



Evaluation of Efficacy and Safety Profile of Alfuzosin and Tamsulosin in Benign Prostatic Hyperplasia

Praveen R^{1*} and Kumar TN²

^{*1}Department of Pharmacology, Venkateshwara Institute of Medical Sciences, Gajraula, Uttar Pradesh, Pin code: 244236, India

²Department of Pharmacology, Sree Narayana Institute of Medical Sciences, Kunnukara, Kerala, Pin code: 683594, India

ABSTRACT

Aim: To compare the safety and efficacy profile of uroselective alpha-1 blocker-Alfuzosin in comparison to an alpha-1A receptor subtype specific antagonist-Tamsulosin in Benign Prostatic Hyperplasia. **Materials and Methods:** A prospective, open labelled, alternative randomised, single centred study in a tertiary hospital where the patient visiting Urology department with diagnosis of Benign Prostatic Hyperplasia (BPH). The data include demographics data like patient ID, age of the patient, dates of visiting to the OPD and other details like history of presenting illness etc. An approved proforma was administered to patients enlisting vital signs like blood pressure, heart rate, systemic examination like cardiovascular system and abdomen examination including digital per rectal examination. Laboratory investigations included RBS, prostate specific antigen and urine analysis. The ultrasonography investigations were done to measure the size of the prostate and post void residual urine. The uroflow meter analysis was done as an OPD procedure to assess the amount of urine voided during urination. **Results:** In our study, patients receiving Tamsulosin 0.4mg once daily and Alfuzosin 10 mg once daily showed a significant improvement in post void residual urine, uroflow rates and symptoms at 1st and 3rd months. The improvement in the above parameters was found to be statistically insignificant between the two groups. The adverse effects like headache, fatigue and dizziness were reported in both the groups. **Conclusion:** The improvement in the treatment of benign prostatic hyperplasia with tamsulosin 0.4mg once daily and alfuzosin 10 mg once daily was similar.

Keywords: Tamsulosin, Alfuzosin, Benign prostatic hyperplasia, Post void residual urine

INTRODUCTION

Elderly males usually get affected by enlarged prostate [1] which has got a huge impact in medical practice nowadays [2]. The pathological changes in prostate results in voiding symptoms and can affect the kidney and urinary bladder. There is a significant improvement in the management of BPH with an advanced science and technology [3]. When it comes to medical therapy, lot of drugs can improve symptoms and restore the prostate function (alpha-1 receptor antagonists, 5-alpha reductase inhibitors,

*Corresponding Author

rajdrpraveen[at]gmaildotcom

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phytotherapy, Gonadotropin releasing hormone analogues and androgen receptor blockers). Among the alpha-1 receptor blockers, the newer alpha-1 blocker Alfuzosin has been claimed to be uroselective [4] and is nowadays being used in the place of specific alpha-1A receptor (bladder neck specific) antagonist Tamsulosin. The present study of comparing the efficacy and the safety profile of the above two drugs has been

undertaken as specific studies are lacking in this aspect.

SUBJECTS AND METHODS

A prospective study was carried-out in patients attending urology department between 2005–2008. Patient details were captured in a standard performa and the study was approved by institutional ethics committee.

The study inclusion criteria

1. Patients greater than 45 years of age with clinical diagnosis of symptomatic BPH
2. IPSS score more than four at the base line
3. Prostate Specific Antigen < 10 (ng/mL)
4. Patients with maximum urinary flow rate of ≤ 12 mL/s but ≥ 4 mL/s for a voided volume of ≥ 120 mL

Exclusion criteria [5,6]

1. Patients suspected to be having carcinoma of prostate
2. PSA > 10 (ng/mL)
3. Neurogenic bladder cases
4. Patients with urethral strictures
5. Patients with urinary bladder stones
6. Any patients with history of prostate surgery
7. Patients with known hypersensitivity to alpha-1 blockers

