

# An Outpatient Medical Expulsive Therapy for Unilateral Single Ureteric Calculi with SOADS Regime: Our 9 Years Experience with 3000 Patients

## Abstract

**Introduction:** The most important recent advances in the management of ureteral calculi have been the development of medical expulsive therapy to facilitate passage of ureteral stones. Drugs like alpha 1 adrenergic blockers with or without corticosteroids along with hydration have been used to facilitate expulsion of stones.

**Material & Methods:** 3000 patients, from January 2008 to December 2017, who were diagnosed to have ureteric calculi either by USG/NCCT and presented to our OPD within first 2 days of colic were enrolled in this study. They were started with SOADS regime which included Tab Alfa blocker (Alfuzocin 10 mg) once daily, Tab Drotaverine Hydrochloride 80 mg + Tab Mefenamic Acid 250 mg Twice Daily, Tab spironolactone 25 mg once daily, Tab ofloxacin 200 mg Twice daily and Syrup Potassium magnesium citrate 2 Tsf with one glass of water three times daily with 2-3 litres of fluid for a period of 2-4 weeks.

**Results:** Out of 3000 pt, 2550 pts (85%) passed the stone with SOADS regime. 65% of pt passed within 2 weeks of therapy and 20% within 4 weeks. Stone size of 4mm, 5mm & 6 mm comprised 65% who passed within 2 weeks and rest 20% pts had stone size of 7mm, 8mm & 9mm. Rest of the 15% were managed by URSL. An interesting observation was noticed that pts with obstructive stone unilaterally had increased BP of 10 mmHg both systolic and diastolic.

**Conclusion:** It is possible to facilitate expulsion of ureteric calculi with SOADS regime in patients who present within first 2 days of colic and thus avoid surgical intervention and thereby reducing the cost and lost working days.

**Keywords:** Ureteric stone; Alfuzosin; Medical expulsive therapy

## Research Article

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## Introduction

As a major health problem, urolithiasis constitutes the third most common disease of the urinary tract, affecting 2-3% of the population, with a high recurrence rate of almost 50% [1]. The incidence of ureteric stones is increasing all over the world. This increase is seen across age, sex, and race. Changes in diet pattern and global warming seems to influence these trends [2]. Recent reviews of published papers suggest that 90% stones of less than 5 mm and 15% stones of sizes between 5mm-8mm will pass spontaneously [3]. For stones less than 5 mm size recommended management includes analgesic, antibiotics and hydration therapy. With medical expulsive therapy, in which Tamsulosin is the main stay, spontaneous passage of stone up to 10 mm has been reported [4].

Among our patients 61.46% of ureteral stones are located in the lower third of the ureter. Similar observations have been made by other authors also. In the last 20 years ureteral stones treatment modalities have changed radically and MET have become a part of the standard protocol for treatment of smaller size stones in the lower third of the ureter. It increases the expulsion rate and

decreases the expulsion time, thereby reducing the cost and lost working days [5]. Stones up to 4 mm size are expelled in almost all cases. Spontaneous expulsion rate for 4-6 mm stones is about 25% and over 8 mm size are rarely expelled [6]. Different procedures have been recommended for stones of greater than 5 mm size. Stones up to 9.5 mm have been successfully expelled with MET, the largest size stone being 1.4 cm [7]. The eventual factors for spontaneous expulsion of ureteral stones size, location, number, spasm in ureteral smooth muscle, mucosal edema, inflammation and ureteral anatomy.

The basis of pharmacotherapy is different for different drug groups. In the case of alpha blockers, the human ureter contains predominantly alphas receptors which are further classified as alpha 1 and alpha 2 receptors. In turn alpha 1 receptors which are divided into subtypes on the bases of their selectivity. Alpha 1a (proximal urethra, prostate, bladder outlet), alpha 1b (smooth muscles of vessels) and alpha 1d (detrusor, lower ureter). Specifically those of alpha type, serve an important role in lower urethral physiology. Nor epinephrine is the main alpha-agonist which exerts positive chronotropic effect on the ureter, thereby

increasing peristaltic frequency. Positive chronotropic effect, increases muscle tone and at high doses may lead to complete ureteral obstruction. In ureter alpha adrenergic receptor antagonists inhibit basal tone and also decrease peristaltic frequency and amplitude. Consequently intraureteral pressure decreases, there is an increase in fluid transport ability which increases the bolus of urine thus exerting pressure above the stone, at the same time peristalsis and intraureteral pressure decrease below the stone. The net effect is an increase in intra ureteral pressure gradient around the stone which ultimately results in stronger expulsive force.

Urolithiasis is one of the commonest urological disorders in our state. Considering the economic condition of the state and various complications of non conservative treatments (ESWL/ureteroscopic lithotripsy/surgery), the MET for ureteric stones can be the preferable, promising and economic choice of treatment. SOADS regime represents a non invasive and cost-effective alternative to interventional approaches with fewer side effects like hypotension, asthenia and retro grade ejaculation.

