Is the Double Dose Alpha-Blocker Treatment Superior Than the Single Dose in the Management Of Patients Suffering From Acute Urinary Retention Caused By Benign Prostatic Hyperplasia?

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Purpose: To compare the efficacy and safety of single (tamsulosin) and double dose (tamsulosin + alfuzosin) alpha-blocker therapy for treating catheterized patients with acute urinary retention (AUR) due to benign prostatic hyperplasia (BPH).

Materials and Methods: Seventy patients with AUR due to BPH were catheterized and randomized into two groups: the single dose group (0.4 mg tamsulosin, 35 patients) and the double dose group (0.4 mg tamsulosin + 10 mg alfuzosin, 35 patients). The catheter was removed after 3 days, and the patients were put on trial without catheter (TWOC).

Results: Seventy males (mean age, 71.2 years) were randomly assigned to receive double or single dose alpha-blocker (35 patients per group). The intent-to-treat population consisted of 70 males. Twenty-seven individuals in the double dose group and 19 in the single dose group did not require re-catheterization on the day of the TWOC (77% and 54%, respectively; P = .003). Success using free-flow variables was also higher in the males who received double dose alpha-blocker compared with single dose therapy (48% vs. 40%; P = .017).

Conclusion: TWOC was more successful in males treated with double dose alpha-blockers, and the subsequent need for re-catheterization was also reduced. The side-effect profiles were similar in the single and double dose alpha-blocker groups and were consistent with the known pharmacology. These results state that double dose alpha-blocker treatment can be recommended for treating males after catheterization for AUR, which may reduce the need for re-catheterization.

Keywords: acute disease; administration; oral; prostatic hyperplasia; drug therapy; treatment outcome; urinary retention; adrenergic alpha-1 receptor antagonists.

INTRODUCTION

Benign prostatic hyperplasia (BPH) is one of the most common urinary disorders in elderly males.[1] The symptoms of BPH include impaired physiological and functional well-being, which interferes with daily living.[2] Although BPH is rarely life-threatening, acute urological complications such as acute urinary retention (AUR) can occur, which is considered to be the most serious complication with the progression of BPH.[3] AUR is particularly painful and distressing for the patient and has considerable economic costs.[4] Early estimates of the incidence of AUR varied widely, but recent population-based studies suggested an incidence of 5-25 per 1000 person-years or 0.5-2.5% per year.[5] However, the risk of AUR is cumulative and increases with age. AUR is one of the primary indications for transurethral resection of prostate (TURP). A large study mentions that the risk of an AUR at 23% for a 60 years old man if he lived for another 20 years.[6] After spontaneous AUR, 15% patients in a long-term study experienced an additional episode of AUR, and 75% underwent subsequent surgery.[7] The initial intervention for AUR is the insertion of a urinary catheter to relieve the symptoms.[8] In addition to being uncomfortable for the patient, this is an avoidable risk factor for blood loss after TURP if surgical intervention is necessary.[9] Therefore, a trial without catheter (TWOC) is preferable compared with leaving the catheter in place, and a 23-28% success rate has been reported.[10,11] Nevertheless, most patients still require TURP, either as an emergency or elective surgery.

Alpha-1 (α_1)-blockers decrease smooth muscle tone in the prostate, thereby rapidly improving urinary symptoms and flow. Currently available α_1-blockers include the selective α_1-blockers terazosin, doxazosin and alfuzosin and the highly selective α_{1A}-blocker tamsulosin. These agents have comparable efficacy, and the major differences between these agents are their tolerability profiles.[12] By decreasing the resistance, α_1-blockers can help relieve AUR and improve the chances of successful TWOC.[13] However, the optimum duration of therapy has not been fully assessed, and there is controversy regarding the length of time a catheter should remain in situ during the initial therapeutic phase. This study aimed to compare the efficacy of modified release single (0.4 mg daily tamsulosin hydrochloride) and double dose (tamsulosin + alfuzosin) combination therapy for the management of patients with AUR who were suitable for TWOC.

