Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/8gj5z148

EFFICACY & SUCCESS RATE OF SILODOSIN, ALFUZOSIN & TAMSULOSIN IN CATHETER-FREE TRIALS AFTER ACUTE URINARY RETENTION CAUSED BY BPH

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Abstract:

Introduction: Acute urinary retention is the incapacity to adequately pass the urine and it has sudden painful onset. This study aims to assess the efficacy of silodosin, alfuzosin and tamsulosin in catheter-free trials after AUR caused by BPH, and also to evaluate the factors that affect the success rate of trial without catheter (TWOC)

Methodology: This randomized control trial was conducted at a Tertiary Care Hospital from Jan to Jun 2023. 84 Patients suffering from acute urinary retention secondary to BPH were enrolled in the study having age was between 40 to 82 years, all of them had acute urinary retention with enlarged prostate (>20 g). Patients were divided into 3 groups Group A tamsulosin; B **silodosin** and Group C alfuzosin respectively. It was also recorded whether TWOC was successful or unsuccessful. Peak flow rate was recorded by uroflowmetry. Further IPSS was recorded after successful TWOC and follow-up visits were planned. All those patients with followed after 2 weeks who had a successful and efficient TWOC and the IPSS was recorded.

Results: 65 patients had successful TWOC, while 56-80 patients had 19 patients with Grade 1 or Grade 2 or Grade 3 TWOC. The overall success of trial without catheter (TWOC) was 61.90% (52 out of 84).

Conclusion: BPH-induced acute urinary retention (AUR) patients can benefit from alfuzosin, silodosin, and tamsulosin, with IPSS improvement after 2 months. All patients should be treated with selective alpha-blockers for efficacy.

Keywords: Acute urinary retention, alfuzosin, silodosin, tamsulosin, BPH

Introduction:
Acute urinary retention is the incapacity to adequately pass the urine and it has sudden painful onset. It is a common urologic emergency [1]. Acute urinary retention is usually seen after benign prostatic hyperplasia in males and it is one of the most common causes of AUR. So, it can be anticipated that without treatment of BPH, the complication of acute urinary retention will increase [2]. The 10-year chances of development of AUR in men who had BPH was reported from 4% to 73% (3). Patients suffering from urinary retention may present with complain of lack of complete voiding, restricted bladder emptying or even with overflow incontinence. Complications of urinary retention involve infection and renal failure [3]. The management strategies of AUR fluctuates, but usually it includes urinary catheter placement either urethral or supra-pubic. It is then followed by medical therapy and immediate admission to hospital or discharge depending upon the severity of cases with outpatient follow-up.
Currently the cause and incidence of AUR is well understood, however, research on preventive and treatment strategies must be conducted. Also, evaluation of effect of treatment strategies on occurrence of AUR on the patient is also necessary [2]. This study will be aimed to determine whether patient having catheter for drainage of urine can spontaneously discharge urine without requiring further catheterization during a trial period of 3 days. It is called trial without catheter (TWOC). Any staged approach that can enhance the success rate of TWOC will have beneficial outcomes for the patients. Determining the cause of urinary retention is essential for effective treatment strategy. For example, if urinary retention is due to prostatic smooth muscle contraction due to increased sympathetic activity, then administration of alpha-blocker will increase the voiding after removal of catheter [3]. The potent most alpha-1 antagonist that was previously observed and investigated for BPH was Tamsulosin. In early 1990s, Alfuzosin was the focus of study for BPH treatment mainly in Europe. Alfuzosin shows high uroselectivity although it is not completely α1A selective. On the other hand, silodosin and tamsulosin have greater α1A selectivity [4]. In previous studies, two alpha-blockers i.e., silodosin and tamsulosin have been compared. But the comparison of alfuzosin, tamsulosin and silodosin for trial without catheter in acute urinary retention is not investigated.
The aim of this study is to assess the efficacy of silodosin, alfuzosin and tamsulosin in catheter-free trials after AUR caused by BPH, and also to evaluate the factors that affect the success rate of trial without catheter (TWOC) by conducting a randomized prospective study.

