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**Original Research Article**

# Role of alpha blockers and 7-days catheterization in enhancing the success of trial void in acute urinary retention due to benign prostatic hyperplasia: a double-blind randomized control trial

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## ABSTRACT

**Background:** Acute urinary retention (AUR) in patients with benign prostatic hyperplasia (BPH) is common. This study evaluated the efficacy of three alpha-blockers with urethral catheterization for 7 days in trial without catheter (TWOC).
**Methods:** This was a prospective, randomized, double-blind, active-control study conducted between November 2013 and May 2016. Patients aged more than 50 years, presenting with first-time painful AUR due to BPH were enrolled in this study. Eligible patients were randomized (1:1:1) to one of the three treatment groups to receive tamsulosin 0.4 mg, alfuzosin 10 mg or silodosin 8 mg for one week. The primary outcome measure was successful TWOC at 7 days.
**Results:** A total of 118 patients were included in the study (tamsulosin, n=40; alfuzosin, n=38; and silodosin, n=40). The baseline parameters were comparable between the three groups. A total of 84 (71.2%) patients had successful TWOC at the end of 7 days (tamsulosin, n=30 (75%); alfuzosin, n=32 (84%); and silodosin, n=22 (55%)) and was significantly (p=0.015) different between three groups. Higher age, larger volume at retention and higher prostate volume were significantly (p<0.05) associated with the failure of TWOC.
**Conclusions:** Results from this study demonstrate that there is a definite role of 7-day catheterization with alpha blockers in improving the rates of success of TWOC in men presenting with AUR due to BPH. The success of TWOC is multifactorial.

**Keywords:** Acute urinary retention, Alfuzosin, Benign prostatic hyperplasia silodosin, Tamsulosin

## INTRODUCTION

Acute urinary retention (AUR) is one of the most common urologic condition requiring emergency intervention. Etiology of AUR in benign prostatic hyperplasia (BPH) is still an enigma. It is reasonable to speculate that AUR in BPH is caused by the dynamic component due to increased sympathetic activity at prostatic smooth muscle. This is because significant men void spontaneously after urethral catheter removal and this benefit may be further enhanced by alpha-blockers.[1] Tamsulosin, alfuzosin and silodosin are alpha blockers commonly used in AUR in patients with BPH.

Trial without catheter (TWOC)after a course of alpha blockers is the traditional practice but the duration of urethral catheter and alpha-blockers is unclear, ranging from 1 to 32 days.[2,3] We aim to identify the efficacy of alpha-blockers with urethral catheterization for 7 days in TWOC.

## METHODS

### *Patient population*

Patients aged more than 50 years, presenting with first-time painful AUR due to BPH were enrolled in this study. Patients with urinary tract infection on urine culture and sensitivity, hydroureteronephrosis on ultrasonography (USG), renal failure, comorbidities, inguinal or ventral abdominal hernia, prostatitis, prostatic abscess, those on alpha blockers, prior urethral stricture, transurethral resection of prostate, recurrent AUR, precipitated AUR following elective operations, were excluded from the study.

### *Study design*

This was a hospital-based prospective, randomized, double-blind, active-control study conducted at the tertiary care center between November 2013 and May 2016. After clinical examination, a 14F per urethral Foley catheter was placed using 25 ml of 2% intraurethral lignocaine jelly (10 minutes of contact time). The residual volume of urine on initial catheterization was recorded. Baseline characteristics including patient's age, duration of lower urinary tract symptoms (LUTS), clinical grade of prostate enlargement by digital rectal examination (DRE), International Prostate Symptom Score (IPSS), prostate volume by transabdominal USG and renal function (serum creatinine) were recorded. Eligible patients were randomized (1:1:1) to one of the three treatment groups to receive tamsulosin 0.4 mg, alfuzosin 10 mg or silodosin 8mg for one week. The primary outcome measure was successful TWOC at 7 days. The TWOC was performed after a week of treatment administration and was considered successful if the post-void residual urine (PVRU) less than 200 ml. If the PVRU was more than 200 ml, TWOC was considered failed and patients were re-catheterized. The baseline parameters were compared based on the use of alpha-blockers and on the success or failure of TWOC.The study protocol was reviewed and approved by the institutional ethics committee. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. Written informed consent was obtained, before enrolling each participant in the study.

