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Research Article

COMPARISON OF EFFICACY OF TAMSULOSIN, ALFUZOSIN, AND SILODOSIN IN THE MANAGEMENT OF BENIGN PROSTATIC HYPERPLASIA

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ABSTRACT

Objectives: This study was done to determine the efficacy of alpha-1 adrenoceptor blockers such as tamsulosin, alfuzosin, and silodosin in patients with the lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH) over 6 months by assessing change in international prostate symptom score (IPSS), quality of life scale for urinary symptoms (Bother score), and improvement in peak urine flow rate (Qmax) from baseline. We also tried to identify any adverse drug reactions (ADRs) caused by these drugs.

Methods: A prospective observational study was conducted in 291 patients with LUTS secondary to BPH attending urology outpatient department of a tertiary care center for 1 year. Ninety-seven patients in each group received tamsulosin, alfuzosin, or silodosin once daily. IPSS, Qmax, and the quality of life scale for urinary symptoms by Bother score were assessed at 1st, 3rd, and 6th month of treatment period. ADR was noted and recorded in ADR reporting form.

Results: IPSS, mean bother score, and mean Qmax showed significant improvement from the baseline in each follow-up visit at 1, 3, and 6 months for all the three groups, but maximum was for alfuzosin and was found to be statistically significant ($p<0.001$). Two patients developed adverse drug reaction during the study; asthenia in tamsulosin group and hypotension in Silodosin group.

Conclusion: Patients on alfuzosin showed maximum improvement in the values of IPSS, Bother score, and Qmax in BPH patients as compared to tamsulosin and silodosin. Alfuzosin would be a better choice in the treatment of LUTS due to BPH.

Keywords: Benign prostatic hyperplasia, Alpha 1 adrenoceptor blocker, Tamsulosin, Alfuzosin, Silodosin, Lower urinary tract symptoms.

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INTRODUCTION

Benign prostatic hyperplasia (BPH) is a common and progressive disease affecting elderly males, often associated with the lower urinary tract symptoms (LUTS) which include nocturia, urgency, urinary frequency, and benign prostatic obstruction [1,2]. BPH develops as an age-related phenomenon in nearly all men, starting at approximately 40 years of age [3]. At present, two main categories of drugs are used for the treatment of symptomatic BPH such as α-1 adrenergic receptor antagonist which blocks the α1-adrenoreceptors (e.g., doxazosin, terazosin, tamsulosin, alfuzosin, and silodosin) and 5α reductase inhibitors which inhibit the enzyme 5α-reductase (e.g., finasteride and dutasteride) thereby preventing the conversion of testosterone to dihydrotestosterone and depriving the prostatic tissue of trophic androgenic influence [4]. The former category provides rapid symptom relief starting within 2–6 weeks, while the latter takes 6 months or longer for symptom relief [5].

Alpha 1-adrenoceptor blockers are currently the recommended first-line therapies for benign prostatic hyperplasia (BPH), because they are efficacious and less expensive with fewer adverse drug reactions (ADRs). They act principally by blocking α1A-adrenoreceptors, which is most prevalent in the prostatic smooth muscle and produce relaxation in the smooth muscle component of the prostate [6]. Our objective was to compare the efficacy and safety of tamsulosin, alfuzosin, and silodosin in LUTS due to BPH.

METHODS

This was a prospective observational study conducted in patients with LUTS [6] secondary to BPH attending urology outpatient department of a tertiary care center, central Kerala. After getting approval from the Institutional Review Board (IRB No- 96/2018) and written informed consent, the study was done on 291 patients. The severity of LUTS was assessed by the international prostate symptom score (IPSS) [7], based on the answers to seven questions regarding urinary symptoms. Peak urine flow rate [8] was assessed by uroflowmetry, a routine follow-up procedure as per the department protocol. Quality of life scale for urinary symptoms was assessed using Bother score [9]. The inclusion criteria were male patients ≥45 years with symptomatic BPH with IPSS of ≥8; Qmax <15 mL/s, but ≥4 mL/s with a voided volume of >150 mL and prostate size ≤40 g. Patients with history of severe hepatic or renal insufficiency, urethral stricture, neurogenic bladder, urethral or prostatic surgery, esophageal or intestinal obstruction, malignancy of genitourinary and gastrointestinal tract, and those with concomitant use of 5α reductase inhibitors were excluded from the study.

The consultant urologist recruited patients into three groups A, B, and C consecutively. Group A received tamsulosin tablet/capsule 0.4 mg (before meals) given once daily at bedtime, Group B alfuzosin SR 10 mg (immediately after meals) once daily at bed time, and Group C silodosin 8 mg (before breakfast) once daily in the morning. The treatment response toward therapy was monitored during follow-up visits after 1, 3, and 6 months. Any adverse reaction during the course of treatment such as asthenia, dizziness, nasal congestion, syncope, hypotension, ejaculation, and erection problem was recorded in ADR reporting form.

