Performance of alpha-blockers in distal ureteral calculus ejection

¹Dr. Prathvi, ²Dr. Rajasekhar Undavalli, ³Dr. Karthik Are

¹Associate Professor, Department of Urology, Rajarajeswari Medical College and Hospital, Bengaluru, Karnataka, India.

^{2,3}Senior Resident, Department of Urology, Rajarajeswari Medical College and Hospital, Bengaluru, Karnataka, India

Corresponding Author:

Dr. Rajasekhar Undavalli

Abstract

Background and objectives: Assessment of effectiveness of α blockers in eliminating distal ureteric calcification and determine Tamsulosin's and Alfuzosin's effectiveness in treating distal ureteric calculus.

Methods: A 120-patients Control Prospective Cohort research was conducted at Department Urology, Rajarajeswari Medical College and Hospital, Bengaluru, Karnataka, India. All individuals presenting a background of ureteric colic who showed up between August 2021 and July 2022 got considered for participation in the research.

Result: Group A patients were 27.0 (range 18 to 45) years old, Group B 26.8 (range 18 to 45), and Group C 25.4. (between range18 to 41 years). Most people were 21 to 30. All 3 groups had comparable age distributions. P = 0. 97, Men and women were equally represented in all 3 groups. Group A needed 3.8%, 16.67%, and 10% intervention in 6mm calculus, respectively. Group A, B, and C required intervention for \geq 6mm calculus at 96.1%, 83.3%, and 90%. All groups showed statistically significant differences. P = 0.03, The placebo group averaged more than 6 analgesic doses.

Conclusion: Tamsulosin and Alfuzosin promote distal ureteric calculus evacuation. Tamsulosin and Alfuzosin had identical distal ureteric calculus ejection rates. Alpha-blockers lessen analgesics needs but not calculus ejection period.

Keywords: Alpha-Blockers, Distal Ureteric Calculus, Analgesics

Introduction

In respect to age, sex, ethnicity, and region, the likelihood of developing renal stones varies between 1% to 15% throughout the course of a person's lifespan. Mature male are usually more frequently affected by kidney stone disease than female population ^[1, 2, 3]. Males are afflicted two to three times greater than females, according to a number of indications, including hospital stays, ambulatory care visits, and emergency room visits. When stones enter the ureter and cause discomfort or blockage, it typically starts to cause symptoms ^[4, 5]. Thorough calculus clearance with least amount of complication is the aim of treatment for individuals with ureteral stone disease. Although the urologist has more choices for treating ureteral calcifications compared to ever before, the majority of people do not necessitate interventions ^[5, 6, 7]. Ureteral calculi that are 4 mm or less typically discharge on their own, but occasionally the person may experience pain and difficulty. If the patient decides anticipatory or active treatment, ureteral calculi of any type can be linked to kidney blockage, thus caution must be exercised to avoid doing irreparable harm to a nephron ^[6, 7].

Different drugs are utilised to improve passaging of kidney stones. Alpha a drenergic

ISSN 2515-8260

Volume 09, Issue 07, 2022

receptors antagonists have been shown to boost the number of stone evacuation, shorten the duration to ejection, and minimize painkiller usage in subjects with ureteric colic brought on by distal ureterolithiasis. The majority of research assessed Tamsulosin's effectiveness as a specific α 1 A and 1 D adrenergic receptor antagonist ^[7, 8]. (The lower intramural section of the kidney has primarily 1D and α 1 A adrenergic receptors where this travels into the detrusors. For the management of BPH, alfuzosin is a medication with a track record of success and is regarded as uroselective with significant sensitivity and specificity ^[8].

In order to determine if Alpha blockers are effective at expelling distal renal calculus, the recent research was conducted. To evaluate the effectiveness of Alfuzosin (a receptor non sub selective alpha blocker) and Tamsulosin (a receptor sub selective alpha blocker) in the treatment of distal ureteral calcification.

Materials & Methods

The controlled prospective cohort study considered all participants who visited the Department Urology, Rajarajeswari Medical College and Hospital, Bengaluru, Karnataka, India, between August 2021 and July 2022 with histories suggesting renal stone for admission.