### *Randomization, allocation concealment, and blinding*

Eligible patients were randomized to one of three groups using block randomization (size = 12) performed by Microsoft Excel 2013. Allocation concealment was performed using serially numbered, opaque and sealed envelopes by an investigator who did not participate in group assignment, data collection or statistical analysis. Envelopes were opened after catheterization by a nursing staff not involved in the research. Study medications were kept inside the sealed envelope with the code. To ensure blinding, study drugs of similar color, shape and size were used. Both the patients and the investigators, who assessed the success of TWOC, were blinded. At the end of the study, the groups were decoded and analyzed.

### *Statistical analysis*

Statistical analysis was performed using SPSS (version 20.0, IBM Corp., Armonk, USA). Variables were presented using mean (standard deviation) or median (interquartile range [IQR]) for continuous variables and proportions or percentages for discrete variables. One-way ANOVA or Kruskal-Wallis tests were used as appropriate, based on Box and Whisker plot. Chi-Square test was used for categorical variables. Logistic regression analysis was performed to assess the factors for successful TWOC. Receiver operator characteristic (ROC) curve analysis was done to identify the cut-off prostate volume and volume at retention for successful TWOC.A p-value of <0.05 was considered statistically significant.

## RESULTS

A total of 118 patients were included in the study, of which 40 (33.9%) patients received tamsulosin, 38 (32.2%) received alfuzosin and 40 (33.9%) received silodosin.

**Table 1: Demographics and baseline characteristics.**

| Parameter | Overall (n=118) | Tamsulosin (n=40) | Alfuzosin (n=38) | Silodosin (n=40) | P value |
|---|---|---|---|---|---|
| Age (years), mean (SD) | 67.7 (6.9) | 65.9(6.1) | 69.1 (6.1) | 69.1 (8.3) | 0.108 |
| Duration of LUTS (months) | 6 (5) | 6 (4) | 6 (3) | 6 (9) | 0.532 |
| Volume at retention (ml) | 600 (563) | 550 (543) | 500 (325) | 712.5 (600) | 0.254 |
| Prostate volume (cc), mean (SD) | 63.1 (26.6) | 63.6 (32.8) | 62.2 (22.4) | 63.5 (23.9) | 0.971 |
| IPSS | 18 (5) | 18 (6) | 17 (6) | 18.5 (4) | 0.911 |
| Post-void residual urine (ml) | 50.5 (124) | 44 (101) | 39 (33) | 63.5 (138) | 0.065 |

Data presented as median (IQR), unless otherwise specified; IPSS: International Prostatic Symptom Score; IQR: Interquartile range; LUTS: Lower urinary tract symptoms; SD: Standard deviation

The flow of participants through the study is depicted in Figure 1. The overall mean age was 67.7 years and was comparable between the three groups. The median duration of LUTS, volume at retention, prostate volume, IPSS score and PVRU were also comparable among the three groups (Table 1).

**Table 2: Comparison of TWOC outcomes.**

| TWOC | Overall (n=118) | Tamsulosin (n=40) | Alfuzosin (n=38) | Silodosin (n=40) | P value |
|---|---|---|---|---|---|
| Success | 84 (71.2) | 30 (75.0) | 32 (84.2) | 22 (55.0) | 0.015 (between three groups) |
| Failure | 34 (28.8) | 10 (25.0) | 6 (15.8) | 18 (45.0) | 0.006 (alfuzosin versus silodosin) |

Data presented as n (%); TWOC: Trial without catheter

On DRE, grade 2 prostatomegaly was seen in 68 (57.6%) patients and grade 3 in 50 (42.4%) of patients. Of these, 25 (62.5%), 21 (55.3%) and 22 (55%) of patients receiving tamsulosin, alfuzosin and silodosin, respectively, had grade 2 prostatomegaly; and 15 (37.5%), 17 (44.7%) and 18 (45%), respectively, had grade 3 prostatomegaly.