The data were entered in Microsoft Excel and analyzed at the end of study using statistical software SPSS 16.0 version. Difference in IPSS, Bother score, and Qmax among the three groups was analyzed using repeated measures analysis of variance with Bonferroni *post hoc* correction. Follow-up visits between the baseline and each visits were analyzed using Paired t-test and significance was fixed at $p<0.001$.

RESULTS

Total number of participants were 291 with 97 in each group. The mean age of participants in years was 66.97±7.34, 57±8.34, and 65.92±8.19 in tamsulosin, alfuzosin, and silodosin groups, respectively.

As shown in Fig. 1 among those in the tamsulosin and silodosin group, 72.16% and 68.04% belonged to 61–75 years, respectively, while those in alfuzosin group, majority 64.94% were in 45–60 years.

There was no statistically significant difference in the baseline values of IPSS; however, the three groups differed in age distribution, Bother Score, and Qmax, as shown in Table 1.

As shown in Fig. 2, when comparing the duration of LUTS among various groups, majority 46.39%, 38.14%, and 45.36% were having a duration of >12 months in tamsulosin, alfuzosin, and silodosin groups, respectively. On Kruskal–Wallis, the duration of LUTS was comparable with p=0.36.

On comparing the IPSS1 and IPSS6 score among various drug groups, the difference was found to be statistically significant, as shown in Table 2. *Post hoc* Bonferroni analysis of showed that there was significant difference between tamsulosin and alfuzosin (IPSS 1-p=0.005; IPSS6-p<0.001) and alfuzosin and silodosin (IPSS 1-p=0.014; IPSS 6-p<0.001). On comparing the Bother 1 and Bother 6 score among the different drug groups, the difference was found to be statistically significant, as shown in Table 2. *Post hoc* Bonferroni analysis of Bother 1 showed that there was significant difference between tamsulosin and alfuzosin (p<0.001) and alfuzosin and silodosin (p=0.001). *Post hoc* Bonferroni analysis of Bother 6 showed that there was significant difference between tamsulosin and alfuzosin (p<0.001), tamsulosin and silodosin (p=0.043), and alfuzosin and silodosin (p<0.001). Qmax 1 and Qmax 2 score among various drug groups was found to be statistically significant. *Post hoc* Bonferroni analysis of showed that there was significant difference between tamsulosin and alfuzosin (Qmax 1 and Qmax 6-p<0.001) and alfuzosin and silodosin (Qmax1-p=0.002; Qmax6-p<0.001).

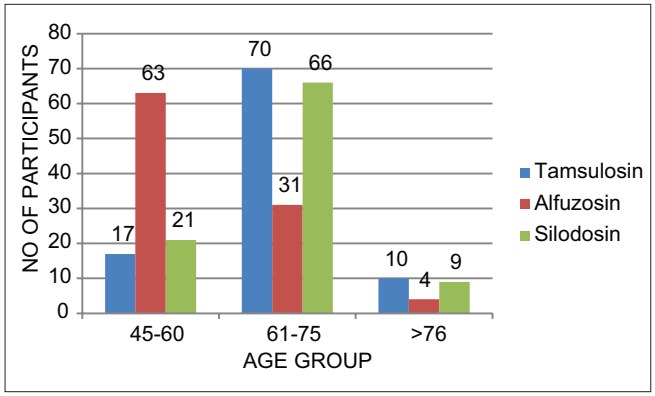

Fig. 1: Age-wise distribution of patients on tamsulosin, alfuzosin, and silodosin

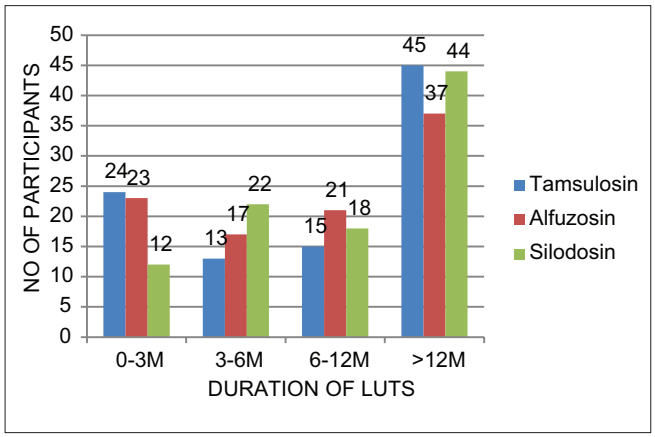

Fig. 2: Distribution of lower urinary tract symptoms in benign prostatic hyperplasia patients