All participants provided their written consent. Subjects got split into three groups: A group received placebo; B group received tamsulosin 0.4 mg daily; and C group received alfuzosin 10 mg daily. The proposal contained all information pertaining to the participant's demographics, tests, result, and problems. Therapy lasted for no longer than 4 weeks or till stone removal.

Age, sex, calculus transit duration and rate with respect to stone size, individuals needing intervention, the justification for the intervention, and the need for painkillers were assessed. Utilizing SPSS, statistical analysis was performed on the dataset using the Chi-Square Test, Multiple Range Test-Turkey-HSD Test, and Levene's Test for Equal Variance.

Inclusion criteria

Radiologically proven distal ureteric calculus as result of renal colic.

Exclusion criteria

- Kidney stone size more than 10mm
- Urosepsis
- Renal colic because of addition calcification.
- Severe hydronephrosis
- Alpha-blockers sensitivity
- Therapy by alpha blockers, beta blockers, calcium, antagonist, nitrates and pregnancy
- Written consent form not provided
- Previous of surgery or endoscopic methods in the UT.
- Previous circumstances of continuous stone ejection
- Ureteral structural known

Results

Table 1: Distribution of Age

| Age groups | Group A | Group B | Group C |
|------------|----------|-----------|----------|
| 15 to 20 | 7(17.5%) | 6(15%) | 7(17.5%) |
| 21 to 30 | 20(50%) | 18(45%) | 26(65%) |
| 31 to 40 | 9(22.5%) | 11(27.5%) | 6(15%) |
| 41 to 50 | 4(10%) | 5(12.5%) | 1(2.5%) |

P = 0.44, Group A participants' average age was 27.0 years (range: 18 to 45 years), Group B patients' average age was 26.8 years (also between 18 to 45 years), and Group C patients' average age was 25.4 years (range between 18 to 41 years). The most of the subjects were determined to be between the ages of 21 and 30. The age range across the three groups was discovered to be comparable.

Table 2: Gender Distribution

| Sex | Group A | Group B | Group C |
|--------|---------|-----------|---------|
| Male | 26(65%) | 25(62.5%) | 24(60%) |
| Female | 14(35%) | 15(37.5%) | 16(40%) |

P = 0.97, with equal numbers of male and female patients in each of the three categories.

Table 3: Side differentiation

| Side | Group A | Group B | Group C |
|-------|---------|---------|-----------|
| Right | 18(45%) | 24(60%) | 17(42.5%) |
| Left | 22(55%) | 16(40%) | 23(57.5%) |

p = 0.5, In none of the groups was a side predominance present.

Table 4: Calculus Size Differentiation

| Calculus size | Group A | Group B | Group C |
|---------------|---------|---------|---------|
| 4 mm | 6 | 9 | 5 |
| 5 mm | 2 | 7 | 5 |
| 6 mm | 2 | 4 | 5 |
| 7 mm | 14 | 7 | 11 |
| 8 mm | 9 | 10 | 8 |
| 9 mm | 7 | 3 | 6 |

p = 0.1382, Mean calculus size for Group A was 6.98 mm (range: 4 to 9 mm), Group B was 6.34 mm (range: 4 to 9 mm), and Group C was 6.78 mm (range between4 to 9mm). It was discovered that the distribution of stone size was uniform across all groupings.

Table 5: Period of Pain

| Groups | Mean | Range |
|--------|----------|-------------|
| A | 1.7 days | 1 to 4 days |
| В | 1.6 days | 1to 4 days |
| С | 1.7days | 1to 5 days |

Prior to manifestation, people experience colicky suffering for an average of 1.7 days, with a variation of (1 to 5 days).

Table 6: Calculus Ejection Rate

| Groups | Expulsion | Failure | Total |
|--------|-----------|-----------|----------|
| A | 18(45%) | 22(55%) | 40(100%) |
| В | 27(67.5%) | 13(32.5%) | 40(100%) |
| С | 25(62.5%) | 15(37.5%) | 40(100%) |

Calculus dismissal rates in Groups A, B, and C were determined to be 45%, 67.5%, and 62.5%, respectively (p=0.00001). There have been significant statistical differences.