**Table 3: Comparison of baseline parameters between successful and failed TWOC.**

| Parameter | Overall (n=118) | Successful TWOC (n=84) | Failed TWOC (n=34) | P value |
|---|---|---|---|---|
| Age (years), mean (SD) | 67.70 (6.9) | 66.8 (6.7) | 69.8 (7.4) | 0.033 |
| Duration of LUTS (months) | 6 (5) | 6 (3) | 6 (9) | 0.924 |
| Volume at retention (ml) | 600 (563) | 450 (250) | 1000 (213) | <0.001 |
| Prostate volume (cc), mean (SD) | 53 (27) | 50.5 (20) | 71 (54) | 0.007 |
| IPSS | 18 (5) | 17.5 (5) | 19 (6) | 0.058 |
| Post-void residual urine (ml) | 50.5 (124) | 35 (25) | 175.5 (31) | <0.001 |
| Volume at retention, ≤800 ml vs >800 ml, n (%) (ratio) | - | 79 (94.0) / 5 (6.0) | 3 (8.8) / 31 (91.2) | <0.001 |

Data presented as median (IQR): Unless otherwise specified; IPSS: International Prostatic Symptom Score; IQR: Interquartile range; LUTS: Lower urinary tract symptoms; SD: Standard deviation; TWOC: Trial without catheter

Out of 118 patients, 84 (71.2%) had successful TWOC at the end of 7 days. The percentage of successful TWOC was significantly different among the three groups (p=0.015). The rate of successful TWOC was significantly (p=0.006) higher in the alfuzosin group compared to silodosin group (Table 2) (Figure 2). However, the PVRU was not affected by any of the alpha blockers used (p=0.105).

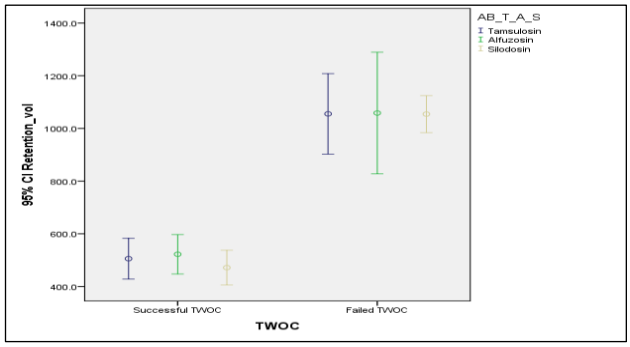


**Figure 2: Error bar graph showing retention volume in patients with successful and failed TWOC stratified by the type of alpha blocker received.**

**Table 4: Factors associated with successful TWOC on day 7.**

| Factors | P value | Odds ratio (95% CI) |
|---|---|---|
| Age >68 years | 0.049 | 2.559 (1.004, 6.522) |
| Prostate volume >62cc | 0.008 | 3.503 (1.392, 8.815) |
| IPSS | 0.151 | 1.096 (0.967, 1.242) |
| Tamsulosin | 0.030 | - |
| Alfuzosin | 0.188 | 0.433 (0.125, 1.504) |
| Silodosin | 0.187 | 2.064 (0.704, 6.053) |
| Constant | 0.004 | 0.024 |

IPSS: International Prostatic Symptom Score; TWOC: Trial without catheter

Higher age (p=0.033), larger volume at retention (p<0.001) and higher prostate volume (p=0.007) were significantly associated with the failure of TWOC. Patients with volume at retention ≤800 ml had a higher chance of successful TWOC (79/84; 94.0%) when compared to those with >800 ml (3/34; 3.7%) (p<0.001). The median PVRU was higher (175.5; 31%) in patients who failed TWOC (Table 3). None of the patients

reported symptomatic or febrile UTI during the 7-day catheterization period. On logistic regression analysis, age (>68 years), large prostate (>62 cc) were significantly associated with failure of TWOC (Table 4).

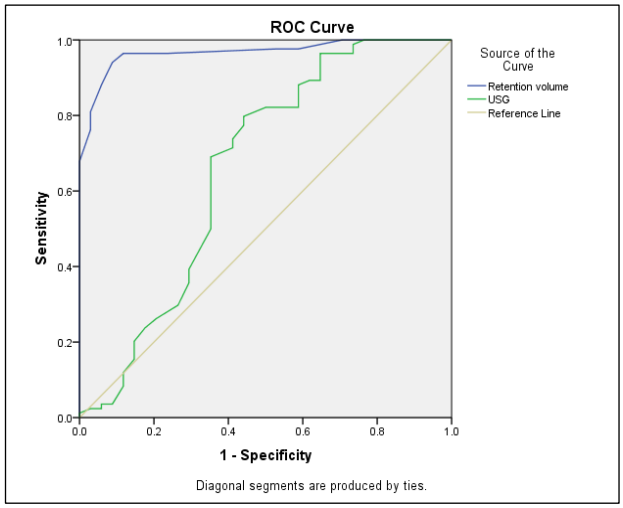


**Figure 3: ROC curve showing the prediction of successful TWOC by retention volume, IPSS and USG measurement.**

On ROC analysis, a cut-off volume at retention of 925 ml with the area under the curve (AUC) was 96.4% sensitive and 88.2% specific for predicting the success of TWOC. A cut off volume of prostate volume 62 cc with AUC was 69% sensitive and 64.7% specific for predicting the success of TWOC (Figure 3).