Relevant data were taken from the patients with benign prostatic hyperplasia. The data included were patient ID, age of the patient, dates of visiting the OPD and the dates of admission and history of presenting illness. The proforma also enlisted general physical examination, vital signs like blood pressure, heart rate, systemic examination like cardiovascular system and abdomen examination including digital per rectal examination. Laboratory investigations included RBS, prostate specific antigen and urine analysis. The ultrasonography investigations were done to measure the size of the prostate and post void residual urine. The uroflow meter analysis was done as an OPD procedure to gauge the voided urine amount. The assessment of the symptoms was done by using International Prostatic Symptom Score (IPSS) which was given to patient on the very first time of visiting the OPD, first month and then the third month, to assess the symptomatic improvement. The uroflowmetry analysis, ultrasonography of the size of the prostate and the post void residual urine was done at the base line, first month, and on the third month of the follow up to assess the clinical improvement. The respective drugs i.e. Alfuzosin 10 mg and Tamsulosin 0.4 mg once daily were given to the consecutive patients. The patients were advised to come for the follow up on the first month and the third month of the treatment. The data obtained were analysed by using student two tailed, independent test to study between the two groups. A repeated measure ANOVA has been used to find the significance of the study parameters between onset, first month and third month in each group.

RESULTS

Age distribution

There was no relevant statistical difference between the treatment groups in terms of demographic changes as the mean being 62.57 years in the tamsulosin group and 64.13 years in the alfuzosin group. Comparison of IPSS scores between the two groups. The comparison of IPSS between the tamsulosin and alfuzosin, the mean change from baseline in the total IPSS of tamsulosin and alfuzosin group till the end of third month was highly significant ($p < 0.001$). But the change is non-significant, when compared across the group at the first and third months (Table 1).

Table 1: IPSS score at baseline and at 3rd month in the treatment arms

IPSS Score	Tamsulosin		Alfuzosin		p-value
	Mean	SD	Mean	SD	
Onset	26.73	4.45	26.60	4.87	0.912
1st Month	15.73	3.25	17.03	3.66	0.437
3rd Month	9.13	2.34	9.10	2.22	0.574
% Change	64.7 %		65.8%		
Significance	<0.001		<0.001		

Comparison of PSA (ng/mL) score between two groups: There is no change in the PSA values in both the groups until the end of the study. The PSA remains unaltered in each and every time point.

Comparison of PVRU (mL) score between two groups: The effects of tamsulosin and alfuzosin treatment on the post void residual urine is shown in the below figure, there were significant reductions from baseline to the end of third month in both the treatment groups ($p < 0.001$). But the alfuzosin has significantly reduced the post void residual urine ($p < 0.001$) at third month more when compared to the tamsulosin group.

Comparison of Prostate Ultra sound (cc) score between two groups: There is no significant change in the size of the prostate in both the tamsulosin and alfuzosin groups.

Comparison of URO flow (mL/s) score between two groups: The changes in Qmax during the active treatment are shown in figure below there was a significant increase in Qmax relative to baseline in both treatment groups at each time ($p < 0.001$). The maximum increase in the Qmax was obtained at third month in both the groups (Table 2).

Table 2: URO Flow analysis at Baseline, 1st and 3rd month between the two treatment arms

URO Flow	Tamsulosin		Alfuzosin		p-value
	Mean	SD	Mean	SD	
Onset	7.37	2.44	6.40	2.01	0.100
1st month	14.47	4.83	14.63	3.86	0.883
3rd month	25.83	6.68	22.80	4.58	0.045
% Change	250.47		256.25		-
Significant	<0.001		<0.001		

