



EVALUATION OF EFFECT OF MET WITH NIFEDIPINE & ALFUZOSIN IN DISTAL URETERIC STONES

Surgery

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ABSTRACT

INTRODUCTION: Ureteric stone is one of the most common urological presentation in surgical emergency department. In last decade medical expulsive therapy (MET) has been used in management of distal ureteric stones as conservative treatment because it would significantly reduce the medical cost and prevent unnecessary invasive. We evaluated the efficacy of nifedipine and alfuzosin in the medical treatment of symptomatic, uncomplicated distal ureteral stones.

METHODS: The prospective study was done on the patients who presented with ureteric stones. Patients ≥ 8 years of either sex with a single, unilateral ureteral stone of ≤ 10 mm were included. Patients were randomly divided into two equal groups of 50 patients each. Patients in Group I received tablet nifedipine 30 mg/day, Group II received alfuzosin 10 mg/day. Patients were followed up weekly up to 28 days; history of stone passage, number of pain episodes were recorded and investigated with routine urine examination, kidney function test, and X-ray KUB. The findings in both groups were compared and statistically tabulated.

RESULTS: Group I had 62% male and 38% female (mean age: 33.28 ± 7.17 years) and Group II had 58% male and 42% female (mean age: 32.19 ± 9.26 years). The mean stone size was 6.3 ± 1.49 mm for Group I and 6.41 ± 1.64 mm for Group II. A statistical significant difference was observed for stone expulsion rate between Group I versus Group II (58% vs. 78%, $P < 0.05$). Average time for stone-expulsion was 12.7 ± 5.48 days in Group I and 12.6 ± 5.3 days in Group II with statistically insignificant difference. Patients taking alfuzosin had fewer pain attacks compared with others. The average number of pain attacks was 2.98 ± 0.98 for Group I and 1.77 ± 0.71 with significant statistical difference. Hospital re-admissions due to uncontrollable pain occurred in 28% and 16% of the subjects in group I and II respectively.

CONCLUSION: Medical expulsive therapy is a useful adjunct to observation in the conservative management of ureteral stones. The use of alfuzosin and nifedipine for uncomplicated distal ureteric stones is safe and effective in term of increased stone-expulsion rate, reduced pain attacks and decrease hospital re-admissions. Alfuzosin was found to be significantly better in terms of stone-expulsion rate and pain attacks as compared to nifedipine.

KEYWORDS

INTRODUCTION:

Ureter stone is one of the most common urological presentation in surgical emergency department and has life time prevalence of 10-15%^[1,2]. It affects 12% of world population. 70% of patient suffers from distal ureteric stones and 53% of distal ureteral stones of < 10 mm dimeters have stone expulsion. Patient in emergency present with symptoms and sign of ureteric colic because of sudden obstruction of ureter and associated complications include hydronephrosis, renal damage, infection of urinary tract, sepsis and deranged renal function⁴. Ureteric stone managed by different modalities depends on stone size, location, composition, clinical factors, equipment availability, surgeon experience and on patients demand, treatment was gradually or jointly adopted^[3]. In last decade medical expulsive therapy (MET) has been used in management of distal ureteric stones as conservative treatment because it would significantly reduce the medical cost and prevent unnecessary invasive procedure^[5].

Alpha receptor blocker and calcium channel blocker had pharmacological effect of smooth muscle relaxation in ureteral tract and in MET. Tamsulosin & nifedipine are the most common drugs adopted in clinical practice and research^[4,5,6]. Tamsulosin is the most common α -1 blocker, however alfuzosin is combined α -1 A an α -1 D selective adrenergic antagonist resulting in relaxation of distal ureteric smooth muscles to facilitate passage of stone and relieving pain. It is easily available and has less cardiac & ejaculatory side effects^[8]. Therefore the present study was planned to evaluate and compare the effect of Nifedipine & Alfuzosin in distal stones.

