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Efficacy and Safety of Tamsulosin-MR Versus Alfuzosin-SR for Treatment of Symptomatic Benign Prostatic Hyperplasia: A Randomized, Prospective Study

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ABSTRACT

INTRODUCTION: Alpha-1 adrenoceptor antagonists are the mainstay for treatment of symptomatic benign prostatic hyperplasia (BPH). Tamsulosin and alfuzosin, the most commonly prescribed drugs, have good efficacy and safety. However, there is paucity of data comparing the modified release (MR) or sustained release (SR) formulas. The purpose of the present study was to compare the efficacy and safety of tamsulosin-MR 0.4 mg with alfuzosin-SR 10 mg in patients with symptomatic BPH.

METHODS: A total of 90 patients participated in the single-blind, parallel-trial design. Patients were randomly assigned to equal groups, receiving tamsulosin-MR (0.4 mg) or alfuzosin-SR (10 mg). Both were taken once daily for 12 weeks. The International Prostate Symptom Score (IPSS) and maximum urinary flow rate (Qmax) were determined before and at 6 weeks and 12 weeks after the initiation of therapy. The number of adverse events was recorded.

RESULTS: Patients in both groups had a significant mean change in both IPSS and Qmax at the end of 6 weeks and 12 weeks of therapy ($P < .001$). There was no significant group difference in mean IPSS or Qmax at 6 weeks. At 12 weeks, the group receiving tamsulosin had a significantly lower IPSS ($P = .048$) and a significantly higher Qmax ($P = .045$) than the group receiving alfuzosin. Adverse events were infrequent and not statistically different between groups. Dizziness and impotence were most common with tamsulosin; dizziness and fatigue were most common with alfuzosin.

CONCLUSION: Tamsulosin-MR was significantly more effective than alfuzosin-SR in improving IPSS score and Qmax at the end of 12 weeks of treatment, although the group differences in outcome measures were small.

Abbreviations and Acronyms

BOO = bladder outlet obstruction
BPH = benign prostatic hyperplasia
IPSS = International Prostate Symptom Score
LUTS = lower urinary tract symptoms
MR = modified release
PVR = postvoid residual
Qmax = maximum urinary flow rate
SR = sustained release

KEYWORDS: Tamsulosin; Alfuzosin; BPH; IPSS; Qmax
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original study

Efficacy and Safety of Tamsulosin-MR Versus Alfuzosin-SR for Treatment of Symptomatic Benign Prostatic Hyperplasia: A Randomized, Prospective Study

INTRODUCTION

Benign prostatic hyperplasia (BPH) is one of the most common diseases that warrant medical consultation for elderly men [1]. Its prevalence increases with age; by 80 years, almost 90% of men have symptoms attributable to prostatic obstruction. Because the elderly constitute a major proportion of the current population, this results in a major impact on medical practice [2].

Management of BPH has changed significantly over time, with considerable advance in the understanding of the demographics and natural history of the disease [3]. Alpha-1 adrenoceptor antagonists are considered the first line of treatment for managing lower urinary tract symptoms (LUTS) that are associated with BPH and suggestive of bladder outlet obstruction (BOO). The newer uroselective α-1 blockers alfuzosin and tamsulosin are most commonly prescribed. They possess a high α_{1A}-receptor affinity and, because of *prostate selectivity* relative to vascular tissues, have the theoretical advantage of improving LUTS and urine flow with few adverse effects [4-8].

Only 2 randomized controlled trials have been published that compare tamsulosin with alfuzosin. Investigators of the first study compared tamsulosin 0.4 mg taken once daily with alfuzosin 2.5 mg taken 3 times daily [9]; investigators of the second study compared tamsulsoin 0.2 mg with alfuzosin 10 mg, both taken once daily [10]. Results showed a similar magnitude of improvement in symptom score and urinary flow rates for patients taking either of the α-blockers.

There is little information available about the newer forms of the drugs: alfuzosin-SR (sustained release) and tamsulosin-MR (modified release). Thus, there is a need for a head-to-head trial on the safety and efficacy of these forms. The present study was conducted to compare efficacy and safety of tamsulosin-MR (0.4 mg) with alfuzosin-SR (10 mg). These formulations are available in India and commonly used in clinical practice.

