

Progesterone Hydrotherapy in Management of Small, Mid and Lower ureteric calculi

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Research Article

Abstract:Aim: To study efficacy of progesterone utilizing its smooth muscle relaxant action for augmenting hydrotherapy for medical management of small mid and lower ureteric calculi.

Materials and methods : Patients of mid and lower ureteric calculi in age group 20 to 50 were selected. They were evaluated for size of calculus, kidney function tests, serum electrolytes as well as cardio-respiratory fitness assessment was done. 80 patients with calculi of size 6mm-1.5 mm, with normal kidney functions, normal lipid profile as well as normal cardio-respiratory fitness were selected for the study. These were randomly divided into two groups; labeled control and test group such that each group had 40 pts with ; 20pts with mid and 20 with lower ureteric or vesico-ureteric junction.(VUJ) calculi .After written informed consent, patients in test group were given following therapy: Inj depot medroxy-progesterone acetate 300mg i.m single dose hydrotherapy : (1pint normal saline + inj Lassix 20 mg) such 3 times daily for 5 days.In control group Plain Hydrotherapy as mentioned above was given.Patients were observed for 7 days in hospital and for 2 weeks on O.P.D basis after discharge and results were tabulated. **Results:** The expulsion rate was significantly higher in group-2 i.e test group where progesterone was used for calculus expulsion (65 & 80 % for mid & lower ureteric calculi) as compared to control group of plain hydrotherapy (30 & 45 % respectively). Average time of extrusion of the calculi for test group was 4 days while for the control group was 10 days.Extrusion with progesterone therapy occurred more for lower ureteric calculi and V.U.J calculi and more so in females as compared to males.Average size of ureteric calculus expelled by progesterone therapy was 9.5mm with largest size being 1.4cm.**Conclusion :** Progesterone due to its smooth muscle relaxant action can be effectively used in medical management of small mid, lower and vesico-ureteric junction calculi up to 1.4mm size. This is an economical and can be practiced at peripheral centers.

Keywords: Mid & lower ureteric calculi, hydrotherapy, progesterone, smooth muscle relaxant action.V.U.J(vesicoureteric junction),L.U(lower ureteric)

Introduction: Ureteric colic is amongst one of the most painful experiences one has. Mostly this is caused by small size calculi that can be dealt with easily. Small ureteric calculi undergo spontaneous extrusion if below 5mm size (1). But above that size treatment is needed.Though ureteroscopy is best method for these - it is not always available at peripheral centers.The current study was for progesterone based hydrotherapy as a easily available, affordable and non-invasive method for management of small mid and lower ureteric calculi .This method

requires no additional expertise beyond general surgical knowledge.

Patients &methods:

Aims: To study efficacy of progesterone utilizing its smooth muscle relaxant action for augmenting hydrotherapy for medical management of small mid and lower ureteric calculi.

Material and Methods:

1. Patients of mid and lower ureteric calculi in age group 20 to 50 were selected.
2. They were evaluated for size of calculus, kidney function tests, serum electrolytes as well as cardio-respiratory fitness assessment was done.
3. 80 patients with calculi of size 6mm-1.5 mm, with normal kidney functions, normal lipid profile as well as normal cardio-respiratory fitness were selected for the study.
4. These were randomly divided into two groups; labelled control and test group such that each group had 40 pts with; 20pts with mid and 20 with lower ureteric or vesico-ureteric junction.(VUJ) calculi.
5. After written informed consent, patients in test group were given following therapy: Inj depot medroxy-progesterone acetate 300mg i.m single dose + hydrotherapy: (1pint normal saline + inj Lassix 20 mg) such 3 times daily for 5 days.
6. In control group Plain Hydrotherapy as mentioned above was given.
7. Patients were observed for 7 days in hospital and for 2 weeks on O.P.D basis after discharge and results were tabulated.

Observations and Results:

Control group implies plain hydrotherapy; Test group implies hydrotherapy with progesterone.

1. Patient characteristics Males: 60 pts, Females 60 pts
2. Age group 20-50 yrs

Table 1: Age-wise and sex-wise distribution

Age group	Sex	Control gp	Test Group	Total Cases
20-30	Male	10	10	28
	Female	4	4	
30-40	Male	18	18	60
	Female	12	12	
40-50	Male	6	6	32
	Female	10	10	

The patients were randomly divided into Control and test groups such that to contain equal number of each sex in each group as well as equal number of patients of a particular age group .Each group had equal number of patients with mid and lower ureteric calculi.

