



## A COMPARATIVE STUDY OF EFFICACY OF NIFEDIPINE, TAMSULOSIN AND THEIR COMBINATION FOR SPONTANEOUS EXPULSION OF DISTAL URETERIC STONES: AN INSTITUTIONAL STUDY

<sup>1</sup>Pankaj Gupta, <sup>1</sup>Sanjay Dosar, <sup>\*2</sup>Dilip Chaurasia and <sup>3</sup>Anil Kumar Saroj

<sup>1</sup>Resident, <sup>1</sup>Resident, <sup>2</sup>Professor, <sup>3</sup>Assistant Professor,  
P.G. Department of Surgery, M.L.N. Medical College, Allahabad, Uttar Pradesh – 211001, India.

Corresponding Author:- **Dilip Chaurasia**  
E-mail: [dilipchaurasia@yahoo.com](mailto:dilipchaurasia@yahoo.com)

Article Info	ABSTRACT
<p>Received 15/02/2015 Revised 27/02/2015 Accepted 05/03/2015</p> <p><b>Key words:</b> Nifedipine, Tamsulosin, Ureteric Stone.</p>	<p><b>Purpose of study:</b> In modern era we are going from open surgery to minimal invasive surgery and non invasive treatment options for distal ureteric stones. Medical expulsive therapy can be a better option. The results of wide spread clinical trials with selective <math>\alpha</math>1A antagonist like tamsulosin and calcium channel blockers like Nifedipine is promising. This study was conducted to compare the efficacy of calcium channel blocker (Nifedipine) and <math>\alpha</math>-1 receptor antagonist (Tamsulosin) alone and both in combination for the spontaneous expulsion of distal ureteric stones in relation to expulsion rate, expulsion time, analgesic use, need for hospitalization and other modalities of treatment. <b>Material and Method:</b> A total 58 symptomatic patients of distal ureteric calculi of less than 10 mm were randomly allocated to home treatment with Tamsulosin, Nifedipine and combination of both drugs (group 1 to 3 respectively). Each group was given Diclofenac (50 mg) twice daily and on demand. The primary end point was expulsion rate and secondary end points were expulsion time, analgesic use, need for hospitalization and other modalities of treatment. <b>Conclusion:</b> In our study Tamsulosin alone was found very effective for distal ureteric stone expulsion. Combination of both Tamsulosin and Nifedipine offered no added advantage and increases the cost of therapy.</p>

### INTRODUCTION

Renal colic is one of the most painful conditions that may occur and it is often caused by stone in the distal portion of the ureter. A watchful waiting approach may be expected to produce spontaneous stone expulsion in upto 50% of the cases but some complications such as urinary infection, hydronephrosis and repeated colic events may occur [1-4]. Endoscopic treatment with ureteroscopy (URS), extracorporeal shock wave lithotripsy (ESWL), and ureterolithotomy allows distal ureterolithiasis to resolve in almost all cases.

However, these procedures are not free from risk or co-morbidities and they require some expertise and costlier too. On the contrary, the role of medical expulsive

therapy (MET) in the treatment of this pathological condition is still unclear. In particular to our knowledge, the most effective treatment regime for spontaneous stone expulsion and for control of painful symptoms has not yet been determined despite the widespread need in clinical practice. A number of trials have demonstrated the utility of pharmacological therapy in spontaneous ureteric stone expulsion and in reducing the duration of pain associated with stone expulsion. The efficacy of calcium channel blocker (Nifedipine) has now been proven in several prospective, randomized clinical trials and recently,  $\alpha$ -1 receptor antagonist (Tamsulosin) demonstrated benefits in the medical management of distal ureteric calculi [2,3,5].



The purpose of this study is to compare the efficacy of two drugs alone and in combination, in medical expulsive treatment of distal ureteric stone.

## MATERIAL AND METHODS

This study was a prospective comparative study of the efficacy of Tamsulosin vs. Nifedipine vs. Tamsulosin + Nifedipine for spontaneous passage of distal ureteric stone, conducted on patients enrolled in urology outdoor and emergency ward of SRN Hospital, Allahabad, as a case of acute renal colic and were randomly allocated to have treatment with Tamsulosin, Nifedipine and both the drugs (Group I to Group III) respectively from September 2008 to September 2009.

**Patient Selection:** All patients with acute renal colic were included in study except those with: Stone not documented on imaging, Stones > 10mm, Pregnancy, Evidence of infection with an obstructing stone, Obstructing stone in a solitary kidney, currently taking Tamsulosin, Nifedipine or other calcium channel blocker, Contraindication or allergy to Tamsulosin or Nifedipine, Patients who were unable to understand the consent, Patients who were unable to comply with follow-up. All selected patients were clinically worked up and investigated appropriately.

**Treatment Protocol –** Patients were randomly allocated to treatment with Tamsulosin (0.4mg OD), Nifedipine (30 mg/day) or, both drugs in combination (Group I to Group III respectively). There was no placebo or control group in this study since objective was prospective comparison of efficacy of these two drugs alone and in combination.

