USING TAMSULOSINE IN THE MANAGEMENT OF LOWER URETERIC CALCULI: OUR EXPERIENCE OF MEDICAL EXPUSIVE THERAPY OF URETERIC CALCULI IN A RANDOMIZED CONTROLLED TRIAL

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Abstract

Background: Lower ureteric calculi can be treated by different modalities. There are many minimally invasive interventional (e.g.,ESWL, ureterorenoscopy, the holmium: YAG laser and basket devices) as well as expectant (watchful waiting) treatments are in practice for the management of distal ureteric calculi. selected method depend on the type of equipment available, location, type and size of stone, needs of the patient and skills of the surgeon. Most of the work on the potency of tamsulosin in lower ureteric calculi expulsion has been done in the developed countries.

Methods: Our randomized controlled trial in Avicenna Hospital Lahore included 100 patients over 18 years of age with stone Size ≤8mm in distal one third of ureter. Patients were randomly assigned into two groups (A & B). Group A Patients were given Capsule Tamsulosin 0.4 mg, once daily up to four weeks while group B patients were given placebo, one Capsule daily up to four weeks. The final result was the expulsion rate. Informed consent was obtained from all the patients. Stone Expulsion time, analgesia requirement, need for hospitalization and drug adverse effects were secondary endpoints.

Results: A total of 49 patients in group A and 48 patients in group B came for follow up, therefore 97 out of 100 patients were evaluated. Mean age of the patients was 36.34 years (range 18–57 years). Mean stone size was 5.78 mm (range 4–8 mm) in largest dimension. A stone expulsion rate of 85.71% (42 patients) was noted in group A and 54.20% (26 patients) in group B. Group A showed a statistically significant advantage in terms of stone expulsion rate (p=0.032). Considering expulsion time in days group A demonstrated statistically significant advantage (p=0.015). Regarding age, sex, stone size and stone lateralization (right/left), there was no remarkable difference between the group A and B. No drug adverse effects were seen in both the groups.

Conclusion: Tamsulosine can be used as medical expulsion therapy in lower ureteric calculi of size less than or equal to 8mm.

Key Words: Tamsulosin, stone expulsion, pharmacologic therapy, ureteric calculi

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The aim of the surgical treatment of patients having ureteral calculi is to observe complete stone clearance with minimal morbidity.[1] There are many minimally invasive interventional (e.g., ESWL, ureterorenoscopy, the holmium: YAG laser and basket devices) as well as expectant (watchful waiting) treatments are in practice for the management of distal ureteric calculi.selected method depend on the type of equipment available, location, type and size of stone, needs of the patient and skills of the surgeon.[2] The stone load remains the main factor in opting the treatment for a patient with ureteral calculi.[3] Most ureteric calculi pass and do not require any procedure. Natural passage depends on stone size, shape, location and associated ureteral factors like edema. Ureteric calculi

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4–5 mm in size have a 40–50% chance of natural passage. In contrast, calculi >6 mm have a <5% chance of natural expulsion. This does not mean that a one cm stone will not pass or that a 1–2 mm stone will always pass uneventfully. Most of the stones that pass do so within a six weeks period after the start of symptoms. Ureteric calculi located in distal ureter at the time of presentation have a 50% probability of natural passage, in contrast to a 25% and 10% chance in the mid and proximal ureter, respectively.[4] Ureteral calculi of any size may be associated with obstructive uropathy, and one must be careful to prevent, nonreversible kidney damage, irrespective of the patient selects conservative or active treatment. Several trials have investigated the role of pharmacologic therapy to assist natural or spontaneous stone passage. Different drugs (e.g., nifedipine and prednisolone) are used for this cause. α1 receptors are the most available adrenergic receptors in the ureteric smooth muscle cells. The blockage of adrenergic receptors by a specific antagonist inhibits tone, peristaltic activity and ureteral contraction. α1 receptors are further divided into four groups, with α1D being found on the lower intramural part of the ureter. Based on these findings, different researchers have tried Tamsulosin (selective α1 adrenergic receptors blocker) to assist spontaneous or natural passage of distal ureteral calculi.[5] Most of the work on the potency of tamsulosin in lower ureteric calculi expulsion has been done in the developed countries. In our county the modern operative facilities are concentrated at tertiary care centres and are scarcely available at district level hospitals. A randomized control trial was planned to compare tamsulosin group with control group in our set up to assess the efficacy of tamsulosin as expulsive pharmacologic treatment for distal ureteral calculi.

METHODS

This randomized controlled trial (RCT) was conducted from 1st june 2016 to 31st october 2021 in Avicenna medical college and hospital Lahore, which is a tertiary care centre. we tried to establish that alpha blockers can be used to ease the passage of lower ureric calculi. Two groups with 50 patients in each group were made. Approval was taken from ethical committee. Informed consent was taken from patients. Inclusion and exclusion criterion were set and followed. All patients with age >18 yrs, stone Size ≤8 mm and stone in distal 1/3 of ureter were included in the study. Patients with ureteric obstruction, distal ureteric stricture, pre-vious ureteric surgery, solitary kidney, abnormal ure-teral anatomy were removed from study. All patients with the diagnosis of ureteral stone in distal 1/3 were included in the study. Group A Patients were given Cap Tamsulosin 0.4 mg, daily up to four weeks while group B patients were given placebo, one Cap daily up to four weeks. Both groups were given tab ibuprofen 400mg, 1 tab thrice a day for pain or on required basis. Patients were evaluated with plain X-Ray KUB after 2 weeks and 4 weeks. The primary result was expulsion rate. Data were analysed using SPSS, We used $P<0.05$ as statisfically significant.

