

Efficacy of Prazosin and Nifedipine in Medical Expulsion Therapy of Ureteric Stones, - A Prospective study

AUB Pethiyagoda*, K Pethiyagoda**

*Department of Surgery, Faculty of Medicine, University of Peradeniya, Sri Lanka

**Department of Community Medicine, Faculty of Medicine, University of Peradeniya, Sri Lanka

DOI: 10.29322/IJSRP.8.6.2018.p7827

<http://dx.doi.org/10.29322/IJSRP.8.6.2018.p7827>

Abstract

Medical expulsion therapy is being used to treat ureteric stones after understanding the pathophysiology of the ureter. The objective of this study was to find out the efficacy of alfa blockers (Prazocin) and calcium channel blockers (Nifedipine) in management of ureteric stones. A prospective study was done in patients who presented with ureteric stones to THP from 1st June 2009 to 31st October 2011. We randomized patients into three groups and identified the patients who were treated with Medical Expulsive Therapy (MET) for urolithiasis. X-ray KUB reports at the diagnosis and after 1 month of treatment with MET were collected. Findings of X-ray KUBs were assessed according to the MET type. A total of 105 patients with mean age of 41.35 years (+/- 12.98) were included. Out of 105, 48 have been given Prazosin 0.5 mg bd (group-A). Nifedipine 10mg bd (group-B) has been given to 29. Both groups have been given Diclofenac Na 50mg tds with Omeprazole 20mg bd. The other 28 have given only Diclofenac and Omeprazole (group-C)

Stone expulsion was observed in 27 of 48 (56.2%) in group A, 16 of 29 (55.2%) in group B, and 12 of 28 (42.9%) in group C. Statistically significant difference was not observed between group A and B with respect to group C. Although successful therapy has been observed with both Prazocin and Nifedipine, compared to the Diclofenac only group, Prazocin and Nifedipine treatment groups yield no difference at success in the management of ureteric stones.

Index terms - Medical expulsion therapy, Prazosin, Nifedipine

I. INTRODUCTION

Urolithiasis affects about 8% to 15% of the population [1]. It has an estimated annual incidence of 12% and is 3 times more common in males, with peak incidence being at 30 years of age [2]. As younger population is affected more, it is clear that urolithiasis remains an important public health concern with substantial economic and quality-of-life impacts [3].

Ureteric stones contribute 20% of all urinary tract stones, 70% of which are located in the distal ureter [4]. Urolithiasis is a chronic disease with repeated attacks, it needs repeated interventions. Half of the patients will develop a recurrence within next 5 years [7].

A ureteric stone has a spontaneous expulsion rate of 50% over time. It mainly depends on the size and site of stone. Meta analysis of studies in which spontaneous ureteral stone passage was assessed: stones <5mm and 5-10mm had 68% and 47% of spontaneous stone passage [9]. The size, localization and stone composition, severity of obstruction, symptoms and anatomy of the urinary system are main factors determine the management option. Medical treatment, extracorporeal shock wave lithotripsy (ESWL) and ureteroscopy are therapeutic options for ureteral stones [5]. Although invasive and minimally invasive treatments for ureteral stones are efficacious, they are not free of complications and are associated with high cost. Medical expulsion therapy (MET) has recently emerged as an alternative strategy for the initial management of small distal ureteric stones [6].

MET developed after identification of the pathophysiology of the ureteric stone disease. Ureter is consisted of smooth muscles that respond according to the calcium ion concentration. Increased calcium ion concentration causes their contraction while reduced levels cause smooth muscle relaxation [8].

Alfa-1 receptors are present throughout the ureter with a high concentration in the distal third of the ureter. Blockage of the receptors will inhibit basal smooth muscle tone and uncoordinated hyper peristalsis. Ureteral calculi also can induce ureteral spasm and it can interfere with the stone passage. Reduction of spasms will increase the expulsion rate with maintaining normal peristaltic activity [10]. Thus alfa-1 blockers and Calcium channel blockers are commonly being used for the effective and safe treatment of ureteric stones. The use of drugs in augmenting stone passage, reducing the morbidity and costs associated with ureteric stone disease, is promising.

Many studies were conducted regarding medical expulsion therapy. They conclude that there is an efficacy of alfa blockers and calcium channel blockers compared to placebos [4-6, 11-13]. As the prevalence, composition of renal stones and risk factors changes with the geography, there could be a difference in the efficacy of the MET. Currently there are no published literature regarding MET urolithiasis in Sri Lankan population. Therefore we aimed our study to identify the place of these drugs in the management of Urolithiasis in patients who attended to THP, Sri Lanka.

