increase in the volume of fluid bolus transmitted through the ureter¹²⁻¹³. These reactions are probable how alpha-blockers help in transferring ureteral stones¹⁴. Alpha-

blockers, especially alpha 1 antagonist, are very operative in upsurgung the proportion of passage of the distal stones in the ureter, shortening the passage time of the stones, and reducing the number of painkillers required during the passage of the stones¹⁵⁻¹⁶. Alpha-blockers might be a valuable assistant in the management of kidney and ureteral stones with ESWL. While greater achievement has been revealed with calcium channel blockers with or without NSAIDs and steroids, alpha1 blockers have become leading candidates for MET due to their excellent safety profile, high success rate, ease of use and low side effect profile and should be used as first-line treatment for any suitable candidate in the distal ureteral stone transit observation protocol¹⁷⁻¹⁸. In addition, alpha1 adrenoceptor antagonists may be accepted during the conventional treatment of middle and proximal stones in the ureter and following surgical interference for kidney stones¹⁹. In our analysis, large number of patients in the tamsulosin alone group experienced ureteral stones expulsion. This finding was among patients with stones smaller or larger than 5mm. This study confirms that patients receiving the tamsulosin have a much shorter time to excrete the stones compared with patients receiving nifedipine²⁰⁻²¹. These results are in line with other results supporting our results. Alpha1 blockers facilitate and accelerate its passage by causing a variation in the pressure gradient around, below and above the blocking stone, reduces mucosal swelling, and nifedipine reduces ureteral spasm, thus facilitating stone excretion²²⁻²³. The shortcomings of this study should be considered. Patients were not blinded, which may have biased the results of the study. The observation time was short. Assessment of pain and analgesic dose was subjective and entirely dependent on patient compliance.

CONCLUSION

The tamsulosin is safe treatment for appropriately sized lower ureteral stones as compared to nifedipine. Patients with lower ureteral stones who received tamsulosin testified pain relief using the Visual Analogue Scale (VAS). Therefore, it is suggested as 1st-line management in patients with stones of the size 4mm-11mm and uncomplicated urolithiasis. This statistic is also important in our environment, where costs and devices are eventually changing the way treatment is delivered.

REFERENCES

- Aydin M, Kiliç MF, Yavuz A, Bayar G. Do alpha-1 antagonist medications affect the success of semi-rigid ureteroscopy? A prospective, randomised, single-blind, multicentric study. *Urolithiasis*. 2018 Nov;46(6):567-72.
- Campschroer T, Zhu X, Vernooij RW, Lock MT. Alpha-blockers as medical expulsive therapy for ureteral stones. *Cochrane Database of Systematic Reviews*. 2018(4).
- Tian D, Li N, Huang W, Zong H, Zhang Y. The efficacy and safety of adrenergic alpha-antagonists in treatment of distal ureteral stones in pediatric patients: A systematic review and meta-analysis. *Journal of Pediatric Surgery*. 2017 Feb 1;52(2):360-5.
- Vermandere M, Kuijpers T, Burgers J, Kunnamo I, van Lieshout J, Wallace E, Vlayen J, Schoenfeld E, Siemieniuk R, Trevena L, Zhu X. Alpha-blockers for uncomplicated ureteral stones: a clinical practice guideline. *BJU international*. 2018;122(6):924-31.
- Oestreich MC, Vernooij RW, Sathianathan NJ, Hwang EC, Kuntz GM, Koziaz A, Scales CD, Dahm P. Alpha-blockers after shock wave lithotripsy for renal or ureteral stones in adults. *Cochrane Database of Systematic Reviews*. 2020(11).
- Amer T, Osman B, Johnstone A, Mariappan M, Gupta A, Brattis N, Jones G, Somani BK, Keeley Jr FX, Aboumarzouk OM. Medical expulsive therapy for ureteric stones: Analysing the evidence from systematic reviews and meta-analysis of powered double-blinded randomised controlled trials. *Arab Journal of Urology*. 2017 Jun 1;15(2):83-93.
- Gnyawali D, Pradhan MM, Sigdel PR, Parajuli P, Chudal S, Poudyal S, Chapagain S, Luitel BR, Chalise PR, Sharma U, Gyawali PR. Efficacy of Tamsulosin plus Tadalafil versus Tamsulosin as Medical Expulsive Therapy for Lower Ureteric Stones: A Randomized Controlled Trial. *Advances in urology*. 2020 Jan 29;2020.