As shown in Table 3, when comparing the IPSS score of tamsulosin at baseline with 1 month, 3 months, and 6 months, the mean±SD was reduced from 23.45±5.4 to 18.85±4.3 at 1 month, 14.95±3.7 at 3 months and 11.66±3.62 at 6 months which was found to be statistically significant with p<0.001. Similarly, the mean±SD for alfuzosin at baseline declined from 21.92±5.6 to 17.09±3.9, 13.2±3.1, and 9.51±2.6 at the follow-ups of 1st, 3rd, and 6th months which was found to be statistically significant with p<0.001. In the silodosin group, also, there was a statistically significant reduction in the mean IPSS score from 23.27±5.0 to 18.68±3.4 and 14.72±2.5 and 11.03±2.4 at 1, 3, and 6 months of follow-ups.

As shown in Table 4, similar to IPSS values, there was a statistically significant difference in the Bother score from the baseline at each visit in all the three groups of drugs.

As shown in Table 5, the Qmax at baseline was 7.79±3.8 which increased to 10.88±4.4, 14.21±4.9 and 17.03±5.6 at 1, 3, and 6 months and was found to be statistically significant with p<0.001. This was similar in the case of alfuzosin and silodosin where the Qmax at baseline increased from 9.82±3.9 to 21.52±5.6 in the Alfuzosin group and from 8.31±3.3 to 17.99±4.9 in the Silodosin group at the end of 3 months. All the values were statistically significant.

As shown in Figs. 3-5, the IPSS score, bother score, and Qmax were found to be improving at each follow-up visits. Decrease in the IPSS score and bother score indicated that the patient was showing improvement of LUTS. Increase in Qmax value indicates that the patient was showing improvement of LUTS.

There were no serious ADRs in any of the study groups warranting discontinuation of study medication. Only two out of 291 patients developed adverse drug reaction. One patient from Tamsulosin group developed asthenia and one patient from silodosin group developed hypotension. However, they did not discontinue the treatment.

DISCUSSION

Table 1: Baseline characteristics

PARAMETERS	Tamsulosin	Alfuzosin	Silodosin	F-value	p-value
Age	66.97±7.34	57±8.34	65.92±8.19	33.79	<0.001
IPSS	23.45±5.1	21.9±5.6	23.27±5.0	2.49	0.084
Bother score	5.24±0.8	4.80±1.0	5.12±0.9	6.06	0.003
Qmax	7.7±3.8	9.82±3.9	8.3±3.3	7.96	<0.001

IPSS: International prostate symptom score

Table 2: Comparison of IPSS, bother, and QMAX at 1st and 6th months of treatment

PARAMETERS	Tamsulosin	Alfuzosin	Silodosin	F-value	p-value
IPSS1	18.85±4.3	17.09±3.9	18.68±3.4	6.09	0.003
IPSS6	11.66±3.7	9.51±2.6	11.03±2.4	13.98	<0.001
Bother1	4.2±0.8	3.65+0.9	4.12±0.8	11.33	<0.001
Bother6	2.12±1.3	1.17±0.9	1.77±0.8	22.70	<0.001
Qmax1	10.88±4.4	13.37±4.3	11.33±3.7	10.06	<0.001
Qmax6	17.03±5.6	21.52±5.6	17.99±4.9	18.70	<0.001

IPSS: International prostate symptom score

Table 3: Comparison of IPSS from baseline in follow-up visits

IPSS	Tamsulosin mean±SD mean diff±SD (95%CI)	Alfuzosin mean±SD mean diff±SD (95%CI)	Silodosin mean±SD mean diff±SD (95%CI)	p-value
Baseline	23.45±5.4	21.92±5.6	23.27±5.0	<0.001
1 month	18.85±4.3	17.09±3.9	18.68±3.4	
	4.61±2.4	4.83±2.9	4.59±2.6	
	(4.12–5.09)	(4.25–5.41)	(4.06–5.13)	
3 months	14.95±3.7	13.2±3.1	14.72±2.5	<0.001
	8.51±3.5	8.71±3.8	8.55±3.8	
	(7.79–9.21)	(7.96–9.47)	(7.77–9.33)	
6 months	11.66±3.62	9.51±2.6	11.03±2.4	<0.001
	11.79±4.3	12.41±4.7	12.24±4.7	
	(10.93–12.66)	(11.47–13.35)	(11.28–13.20)	