Table 2: Patient groups

Group	Patients with mid ureteric calculus	Patients with lower ureteric / V.U.J calculus.
Test	30	30
Control	30	30

V.U.J – Vesico-ureteric junction

3. Average size of calculus:

Table 3: Calculus size

Study group	Avg size of mid-ureteric calculus (mm)	Avg size of lower ureteric/ V.U.J calculus (mm)
Test group	7	9
Control Group	7.5	8

V.U.J – Vesico-ureteric junction

4. Results of hydrotherapy:

A. Success of hydrotherapy was determined by extrusion of calculus

Table 4: Success of hydrotherapy

Group	Site of calculus	Total Cases	Success of hydrotherapy	%
Control	Mid ureteric	30	10	33.33
		30	14	46.66
	L.U	15	6	
		V.U.J	15	8
Test	Mid ureteric	30	23	76.66
		L.U/V.U.j		90
	L.U	15	13	
		V,U,J	15	14

B. Average time of extrusion of calculus :

Table 5: Avg calculus extrusion

Group	Avg time of calculus extrusion
Test	4
Control	9

5. Statistical analysis:

Table 6: mid-ureteric calculi

Category	Observed	Expected
Extruded	23	9
Non-extruded	7	21

By applying Chi-square test the result had chi-squared value of 31.11 with p value <0.001 which is statistically significant.

Table 7: Lower ureteric and vesico-ureteric junction calculus

Category	Observed	Expected
Extruded calculus	27	14
Non-extruded	3	16

By applying Chi-square test the result had chi-squared value of 22.63 with p value <0.001 which is statistically significant.

Progesterone hydrotherapy resulted in statistically significant success in extrusion of the small mid and lower ureteric calculi with p value <0.001.

6. Extrusion with progesterone therapy occurred more for lower ureteric calculi and V.U.J calculi and more so in females as compared to males. No adverse effects were noted.

Table 8: Results of progesterone based hydrotherapy

Sr no	Site of calculus	Calculi extruded	Percentage
1	Mid-ureteric	23	76.66
2	Lower ureteric/V.U.J	27	90

Table 9: Comparison with plain hydrotherapy control group:

Group	Site of calculus	Extruded	Non-extruded	Percentage
Control	L.U	6	9	40
	V.U.J	8	7	53.33
Test	L.U	13	2	86.66
	V.U.J	14	1	93.33

V.U.J – Vesico-ureteric junction L.U – lower ureteric

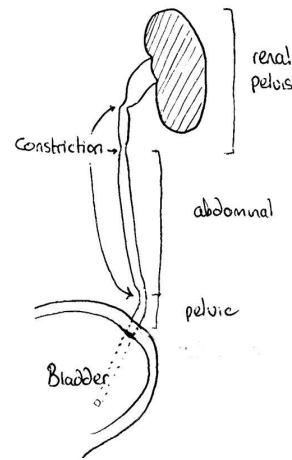
C. Test group (progesterone based hydrotherapy) sex-wise results.

Table 10:

	Extruded	Non-extruded	Total pts	Percentage
Male	26	8	34	76.47
Female	24	2	26	92.30

Overall success rate of progesterone based hydrotherapy combining results of both mid-ureteric, lower ureteric and V.U.J calculi was in total was 83.33 % .

**Discussion:
Anatomy: (1)**



The ureters are two muscular tubes whose peristaltic contractions convey urine from the kidneys to the urinary bladder. Each measures 25–30 cm in length, is

thick-walled and narrow, and is continuous superiorly with the funnel-shaped renal pelvis. Each descends slightly medially, anterior to psoas major, and enters the pelvic cavity where it curves initially laterally, then medially, to open into the base of the urinary bladder.

The diameter of the ureter is normally 3 mm, but is slightly less at

1. junction with the renal pelvis,
2. brim of the lesser pelvis near the medial border of psoas major,
3. where it runs within the wall of the urinary bladder, which is its narrowest part.

These are the commonest sites for renal stone impaction.