Table 7: Removal of Calculus with respect to Kidney Stone Size

| Calculus size | Group | Group A Group B Group C | | Group B | | C |
|---------------|-----------|-------------------------|-----------|---------|-----------|---------|
| Calculus size | Expulsion | Failure | Expulsion | Failure | Expulsion | Failure |
| ≤6mm | 9 | 1 | 19 | 2 | 14 | 2 |
| > 6mm | 3 | 27 | 10 | 9 | 17 | 9 |

p = 0.000001, p = 0.00016, p = 0.013

Only 5/47 (7.1%) cases experienced failures in group less than 6 mm, as opposed to 45/75 (60.6%) in groups larger than 6 mm. In each group, this difference was highly statistically significant.

Table 8: Ejection time in regards to management

| Groups | No of days of treatment |
|--------|------------------------------|
| A | $8.62 \pm 3.25 \text{ days}$ |
| В | $7.74 \pm 3.13 \text{ days}$ |
| С | $8.56 \pm 4.51 \text{ days}$ |

p = 0.5961, In none of the 3 groups was the calculus ejection period statistically significant.

Table 9: Ejection period of calculus size ≤ 6 mm

| Groups | No of days of treatment |
|--------|-------------------------|
| A | 7.35 ± 2.90 |
| В | 6.50 ± 2.50 |
| С | 5.52 ± 1.24 |

P =0.1155, none of the three groups' discharge times for calculus 6 mm were statistically significant.

Table 10: Removal period of caliculi size > 6 mm

| Groups | No of days of treatment |
|--------|-------------------------|
| A | 11.40 ± 2.07 |
| В | 10.25 ±2.83 |
| С | 11.15 ± 4.70 |

There was no statistically significant difference in the evacuation period of calculus ≥ 6 mm among the 3 groups (p = 0.7844).

Table 11: Need of Intervention

| Groups | No of cases |
|--------|-------------|
| A | 26(65%) |
| В | 12(30%) |
| С | 10(25%) |

In Group A, Group B, and Group C, the intervention requirement (URS) was discovered to be 65%, 30%, and 25%, respectively (p=0.00001). There were statistically significant differences.

Table 12: Intervention needed in repect to calculus size

| Calculus size | Group A | Group B | Group C |
|-----------------|-----------|-----------|---------|
| ≤ 6mm | 1 (3.8%) | 2(16.67%) | 1(10%) |
| <u>></u> 6mm | 25(96.1%) | 10(83.3%) | 9(90%) |
| p value | 0.00001 | 0.00016 | 0.0134 |

Intervention requirements in 6mm calculus were 3.8%, 16.67%, and 10% in Groups A, B, and

ISSN 2515-8260

Volume 09, Issue 07, 2022

C, respectively. Intervention requirements in \geq 6mm calculus were 96.1%, 83.3%, and 90% in Groups A, B, and C, respectively. In each group, this difference was highly statistically significant.

| Table | 13: | Anal | lgesics | N | leed | led | |
|-------|-----|------|---------|---|------|-----|--|
|-------|-----|------|---------|---|------|-----|--|

| Groups | No. of doses of analgesic requirement |
|--------|---------------------------------------|
| A | 6.60 ± 1.81 |
| В | 3.85 ± 2.50 |
| С | 4.17 ± 3.01 |

P =0.03, The placebo group's average duration of much more than 6 doses had a greater need for analgesics.

Discussion

In total, there were 120 participants in the research, subjects differentiated in 3 distinct categories. Patients in Group A received a placebo, People in Group B received tamsulosin at a dosage of 0.4 mg per day, and People in Group C received alfuzosin at a dosage of 10 mg per day. Pills of painkillers with a 100 mg extended release were provided upon request. There were fifty individuals in each of the groups. Patients in the placebo (Group A) group had an mean age of 27.0 years (range: 18 to 45 years), those in the tamsulosin (Group B) group had an mean age of 26.8 years (range: 18 to 45 years), and those in the alfuzosin (Group C) group had a mean age of 25.3 years (range between 18-41 years) [9, 10, 11]. It was revealed that the most individuals in the age between 21 to 30 years old. Its discovered that there was a comparable dispersion of ages among all 3 groups. The female to male ratio was discovered to be 1:1.6, 1:1.5, and 1:1.6 accordingly in the groups that received the placebo (Group A), Tamsulosin (Group B), and Alfuzosin (Group C). Average calculus dimensions in Placebo (6.98± 1.6 mm), in Alfuzosin (6.7±1.5 mm) and Tamsulosin (6.34±1.7 mm). Everything was discovered that the amount of calculus is split up similarly among all three groups. The average duration of the patients' colicky pain prior to diagnosis was approximately 1.8 days, however it ranged between (1 to 5 days) [11, 12].