Material and methods:
This prospective randomized control trial was conducted at a Tertiary Care Hospital from Jan to Jun 2023. A sample size of 84 was calculated using Rao Soft calculator. Consecutive sample collection technique was utilized. This study has been registered in Research Registry having UIN researchregistry9303 [5].

Patients suffering from acute urinary retention secondary to BPH were enrolled in the study. All the patients fulfilled the following criteria: all the patients age was between 40 to 82 years, all of them had acute urinary retention with enlarged prostate (>20 g), and all of them were willing to report for follow-up visits on predicated dates in OPD. All those patients were excluded who had used finasteride or any alpha blocker earlier (last 6 months), who had prostate size more than 100 g. Those patients were also excluded who were on anti-hypertensives, antipsychotics, sympathomimetics, anticholinergics drugs. Exclusion criteria also included those patients who had malignancy of prostate, underwent any prostatic surgery in past; were suffering from any other cause of urine retention including UTI, malignancy of bladder, neurogenic bladder, urethral stricture and prostatitis etc.; had severe cardiac disease; orthostatic hypotension; any mental condition with impaired cognitive function, hypersensitivity towards the drugs used in trial and alcohol abuse.

A computer-generated algorithm was used for the purpose of randomization of the patients. All the patients were categorized into 3 groups after randomization making it 28 patients in each group.

Group A, B, C contained patients who underwent trial with tamsulosin; silodosin and alfuzosin respectively. Different doses for each drug were used at bedtime i.e., 0.4 mg dose of Tamsulosin, 10 mg dose of Alfuzosin, and 8 mg dose of silodosin.

Before enrolling patients, ethical approval was obtained from the ethical review committee, ref no ERC/KRL/152/23 & a written informed consent was taken from all patients. Detailed history was recorded and then general and systemic examination was done. Prostate consistency was assessed by digital rectal examination. Spinal reflexes were examined. Size of the prostate and presence of residual urine was determined by transabdominal ultrasonography. IPSS was determined and recorded at presentation and 2 months after conducting the trial. Abdominal ultrasound was used to determine the prostate volume. Careful examination of all the patients with AUR was done, and those having AUR not due to BPH were not included in the study. 3 days after drug administration, the catheter-free trial was conducted. Uroflowmetry and post-void residual urine measurements was done in all those patients who voided. Patients whose post-void residual volume was more than 150 ml were categorized as failed trial without catheter (TWOC). Treatment was continued. Re-catheterization and TURP was planned in all those patients who failed to void. Various parameters like prostate grade on digital rectal examination, size of prostate, volume of retained urine, medicine used and IPSS at time of patient presentation were recorded. It was also recorded whether TWOC was successful or unsuccessful. In successful scenarios, peak flow rate was recorded by uroflowmetry. Further IPSS was recorded after successful TWOC and follow-up visits were planned. All those patients with followed after 2 weeks who had a successful and efficient TWOC and the IPSS was recorded.

Data was analyzed using SPSS version 26. Chi square test was applied to see the efficacy & the factors that affect the success rate of trial without catheter (TWOC).

Results

All the patients age was between 40 to 82 years, all of them had acute urinary retention with enlarged prostate (>20 g). The patients were randomized into three groups. Group A (tamsulosin), Group B (Silodosin), and Group C (alfuzosin): The Groups A, B, and C had 28 patients, respectively. The Mean, Median and Std Deviation between age group were 51.2738, 51.0000 and 7. 91727.The PFR-A, PFR-B, PFR-C, IPSS-A, IPSS-B and IPSS-C groups were as follows in [Table-1].