**Follow up –** Each group of patients were started with respective drug therapy with analgesic and followed up to 30 days. Every 10th day, patients were evaluated with X-ray KUB, USG KUB, analgesic use and need for hospitalization. If no evidence of stone on imaging was found, then the treatment was stopped. If stone was present, the same drug was continued for next 10 days and the patient was re-evaluated. If stone was found, same treatment was continued for next 10 days and patient again evaluated.

If stone persisted even after 30 days of drug trial, other modalities of treatment were chosen like ESWL, ureterolithotomy or Ureteroscopic removal of stone.

All the results were analysed statistically by students t-test, test of significance for difference of proportion (using SPSS 10.0 programme, Inc.,Chicago, IL).

## RESULTS

Total 58 patients were evaluated for study. No statistical significant difference was observed among 3 groups in relation to age or size of stone. Group I to III contained 21 patients, 19 patients and 18 patients respectively (Table -1). Stone expulsion was observed in 47 (80.03%) out of 58 patients. None of patient was lost during follow-up. In 9 patients (15.51%) where stone expulsion did not occur ureteroscopic removal of stone was done and ureterolithotomy was done in 2 patients (3.44%) Expulsion occurred in 19 (90.45) out of 21 patient in Group I, 11 (57.83%) out of 19 patients in Group II and 17 (94.44%) out of 18 patients in Group III. Group I and III showed the higher expulsion rate in comparison to Group II, which was statistically significant ( $p < 0.05$ ). Group III also showed higher expulsion rate as compared to Group I, but it was not statistically significant. Stone expulsion was more rapid in Group I and Group III than Group II on 10th day. Group I showed 68.42% expulsion and Group III showed 64.70% which was higher than Group II (35.36%). Mean time of expulsion was 13.68, 18.18 and 14.11 days in Group I to III respectively. Group I and III showed the lower time of expulsion than Group II which was statistically significant. There was no statistical significant difference in mean time of expulsion between Group I and Group III. In Group I, and Group III none of the patient required increased dose of analgesics. Only 2 patients (10.52%) out of 19 patients in Group II required increased dose of analgesics during the treatment. Thirteen out of total 59 patients needed hospitalization. Two patients needed hospitalization for increased pain in Group II. Eleven patients who did not pass the stone spontaneously, needed hospitalization for other treatment like ureteroscopic removal or ureterolithotomy. Two patients (9.52%) in Group I, 8 patients (40.10%) in Group II and 1 patient (5.55%) in Group III needed hospitalization. Ureteroscopic removal was done in 2 patients in Group I, 6 patients in Group II and 1 patient in Group III. Ureterolithotomy was done in 2 patients in Group II.

**Table 1. Patient's characteristics**

Patient characteristics	Group I	Group II	Group III
Mean age (SD)	29.23( 11.02)	25.94 (7.77)	27.05 (11.29)
Male/Female	20/1	13/6	14/4
Mean stone size (SD)	7.09 (1.68)	6.89 (1.148)	7.23 (1.21)
Median (Range)	7 (3.9-9.8)	7 (4.5-8.6)	7.5 (5-9.3)

**Table 2. Results of Study**

Patient status	Group 1	Group 2	Group 3
Pt. With stone expulsion	19/21 (90.48%)	11/19 (57.89%)	17/18 (94.44%)
Stone expulsion at 10 <sup>th</sup> day	13 (68.42%)	4 (36.36%)	11 (64.70%)



Mean time of stone expulsion in days ( SD)	13.68 (5.97)	18.18 (7.5)	14.11 (6.18)
No. Of pt. needed more analgesia	0	2 (10.52%)	0
No. Of pt. needed hospitalization	2	10	1
Ureteroscopic removal	2	6	1
Ureterolithotomy	0	2	0

## DISCUSSION

Distal ureteric stones are very common in our society and currently ESWL, ureteroscopic removal and open surgery (Ureterolithotomy) is the most popular treatment modality. Although watchful expectancy may produce spontaneous stone expulsion in up to 50% of cases but some complication such as urinary infection, hydronephrosis and repeat colic events may occur [1,6]. Lots of randomized control trials have been done about medical expulsive therapy with selective  $\alpha$ -antagonist, calcium channel blockers and have suggested that they have role in speedy expulsion, better control of painful symptoms and decreased need for hospitalization. These agents have been used to decrease obstruction induced phasic peristaltic contraction, and to maintain tonic contraction which would allow distal migration to stone [4]. In this study, we compared the clinical efficacy of 2 drugs Tamsulosin and Nifedipine alone and in combination. In our study 47 cases (81.03%) out of total 58 patients showed spontaneous expulsion of stone, suggesting that MET have higher expulsion rate than watchful waiting approach. In Present study, stone expulsion occurred in 90.48% with Tamsulosin (Group I) 57.89% with Nefedipine (Group II) and 94.44% with combination of both Tamsulosin and Nifedipine (Group III). This study shows Tamsulosin is better drug in rapid stone expulsion than Nifedipine (Statistically significant) but combination of both drugs offer no more advantage but the difference was statistically insignificant. This study showed that Tamsulosin also reduces the eliminative time (68.42% within 10 days) than Nifedipine (36.36% within 10 days) and with both drugs (64.70% in 10 days). Mean time of stone expulsion with Tamsulosin was 13.68 days, 18.18 days with Nifedipine and 14.11 days with drug combination. Our trial confirms the excellent efficacy of Tamsulosin above in favour of rapid stone expulsion. The combination of both drugs offered no advantage.

