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Alpha-Adrenergic Blockers with or without Deflazacort for the Expulsion of a Lower Ureteric Calculus ≤ 10 mm: A Comparative Study

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ABSTRACT

Introduction: A lower ureteric calculus is one of the most commonly encountered conditions in daily urological practice. There are various options for management of lower ureteric calculus, which includes watchful waiting, extracorporeal shock wave lithotripsy (ESWL), and ureteroscopic lithotripsy (URSL). The aim of our study was to evaluate the efficacy of following drugs in the expulsion of a lower ureteric calculus ≤ 10 mm. The drugs used are (1) tamsulosin, (2) naftopidil, (3) tamsulosin and deflazacort, and (4) naftopidil and deflazacort.

Methods: A prospective study was carried out in the Department of Urology from August 2012 to January 2013. A total of 150 patients were enrolled and were randomized into 5 equal groups of 30: A (control), B (naftopidil), C (tamsulosin), D (naftopidil and deflazacort), and E (tamsulosin and deflazacort). Complete hemograms; blood urea; serum creatinine; urine routine examination and culture and sensitivity; X-ray of the kidney, ureter, and bladder (KUB); and/or ultrasonography were done in all cases. Cases were followed up to 30 days or upon spontaneous passage of the calculus, whichever was earlier. X-ray KUB and/or ultrasonography were done to confirm the passage of the stone.

Results: The expulsion rate for a calculus ≤ 10 mm was statistically significant in all the groups in comparison to the control group. The mean days of expulsion and use of analgesics was also low in all the groups compared to control. Amongst all groups, the stone expulsion rate was highest, and episodes of pain and mean days of expulsion were lowest for the D group.

Conclusion: It is concluded that alpha-adrenergic blockers facilitate the expulsion of lower ureteric stones ≤ 10 mm and decreases the episodes of colic, which is further improved by the addition of deflazacort. Naftopidil plus deflazacort gives the best results in regards to stone expulsion rates, mean days of expulsion, and episodes of colic.

INTRODUCTION

A lower ureteric calculus is one of the most commonly encountered conditions in daily urological practice. There are various options for the management of lower ureteric calculus, which includes watchful waiting, extracorporeal shock wave lithotripsy (ESWL), and ureteroscopic lithotripsy (URSL). Though URSL is the gold standard for management of lower ureteric calculi, it is invasive, requires anesthesia, and facilities are not available everywhere in developing countries like India. The

KEYWORDS: Lower ureteric calculus, medical expulsive therapy, alpha-adrenergic blocker

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size of the calculus remains the main deciding factor for the type of intervention.

There are various studies that show positive results with medical expulsive therapy (MET) for lower ureteric calculi in relation to expulsion rates and duration. The various drugs that are used for MET for lower ureteric calculi are α-adrenergic antagonists and calcium channel blockers. There are 3 types of α-blockers; namely α1a, α1b, and α1d, of which α1a and α1d are present in high densities in the lower ureter. Both α-antagonists and calcium channel blockers inhibit the contraction of ureteral muscle responsible for ureteral spasms while allowing antegrade stone propagation. Ureteric stones cause inflammatory changes in the ureteric wall and that submucosal edema in and around the stone, which worsens the ureteric obstruction. This submucosal edema can be reduced by corticosteroids like deflazacort. We did a prospective study to look for the efficacy of α-adrenergic blockers (tamsulosin and naftopidil) with or without deflazacort for the expulsion of distal ureteric calculi ≤ 10 mm. The aim of our study was to evaluate the efficacy of the following drugs in the expulsion of lower ureteric calculi ≤ 10 mm.