MATERIAL AND METHOD:

The present prospective study was conducted in Department of Surgery, from January 2019 to January 2020. Patients were assessed with history, physical examination and investigated with complete blood count, blood urea, serum creatinine, routine urine analysis, X-rays kidney, ureter, and bladder (KUB), ultrasonography, intravenous urography and helical computed tomography (CT) whenever was necessary. Patients ≥ 8 years of either sex with a single, unilateral ureteral stone of ≤ 10 mm were included. The distal ureter was defined as the segment from the lower border of the sacroiliac joint to the vesico-ureteric junction. Patients having previous surgery on the ipsilateral ureter, bilateral ureteric stones, multiple stones, solitary kidney, urinary tract infection, moderate or severe hydronephrosis, contraindications for nonsteroidal antiinflammatory drugs (e.g. gastritis), known allergy to tamsulosin or alfuzosin, renal insufficiency, or currently on α blocker therapy, and pregnant or lactating women were excluded. The study was approved by the ethical committee of hospital.

After taking written informed consent, patients received tablet nifedipine 30 mg/day in Group I and tablet alfuzosin 10 mg/day in Group II. Patients in both groups received tablet diclofenac sodium (50 mg) every 12 hourly for 1 week and injection diclofenac sodium (75mg) as needed. An intramuscular injection Tramadol hydrochloride 100 mg was given for persistent pain.

Sample Size: Spontaneous expulsion rate for lower ureteric stones

ranges between 25% and 60%. We took an average rate of spontaneous stone expulsion as 40% and also considered an expected increase of this rate by 35% from baseline after MET. Taking significance level α at 95% and power of study 80%, the sample size was calculated by using formula $[N = 2 \times \{Z_{1-\alpha} + Z_{1-\beta}/d\delta\}^2 \times p(1-p)]$, where N = size/group; P = spontaneous expulsion rate; $Z\alpha$ = standard normal deviate for one sided test; d = expected difference; $\delta\theta$ = clinically acceptable margin (taken as 0.05). The sample size required for each group was 35 per group, but considering the unknown error and attrition, the sample was increased to 50 per group. In this way a total of 100 subjects were recruited, which were then randomly distributed into two groups i.e. Group I and II.

Procedure: Patients were followed up weekly up to 28 days; history of stone passage, number of pain episodes were recorded and investigated with routine urine examination, kidney function test and X-ray KUB. Patients were advised to watch for stone expulsion. Medications were stopped after spontaneous stone expulsion, any intervention before the end of the study, and adverse effect. For patients with a stone free ureter on the last imaging, but no documented stone expulsion, the last date of positive stone status was recorded. Abdominal CT was performed for patients with radiolucent stones if the stone was not expelled by the end of the study. Patients underwent ureteroscopic stone removal for persistent stones after 28 days. Patients having uncontrollable pain were readmitted for injectable analgesics and medication was continued. The blood pressure, stone position on imaging, number of pain attacks, time of stone expulsion, hospital re-admission and any adverse events were recorded.

Statistical analysis: Data analysis was performed using Statistical Package for the Social Sciences trial version 24 statistical software. Student's t-test and Chi-square test were applied as required. The power of the study was 0.80, and the level of significance was set at <0.05.

RESULTS:

Group I had 62% male and 38% female (mean age: 33.28±7.17 years) and Group II had 58% male and 42% female (mean age: 32.19±9.26 years). The mean stone size was 6.3 ± 1.49 mm for Group I and 6.41±1.64 mm for Group II. There were no statistically significant differences between the groups in terms of sex, age, stone size and side ($P > 0.05$) as shown in table 1.

A statistical significant difference was observed for stone expulsion rate between Group I versus Group II (58% vs. 78%, $P < 0.05$). Average time for stone expulsion was 12.7±5.48 days in Group I and 12.6±5.53 days in Group II with statistically insignificant difference. Patients taking alfuzosin had fewer pain attacks compared with others. The average number of pain attacks was 2.98±0.98 for Group I and 1.77±0.71 with significant statistical difference. Hospital re-admissions due to uncontrollable pain occurred in 28% and 16% of the subjects in group I and II respectively (table 2).