RESULTS

A total of 49 patients in group A and 48 patients in group B reported for follow up on designated time. Three patients did not come for follow up, therefore 97 out of 100 patients were evaluated. Mean age of the patients was 36.34 years (rang 18–57 years). 43 patients had right ureteral calculus and 54 patients had left ureteral calculus. There was almost equal distribution of right and left ureteral calculi in both the group. Mean stone size was 5.78 mm (range 4–8 mm) in largest dimension. A stone expulsion rate of 85.71% (42 patients) was seen in group A and 54.20% (26 patients) in group B. Group A revealed a statistically significant advantage in term of stone expulsion rate ($p=0.032$). In group A 23 patients (46.93%) expelled their stone within seven days of treatment, 13 patients (26.53%) expelled stone within 14 days, 4 patients (8.16%) expelled stone within 21 days of treatment and 2 patients (4.08%) expelled stone within 28 days of treatment. in group B, 9 patients (18.75%) expelled their stone within seven days of management, 5 patients (10.41%) passed stone within 14 days, 2 patients (4.61%) expelled stone within 21 days and 10 patients (20.83%) expelled their calculi within 28 days of management. Considering expulsion time in days group A showed statistically notable advantage ($p=0.015$). (Table-1) Nine patients (18.36%) in group A required analgesia (ibuprofen) while in group B, 19 patients (39.58%) required analgesia. There were statistically

significant less number of pain episodes in group A as compared to group B (p=0.006). None of the patient in group A required admission in hospital while 1 patient in group B was hospitalized during this study. Regarding age, sex, stone size and stone lateralization (right/left), there was no significant difference between the group A and B. No drug adverse effects were seen in both the groups. All those patients who did not expell stone at the end of 28 days were successfully treated with ureterorenoscopy.

Table 1: Stone expulsion time in days (p=0.015)

Expulsion time iu days	Group-A(n=49) N (%)	Group-B (n=48) N (%)
<7	23 (46.93)	9(18.75)
8-14	13 (26.53)	5(10.41)
15-21	4(8.16)	2(4.16)
22-28	2 (4.08)	10(20.83)
Stone not passed	7(14.29)	22 (45.80)

DISCUSSION

Lumbar pain from acute renal colic is a common presenting complaint to emergency departments.[6] Approximately 13% of men and 7% of women will be having kidney stone at some time in their life.[7] The majority of ureteral stones cause pain that is severe and of rapid onset, causing patients to seek medical care. Recent advances in endoscopic urology and fine instruments has largely replaced the management of ureteral stones by open surgery to either minimal invasive methods like ESWL and ureteroscopy or to watchful waiting. The minimally invasive treatment for ureteral stone are now the gold standard options. Although, these techniques are not risk free, are quite expensive and are available at tertiary care centers.

Waiting for the spontaneous or natural passage is an option, only for the smaller ureteric calculi. It may be associated with discomfort or pain. Smaller, more distal and right sided stones are more likely to expel spontaneously.[9] However the expectant approach may result in complications, such as infection of urinary tract, hydronephroureter and renal compromise.[10] In this study the mean stone size was 5.78 mm (range: 4–8 mm) in largest dimension. Ureteral calculi usually lodge at three distinct sites where calibre of the ureter narrows: the ureteropelvic junction, the iliac vessels and the ureterovesical junction. α1A and α1D adrenergic receptors are concentrated more densely in the distal 1/3 of ureter (including intramural part) than other adrenergic receptors. α1 antagonist can result in inhibition of tone, peristaltic wave frequency and ureteral contractions even in the intramural part of ureter. Therefore α1 antagonists have a crucial role in spontaneous natural painfree expulsion of stones ≤8 mm located in distal 1/3 of ureter. Dellabella and colleagues (2003), in a study conducted to investigate the efficacy of tamsulosin in facilitating ureteral stone expulsion, found that treatment with tamsulosin was associated with an increased stone expulsion rate and a decreased time to stone expulsion. In our study a stone expulsion rate of 85.71% was found in group A and 54.20% in group B. Group A revealed a statistically significant advantage in terms of stone expulsion rate as compared to group B (p=0.032). These results are comparable to similar studies by Griwan[2], De Sio5 and porpglia.[11] Considering expulsion time in days group A showed statistically significant advantage as compared to group B (p=0.015). Dellabella et al, used tamsulosin as spasmolytic drug during episodes of ureteral colic due to calculi at VUJ, observed an increased stone expulsion rate, decrease in stone expulsion time, decreased requirement for hospitalization/ endoscopic procedures and provided good control of colic pain.[12] In this study 18.36% patients in group A and 39.58% patients needed analgesic. Tamsulosin can be used in association with ESWL for larger ureteral calculi, to gain a higher stone clearance rate.[13] Because the patient symptoms and stone size do not predict loss of kidney function, and because there is no clear time threshold for irreversible damage, surgical intervention should be considered in any patient with ureteral obstruction unless the ability to closely monitor renal function test is available.

CONCLUSIONS

Alpha blockers can be used as medical expulsive therapy in patients with stone size of less than or equal to 8mm in distal ureter. More trials can be conducted to confirm the findings of above mentioned article.

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Not all angels have wings,
some have stethoscopes

-Dr. Seuss