

## Research Article

# Medical expulsive therapy for the management of ureteric calculi

Yogendra D. Shah<sup>1,2\*</sup>, Pukur I. Thekdi<sup>3</sup>, K. G. Patel<sup>3</sup>

<sup>1</sup>Assistant Professor in Surgery, C U Shah Medical College and Hospital, Surendranagar, Gujarat, India

<sup>2</sup>Presently as Assistant Professor in Surgery, GMERS Medical College and Hospital, Dharpur, Patan, Gujarat, India

<sup>3</sup>Professor in Surgery, C U Shah Medical College and Hospital, Surendranagar, Gujarat, India

**Received:** 23 June 2013

**Accepted:** 29 June 2013

### \*Correspondence:

Dr. Yogendra D. Shah,

E-mail: drydshah@gmail.com

© 2013 Shah YD et al. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

## ABSTRACT

Ureteric stones in endemic areas if treated on OPD basis with helps of oral drugs saves hospitalization and economic burden to the patient and the hospital. A prospective study was carried out for 9 and half years in two medical colleges by offering two different regimes to patients on random basis and regular follow-up was done on OPD basis. The stone passage rate was highest in the lower ureter 1/3rd (80%) followed by middle 1/3rd (45%) and upper 1/3rd (40%). The patients who were offered regime 1 which included diuretics had less success rate then that with regime 2 which included drugs like nifedipine and steroids. Treatment of ureteric stones on OPD basis in endemic areas is a boon for the patients and for the health management system in terms of cost and health care system.

**Keywords:** Ureteric stone, Dicontin-K, Nifedipine, Prednisolone

## INTRODUCTION

While treating the urinary stones the surgeon should take into consideration the epidemiologic criteria, metabolic status, life styles and of course the patients wish. The specialty of urologic surgery dates back up to work of Hippocrates who has quoted in his famous oath that 'I will not cut, even for stone, but leave such procedures to practitioners of the craft. It is quiet known that large number of patients passes stones spontaneously with adequate hydration. Based on meta-analysis, according to American Urological Association, up to 98% of ureteral stones 4 mm or smaller size will pass spontaneously.<sup>1</sup> Hence, both nonsurgical and surgical aspects of stone treatment are equally important. The aim of study is to establish that ureteric stone can be treated with calcium channel blocker and steroid without admission to the hospital. Urolithiasis is quiet prevalent with incidence of up to 10% in USA. Once the diagnosis of ureteric stone

has been confirmed by history and investigation, size and location of the stone determines the management.<sup>2</sup> Sandeguard describes the fate and outcome of ureteric calculi treated conservatively. Longer the duration of obstruction due to stone, effect on the renal function is worse. Kidney partially obstructed for 14 days shows recovery of renal function better as compared to obstructed for 2 month (i.e. 31% vs. 8%). We present our result of prospective study of 400 patients treated with medical expulsive therapy

## METHODS

In this prospective study carried over a period of 9 & 1/2 years between January 2000-June 2009 in M.P. Shah Medical College, Jamnagar for first 3 years and subsequently in C.U. Shah Medical College and Hospital, Surendranagar. Total number of patients were 400 out of which 240 patients were male as compared to female 140

female patients. Age of the patients varies between 17-58 years with average age being 26.5 years.

**Inclusion criteria:**

- 1) All patients attended emergency department as well as surgical OPD with stone size <10mm (width) on plain X-ray KUB.
- 2) Patients with any age group having mild to moderate hydronephrosis on USG.

**Exclusion criteria:**

- 1) All patients with high grade obstruction.
- 2) Patients with pyonephrosis.

All patients were subjected to complete blood count, urine analysis, serum creatinine, blood urea.

All patients with stone size for than 5mm and hydronephrosis had undergone Intravenous urography.

We have used 2 regimes for medical management of ureteric stone. All patients with >5mm stone were offered regime 2. Those patients who were not responded to regime 1 were switched over to regime 2.

**Regime 1:** consist of-

1. Plenty of liquids orally,
2. Tablet Dicontin-K (furosemide plus potassium) 20mg once a day,
3. Diclofenac sodium 50mg three times a day,
4. Ranitidine 150mg two times a day.

All these medication were given for 2 weeks.