### Materials and Methods

This study was non-interventional and prospective cross sectional conducted in the Urological Departments of Super speciality hospital GMC, Srinagar and Kidney hospital & Research centre Srinagar, Kashmir, J&K, India from January 2008 to December 2017. A total of 3000 patients were enrolled during these Nine (9) years, both sexes who were over above 9 years up to 85 yrs (Table 1&2), having single stone size less than or equal to 9mm reporting within 2 days of colic. Patients with pregnancy, breast feeding, contraindication to SOADS regime, complication needing surgery, renal/Liver failure, solitary kidney, Bilateral ureteric stones were excluded from the study. An explanation was given to the patients including the reason why he or she was prescribed the SOADS regime, the possible side effects and effectiveness of the drug and their written approval was taken.

Table 1: Showing male/female ratio.

S. no	Sex	Number	% Percentage
1.	Male	1977	65.9%
2.	Female	1023	34.1%

Table 2: Showing Age Groups.

1.	9 yrs - 18 yrs	419	13.96 %
2.	19 yrs - 30 yrs	1001	33.36 %
3.	31 yrs - 50 yrs	894	29.80%
4.	51 yrs - 70 yrs	558	18.62%
5.	71 yrs - 85 yrs	128	04.26%
Total		3000	100 %

All patients who reported within 1-2 days of ureteric colic were examined, and subjected to Haemogram, KFT, Urine examination, Ultrasound and NCCT Scan (Figure 1&2) to document ureteric

calculi at the time of colic with respect to location, side and size of the stone. Age and sex of the patient was noted down and SOADS regime was started for a period of 4 weeks maximum after which this MET was stopped. The routine follow up examination were performed, using the same tools to evaluate the success of the treatment after every week till 4 weeks of study period. Patients were instructed to discontinue the study medication after spontaneous stone expulsion and date of expulsion is to be recorded. For patients without stone in urinary tract on final USG/NCCT but unnoticed stone expulsion, the date of last positive stone status is to be recorded (Figure 3). For the children the dosage of the SOADS regime was half the dosage. Two - three litres of fluid which consists of Lemon juices, Oranges juices and clear water or Tea. This regime was continued for 2 weeks after which again assessment was made and if the stone did not pass then it was continued for another 2 weeks. Treatment was considered successful when stone was expelled within 4 weeks. After 4 weeks, patients who did not pass the stone were advised to undergo minimally invasive surgery depending upon the stone size and location.



Figure 1: X-ray KUB showing multiple lower ureteric calculi.

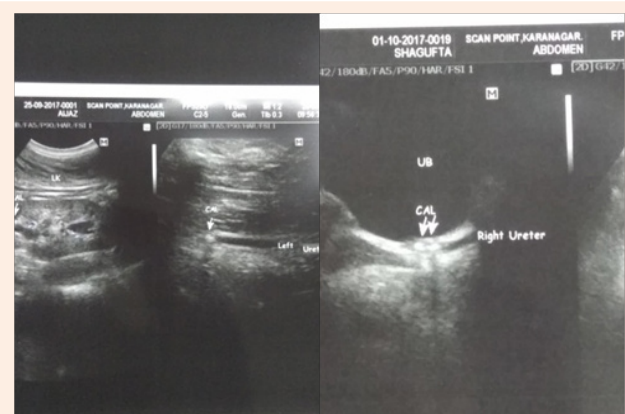


Figure 2: Ultrasound showing upper ureteric calculi and uvj calculi.

## Results

The diagnosis of the ureteric stone was established in 3000 patients, by ultrasound and NCCT Abdomen & Pelvis. Out of 3000 pts, there were 1977 males and 1023 females with age range from 9 years to 85 years. Out of 3000 pts, 2550 pts (85%) passed stone with SOADS regime within 4 weeks. Of 2550 pts, 1657 (65%) passed stone within 2 weeks of therapy and rest 893 pts (35%) passed stone within 4 weeks of therapy (Table 3-5). 4-6 mm stone size, comprises about 1814 pts (60.46 %), while 7-9 mm comprises about 1186 pts (39.53 %). Lower the size greater the chance of the stone to pass. Stones at UVJ and lower ureter had higher incidence of passage than stones in the upper ureter. Sex had no impact on stone passage. Right sided stones (1553/1678) had increase chance of passage than left (997/1322). In patients of unilateral obstruction, there was 10 mmHg increases in both

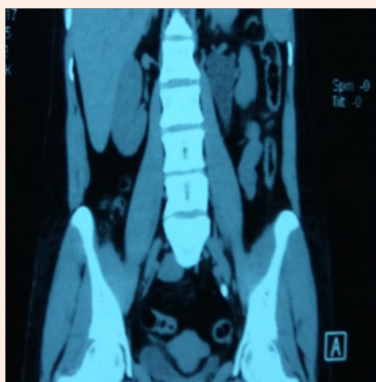
systolic/diastolic blood pressure. Uric acid stone had increased chance of passage than calcium oxalate monohydrate calculi. Fluids like Lemon, Orange and Tea consumption were associated with increased stone passage. NCCT abdomen/Pelvis was the best investigation to confirm the presence of calculi with respect to size, composition, side, location and upper tract dilatation.