Ureteral calculi originate from kidneys, and while passing down the ureter, get lodged at different sites manifesting with loin pain, urinary obstruction and renal damage or urosepsis with rigors and chills. These are sites where ureteric calculi can get lodged and cause painful colicky symptoms Further retension of calculi will lead to backpressure changes on the kidney leading to hydronephrosis and hydroureter compromising kidney function of that site.

As per observations in literature calculi above size 6mm have <5% chance of spontaneous extrusion undergo spontaneous extrusion (lower ureteric calculi upto 50% and mid ureteric calculi upto 25 %)(2).

Such calculi can be

- 1: Ureteroscopically removed
- 2: Where such facilities and expertise are not available, plain hydrotherapy or medical expulsive therapy is used as an attempt of treatment for the calculi.

Plain hydrotherapy is not uniformly successful and also cannot be given for a prolonged period due to backpressure in the already hydronephrotic kidney(3) Ureteroscopy is a invasive procedure though minimally invasive . It has a complication rate of 5-30% .(4)

Success rate of plain hydrotherapy as per studies carried in various trials ranges from 18-60 % according to various trials.

Medical expulsive therapy has been attempted with acceptable success for small size ureteric calculi. The other option is by ureteroscopic removal which is an invasive procedure and also costly to the patient. Further not always urourgeons are available in peripheral rural areas. Non-affording patients many times just don't take endoscopic treatment due to the high cost.

Various methods have been studied for medical i.e drug based management of ureteric calculi. These include use of

1. Tamsulosin
2. Nifedipine
3. Progesterone

The main principle of these therapies involves smooth muscle relaxant action of the above drugs so as to relax the ureteric musculature and allow dilatation of the ureteric lumen . This enable naturally formed urine or forced diuresis using hydration with diuretic agent to cause extrusion of the calculus from the ureter to bladder and subsequently it is passed per urethra .

If we compare above therapies :

	Progesterone	Tamsulosin	Nifedipine
Principle	Progesterone has a smooth muscle relaxant action which helps in augmentation of hydrotherapy and extrusion of calculus. (5)	Action on alpha 1a and alpha 1d receptors in lower ureter causing ureteric smooth muscle relaxation . (6, 7, 8)	Nifedipine is a calcium channel blocker which causes relaxation of the smooth muscles thus causing dilation of the ureter and facilitates extrusion of the ureteric calculus .(9)
Advantage	It requires single dose in most cases for relaxant action on the ureter . There are no significant side effects	Oral based therapy that can be carried out at O.P.D. basis	Oral therapy
Disadvantage	No significant disadvantage . The only important contraindication is for pregnant women (10)	Success of therapy depends on compliance of patients which is less in rural and less educated population	This is a therapy which requires carefull monitoring and especially is unsuitable for hypertensive and elderly patients due to sudden hypotensive action of nifedipine.(11, 12, 13). It requires strict blood pressure monitoring
Total cost (approximate)	Rs 180-300(if 2 doses)	Rs 500	Rs 100

If efficacy of the various medical expulsive therapies and plain hydrotherapy are compared as per earlier studies:

Therapy	Study	Percentage of calculus expulsion
Plain Hydrotherapy	A. L. MIKKELSEN,H.-H. MEYHOFF, F et al (14)	18-30 %
	Priminger GM et al (15)	47 %
Progesterone	Hübner WA, Irby P, Stoller ML (16)	22-45%
	A. L. MIKKELSEN,H.-H. MEYHOFF, F et al (14)	66%
Tamsulosin	B.Lojanavivat et al (17)	68%
	MARCO DELLABELLA et al. (18)	100%
Nifedipine	FRANCESCO PORPIGLIA et al. (11)	85%
	FRANCESCO PORPIGLIA et al. (11)	79%
	Borghi L, Meschi T (13)	87%
	Beach MA, Mauro LS(12)	79-80%

In our study patients treated with progesterone + hydrotherapy showed a significant better efficacy in extrusion of ureteric calculi more notably for lower ureteric and vesicoureteric junction calculi as compared to plain hydrotherapy.

1. 90% lower ureteric calculi and
2. 76.66 % mid-ureteric calculi were extruded successfully.

Success was more for lower ureteric and V.U.J calculi and more in females as compared to males.