- Tamsulosin
- Naftopidil
- Tamsulosin and deflazacort
- Naftopidil and deflazacort

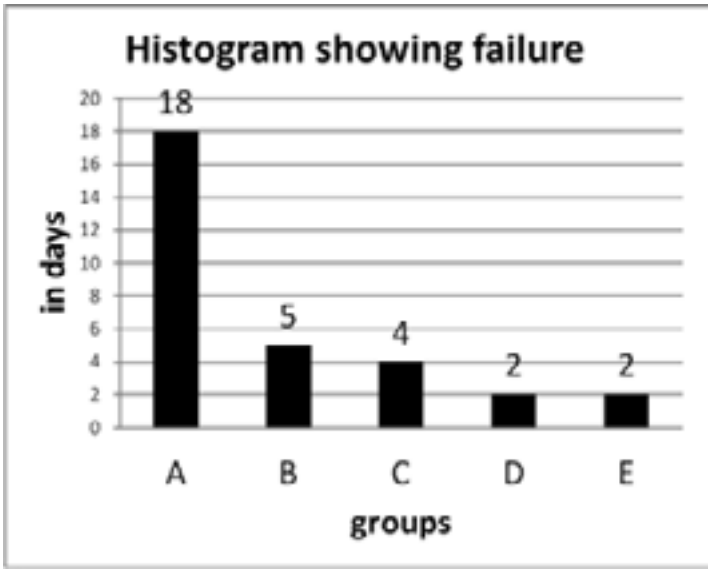
METHODS

A prospective study was carried out in the Department of Urology, from August 2012 to January 2013. A total of 150 patients were enrolled and were randomized into 5 equal groups of 30:

- A – control: high fluid intake along with drotaverine (80 mg) whenever required
- B – naftopidil: naftopidil (50 mg) once daily at bedtime
- C – tamsulosin: tab. tamsulosin (0.4 mg) once daily at bedtime
- D – naftopidil and deflazacort: naftopidil (50 mg) and deflazacort (6 mg) at bedtime
- E – tamsulosin and deflazacort: tamsulosin (0.4 mg) and deflazacort (6 mg) at bedtime

The above-mentioned drugs were given for a maximum period of 30 days or until the spontaneous passage of a stone (whichever was first). Complete hemograms; blood urea; serum creatinine; urine routine examination and culture and sensitivity; X-ray of the kidney, ureter, and bladder (KUB); and/or ultrasonography were done in all cases. Patients with symptomatic unilateral, solitary lower ureteral calculi proved either on a skiagram or sonography of the KUB. Calculus size ≤ 10 mm (in the major axis) were included in the study. Patients with active urinary tract infection, acute/chronic renal failure, history of urinary tract surgery, uncorrected distal obstruction, marked hydronephrosis, and patients < 18 years old were excluded. Ethical committee clearance was taken for the study.

Figure 1. A histogram showing failure rate.



During follow-up, patients were asked to pass urine in a stone collector. Follow-up was done with a USG KUB after 2 and 4 weeks. Successful MET was considered when a stone was not seen in USG/X-ray KUB. Failure was considered if 1) the patient failed to pass the stone at the end of 30 days, or 2) uncontrolled pain and/or uroseptic fever led to hospitalization during the study period.

RESULTS

The study included 150 patients with an age range of 19 to 57 years (mean = 32.81). The male and female ratio was 2.6:1 (109:41). The smallest stone size was 3.7 mm and the largest was 10 mm. Mean stone size < 5 mm was 4.7 mm, and 5 to 10 mm was 7.37.

The stone expulsion rates in groups A, B, C, D, and E was 40%, 83%, 86%, 93%, and 93%, respectively (Table 1). Groups B, C, D, and E showed statistically significant stone expulsion rates as compared to group A, as determined by a statistical test of proportion (P value for B = 7.65 x 10 to 7, C = 1.355 x 10 and 7, D = 1.6 x 10 and 9, and E = 1.6 x 10 to 9). However, there was no difference between C and D and between C and E (P value = 0.4014). Similarly, there was no difference between D and E (P value = 0.50). Also there was no difference between B and C (P value = 0.4497) and there was no difference among B, D, or E (P value = 0.3522).