In patients who received placebo (Group A), only 18 out of 40 (45%) of calculus was discovered to be evacuated, while 27 out of 40 (67.5%) patients needed treatments. In subjects receiving tamsulosin (Group B), 25 out of 40 (62.5%) of calculus was discovered to be evacuated, whereas only 14 out of 40 (35%) patients needed treatments. In participants using alfuzosin (Group C), 29 out of 40 (72.5%) of calculus was determined to be ejected, while 11 out of 40 (27.5%) individuals needed treatments. The ejection rate for calculus was 45% in the placebo group, 67.5% in the Tamsulosin group, and 62.5% in the Alfuzosin group, according to multivariate analysis [12, 13].

Patients in Group A who received the placebo (Group A) and Tamsulosin (Group B) had a much higher rate of calculus expulsion than patients in Group A who received the Alfuzosin treatment (Group C). This difference was statistically significant ^[14, 15]. (These outcomes are correlated to those of other studies), although there wasn't substantial difference between both the patients using tamsulosin (Group B) and those taking alfuzosin (Group C), which means that receptor sub selectivity is insignificant reason for concern. Just 5 out of 47 instances, or 10.6%, had failures in the 6mm group when compared with 45/75 (60%) in > 6mm groups ^[15, 16].

Study contrast demonstrated a high level of statistical significance across all three groups [(Placebo) p value = 0.000001, (Tamsulosin) p = 0.00016, and (Alfuzosin) p = 0].013]. The results showed that the time it took for calculus to be expelled was 8.63 ± 3.24 days in the Placebo Group A, 7.75 ± 3.14 days in the Tamsulosin Group B, and 8.57 ± 4.52 days in the Control Group C. It was determined that there was not a statistically significant difference between the groups. In each of the three groups, there was no statistically significant difference in the amount of time it took chunks larger than or equal to six millimetres to be

ISSN 2515-8260 Volume 09, Issue 07, 2022

expelled ^[15, 16, 17]. The need for analgesics was significantly higher in placebo groups, and the average period is greater than six days. 59 out of 120 patients needed to have an ureteroscopy and/or lithotripsy performed [Placebo (Group A) 26 (65%), Tamsulosin Group B 12(30%), and Alfuzosin Group C 10(25%)]. In patients, persistent pain was found to be the cause for intervention. Non-expulsion of calculus was found to be the cause for intervention in 9 patients, while dizziness caused by Tamsulosin was the cause for intervention in 1 patient. It was discovered that patients in the Placebo Group A had a higher incidence of interventions 25 (96.1%). The risk of the patient needing to stop receiving therapy as a result of adverse reactions to the medication is extremely low. It is possible that no patients complained of retrograde ejaculation because the treatment was only administered for a brief period of time or because ureteric colic caused a reduction in the amount of coitus or an absence of coitus altogether ^[16, 17, 18].

Conclusion

The spontaneous ejection rates of distal renal calcification is improved by the administration of alpha blockers, such as Tamsulosin and Alfuzosin. There is no discernible distinction in the rate at which Tamsulosin and Alfuzosin expel calcification from the distal ureter when compared to Alfuzosin. Although alpha blockers decrease the need for analgesics, they do not speed up the elimination of calculus.