II.METHODOLOGY

This study was conducted as a retrospective cohort study. We used medical records from 1st June 2009 to 31st October 2011, in Teaching Hospital Peradeniya (THP). We first identified the patients who have been diagnosed to have single ureteral urolithiasis from the X-ray KUB and USS KUB. From them the patients who have been given Prazocin or Nifedipine with analgesics or analgesics only for maximum of 4 weeks were included to the study.

We grouped them: Group A-Prazosin 0.5 mg bd + Diclofenac Sodium 50 mg tds, with a proton pump inhibitor Group B- Nifedipine 10mg bd + Diclofenac Sodium 50 mg tds and an proton pump inhibitor Group C- Diclofenac Sodium 50mg tds an proton pump inhibitor only. Prazocin and Nifedipine have been given for maximum of 4 weeks and Diclofenac and Omeprazole for 2 weeks.

Patients who had acute ureteric obstruction with elevated serum creatinine or with chronic renal failure, urinary tract infections and already on Prazocin or Nifedipine (as antihypertensive, for the treatment of BPH etc) also patients with radio lucent stones were excluded from the study. Socio demographic data presenting symptoms and findings of the 1st X-ray and /or USS KUB which had been done at the time of the diagnosis were obtained with regard to side, site and the size of the stone. Results of the urine full report and Serum creatine levels were also collected. Then the 2nd X-ray which had been done after 1 month of treatment was evaluated for passage of stones.

One-way analysis of variance (ANOVA) was used to compare continuous variables between the three groups (age, Stone size), and also continuous variables between each two groups were tested by using Student's t-test. Nominal parameters (Categorical data) were analyzed by using Pearson's chi-square and Fischer's exact test. A p-value<0.05 was considered significant. Statistical analysis was performed by using SPSS ver. 20.0 (SPSS Inc., Chicago, IL, USA) software.

III.RESULTS

A total of 152 patients with ureteric urolithiasis diagnosed from their X-ray KUB and USS KUB from 1st June 2009 to 31st October 2011 were included in the study. Out of them, 105 patients with their mean age of 41.11 years (+/-13.08) have been prescribed medical Expulsion therapy for their ureteric stone. There were 80 (76.2%) males and 25 (23.8%) females. There were 48 patients into group A (Prazosin), 29 into group B (Nifedipine), and 28 into group C.

There was no significant difference between 3 groups according to the age, stone size or serum creatinine levels. (Table 1)

Table 1- Demographic information and results of the three groups

	Group A (n=48)	Group B (n=28)	Group C (n=27)	P value (A & B)	P value (A & C)	P value (B & C)	ANOVA
Mean Age + Std Deviation (years)	42.63 +/- 13.884	39.43 +/- 13.198	40.26 +/- 11.624	0.330	0.458	0.806	0.554
Mean stone size (mm)	6.79	8.96	8.77	0.010	0.082	0.902	0.071
Mean serum creatinine levels (Umol/l)	91.19	91.18	92.74	0.999	0.848	0.888	0.983

In group A the mean size of the stone was 7.41mm and had 27 stones passage out of 48 (56.25%). In group B had 16 stones passage out of 28 patients (55.2%) with mean stone size of 8.96mm. In group C the mean stone size was 8.77 mm and stone passage was noted in 12 out of 28 (42.9%). Statistical significance was not noted between groups A and B ($p=0.926$) or groups A and C ($p=0.260$) or groups B and C ($p=0.352$) according to the Chi-square test. Statistical significant difference was also not observed between group A and B with respect to group C. (Z-ratios 1.127, 0.93 respectively) according to the odds ratios. (Table 2)

Table 2 – Success of treatment according to three drug groups.

	Stone passage			P values-Chi squire			Z ratios		
	Group A	Group B	Group C	A & B	A & C	B & C	A & B	A & C	B & C
Stone passage	56.25%	55.2%	42.9%	0.926	0.260	0.352	1.234	1.127	0.930

According to 1stX ray KUB, there were 20 stones at the upper ureter (L2-L4), 2 at the mid ureter, and 83 at the lower ureter. There was no significant difference between 3 site groups according to age, mean stone size and serum creatinine levels. (Table 3)

Table 3- Success of treatment according to stone site in the ureter

	Upper ureter (n=20)	Mid ureter (n=2)	Lower ureter (n=83)	P value for 3 groups
Mean Age (Years)	38.70 +/- 11.012	36.50 +/- 7.778	41.84 +/- 13.649	0.561
Mean stone size (mm)	9.81 +/- 3.291	7.50 +/- 0.707	7.32 +/- 4.031	0.076
Serum creatinine level (Umol/l)	88.53	115.00	91.2626	0.485

A statistical significant difference was noted in success with respect to the anatomical site of the ureteric stone. The calculi passed through the ureter spontaneously in 25.0% in upper ureter group 50.0% in mid ureter and 59.0% in lower ureter group. A statistical difference was not noted between 3 groups ($p=0.240$). Comparison between upper and lower ureteric stones yield p value of 0.06. (Table 4)

Table 4- Comparison of upper, mid and lower ureteric stones on outcome

	Upper ureter (n=20)	Mid ureter (n=2)	Lower ureter (n=83)	P value for 3 groups	P value (Upper & Lower)
Stone passage	N= 5 (25%)	N=1 (50%)	N=49 (59%)	0.24	0.06

There was no significant difference in the success with regard to age or gender.