**Regime 2:** consist of-

1. Capsule Nifedipine - sustained released 20mg once a day,
2. Norfloxacin 400mg, Diclofenac sodium three times a day
3. Prednisolone tablet 5 mg, 2 tablet three times a day for 3 days followed by two tablet two times a day for 3 days then one tablet three times a day for 3 days and one tablet two times a day for 1 day.
4. Ranitidine 150mg 2 times a day.

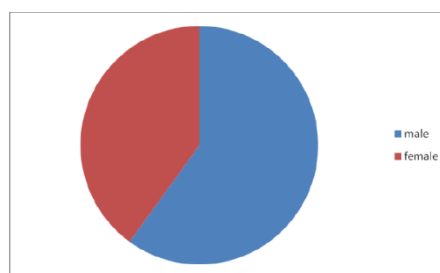
Total duration of therapy in regime 2 was 10 days.

All patients of stone >5mm were offered regime 2. Success rate was compared between two regimes. Stone free rate or clearance was assessed by plain X-ray KUB and USG KUB on 14<sup>th</sup> day in regime 1 group while on 10<sup>th</sup> days in regime 2 group.

**RESULTS**

The 400 patients of ureteric stone during the period of January 2000 – June 2009 were included in this prospective the study.

In this study 240 patients were male as compared to female 140 female patients. Age of the patients varies between 17-58 years with average age being 26.5 years.



**Figure 1: Distribution of male and female patients.**

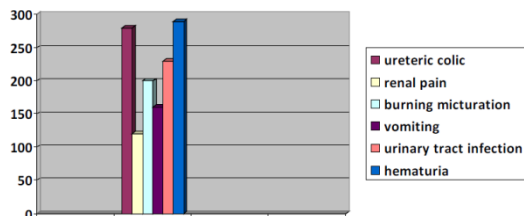
**Table 1: Shows that incidence of ureteric stone was highest in lower 1/3<sup>rd</sup> of ureter. Up to 4mm stone.**

Regime	I		II		I to II				Chi square	p-value
	Up to 4mm		5-6 mm		7-10 mm					
	Total	Passed	Total	Passed	Total	Passed	Total	Passed		
Upper 1/3 <sup>rd</sup>	20	8	8	2	12	1	20	13	6.33	0.011*
Middle 1/3 <sup>rd</sup>	10	3	4	4	13	3	13	8	0.17	0.676
Lower 1/3 <sup>rd</sup>	120	109	28	24	125	80	27	27	28.22	0.000**
Total	150	120	40	30	150	84	60	48	-	-

\*\* denote significance at 1% level

\* denote significance at 5% level

Most common presentation in this study was ureteric colic (70%) followed by burning micturition (50%) followed by vomiting (40%) and fixed renal pain in 30% cases. Most common sign was haematuria (80%).



**Figure 2: Distribution of various symptoms of patients with ureteric stone.**

## DISCUSSION

A stone in the ureter usually arises in the kidney and enters in to the ureter subsequently. Most calculi are small and pass spontaneously. Typically most patients present with sudden onset of agonizing pain, which may radiate to the groin, sacrum, labia, scrotum and the anterior surface of thigh. Presence of stone in ureter does not necessitate the surgical intervention. Important factors that decide spontaneous passage of stones are its size, location and degree of obstruction at the initial presentation.<sup>3</sup> Conservative treatment or medical treatment is probably most effective for stone size of 3-10mm. Overall incidence of stone passage with medical treatment is >65%. Many randomized trials prove the efficacy of conservative or medical treatment and helps in reducing the pain and helps in stone passage. Thus overall rate of surgical intervention is reduced with medical treatment.<sup>4,5</sup> Conservative treatment using medical therapy is found to be cost-effective before embarking upon surgical option.<sup>6</sup> Most stone that will pass spontaneously with conservative management, will pass within 4-6 weeks.<sup>7</sup> According to meta-analysis done by Marlene Busko conclude that all patients with stone size up to 1 cm who are candidate for observation should be offered trial of medical therapy. Conservative or medical management should not be offered to patients with >1cm size stone, high grade obstruction or patients in sepsis.<sup>8</sup>