8. Sung SY, Le TT, Chen JH, Hsieh TF, Hsieh CL. Alpha-1 blocker use increased risk of subsequent renal cell carcinoma: A nationwide population-based study in Taiwan. *Plos one*. 2020 Nov 19;15(11):e0242429.
9. Liu XJ, Wen JG, Wan YD, Hu BW, Wang QW, Wang Y. Role of silodosin as medical expulsive therapy in ureteral calculi: a meta-analysis of randomized controlled trials. *Urolithiasis*. 2018 Apr;46(2):211-8.
10. Raison N, Ahmed K, Brunckhorst O, Dasgupta P. Alpha blockers in the management of ureteric lithiasis: A meta-analysis. *International Journal of Clinical Practice*. 2017 Jan;71(1):e12917.
11. Türk C, Knoll T, Seitz C, Skolarikos A, Chapple C, McClinton S, European Association of Urology. Medical expulsive therapy for ureterolithiasis: the EAU recommendations in 2016. *European Urology*. 2017 Apr 1;71(4):504-7.
12. Sentürk AB, Aydin C, Ekici M, Yaytokgil M, Akkoc A, Baykam MM. Comparison of three most frequently used alpha blocker agents in medical expulsive therapy for distal ureteral calculi, result of a retrospective observational study. *Archivio Italiano di Urologia e Andrologia*. 2018 Mar 31;90(1):25-8.
13. Aboumarzouk OM, Jones P, Amer T, Kotsiris D, Emiliani E, Somani B, Kallidonis P, Taily T, Atis G, Greco F, Hruby S. What is the role of α -blockers for medical expulsive therapy? Results from a meta-analysis of 60 randomized trials and over 9500 patients. *Urology*. 2018 Sep 1;119:5-16.
14. Ye Z, Zeng G, Yang H, Tang K, Zhang X, Li H, Li W, Wu Z, Chen L, Chen X, Liu X. Efficacy and safety of tamsulosin in medical expulsive therapy for distal ureteral stones with renal colic: a multicenter, randomized, double-blind, placebo-controlled trial. *European urology*. 2018 Mar 1;73(3):385-91.
15. Koo KC, Yoon JH, Park NC, Lee HS, Ahn HK, Lee KS, Kim DK, Cho KS, Chung BH, Hong CH. The impact of preoperative α -adrenergic antagonists on ureteral access sheath insertion force and the upper limit of force required to avoid ureteral mucosal injury: a randomized controlled study. *The Journal of Urology*. 2018 Jun 1;199(6):1622-30.
16. Zhang Y, Ouyang W, Li H, Liu H, Yuan P, Lu H, Sun X, Ye Z, Xing J, Chen Z, Xu H. Cost-effectiveness of Medical Expulsive Therapy with α -blockers for Large Distal Ureteral Stones in China. *Urology Journal*. 2020 Mar 14;17(05):462-8.
17. Tao RZ, Qin ZQ, Lv JL. Efficacy and safety of Tamsulosin in the medical expulsion therapy for distal ureteral calculi: a systematic review and meta-analysis of placebo-controlled trials. *Urology journal*. 2019 Jun 17;16(3):224-31.
18. Nazir SS, Bashir SA, Khan N, Iqbal T, Jeelani SA. An Outpatient Medical Expulsive Therapy for Unilateral Single Ureteric Calculi with SOADS Regime: Our 9 Years Experience with 3000 Patients. *Urol Nephrol Open Access J*. 2017;5(6):00192.
19. Sridharan K, Sivaramakrishnan G. Medical expulsive therapy in urolithiasis: a mixed treatment comparison network meta-analysis of randomized controlled clinical trials. Expert opinion on pharmacotherapy. 2017 Sep 22;18(14):1421-31.
20. Meltzer AC, Burrows PK, Wolfson AB, Hollander JE, Kurz M, Kirkali Z, Kusek JW, Mufarrij P, Jackman SV, Brown J. Effect of tamsulosin on passage of symptomatic ureteral stones: a randomized clinical trial. *JAMA internal medicine*. 2018 Aug 1;178(8):1051-7.
21. Nuraj P, Hyseni N. The role of the tamsulosin in the medical expulsion therapy for distal ureteral stones. *Medical Archives*. 2017 Apr;71(2):137.
22. Sun Y, Lei GL, Yang L, Wei Q, Wei X. Is tamsulosin effective for the passage of symptomatic ureteral stones: A systematic review and meta-analysis. *Medicine*. 2019 Mar;98(10).
23. Urkmez A, Tokuc E, Topaktas R, Sahin A, Yuksel OH. Mirabegron: a novel and promising medical expulsive treatment for ureteral stones?. *J Coll Physicians Surg Pak*. 2019 Jan 1;29(01):73-4.