## DISCUSSION

The etiology of AUR in BPH remains elusive. The AUR due to BPH is mostly classified as spontaneous though a thorough search is performed to look into the causes which could have precipitated this episode of AUR.[4] The concept of TWOC is popular because immediate surgery after AUR is associated with greater 30-day perioperative morbidity. Advantages of postponing the

surgery also include bladder recovering its contractility and reduction in prostatic edema. The traditional practice in the management of AUR is the addition of an alpha-blocker along with catheterization.[3]

Men were more likely to void successfully after their prostatectomy if they had had a period of catheterization.[5] They were also less likely to require a second procedure because of bleeding. However, catheterization did not affect the clinical outcome.[6]

This suggests that prostatectomy for AUR could be risky than performed for LUTS. It has been previously reported that men who had prostatectomy after AUR had an increased risk of intraoperative complications than patients who had prostatectomy for LUTS (Relative risk [RR] 1.8), transfusion (RR,2.5), postoperative complications (RR, 1.6) and hospital death (RR,3.3)[6]. Hence, TWOC is considered in patients with AUR to avoid having a catheter at the time of surgery. Furthermore, few patients may not need surgery after an isolated episode of AUR. The duration of catheterization and AB is highly variable across studies, ranging from 1-32 days. In a systematic review by Fisher et al, a total of nine studies with 1044 men were included and found that alpha blockers increase the success rates of trial without catheter.[3]

There is enough evidence in the literature on the role of alpha-blockers in increasing the chances of a trial void in these patients in particular treatment with alfuzosin, tamsulosin as well others but limited literature available on the use of silodosin.[1,7-12] The risk of UTI increases by 10% with every day of catheter.[13,14] Although long-term chronic indwelling catheter would increase bacterial colonization with morbidity.[15] We noticed no episodes of febrile or symptomatic UTI in present study population.

In a large study by Desgrandchamps which included 2618 men who were catheterized for AUR and found that around 63%, 53% and 43% of patients had successful TWOC for 1-day, 3- days and >7-days catheterization, respectively.[16] However, this population of men was heterogeneous and clinical profile patients could have altered the rate of success of TWOC.[16] Of the 1906 men who had a TWOC, 1505 (79%) received alpha 1 -adrenergic blocker at the time of catheter removal (alfuzosin 76%, tamsulosin 6%, unspecified 18%). The TWOC success rate was significantly higher in those men receiving an alpha-1 -blocker (53.0% vs. 39.6% without alpha-1-blocker).[16]

Several clinical trials have been conducted to assess the usefulness of alpha-blockers in improving the outcomes of TWOC.[1,7-12] McNeill et al evaluated the effect of alfuzosinin patients with the first episode of spontaneous AUR related to BPH who underwent emergency catheterization in a large randomized, double-blind, placebo-controlled study and found that alfuzosin when administered for two consecutive days significantly improved voiding after catheter removal.[1,17] Djavan et al in a prospective RCT of 114 men with AUR found 44% and 62% success rate following 1-day and 7-day catheterization.[18] Overall, our results were consistent with previous reports supporting the use of alpha-blockers in patients with AUR due to BPH.

In the present study, the higher success rate (71.2%) could be attributed to the addition of an alpha-blocker; the maximum being for alfuzosin (84.2%), followed by tamsulosin (75%) and then silodosin (55%).

Author acknowledges the following limitations of the study. A placebo arm was not added to assess the role of only catheterization and no alpha-blocker. However, considering that there is a lot of literature available

demonstrating the benefits of alpha blockers, it was not ethical to have a placebo arm. The comparison with literature is not correct because of heterogeneity and non-randomized nature of the patient population. We could not assess the pain and discomfort associated with a catheter for 7-day duration and patient satisfaction following catheterization.

## CONCLUSION

Results from this study demonstrate that there is a definite role of 7-day catheterization with alpha blockers in improving the rates of success of TWOC in men presenting with AUR due to BPH. The success of TWOC is multifactorial. Among the modifiable factors, alfuzosin seems to have the maximum efficacy followed by tamsulosin. This needs to be confirmed in large multicenter studies.

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