The mean duration of stone expulsion in groups A, B, C, D,

and E was 12.42 days, 11.8 days, 12.27 days, 6.4 days, and 9.92 days, respectively (Table 1). Group D showed a statistically significant mean duration of expulsion compared to group A (P value of 0.0031) as determined by student t test. There was no statistically significant mean duration of expulsion in groups B, C, and E compared to group A (P value for group B = 0.351, C = 0.466, and E = 0.063), as determined by student t test. The difference between the means of groups B and D was found to be significant with P value = 0.000354, and also the difference between the means of groups C and D was found to be significant with P value = 0.000443, as determined by student t test.

The patients with episodes of pain in group A, B, C, D, and E was 22 (73.3%), 19 (63.3%), 15 (50%), 10 (33.3%), and 13 (43.3%), respectively (Table 1). There was a statistically significant advantage in groups C, D, and E compared to group A (P value in group C = 0.002, D = 4.009 x 10 to 7, and E = 0.0001), as determined by a statistical test of proportion.
The failure rate in groups A, B, C, D, and E was 18 (60%), 5 (16.6%), 4 (13.3%), 2 (6.6%), and 2 (6.6%) (Figure 1).

One patient from group A required hospitalization because of severe abdominal pain and fever, and he was considered a failure. The patients who were not stone free with MET were successfully managed by ureteroscopic lithotripsy.

Table 1. Showing the stone expulsion rates ,mean duration of expulsion, and episodes of pain in all the groups.

Groups	Stone expulsion rate (%)	Mean duration of expulsion (in days)	Patients having pain (%)
A	12 (40%)	12.42	22 (73.3%)
B	25 (83%)	11.8	19 (63.3%)
C	26 (86%)	12.27	15 (50%)
D	28 (93%)	6.4	10 (33.3%)
E	28 (93%)	9.92	13 (43.3%)

DISCUSSION

For lower ureteric stones, the spectrum of treatment options includes watchful waiting, ESWL, ureterolithotomy, and URSL. URSL is considered to be the gold standard for lower ureteric stones, but it is not risk free, requires general anesthesia, is expensive [1], and facilities are not widely available in developing countries like India. To have a treatment modality that is safe, noninvasive, and effective, non-complicated lower ureteric stones need time. According to the European Association of Urology Guidelines on Urolithiasis for 2013, medical expulsive therapy is recommended for any ureteric calculus < 10 mm if active stone removal is not indicated and alpha-blockers are used for MET.

Three different types of adrenergic receptors are identified: α1a, α1b, and α1d [2]. The distribution of adrenergic receptors throughout the inner and outer smooth muscles of the ureter is highest for α1d, followed by α-1a and α1b [3]. Blocking these α-adrenergic receptors inhibits basal smooth muscle tone and hyperperistaltic uncoordinated frequency while maintaining tonic propulsive contractions [4]. Calculi in the ureter induce uncoordinated ureteric contractions, which interfere with calculi expulsion. Muscle relaxation with maintenance of normal antegrade peristaltic activity will facilitate expulsion of a stone. The ureteric calculus stimulates inflammatory changes in periuretric tissues with submucosal edema hampering further calculi expulsion [5]. Hence, the drugs that can block these α

-adrenergic receptors in the distal ureter or those that can reduce the edema in and around the ureteric calculi can facilitate calculi expulsion. Such drugs include α-adrenergic receptor blockers and anti-inflammatory drugs like corticosteroids. A number of randomized clinical trials (RCTs) have tested these drugs, and the resulting findings have almost always been interpreted and proclaimed as proof of efficacy [6].

Griwan et al. reported a calculus expulsion rate of 90% using tamsulosin [7]. They also found a statistically significant decreased number of pain episodes in the tamsulosin group compared to the control group. Al-Ansari found statistically significant stone expulsion rates (82%) in the tamsulosin group compared to the control group (61%) [8]. In our study, the calculus expulsion rate in lower ureteric calculi was 86% and a statistically significant decrease in the number of pain episodes in the tamsulosin arm (50%) compared to control arm (73.3%). Deliveliotis et al. found decreased stent-related urinary symptoms and pain with alfuzosin in patients who opted for conservative management for ureteric calculi with an indwelling DJ stent [9].