Our study shows that Tamsulosin has better control of painful symptoms than Nifedipine. Only two patients in Group II showed the increased analgesic use. The cause of pain was related to ureteric colic and due to straining of muscular nerve ending and mucosa, which was due to increase in ureteral intraluminal pressure resulting from stone obstruction and the production of lactic acid due to smooth muscle spasm [1,6]. It also includes the

inflammation of the ureteral tract, where stones are impacted. The pain stimulus is conveyed to the spinal cord through type A slow fibers and type C fast fibers and then to the cerebral centre. The visceral pain is referred to the somatic distribution which corresponds to the spinal segment from where sympathetic innervations of the ureter originates. Evidences indicate that  $\alpha$ -1 receptor blockage results in the alleviation of visceral referred pain and it has been supposed that the  $\alpha$ -adrenergic blockage occurs in C fibers [5,6]. Therefore according to the final results of our trial, it would be possible to suppose a double action of Tamsulosin over the control of pain associated with ureteric colic, that is first action on smooth muscle preventing spasm, where Nifedipine would also be able to act, and the second action on C fibers or sympathetic post-ganglionic neurons, which blocks the pain conduction to the central nervous system.

In our study excellent pain control was observed in Groups treated with Tamsulosin (Group I) and Tamsulosin + Nifedipine (Group III). It also demonstrated the fact that none of the patients in these groups were urgently hospitalized during the study period. Only 2 patients in Group II required urgent hospitalization for increase in pain. Total 8 patient in Group II required hospitalization in which 6 patient treated with Ureteroscopic removal of stone and Ureterolithotomy done in 2 patient. One patient in Group II required admission for Ureteroscopic removal. Tamsulosin therapy proved superior to Nifedipine therapy for relieving pain associated with ureteric colic, decreased the use of analgesics and also decreased the need for hospitalization. Tamsulosin therapy also reduced the number of ureteroscopy or ureterolithotomy, thus decreased the need for hospitalization and also the cost of treatment.

## CONCLUSION

Medical expulsion therapy with Tamsulosin alone can be suggested as first choice of treatment for distal ureteric stones without complication, due to its excellent expulsive efficacy and good pain control, therefore allowing patient to perform daily activities regularly.

## Footnotes:

Source of support: Nil.

Conflicts of interest: None declared.

## REFERENCES

1. Beach MA, Mauro LS. (2006). Pharmacologic expulsive treatment of ureteral calculi. *Ann Pharmacother*, 40(7-8), 1361-8.
2. Hollingsworth JM, Rogers MA, Kaufman SR, Bradford TJ, Saint S, Wei JT, et al. (2006). Medical therapy to facilitate urinary stone passage: a meta-analysis. *Lancet*, 368, 1171-1179.



3. Francesco Porpiglia. (2004). Nifedipine and Tamsulosin Both Effective Therapy for Lower Ureteral Stones. *J Urol*, 172, 568-571.
4. Liu M, Henderson SO. (2007). Myth: nephrolithiasis and medical expulsive therapy. *CJEM*, 9(6), 463-5.
5. Parsons JK, Hergan LA, Sakamoto K, Lakin C. (2007). Efficacy of alpha-blockers for the treatment of ureteral stones. *J Urol*, 177(3), 983-7.
6. Sterrett SP, Nakada SY. (2008). Medical expulsive therapy. *Semin Nephrol*, 28(2), 192-9.
7. Borghi L, Meschi T, Amato F, Novarini A, Giannini A, Quarantelli C et al. (1994). Nifedipine and methylprednisolone in facilitating ureteral stone passage: a randomized, double-blind, placebo-controlled study. *J Urol*, 152, 1095.
8. Porpiglia F, Destefanis P, Fiori C and Fontana D. (2000). Effectiveness of nifedipine and deflazacort in the management of distal ureter stones. *Urology*, 56, 579.
9. Dellabella M, Milanese G and Muzzonigro G. (2005). Randomized trial of the efficacy of tamsulosin, nifedipine and phloroglucinol in medical expulsive therapy for distal ureteral calculi. *J Urol*, 174, 167.
10. Yilmaz E, Batislam E, Basar MM, Tuglu D, Ferhat M and Basar H. (2005). The comparison and efficacy of 3 different alpha1-adrenergic blockers for distal ureteral stones. *J Urol*, 173, 2010.