Funding source: None

Conflict of Interest: None

References

- 1. Latifpour Jamshid, Kondo Shun, O'Hollaren Brian, Morita Takashi, Weiss RM. Autonomic receptors in urinary tract: sex and age differences. Journal of Pharmacology and Experimental Therapeutics. 1990;253(2):661-667.
- 2. Latifpour J, Morita T, O'Hollaren B, Kondo S, Weiss RM. Characterization of autonomic receptors in neonatal urinary tract smooth muscle. Developmental pharmacology and therapeutics. 1989;13:1-10.
- 3. Sigala S, Dellabella M, Milanese G, Fornari S, Faccoli S, Palazzolo F, *et al.* Evidence for the presence of α1 adrenoceptor subtypes in the human ureter. Neurourology and Urodynamics: Official Journal of the International Continence Society. 2005;24(2):142-148.
- 4. Morse RM, Resnick MI. Ureteral calculi: natural history and treatment in an era of advanced technology. The Journal of urology. 1991;145(2):263-265.
- 5. Song HJ, Cho ST, Kim KK. Investigation of the location of the ureteral stone and diameter of the ureter in patients with renal colic. Korean Journal of urology. 2010;51(3):198-201.
- 6. Cimentepe E, Unsal ALI, Saglam R, Balbay MD. Comparison of clinical outcome of extracorporeal shockwave lithotripsy in patients with radiopaque v radiolucent ureteral calculi. Journal of endourology. 2003;17(10):863-865.
- 7. Cooper JT, Stack GM, Cooper TP. Intensive medical management of ureteral calculi. Urology. 2000;56(4):575-578.
- 8. Porpiglia F, Destefanis P, Fiori C, Fontana D. Effectiveness of nifedipine and deflazacort in the management of distal ureter stones. Urology. 2000;56(4):579-582.
- 9. Dellabella M, Milanese G, Muzzonigro G. 1151: The Medical-Expulsive Therapy for Distal Ureteral Stones: Which is the Optimal Choice? The Journal of Urology. 2004;171(4S):303-304.
- 10. Tekin A, Alkan E, Beysel M, Yucebas E, Aslan R, Sengor F. 1152: Alpha-1 Receptor

ISSN 2515-8260 Volume 09, Issue 07, 2022

- Blocking Therapy for Lower Ureteral Stones: A Randomized Prospective Trial. The Journal of Urology. 2004;171(4S):304-304.
- 11. Zwergel U, Zwergel T, Ziegler M. Effects of prostaglandins and prostaglandin synthetase inhibitors on acutely obstructed kidneys in the dog. Urologia internationalis. 1991;47(2):64-69.
- 12. Nakada SY, Jerde TJ, Jacobson LM, Saban R, Bjorling DE, Hullett DA. Cyclooxygenase-2 expression is up-regulated in obstructed human ureter. The Journal of urology. 2002;168(3):1226-1229.
- 13. Nakada SY, Jerde TJ, Bjorling DE, Saban R. Selective cyclooxygenase-2 inhibitors reduce ureteral contraction *in vitro*: A better alternative for renal colic? The Journal of urology. 2000;163(2):607-612.
- 14. Becker AJ, Stief CG, Meyer M, Truss MC, Forssmann WG, Jonas U. The Effect of the Specific Phosphodiesterase-IV-Inhibitor Rolipram on the Uretheral Peristalsis of the Rabbit *In vitro* and *In vivo*. The Journal of urology. 1998;160(3-1):920-925.
- 15. Taher A, Schulz-Knappe P, Meyer M, Truss M, Forssmann WG, Stief CG, *et al.* Characterization of cyclic nucleotide phosphodiesterase isoenzymes in the human ureter and their functional role *in vitro*. World Journal of urology. 1994;12(5):286-291.
- 16. Kühn R, Ückert S, Stief CG, Truss MC, Lietz B, Bischoff E, *et al.* Relaxation of human ureteral smooth muscle *in vitro* by modulation of cyclic nucleotide-dependent pathways. Urological research. 2000;28(2):110-115.
- 17. Romics I, Molnar DL, Timberg G, Mrklic B, Jelakovic B, Köszegi G, *et al*. The effect of drotaverine hydrochloride in acute colicky pain caused by renal and ureteric stones. BJU International. 2003;92(1):92-96.
- 18. Preminger GM, Tiselius HG, Assimos DG, Alken P, Buck C, Gallucci M, *et al.* Guideline for the management of ureteral calculi. The Journal of urology. 2007;178(6):2418-2434.