Average time of stone extrusion was 4 days. Thus in most patients the calculi were extruded during the 5 day I.P.D period. The patients were thus quickly relieved of their disorder. No adverse effects were observed

Progesterone based hydrotherapy treatment has

1. Comparable success rates with respect to other medical expulsive treatments for management of ureteric calculi.
2. Quicker results
3. Can be done at peripheral centres and taluka and rural hospitals

The advantages of progesterone based treatment over above other medical expulsion methods:

1. Low cost
2. Ease of administration
3. No significant side effects
4. Ease for monitoring patients
5. Easy patient compliance
6. Quick results.

Conclusion:

Progesterone due to its smooth muscle relaxant action can be effectively used in medical management of small mid, lower and vesicoureteric junction calculi. This is an economical and can be practiced at peripheral centres

References:

- [1] Marshall L. Stoller: Urinary stone disease .Smith General Urology: Editors: Emil A. Tanagho, Jack .W. McAninch 17th edition pg 262
- [2] Susan Standring, PhD, DSc, Neil R Borley, FKC Gray's Anatomy, 40th Edition By Susan Standring, PhD, DSc, FKC.
- [3] Marshall L. Stoller: Urinary stone disease .Smith General Urology: Editors: Emil A.Tanagho, Jack .W. McAninch 17th edition Pg no 268.
- [4] Shlomo Raz M.D., Marcia Zeigler B.S., Marco Caine M.S., and F.R.C.S Hormonal influence on the adrenergic receptors of the Ureter: Article first published online: 5 Dec 2008 DOI:10.1111/j.1464-410X.1972.tb10100. British Journal of Urology. Volume 44, Issue 4, pages405–410; 14.2, August 1972
- [5] Weiss RM, Bassett AL, Hoffman B FInvest Urol., 16(2):123-7.Adrenergic innervation of the ureter, Sept. 1978.
- [6] Parsons JK, Hergan LA, Sakamoto K, Lakin C. Source Division of Urology, University of California San Diego School of Medicine, San Diego, California 92103, USA. J Urol., 177(3):983-7; discussion 987.Efficacy of alpha-blockers for the treatment of ureteralstones, Mar 2007.
- [7] Cervenákov I, Fillo J, Mardiak J, Kopečný M, Smirala J, Lepies P Int Urol Nephrol., 34(1):25-9.Speedy elimination of ureterolithiasis in lower part of ureters with the alpha 1-blocker—Tamsulosin SourceTabakova- Str,No: 8, 811 07 Bratislava, Slovak Republic, Europe, 2002.
- [8] Canda AE, Turna B, Cinar GM, Nazli O. Urol Int., 78(4):289-98.Physiology and pharmacology of the human ureter: basis for current and future treatments, 2007.
- [9] Progesterone information from Drugs Update www.drugupdate.com/generic/view/658
- [10] Francesco Porpiglia et al Title: Nifedipine versus tamsulosin for the management of lower ureteral stone E Journal: The Journal Of Urology ® Vol. 172,568–571, August 2004
- [11] Beach MA, Mauro LS Pharmacologic expulsive treatment of ureteral calculi. Ann Pharmacother. 2006 Jul-Aug; 40(7-8):1361-8. Epub, Jul 18 2006
- [12] Borghi L, Meschi T, Amato F, Novarini A, Giannini: Nifedipine and methylprednisolone in facilitating ureteral stone passage: a randomized, double-blind, placebo-controlled study. A J Urol., 152(4):1095-8, Oct 1994.
- [13] A.L Mikkelsen et al. Title: The Effect of Hydroxyprogesterone on Ureteral Stones Journal: International Urology and Nephrology 20 (3), pp. 257-260, 1988
- [14] Miller O.F, Kane C.J: Time to stone passage for observed ureteral calculi; A guide for patient education: J Urol., 162-688-91, 1999
- [15] Hübner WA, Irby P, Stoller ML; Natural history and current concepts for the treatment of small ureteral calculi; Euro. Urol., 24(2):172- 6, 1993
- [16] B.Lojanavivat et al. Title: Effect of low dose & standard dose tamsulosin in the treatment of distal ureteric stones; A randomized controlled study. Journal of international medical research; 36:529-536, 2008
- [17] Marco Dellabella et al Title:The efficacy of tamsulosin in management of juxtavesical ureteral stones Journal: Vol. 170, 2202; The journal of Urology, Dec 2003