Grades of success of TWOC were as follows by 40-55 age, 23 patients had Grade 1, 33 patients had Grade 2, 9 patients had Grade 3 which showed total 65 patients having successful TWOC. With age 56-80, 6 patients had Grade 1, 9 patients had Grade 2 and 4 patients had Grade 3 which showed total 19 patients having successful TWOC. Thus, total 29 patients had Grade 1, 42 patients had Grade 2, 13 patients had Grade 3 which showed total 84 patients with successful TWOC as shown in [Table-2].

The bar chart showed the age and count of round cells. Patients having age 55 was in Grade 2 with successful TWOC, 45 age was in Grade 1 and 40 age was in Grade 3 of one side count round cells. Similarly, the patients having age 80 was in Grade 2 with successful TWOC, 70 was in Grade 1 and 56 was in Grade 3 of other side count round cells. There was a statistically significant difference and also a correlation in successful TWOC between Grade 2 of either round cells, and lower grades between Grade 3 as shown in [Figure-1].

The patients were divided into three groups. Grades of median lobe enlargement are as follows: Grade 1: <5 mm, Grade 2: 5–10 mm, and Grade 3: >10 mm: The Grade 1, 2, and 3 had 11, 13, and 4 patients with total 28 patients, respectively in Group A patients. The success of TWOC was as follows: In Group 1: out of 11 patients, 6 and 5 patients. In Group 2: out of 13 patients, 8 and 5 patients, and in Group 3: out of 4 patients, 2 and 2 patients had successful TWOC in Group A.

The success of TWOC Group B patients was as follows: In Group 1: out of 11 patients, 7 and 4 patients. In Group 2: out of 13 patients, 9 and 4 patients, and in Group 3: out of 4 patients, 3 and 1 patients had successful TWOC in Group B patients. The success of TWOC group C was as follows: In Group 1: out of 11 patients, 7 and 4 patients. In Group 2: out of 13 patients, 8 and 5 patients, and in Group 3 out of 4 patients, 2 and 2 patients had successful TWOC in Group C patients. The overall success of trial without catheter (TWOC) was 61.90% (52 out of 84), as follows in [Table-3].

Discussion:

The aim of treating benign prostatic hyperplasia involve, decreasing bladder outlet obstruction, relieving LUTS, enhancing emptying of bladder, improving bladder instability, preventing the future occurrence of gross hematuria, urinary retention and UTIs. It is also done to reverse the renal insufficiency. For the purpose of immediate management of acute urinary retention, bladder decompression is done by the aid of catheterization. Use of TWOC has been increased due to the evidence that immediate surgery after acute urinary retention is linked with higher morbidity than delayed prostatectomy by lowering the risk of catheter induced infection. It helps in treating patients without surgery that enables other patients to schedule the operation without use of catheter. According to recent guidelines by AUA, BPH surgery is not obligatory after the first episode of acute urinary retention with successful TWOC (6). Transabdominal ultrasound (TAUS) was used in our study because the facility of transrectal ultrasound was not available. We considered average prostate of more than 20 g for our study. According to veterans' affairs comparative medical therapy trial, the use of selective alpha-1 blockers irrespective of the prostatic volume, have beneficial outcomes when used as first-line medical therapy for BPH. According to a study, the alpha-blockers have superiority over hormonal therapy for BPH treatment (7). Tamsulosin was considered as the potent most alpha-1 antagonist for BPH (8). Narayan et al. conducted a double-blind, randomized and placebo-controlled trial that compared the safety and effectiveness of tamsulosin and placebo (9). 735 men were included in this randomized study that continued for 13 weeks. Results regarding improvements after treatment in acute urinary retention symptom and peak flow-rates were reported similar to that of Lepor et al. (7)