**Table 3:** SOADS regime.

Tab Alfuzosin 10 mg at bed time daily once
Tab Ofloxacin 200 mg BD daily
Tab Drotaverine hydrochloride 80 mg + Tab Mefenamic Acid 250 mg one tab BD daily
Tab Spirinolactone 25 mg daily once after breakfast
Syrup Potassium magnesium citrate , 2 tsf with one glass of water TDS

**Table 4:** Passed stone within 4 weeks of therapy.

Stone Characteristics	Within 2 Weeks		Between 2-4 Weeks		Within 4 Weeks		Did not Pass Stone		P -Value
	Number	%	Number	%	Number	%	Number	%	
Stone Size (mm)									
4 mm	680	79.6	154	18.0	834	97.7	20	2.3	<0.001
5 mm	371	66.5	120	21.5	491	88.0	67	12.0	
6 mm	285	70.9	47	11.7	332	82.6	70	17.4	
7 mm	189	37.1	235	46.1	424	83.1	86	16.9	
8 mm	93	20.7	269	59.9	362	80.6	87	19.4	
9 mm	39	17.2	68	30.0	107	47.1	120	52.9	
Location of stone									
Upper ureter	99	23.7	202	48.3	301	72.0	146	34.9	<0.001
Mid ureter	316	42.8	291	39.4	607	82.2	130	17.6	
Lower ureter	651	66.4	224	22.8	875	89.2	93	9.5	
UVJ Calculi	591	68.5	176	20.4	767	88.9	81	9.4	



**Figure 3:** NCCT Scan of abdomen & Pelvis showing left lower ureteric calculi.

## Discussion

Urolithiasis is a common problem in northern part of India. Most of these patients also have ureteric calculi of varying sizes. Most of the small ureteric calculi usually pass spontaneously but with severe pain during expulsion and microscopic haematuria. In recent years, significant advances have been made in every medical field, ESWL and ureteroscopy have been widely used for the treatment of ureteric stones, however these procedures are not risk free [8]. MET is aimed at facilitating the passage/expulsion of ureteric stone with minimal symptoms. The main factors associated with obstruction by stones are ureteral smooth muscle spasm, mucosal edema, pain and infection. Medical therapy is aimed at addresses these factors. Various drug combinations have been described. Drugs like corticosteroids, hormones, NSAID, calcium channel blockers and alpha- 1 adrenergic blockers have been evaluated. Encouraging results have been reported with

use of calcium channel blockers and alpha-1 adrenergic blockers. Calcium channel blockers suppress smooth muscle contraction and reduce ureteral spasm, whereas alpha-1 adrenergic blockers decrease ureteral muscle tone and frequency and force of peristalsis [9]. Corticosteroids reduce inflammatory reaction and sub mucosal oedema in the vicinity of stone [10].

**Table 5:** Patient/stone characteristics.

Patient/Stone Characteristic	Number	Percentage
<b>Sex</b>		
Male	1977	65.9
Female	1023	34.1
<b>Age ( Years )</b>	36.3 ( 9-85 )	
<b>Time to Pass Stone</b>		
Within 2 weeks	1657	55.2
2-4 weeks	893	29.8
Within 4 weeks	2550	85.0
Did not pass stone	450	15.0
<b>Stone Size ( mm )</b>		
4	854	28.5
5	558	18.6
6	402	13.4
7	510	17.0
8	449	15.0
9	227	7.6
<b>Location of Stone</b>		
Upper ureter	418	13.9
Mid ureter	738	24.6
Lower ureter	981	32.7
UVJ Calculi	863	28.8
<b>Laterality</b>		
Right	1678	55.9
Left	1322	44.1

In our study 85% (2550 out of 3000 pts) of patients passed stone with SOADS regime within 4 weeks. A meta-analysis of nine randomised clinical trials has compared calcium channel blockers or alpa-1 blockers with or without corticosteroids against placebo or no treatment. This has shown that patients treated with MET had a 65% of greater chance of spontaneous passage of stone than the control group. In this analysis there was no significant benefit of adding corticosteroid with calcium channel or alpha-1 blockers which was also proved in our study as we exclude corticosteroid

in our group. Cooper and associates treated 70 patients having ureteral calculi and found that addition of nifedipine, prednisone, acetaminophen and antibiotics to standard medical therapy resulted in higher stone passage rate and fewer workday lost, emergency visits and surgical interventions [9].

### Conclusion

A conservative approach should be considered as an option in the management of ureteric calculi in patients who present within 1-2 days of colic in uncomplicated, unilateral and stone size of less than 10mm with SOADS regime as an outpatient treatment for maximum of 4 weeks after which they should be advised other viable options.

### Conflict of Interest

None.

### Acknowledgement

None.

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