IV. Discussion

The three groups in our study were similar demographically and clinically. There was no significant difference between the stone sizes either. At presentation most of the stones were seen in the lower ureter. Although there was no statistically significant difference higher serum creatinine level was seen in the patients with mid ureteric stones, Further studies would be needed for find why it is so. As noted in previous studies spontaneous passage of upper ureteric stones was less and the difference between the mid ureteric stones and the lower ureteric stones in spontaneous passage of stones was not significantly different in our study. Although it has been noted on previous occasions by researches that stones less than 5mm would pass spontaneously we did observed stones of larger size passing spontaneously, Majority of Sri Lankans have a smaller stature and how they were able to expel stones larger than 5mm warrants larger studies in the future.

V. CONCLUSION

Although successful therapy has been observed with both Prazosin and Nifedipine, compared to the Diclofenac only group, Prazosin and Nifedipine treatment groups yield no statistically significant difference in the success of management of ureteric stones

REFERENCES

1. M. Dellabella, G. Milanese, G. Muzzonigro Efficacy of tamsulosin in the medical management of juxtavesical ureteral stonesJUrol, 170 (2003), pp. 2202–2205
2. Kidney and ureteric stones.*Urogy care foundation* (available @<http://www.urologyhealth.org/urology/index.cfm?article=32&display=1>)
3. Stamatelou KK, Francis ME, Jones CA, Nyberg LM, Curhan GC. Time trends in reported prevalence of kidney stones in the United States: 1976-1994. *Kidney Int.* 2003;63(5):1817-1823.
4. Menon M, Parulkar BG, Drach GW. Urinary lithiasis: etiology, diagnosis and medical management, In Walsh PC, Retik AB, Vaughan ED jr ,et al, editors. Campbell's Urology, 7thed. Philadelphia: W B Saunders; 1998, 2261-2733.
5. Sáenz Medina J¹, Alarcón Parra RO, Redondo González E, Llanes González L, Crespo Martínez L, Fernández Montarroso L, Durán Poveda M, Páez Borda A. Prognostic factors of spontaneous expulsion in ureteral lithiasis Actas Urol Esp. 2010 Nov;34(10):882-7. (Available @<http://www.ncbi.nlm.nih.gov/pubmed/21159285>)
6. Tzortzis V¹, Mamoulakis C, Rioja J, Gravas S, Michel MC, de la Rosette JJ. Medicalexulsive therapy for distal ureteral stones.*Drugs*.2009 ;69(6): 677-92. doi: 10.2165/00003495-200969060-00003.
7. Rahim J, Mahmood A, Ashraf S, Tahir M, Khan MU,Efficacy of Tamsulosin Spontaneous Expulsion in the Treatment of Distal Ureteric Stones,
8. Andersson KE, Forman A. Effects of calcium channel blockers on urinary tract *Acta Pharmacol Toxicol*1986;58:193–200.

- 9.Preminger GM, Tiselius H-G, Assimos DG, et al., American Urological Association Education and Research, Inc. European Association of Urology.2007 guideline for the management of ureteral calculi.EurUrol2007;52:1610–31.
- 10.GianlucaGiannarinia,*Riccardo Autorino,RecommendingMedicalExpulsiveTherapyforDistalUretericCalculi:AStepBack?, European Journal of Urology 2009;56; 413-417,
11. Campschroer T, Zhu Y, Duijvesz D, Grobbee DE, Lock M - Alpha-blockers as medical expulsive therapy for ureteral stones,(available@<http://summaries.cochrane.org/CD008509>)
12. Kumar S, Jayant K, Agrawal S, Singh KS ,Comparative Efficacy of Tamsulosin Versus Tamsulosin With Tadalafil in Combination With Prednisolone for the Medical Expulsive Therapy of Lower Ureteric Stones: A Randomized Trial, Korean J Urol. 2014 Mar;55(3):196-200.
- 13.Al-Ansari A¹, Al-Naimi A, Alobaidy A, Assadiq K, Azmi MD, Shokeir AA.Efficacy of tamsulosin in the management of lower ureteral stones: a randomized double-blind placebo-controlled study of 100 patients.Urology. 2010 Jan;75(1):4-7. doi: 10.1016/j.urology.2009.09.073.