METHODS

Participants

A total of 104 patients were evaluated for possible inclusion in the study between June 2008 and March 2009 at the outpatient clinic of the Department of Urology, Sir Sunderlal Hospital, Banaras Hindu University, Varanasi, India (a tertiary care government medical center). Inclusion was based on the patient's medical history, intake of medication, and a physical examination.

The inclusion criteria were: (1) males age 45 years of age or older who presented with voiding difficulty and a clinical diagnosis of BPH; (2) at least a 6-month history of LUTS; (3) an International Prostate Symptom Score (IPSS) of at least 13; (4) a maximum urinary flow rate (Qmax) between 4 mL/s and 15 mL/s after 2 uroflowmetry evaluations, with voided urine volumes of at least 120 mL; (5) able to read and comprehend English or Hindi. The exclusion criteria were: (1) suspected or proven prostatic malignancy; (2) urinary retention, defined as a postvoid residual (PVR) volume of at least 100 mL as measured on a bladder scan; (3) active, untreated urinary tract infection; (4) history of prostatectomy; (5) significant, untreated or uncontrolled medical disease such as diabetes mellitus, hypertension, renal failure, hepatic dysfunction, cardiac failure, or senile dementia; (6) intake of any medication for the treatment of BPH (eg, α-blockers, 5α-reductase inhibitors, plant extracts) in the preceding 2 weeks; (7) intake of α-blockers (eg, doxazosin, terazosin, prazosin), 5α-reductase inhibitors, cholinergic agents, anticholinergics, or antispasmodics for any other reason.

A total of 90 participants met the criteria and were enrolled in the study; 14 were ineligible because of a suspected malignancy or significant urinary retention. The age range for all patients was 48-78 years. The mean (standard deviation) age of the group receiving tamsulosin-MR was 63.25 (7.54) years; the age of the group receiving alfuzosin-SR was 64.48 (8.85) years. The baseline demographic and clinical data of the patients in the 2 groups were similar, with no significant group differences in any of the characteristics.

Procedures

The protocol for this trial was reviewed and approved by the Institutional Ethics Committee of the college and was conducted in accordance with the Good Clinical Practice guidelines. Patients were given full information on the purpose, procedures, advantages, disadvantages, and other matters associated with the conduct of the trial. Written informed consent was obtained.

The study had a randomized, single-blind, parallel-trial design. Patients were randomly assigned to groups using a computer-generated list of random numbers. Patients in group 1 (n = 45) received tamsulosin-MR (0.4 mg) once daily; patients in group 2 (n = 45) received alfuzosin-SR (10 mg) once daily. Both medications were taken in the morning after breakfast for 12 weeks, with no initial dose titration. Patients were not informed of the treatment group to which they were allocated. The drug and instructions were dispensed in packets by the resident doctor.

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Figure 1. Schematic of the Study Design.
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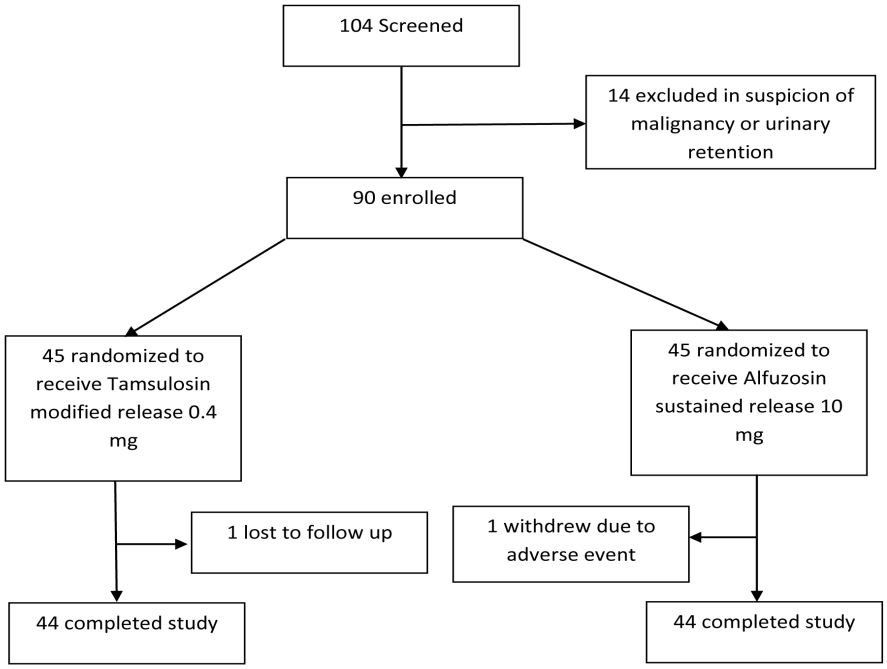