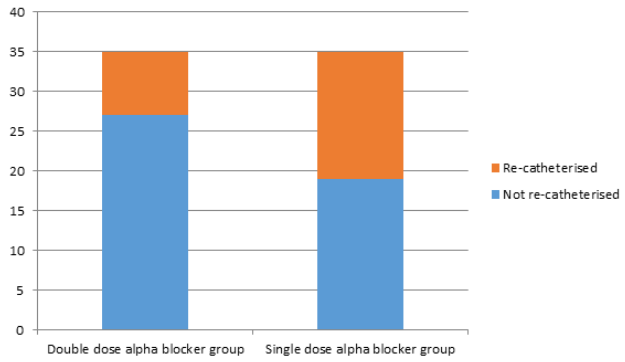

Figure . Successful trial without catheter in each study group.

MATERIALS AND METHODS

Between 2008 and 2013, 70 males aged 48-85 years (mean, 71.2 years) were enrolled in the study. Thirty-five patients received single dose α-blocker therapy with a modified-release tamsulosin hydrochloride capsule (0.4 mg), and the remaining 35 received double dose combination therapy comprising modified-release tamsulosin hydrochloride (0.4 mg) and alfuzosin hydrochloride (10 mg), consumed daily in the tablet form. All patients were admitted to the urology and emergency department of the hospital for AUR and had been catheterized in the previous 72 h. Before catheterization and therapy, informed consent was received from all patients.

Males with initial catheterization volumes off > 1500 or < 500 mL were excluded from the study. Other exclusion criteria included, evidence of renal or hepatic dysfunction, previous urinary tract surgery, neurogenic or other diseases of the bladder, upper urinary tract diseases such as uremia, any malignancy or the use of retention-enhancing medications. The study received Ethics Committee approval and conformed to the international guidelines for clinical trials. It was performed according to the Declaration of Helsinki, and all patients provided written informed consent.

The duration between catheterization and the initial dose of medication was 72 h. In the single-dose group, a 0.4-mg

Table 3. Difference of related indicators among 2 or more than 2 groups.

Criteria	Double Dose Alpha-Blocker Group	Single Dose Alpha-Blocker Group	Total	*p*
Number of patients	35	35	70	
Primary analysis*	14 (42)	11 (31)	25 (35)	.175
Any two free-flow criteria	17 (48)	14 (40)	31 (44)	.017
Two specified criteria**	22 (62)	18 (51)	40 (57)	.035
Any two criteria†	24 (68)	20 (57)	44 (62)	.028

* Primary analysis included three criteria: flow rate > 5 mL/s, voided volume > 100 mL and residual urine volume 200 mL.
**Flow rate > 5 mL/s and voided volume > 100 mL.
†Flow rate > 5 mL/s, voided volume > 100 mL and residual urine volume 250 mL.

tamsulosin hydrochloride tablet was administered once daily before bed. In contrast, in the double-dose group, a 10-mg alfuzosin hydrochloride tablet was administered daily after breakfast, and 0.4-mg tamsulosin hydrochloride tablet once daily before bed. The duration of therapy was determined at the physician's discretion (three or eight doses) according to their normal practice. Patients were allowed to return home after a successful catheter-free void (flow rate of > 5 mL/s, a voided volume of > 100 mL and residual volume of 200 mL). In the absence of any internationally agreed outcome measures, investigators regarded a successful TWOC as effective bladder emptying. Patients were observed weekly (flow rate, ultrasound) and they could continue to consume medications for up to 36 weeks, but if re-catheterization was required (residual volume of > 200 mL) they were withdrawn from the study.