DISCUSSION

Benign prostatic hyperplasia is one of the most common conditions affecting elderly males with a resultant impact on the medical practice as the elderly constitute an increasing population not only in India but also throughout the world [2]. A decade back, surgery and watchful-waiting were the only accepted management options for BPH [7]. Now there has been a drastic decline in the surgery as medication has become the most frequently used treatment for BPH that has been a major change in urological clinical practice. Alpha-1 blockers have become the major drugs for BPH among which Alfuzosin has been claimed to be uroselective Alpha-1 blocker and Tamsulosin Alpha-1A prostate specific blocker [8]. In our study, we have analysed the efficacy of Alfuzosin 10mg once daily, and tamsulosin 0.4mg once daily on IPSS, PSA, PVRU, size of the prostate, uroflow analysis and per rectal examination. When IPSS between tamsulosin and alfuzosin was compared, treatment with tamsulosin resulted in a significant decrease in the mean change from baseline in the total IPSS. The improvement in the total IPSS with tamsulosin was apparent at the first assessment (4 weeks) and was maintained throughout the study. The mean change from baseline in the total IPSS after 12 weeks of treatment was significant ($p < 0.001$) in concurrence with the study of Nordling J [8]. With regard to that of alfuzosin, though there was decrease in total IPSS, the change was apparent like that of tamsulosin but less so though statistically significant. The mean reduction in total symptom score at the endpoint was 9.43(64.7%) in the tamsulosin group and 9.10(65.8%) in alfuzosin group [5]. Perhaps a study of longer duration of six months or more may show defined difference in improvement in the effect of one drug over the other. In analysing the PSA values, in our study where the follow-up was up to 12 weeks has shown no statistical change in both the groups. In the study conducted by Park CH et al, which involved 211 patients treated with tamsulosin, also shows non-significant change in the PSA values up to 52 weeks [1].

In the present study with both Tamsulosin and Alfuzosin the post void residual urine showed a significant reduction from the baseline till the third month ($p < 0.001$), in concurrence with the study of Van et al. [9] involving 101 patients on Alfuzosin and 86 patients on tamsulosin. In the present study, it was also observed that post void residual urine in the alfuzosin group was lower than tamsulosin at the end of third month, whereas in the first month the values were practically same and the difference was insignificant, however it needs much longer follow-up to say that in the long run alfuzosin will be superior to tamsulosin or not in reducing the post void residual urine. As for the efficacy is concerned, in reduction of IPSS score and post void residual urine, both the drugs, have not shown any superiority of one over the other. In the uroflowmetry analysis, there was a significant increase in Qmax relative to baseline in both treatment groups at each time ($p < 0.001$). i.e. Baseline to first month and from first month to third month. The maximum increase in the Qmax was obtained at third month in both the groups. As per the meta-analysis of two European randomized, double blind, multicentric studies with tamsulosin for 12 weeks, a significant improvement in Qmax from baseline has been reported [6], and similar findings have been found in the present study also [7].

As for the size of the prostate is concerned, in our study there was non-significant change in the size of the prostate in both the groups which was also similar to a study done by Rossette JJ [8]. Both the drugs may not have altered the prostatic size because the enlargement of the prostate depends on the tissue androgen namely dihydrotestosterone which is converted from testosterone by 5-alpha reductase. In the present study side effects were low and compliance was equally good with both the drugs. Retrograde ejaculation was not complained by any of our patients in the study, however most of the patients were elderly coming from a low socio-economic status with a rural background who also followed good old Indian traditions like staying in a joint family how much ever the couples believed in

the indulgence of the sexual activity is uncertain. After the present study, it appears that both Alfuzosin and Tamsulosin have been almost similar in their effects and neither of them showing significant improvement over the other in the parameters studied except in PVRU. Even the safety profile also is not better in one over than the other. With the limited study period as in the present study, it may be that either drug may be used in BPH with almost equal effectiveness, except better tolerability of tamsulosin because of lesser alterations in the blood pressure [7].

CONCLUSION

The results of the present study show that tamsulosin 0.4mg once daily and alfuzosin 10 mg once daily in the treatment of BPH produce comparable improvement in urinary flow rates, symptoms and post void residual urine and both the drugs were well tolerated, thus maintaining the improvement in the lower urinary tract symptoms. However, alfuzosin significantly improved the post void residual urine at the third month when analysed with tamsulosin at the same month.

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