All patients were evaluated before treatment (baseline) and at 6 weeks and 12 weeks during treatment. They were seen by a urologist who assessed the progress of treatment according to standard clinical practice. In addition, questionnaires were completed and the occurrence of adverse events was recorded. Uroflowmetry and PVR volume measurements were performed. Compliance was determined by a resident doctor on the basis of the number of tablets returned at each visit; poor compliance was defined as consumption of less than 80% of the expected number of tablets.

Data Analysis

The study was designed to compare the 2 active treatment groups. The primary outcome was the mean change in IPSS from baseline to the end of 12 weeks of treatment. Other outcomes studied were mean change in the IPSS, mean change in Qmax, and the incidence of adverse events.

A study sample size of 90 patients (at least 45 in each arm) was calculated to have 80% power with a 95% confidence interval of detecting a 5-point difference in the IPSS between tamsulosin-MR and alfuzosin-SR at the end of treatment. Trial data were entered into a database using SPSS software version 15.0 (SPSS Inc, Chicago, IL, USA). The mean IPSS, mean Qmax, and mean percentage change in IPSS were compared between the 2 groups at each visit using the *t* test; $P < .05$ was considered statistically significant.

RESULTS

At the end of the study, data were available for 88 patients (Figure 1). One patient in the group receiving tamsulosin-MR was lost to follow-up after the initial (6-week) visit, and 1 patient withdrew from alfuzosin-SR at the end of the first week of therapy because of adverse events.

IPSS and Qmax

Table 1 contains the means and standard deviations for IPSS and Qmax at the baseline, 6-week, and 12-week evaluations for patients in both groups. There was progressive improvement in the IPSS of all patients during the treatment period. When compared with the baseline IPSS, patients in both groups showed significant improvement in the mean IPSS at both the 6-week and 12-week evaluations. There was no significant group difference in mean IPSS at 6 weeks. The mean (SD) change in IPSS score from baseline to the end of the study was 9.98 (0.95) in the group receiving tamsulosin-MR ($P < .001$) and 8.38 (0.45) in the group receiving alfuzosin-SR ($P < .001$). At the end of 12 weeks, the group receiving tamsulosin-MR had significantly lower IPSS than the group receiving alfuzosin-SR ($P = .048$).

Table 1. Means and Standard Deviations (SD) for the International Prostate Symptom Score (IPSS) and Maximum Urinary Flow Rate (Qmax) at Baseline and During Treatment With Tamsulosin-MR or Alfuzosin-SR; Probability of Significant Differences (N = 88).
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Outcome Measure	Tamsulosin-MR (n = 44)		Alfuzosin-SR (n = 44)		*P*
	Mean	SD	Mean	SD	
IPSS					
Baseline	20.08	3.52	19.60	3.26	.542
6 weeks	15.18	2.97	15.52	2.89	.433
12 weeks	10.10	2.57	11.22	2.81	.048
Qmax					
Baseline	7.37	2.44	6.40	2.01	.100
6 weeks	14.47	4.83	14.63	3.86	.883
12 weeks	25.83	6.68	22.80	4.58	.045

There was progressive improvement in the Qmax of all patients during the treatment period. At 6 weeks and 12 weeks, patients in both treatment groups showed a significant improvement in Qmax when compared with the baseline ($P < .001$). There was no significant difference in the mean Qmax of patients in the 2 treatment groups at 6 weeks. However, at 12 weeks, the group receiving tamsulosin-MR had a significant increase from baseline of 18.46 mL/s (4.24), compared with 16.40 ± 2.54 mL/s for the group receiving alfuzosin-SR ($P = .045$).