RESULTS

The mean age of patients in the single- and double-dose groups was 69.4 ± 8.8 and 72.2 ± 8.5 years, respectively, and the initial catheterization volumes recorded were 673.2 ± 80.3 and 723.7 ± 90.7 mL. Therefore, these parameters were comparable between groups. Single (tamsulosin) and double dose (tamsulosin + alfuzosin) therapies resulted in successful TWOC in 54% (19/35) and 77% of (27/35) patients, respectively. Twenty-seven individuals in the double dose group and 19 in the single dose group did not require re-catheterization on the day of the TWOC (77% and 54%, respectively; $P = .003$) (Figure). Pre-determined criteria for defining a successful TWOC revealed no significant benefits of double-dose therapy compared with single-dose therapy (42% vs. 31%, respectively, $P = .175$; Table). However, secondary analysis of study data using two free-flow criteria revealed that double-dose α-blocker therapy resulted in a significantly better outcome compared with single-dose therapy (Table).

Both single and double dose α-blockers were well tolerated. A common adverse effect reported in the double-dose group was dizziness (8.7% vs. 6.5% in the single-dose group). Headache was the most common adverse effect in the double-dose group (11.4% vs. 9.3% in the single-dose group). Moreover, retrograde ejaculation was reported in 13.4% and 11.7% of patients receiving double and single doses, respectively. None of the differences in adverse events between the single and double dose groups were statistically significant, and no severe hypotension event is recorded in each group that requires the discontinuation of therapy.

DISCUSSION

BPH is a progressive disease that is primarily characterized by the deterioration of symptoms over time, the incidence of serious complications such as AUR and the need for BPH-related surgery in some patients.[14] AUR is a common urological emergency that is characterized by the sudden and painful inability to pass urine. The incidence of AUR in patients with BPH varies widely from 0.4% to 25%.[15] The management of AUR requires bladder decompression, usually through a urethral catheter. Until recently, subsequent management almost exclusively comprised prostatic surgery within a few days (emergency surgery) or a few weeks (elective surgery) after the first AUR episode. However, increased morbidity and mortality associated with emergency surgery and the potential morbidity associated with prolonged catheterization have led to an increased use of TWOC. This involves catheter removal after 1-3 days, which allows the patient to void in 23-40% cases. Surgery, if

required, can then be planned at a later stage in patients with unsuccessful TWOC.[7]

The primary objective of the present study was to evaluate the efficacy of tamsulosin compared with tamsulosin + alfuzosin for the management of catheterized patients with AUR caused by BPH by comparing the number of patients voiding successfully after catheter removal. The pre-determined primary criteria for defining a successful TWOC revealed significant beneficial effects of double-dose α-blocker therapy. Furthermore, the success rate of TWOC with tamsulosin (54%) was comparable to previous observations by Lucas and colleagues[16] and Hua and colleagues,[17] who reported success rates of 48% and 61%, respectively. Double dose α-blocker therapy resulted in a 77% success rate of TWOC in our study. In addition, it was well tolerated and resulted in outcomes that were superior to those previously reported: 55% by McNeill and colleagues[18] 61.3% by Gopi and colleagues[19] and 61.9% by McNeill and colleagues.[20] However, these outcomes were obtained using single-dose alfuzosin therapy. Moreover, in a systematic review of meta-analysis group assessing the role of alfuzosin, tamsulosin, silodosin, doxazosin compared with placebo for TWOC in patients with AUR due to BPH have been reported. Compared to 38.9% (161/414) in control groups 56.8% (362/637) of patients receiving a1-blockers had a successful TWOC.[21] The success rates were similar with our single dose tamsulosin group (56.8-54%). To the best of our knowledge, the present study is one of only a small number of prospective randomized trials performing a head-to-head comparison between single- and double-dose α-blocker therapies for TWOC in AUR.

The common adverse events included hypotension, dizziness, and retrograde ejaculation. For drug related adverse events the results were statistically insignificant between two groups. In our study adverse events were low and comparable across studies which are made with selective α1-blockers.[16-18,20,22-26]

CONCLUSION

In males catheterized for AUR, previous studies revealed that TWOC was more successful when treated with alfuzosin or tamsulosin compared with placebo. In addition, our study suggests that, compared with single-dose therapy, double dose α-blocker therapy with alfuzosin and tamsulosin was well tolerated and improved the TWOC success rates in patients with AUR.

CONFLICT OF INTEREST

None declared.

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