Alfuzosin was investigated for treating BPH that exhibits uroselectivity. However, Silodosin and tamsulosin have greater α1A selectivity. Jardin et al. reported the safety and efficacy of alfuzosin for treating BPH after conducting a multicenter, large scale and randomized trial (10). Alpha-1 blockers are beneficial for treatment of lower urinary tract symptoms indicative of BPH. They act by lowering the sympathetic tone that will decrease outlet resistance of bladder and also post void residual volume of urine. According to some studies, alpha-1 blockers enhance the rate and chances of successful TWOC (11). So, alpha-1 blockers are frequently used before removing catheter. All the patients in this prospective study were randomly divided into three groups, tamsulosin (0.4 mg), alfuzosin (10 mg), and silodosin (8 mg). Drugs were administered once a day at bedtime. Constipation was treated to avoid the side effects of the drug. The primary aim of our study was to determine the efficacy of tamsulosin, alfuzosin and silodosin for treating patients with acute urinary retention due to BPH by comparing patients who voided successfully after removal of catheter. When the 3 drugs were collectively compared, it was found that the difference for successful TWOC was not statistically significant ($P > 0.005$). According to our knowledge, no previous study has compared the effect of these three drugs in acute urinary retention because of BPH. According to a study conducted by Maldonado-Ávila et al. illustrates the safety and efficacy of alfuzosin and tamsulosin in these patients. Statistically insignificant results were obtained while comparing both groups. However, tamsulosin was proven to be more effective in successful removal of catheter (12). The highest success rate was seen in the A study conducted by Kumar et al. showed the highest rate of success (13) and the study by Lucas et al. showed the lowest success rate (10). However, our study yielded a comparable successful result. A study by Ginka showed higher rate of success for silodosin versus tamsulosin (72.33% for silodosin and 66.7% for tamsulosin). Patil et al found efficacy slightly higher efficacy with tamsulosin when compared with silodosin (14). Our study compared silodosin, alfuzosin, and

tamsulosin and there was no significant difference in success after conducting a catheter-free trial for these three drugs.

The results were insignificant while considering the prostate size of patients who voided (mean size 41.9g) and the patients who did not void (mean size 42.6 g). The patients having size of prostates greater than 50 g had less chances to void (57.2%) than those patients whose prostates were less than 50 g (62.5%). Our study finds this difference statistically insignificant. Whereas Fitzpatrick et al. conducted a worldwide survey comprising of 6074 men to conclude that a prostate size less than 50 g is highly significant to predict the success of TWOC (15). All the patients in our study who underwent successful TWOC were observed and assessed of, post-void residual volume of urine, IPSS and peak flow rate. During follow-up, there was a significant decrease in IPSS in all patients. It was interesting to note that results for comparison between three groups were statistically insignificant. Many RCTs and open-label studies found that an enhancement of 4 to 6 points in the IPSS can be expected while treating BPH (16).

A change of 2.5 to 4.2 in IPSS was seen in a study conducted by Senkul et al for those patients who were administered with alpha-blockers. An improvement in IPSS of 2.9 to 3.2 points is seen in our study. There was sufficient rates of flow and no noticeable post-void residual urine after the treatment. Our study has a limitation that it is conducted in small population of patients. However, results of our study are can contribute in conducting future studies in this stream.

Patients with AUR caused by BPH can benefit from the use of alfuzosin, silodosin, and tamsulosin. After 2 months of treatment, the IPSS has improved dramatically with all three medicines. Catheter-free trials and improvements in the International Prognostic Scoring System (IPSS) show no discernible difference between the three medications. All patients experiencing their first episode of AUR owing to BPH should be offered medical therapy with selective or sub-selective alpha-blockers because of its efficacy.

Declarations

Competing Interests: No conflict of interests declared by the authors.