According to Pak et al, high fluid intake in such ways that urine output remains above 3 liters per day, has shown that there is reduction in saturation of calcium phosphate, calcium oxalate thus decreasing the chances of stone formation. High fluid intake is associated with increase in inhibitory activity of Tamm-Horsfall protein. Diuretics like Dicontin-K inhibits the sodium-potassium chloride channel in the ascending limb of loop of henle. It increases the urine output. Calcium channel blockers and  $\alpha$ -blockers have been found to be associated with antegrade propulsion of stone by inhibiting ureteral spasm.<sup>9</sup> Diclofenac sodium inhibits the formation of

prostaglandins and helps in relieving pain of stone colic. In addition to anti-inflammatory action, Diclofenac sodium interferes with auto-regulatory response by reducing renal blood flow and does not affects the renal function in normal kidney.<sup>10</sup> Calcium channel blockers are smooth muscle relaxant. Few small prospective studies show that it facilitates spontaneous passage of stone if it is combined with prednisolone which is strong anti-inflammatory drug.

In this study, there was a male preponderance (60%) and median age of presentation was 26.5 years with age varies between 18-75 years. Ureteric stone was more common on right side as compared to left side (60% vs. 40%) in this study.

Most common presentation was ureteric colic in 280 patients (70%), followed by burning micturition in 200(50%) followed by vomiting (40%) and fixed renal pain in 30% cases. Most common sign was haematuria in 290 (80%) followed by urinary tract infection in 230(60%) of patients. Absence of haematuria does not rule out present the stone. According to one study, 67% of patients with ureteric stone had more than 5 RBC per high power field and 89% of patients had more than 0 RBC/hpf on urine microscopic examination.<sup>11</sup> Total number of patients with stone up to 4mm size were 210(52.5%), 5-6mm were 40(10%) and 7-10mm were 150(37.5%). Patients with stone size up to 4mm were offered regime 1 out of 210 ,120 patients had passed stone with regime 1& 30 patients were referred for surgery because of high grade obstruction they develop. Remaining 60 patients were switch over to regime 2, out of those 48 (80%) patients had passed stone. Those patients of 5-6mm and 7-10 mm were offered regime 2.out of 190 patients,114 patients had passed stone with success rate of 60%.comparing the efficacy of regime 1 to 2, regime 2 was found to be more effective for upper 1/3<sup>rd</sup>(P:0.011) and lower 1/3<sup>rd</sup> (p=0.000). For middle 1/3<sup>rd</sup>, there was no statistical significant difference was found (p:=0.676).Overall success rate with regime 2 was 80%. Stone passage rate was highest in the lower ureter 1/3<sup>rd</sup> (80%) followed by middle 1/3<sup>rd</sup> (45%) and upper 1/3<sup>rd</sup> (40%). According to Ueno et al<sup>12</sup>, width is a critical determinant of spontaneous passage of stone. So we considered width as a parameter for patient's selection. We found that stones measuring 5 mm or smaller in size will usually pass spontaneously in 80% cases, while stones measuring 6mm or larger in size will pass spontaneously in 60% cases. Though Stone size and location is very important predictor of stone passage, many other factors decide the fate of stone. It is known that the larger the stone lower the probability of spontaneous passage. With regard to the location of stone, our study showed that if a stone was present in the upper 1/3<sup>rd</sup> of ureter at the time of diagnosis, the overall frequency of spontaneous passage was 40%. The frequency of spontaneous passage of stones in the distal

1/3<sup>rd</sup> of ureter was significantly higher than that of stones in the upper 1/3<sup>rd</sup> (80%). A review of the literature published by Hubner et al<sup>13</sup> in 1993 included 2,704 cases derived from six studies; they reported frequencies of spontaneous passage of 12% for proximal ureteral stones, 22% for mid ureteral stones, and 45% for distal ureteral stones. Review by Singh et al show that medical treatment using either  $\alpha$ -blockers or calcium channel blockers improve the stone passage rate for moderately sized distal ureteral stones. Adverse drug reactions were noted in 4% of those taking  $\alpha$ -blockers and in 15.2% of those taking calcium channel blockers.<sup>14</sup> Meta-analysis by Hollingsworth et al also concludes that medical therapy with either calcium channel blockers or  $\alpha$ -blockers may increase the chance of spontaneous passage of stone.<sup>15</sup> Steroid has also found to important in the conservative management of ureteric stone. Addition of steroid to  $\alpha$  blocker has been found to shorten the time for spontaneous passage.