Porpiglia et al. studied the efficacy of tamsulosin and deflazacort for the expulsion of lower ureteric calculi less than or equal to 1 cm, and found statistically significant increased calculi expulsion rates, decreased calculi expulsion duration, and decreased pain episodes compared to control [10]. In our study, we also found a statistically significant increased calculi expulsion rate, decreased calculi expulsion duration, and decreased pain episodes compared to control.

Xizhao Sun et al. found statistically significant calculi expulsion rates with naftopidil (90%) compared to the control group (26.6%) [11]. In our study, we found a statistically significant calculi expulsion rate in the naftopidil group (83%) compared

to the control group (40%).

In our study, the naftopidil plus deflazacort group had a statistically significant advantage over the control group with stone expulsion rates, the mean duration of expulsion, and decreased pain episodes.

CONCLUSION

Medical expulsive therapy should be considered for uncomplicated distal ureteral calculi less than or equal to 1 cm as the first line of treatment. Alpha-adrenergic blockers have been found to increase and hasten stone expulsion rates, reduce mean days to stone expulsion, and decreases pain episodes. The addition of deflazacort further hastens the calculus expulsion rates, reduces mean days to stone expulsion, and decreases pain episodes. In our study, we got the best results with naftopidil plus deflazacort. However, larger prospective randomized controlled trials will provide more information into the effectiveness of MET for uncomplicated lower ureteric calculi.

REFERENCES

1. Leicht, W., et al. (2012). "[Colovesical fistula caused by diverticulitis of the sigmoid colon: diagnosis and treatment]." *Urologe A* 51(7): 971-974. PubMed | CrossRef

2. Niebling, M., L. Van Neenspeet, et al. (2013). "Management of colovesicle fistula caused by diverticulitis: Twelve years experience in one medical centre." *Acta chir belg* 113(1): 30-34.

3. Kang, J. Y., et al. (2004). "Epidemiology and management of diverticular disease of the colon." Drugs Aging 21(4): 211-228. PubMed

4. Melchair, S., D. Cudovic, et al. (2009). "Diagnosis and management of colovesicle fistula due to sigmoid diverticulitis." *J Urol* 182(3): 978-982.

5. Zonca, P., et al. (2009). "[The current view of surgical treatment of diverticular disease]." *Rozhl Chir* 88(10): 568-576. PubMed

6. Najjar, S. F., et al. (2004). "The spectrum of colovesical fistula and diagnostic paradigm." *Am J Surg* 188(5): 617-621. PubMed | CrossRef

7. Pontari, M. A., et al. (1992). "Diagnosis and treatment of enterovesical fistulae." *Am Surg* 58(4): 258-263. PubMed

8. Chen, S. S., et al. (1990). "Sonographic features of colovesical fistula." *J Clin Ultrasound* 18(7): 589-591. PubMed

9. Amendola, M. A., et al. (1984). "Detection of occult colovesical fistula by the Bourne test." *AJR Am J Roentgenol* 142(4): 715-718. PubMed | CrossRef

10. Jorett, T. W. and J. H. Vaughan. (1998). "Accuracy of CT in the diagnosis of colovesicle fistula secondary to diverticular disease." *J Urol* 153(1): 44-46.

11. Amin, M., et al. (1984). "Conservative treatment of selected patients with colovesical fistula due to diverticulitis." *Surg Gynecol Obstet* 159(5): 442-444. PubMed

12. Marney, L. A. and Y. H. Ho (2013). "Laparoscopic management of diverticular colovesical fistula: experience in 15 cases and review of the literature." *Int Surg* 98(2): 101-109. PubMed | CrossRef