DISCUSSION:

Recent advances in ureteric stone management have allowed these to be treated using minimally invasive techniques, which have increased success rates and decreased treatment related morbidity. These advances include shock wave lithotripsy and ureteroscopic lithotripsy. Although these approaches are less invasive than traditional open surgical methods, they are expensive and have inherent risks. Consequently, observation has been advocated for small ureteral stones which have a high probability to pass spontaneously. Observation can be supplemented by using MET. Hellstrom and Sikka^[9] studied the effect of tamsulosin and alfuzosin on ejaculatory function and concluded that marked decrease in ejaculatory volume in almost 90% of subjects and anejaculation in approximately 35% of individuals taking tamsulosin. Thus, we chose to study alfuzosin to avoid ejaculatory disturbance.

A meta-analysis compared stone passage rates in patients who were given calcium channel blockers or α 1-adrenergic receptor antagonist versus controls who did not receive these medications. They demonstrated a 65% greater chance of passing a ureteral stone in patients who received either medication. Another study also showed that calcium channel antagonist could promote distal calculi expulsion and reduce analgesia requirement, renal colic rate, and hospitalization rate.

Sameer et al^[10] in their study revealed statistically significant difference

in alfuzosin (85.7%) and nifedipine (60%) for stone expulsion rates ($P < 0.05$) when compared with control group (20%). In another randomized placebo controlled trial study done by Pirzada et al^[11] on 60 patients to test the efficacy of alfuzosin in kidney stones which are fragmented by extracorporeal shock wave lithotripsy and authors concluded that stone expulsion was significantly higher in alfuzosin group when compared to placebo (76.7% and 46.7% respectively, $P = 0.01$). Similar results were found in the present study i.e. statistical significant difference was observed for stone expulsion rate between Group I (nifedipine) versus Group II (alfuzosin) (58% vs. 78%, $P < 0.05$).

Nifedipine and alfuzosin also decreased the frequency of pain attacks. Patients taking alfuzosin had significantly less pain as compared to nifedipine group ($P < 0.001$). Use of α -blockers for expulsion of ureteral stones probably decreases the analgesic requirement in two ways: Expulsion of stones, leading to longer stone free periods, and blockade of C-fibers. It is difficult to assess which of these may be primarily responsible for decreasing the analgesic requirement, because α -blockers are known to be associated with both. Similar results were reported by Sameer et al in their study.

No patients developed serious side effects during the study period. Patients who were not stone free after the 4 week follow up were successfully treated with ureteroscopy. This study demonstrated that neither watchful waiting nor medical therapy seems to negatively affect the success rate of stone removal. Our results confirmed the efficacy of nifedipine and alfuzosin for distal ureteric stones. 58% of patient taking nifedipine and 78% of patients taking alfuzosin were able to expel their stones at the end of study. Alfuzosin was found to be significantly better in term of stone expulsion compared to nifedipine group ($P < 0.05$).

CONCLUSION:

Medical expulsion therapy is a useful adjunct to observation in the conservative management of ureteral stones. The use of alfuzosin and nifedipine for uncomplicated distal ureteric stones is safe and effective in term of increased stone expulsion rate, reduced pain attacks and decrease hospital re-admissions. Alfuzosin was found to be significantly better in terms of stone expulsion rate and pain attacks as compared to nifedipine

Table 1: Demographic data, stone size and side among the study groups

Variables	Group I Nifedipine (N=50)	Group II Alfuzosin (N=50)	t Test	p value
Gender				
Male, N (%)	31 (62)	29 (58)		
Female, N (%)	19 (38)	21 (42)		
Age in years (Mean±SD)	33.28±7.17	32.19±9.26		
Stone Size (mm)	6.3±1.49	6.41±1.64	0.37	0.71
Stone Side			Chi Square	p value
Right, N (%)	36 (72)	38 (76)	0.17	0.83
Left, N (%)	14 (28)	12 (24)		

Table 2: Stone expulsion, duration of stone expulsion, pain and re-admission rate among the study groups

Variables	Group I Nifedipine (N=50)	Group II Alfuzosin (N=50)	Chi Square Test	p value
Stone Expulsion Rate, N (%)	29 (58)	39 (78)	6.81	0.02*
			t test	
Duration of Stone Expulsion (Days), Mean±SD	12.7±5.48	12.6±5.53	0.13	0.89
Episodes of Pain	2.98±0.98	1.77±0.71	4.98	0.002*
			Chi Square Test	p value
Hospital re-admission rate, N (%)	14 (28)	8 (16)	2.31	0.37

*: statistically significant

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