Overall success rate is 70.5% in this study for stone up to 10 mm in size (282 patients have passed stone out of 400) In our study, higher stone clearance rate was noted with regime 2. Those patients who were not responded to regime-1 were switch over to regime-2 and responded very well (80%). There was a statistically significant difference was noted with regime 2 for at least lower 1/3<sup>rd</sup> (p=0.000) and upper 1/3<sup>rd</sup> calculus (p=0.011). Better response rate was probably because of addition of calcium channel blockers and steroids.<sup>14</sup>

Only those patients who required intervention were admitted to the hospital. All other patients were managed at home by medical treatment.

No patients in our study showed any significant side effects associated with drugs.

Medical expulsive therapy using calcium channel blocker and steroid is a rational approach for management of ureteric calculi. It is cost effective and patients can be treated on outpatients' basis. Patients can carry out his day to day work with medical expulsive therapy without significant side effect.

## CONCLUSION

Medical expulsive therapy using calcium channel blocker and steroid is a rational approach for management of ureteric calculi. It is economical for the patients and they can be treated on outpatients' basis and can carry out their day to day work with medical expulsive therapy without significant side effect. Hence, in endemic areas if we can treat the patients on OPD grounds it is a boon both for the patients and for the health management system in terms of cost and health care system.

## REFERENCES

1. Segura JW, Preminger GM, Assimos DG, et al. Ureteral stones: clinical guidelines-panel summary report on the management of ureteral calculi. *Journal of Urology* 1997; 158: 1915-1921.
2. O'Flynn JD. The Treatment of Ureteric Stones: Report on 1120 Patients. *British Journal of Urology* 1980; 52: 436-438.
3. Miller OF, Kane CJ. Time to stone passage for observed ureteral calculi: A guide for patient education. *Journal of Urology* 1999; 162: 688-91.
4. Cooper JT, Stack GM, Cooper TP. Intensive medical management of ureteral calculi *Journal of Urology* Oct 1 2000; 56(4):575-8.
5. Porpiglia F, Ghignone G, Fiori C, Fontana D, Scarpa RM. Nifedipine versus tamsulosin for the management of lower ureteral stones. *Journal of Urology.* Aug 2004; 172(2): 568-71.
6. Bensalah K, Pearle M, Lotan Y. Cost-effectiveness of medical expulsive therapy using alpha-blockers for the treatment of distal ureteral stones. *Euro Urology* 2008;53:411-8.
7. Tiselius HG, Ackermann D, Alken P, Buck C, Conort P, Gallucci M. Guidelines on urolithiasis. *Euro Urology* 2001; 40:362.
8. Priminger GM, Tiselius HG, Assimos DG, Alken P, Buck C, Gallucci M, Knoll T, Lingeman JE et al. 2007 Guideline for the Management of Ureteral Calculi. *Journal of Urology* 2007; 178:2418.
9. Troxel SA, Jones AW, Magliola L, Benson JS. Physiologic effect of nifedipine and tamsulosin on contractility of distal ureter *Journal of Endourology* 2006; 20: 565-8.
10. Shokeir AA, Abdulmaaboud M, Farage Y, Mutabagani H. Resistive index in renal colic: The effect of nonsteroidal anti-inflammatory drugs. *British Journal of Urology* 1999; 84:249-51.
11. Bove P, Kaplan D, Dalrymple N, et al. Re examining the value of hematuria testing in patients with acute flank pain. *Journal of Urology.* Sep 1999; 162:685-7.
12. Ueno A, Kawamura T, Ogawa A, Takayasu H. Relation of spontaneous passage of ureteral calculi to size. *Journal of Urology* 1977; 10: 544 -546
13. Hubner WA, Irby P, Stoller ML. Natural history and current concepts for the treatment of small ureteral calculi. *Euro Urology* 1993; 24: 172-6.
14. Singh A, Alter HJ, Littlepage A. A systematic review of medical therapy to facilitate passage of ureteral calculi *Annals Emergency Medicine.* Nov 2007; 50(5):552-63.
15. Hollingsworth JM, Rogers MA, Kaufman SR, et al. Medical therapy to facilitate urinary stone passage: a meta-analysis. *Lancet* 2006;368:1171-9.

DOI: 10.5455/2320-6012.ijrms20130821

**Cite this article as:** Shah YD, Thekdi PI, Patel KG. Medical expulsive therapy for the management of ureteric calculi. *Int J Res Med Sci* 2013;1:267-70.