Funding: No Funding has been received

Acknowledgements: Nil

Contribution statement: All authors have equally contributed to the manuscript and have approved the final manuscript to be published

ETHICAL CONSIDERATION

Approval of the research protocol by an Institutional Reviewer Board and the approval: ERC/KRL/152/23

Informed Consent: Obtained from all the participants Registry and the Registration No. of the study/trial: researchregistry9303

Animal Studies : NA

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Tables:

	AGE	PFR A	PFR B	PFR C	IPSS A	IPSS B	IPSS C
Mean	51.2738	10.8521	10.7107	12.1307	3.1050	3.7975	2.2857
Median	51.0000	10.8000	10.5000	11.8900	2.9500	3.3500	2.0000
Std. Deviation	7.91727	1.08347	1.61606	1.68439	.49277	1.86629	.64101

Table 1. Statistical analysis of age, PFRA, PFRB, PFRC, IPSSA, IPSSB and IPSSC groups

AGE_CATEGORY	GRADE 1	GRADE 2	GRADE 3	P value
40-55	23	33	9	0.745
56-80	6	9	4	

Table 2. Successful trial without catheter in each group of patients

		GRADE 1	GRADE 2	GRADE 3	**P value**
TWOC A	SUCCESSFULL	6	8	2	**0.898**
	RECATHETERIZE	5	5	2	
TWOC B	SUCCESSFULL	7	9	3	**0.907**
	RECATHETERIZE	4	4	1	
TWOC C	SUCCESSFULL	7	8	2	**0.889**
	RECATHETERIZE	4	5	2	

Table 3: Successful trial without catheter in each group of patients

Figure Legend:

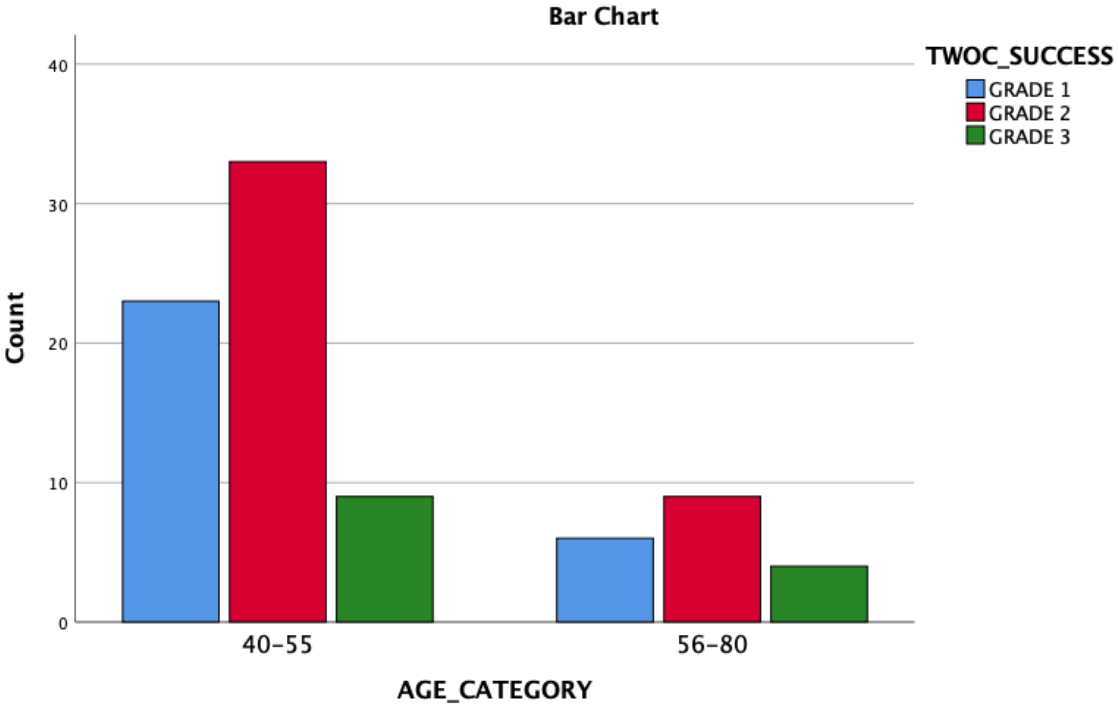

Figure 1. Difference in success of trial without catheter between Grades 1, 2, and 3