Adverse Events

A total of 25 adverse events were reported by 14 patients (Table 2). Of these, 9 adverse events were reported by 6 patients (13.63%) taking tamsulosin-MR; 16 adverse events were reported by 8 patients (17.78%) taking alfuzosin-SR. There was no statistically significant difference in the adverse event rate between the groups. All adverse events were mild and transient except for that reported by the 1 patient taking alfuzosin-SR, who withdrew from the study because of severe dizziness and syncope. Dizziness (n=4) and impotence (n=2) were the most common adverse events reported in the group taking tamsulosin-MR; dizziness (n=5) and fatigue (n=4) were the most common adverse events in the group taking alfuzosin-SR.

Table 2. Number of Adverse Events During Treatment With Tamsulosin-MR or Alfuzosin-SR (n = 14; N = 88).
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Adverse Event	Tamsulosin-MR (n = 6)	Alfuzosin-SR (n = 8)
Dizziness	3	5
Headache	1	2
Syncope	1	2
Malaise	0	1
Hypotension	0	2
Fatigue	1	4
Impotence	2	0
Ejaculatory disorder	1	0
Total	9	16

DISCUSSION

A decade ago, surgery and watchful waiting were the only accepted management options for BPH. With the advent of urospecific alpha blockers, the paradigm has shifted from surgical to medical intervention and from an inpatient to an outpatient setting. The α-1 blockers tamsulosin and alfuzosin have become the most commonly prescribed drugs for BPH. The present study was designed to compare the effects of tamsulosin-MR 0.4 mg once daily and alfuzosin-SR 10 mg once daily on IPSS, uroflow analysis, and adverse events.

Both patient groups had significant, progressive changes in IPSS score from baseline to the end of the study. The mean decrease in IPSS score from baseline to the end of the study was 9.98 in the group receiving tamsulosin-MR and 8.38 in the group receiving alfuzosin-SR. Previous clinical studies with tamsulosin for 4-24 weeks showed a mean decrease in IPSS ranging from 4.9-9.7 [11-14]. At the end of 12 weeks, the group receiving tamsulosin-MR in the present study had a significantly lower IPSS than the group receiving alfuzosin-SR ($P = .048$). The group difference was small, with the mean values differing only by 1 point. Lapitan et al [10] compared tamsulosin 0.2 mg and alfuzosin 10 mg once daily and found that patients receiving

both medications had reductions in IPSS, with no statistically significant group difference after 8 weeks of treatment. Similar results were reported by Buzelin et al [9], who compared tamsulosin 0.4 mg once daily with alfuzosin 2.5 mg 3 times daily and found no significant group difference in the Boyarsky symptom score at the end of 12 weeks.

Both groups in the present study had significant, progressive changes in Qmax from baseline to the end of the investigation. The largest increase in Qmax was obtained at 12 weeks in both groups, but the group taking tamsulosin-MR had a significantly higher Qmax at 12 weeks (P = .045). The group difference was small, with the mean Qmax differing by only 3 mL/s. Neither Buzelin et al [9] nor Lapitan et al [10] found any statistically significant difference in Qmax between the groups taking tamsulosin or alfuzosin after 12 weeks and 8 weeks, respectively.

In the present study, tamsulosin-MR and alfuzosin-SR were both well tolerated. With 1 exception, the treatment adverse events were not serious enough to warrant withdrawal from the study. Side effects were infrequent and compliance was equally good with both drugs. There was no statistically significant difference in the adverse event rate between the groups. Schwinn et al [15] reviewed reports of frequent dizziness, fatigue, and headache associated with alfuzosin; 1 adverse event warranted discontinuation of therapy. Retrograde or abnormal ejaculation has been previously reported in association with tamsulosin [16,17]. This was a complaint of only 1 patient receiving tamsulosin in the present study. No patients taking alfuzosin reported sexual side effects. Patient sexual activity was not specifically determined as part of the present study, so it is possible that they were not sexually active.

It appears that both tamsulosin-MR and alfuzosin-SR have good efficacy in improving symptoms of BPH. Tamsulosin-MR showed significant improvement in IPSS score and Qmax over alfuzosin-SR after 12 weeks of therapy, but the group differences were small. The safety profile is comparable and both drugs were well tolerated by the patients. The fact that the significant group difference did not appear until the evaluation at 12 weeks indicates that a study of longer duration may show a more clear-cut dissimilarity between treatments.

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Conflict of Interest: none declared

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