IPSS: International prostate symptom score

Table 4: Comparison of bother score of baseline with follow-up visits

Bother score	Tamsulosin mean±SD mean diff±SD (95%CI)	Alfuzosin mean±SD mean diff±SD (95%CI)	Silodosin mean±SD mean diff±SD (95%CI)	p-value
Baseline	5.24±0.8	4.40±1.0	5.12±0.9	<0.001
1 month	4.20±0.8	3.65±0.9	4.12±0.8	
	1.04±0.7	1.14±0.8	1.00±0.7	
	(0.91–1.18)	(0.99–1.29)	(0.85–1.15)	
3 months	3.00±0.9	2.37±0.8	2.89±0.8	<0.001
	2.24±0.8	2.43±0.9	2.24±0.9	
	(2.07–2.41)	(2.25–2.61)	(2.04–2.44)	
6 months	2.12±1.2	1.17±0.9	1.77±0.8	<0.001
	3.11±1.3	3.62±1.2	3.35±1.1	
	(2.85–3.38)	(3.38–3.86)	(3.13–3.57)	

Table 5: Comparison of Qmax from baseline with follow-up visits at 1, 3, and 6 months

Qmax	Tamsulosin mean±SD mean diff±SD (95%CI)	Alfuzosin mean±SD mean diff±SD (95%CI)	Silodosin mean±SD mean diff±SD (95% CI)	p-value
Baseline	7.79±3.8	9.82±3.9	8.31±3.3	<0.001
1 month	10.88±4.4	13.37±4.3	11.33±3.7	
	−3.08±1.5	−3.55±1.3	−3.02±2.0	
	(−3.38−−2.78)	(−3.82−−3.28)	(−3.43−−2.61)	
3 months	14.21±4.9	17.34±4.9	14.67±4.1	<0.001
	−6.42±2.4	−7.52±2.4	−6.36±2.8	
	(−6.91−−5.94)	(−7.99−−7.04)	(−6.93−−5.77)	
6 months	17.03±5.6	21.52±5.6	17.99±4.9	<0.001
	−9.24±3.4	−11.70±3.5	−9.68±4.1	
	(−9.92−−8.56)	(−12.41−−10.99)	(−10.50−−8.86)	

BPH is the most common urological problem in ageing men manifesting as urinary flow obstruction [10]. According to the European Association of Urology 2011 guidelines, α-blockers are currently the preferred first-line therapy for all men with moderate or severe LUTS [7,11].

In our study, the minimum age of patients included was 46 years and the maximum was 87 years. The mean age of those in tamsulosin, alfuzosin, and silodosin was 66.97±7.34 years, 57±8.34 years, and 65.92±8.19 years, respectively. In the study by Manjunatha *et al*., the mean age of those in tamsulosin, alfuzosin, and silodosin group was 63.60±9.05, 63.43±8.91, and 64.00±11.14, respectively. In the study by Manohar *et al*., the mean age of patients was 58.47±6.16, 56.90±10.26, and 59.10±8.79 in tamsulosin, alfuzosin, and silodosin groups, respectively. Majority patients were having >12 months of duration of LUTS in tamsulosin, alfuzosin, and silodosin group in our study.

All three drugs showed statistically significant reduction in IPSS scores at 1, 3, and 6 months compared to baseline.

The mean IPSS values were decreasing in each follow-up visit for all the three drugs and the maximum improvement was seen with alfuzosin. In the study by Manjunatha *et al*., there was progressive decrease in the baseline IPSS at different follow-up visits at 2 weeks, 4 weeks, 8 weeks, and 12 weeks for tamsulosin, alfuzosin, and silodosin [1]. The net decrease after 12 weeks was 72.12%, 88.18%, and 82.23% for tamsulosin, alfuzosin, and silodosin, respectively, and the maximum improvement in IPSS was seen with alfuzosin which is concurrent to our study. In the study by Manohar *et al*., the mean IPSS scores were improving in follow-up visits at 1 week, 4 weeks, and 12 weeks in all the three drugs and the maximum improvement was seen in the Silodosin group [6]. In the study by Manjunatha *et al*., they also analyzed the voiding and storage scores of IPSS and followed up at 2, 4, 8, and 12 weeks. In the study by Manohar *et al*., they also analyzed the post void residue by transabdominal ultrasound scan and followed up at 1, 4, and 12 weeks.

The mean bother score was also increasing in each follow-up visit for all the three drugs and the maximum improvement was seen with alfuzosin. In the study by Manjunatha *et al*., the rate of decrease in bother score at the end of study period for tamsulosin, alfuzosin, and silodosin was 77.75%, 90.06%, and 82.23%, respectively, and the maximum improvement was seen with alfuzosin group which is concurrent to our study [1]. In the study by Manohar *et al*., the mean bother score was improving in follow-up visits at 1 week, 4 weeks, and

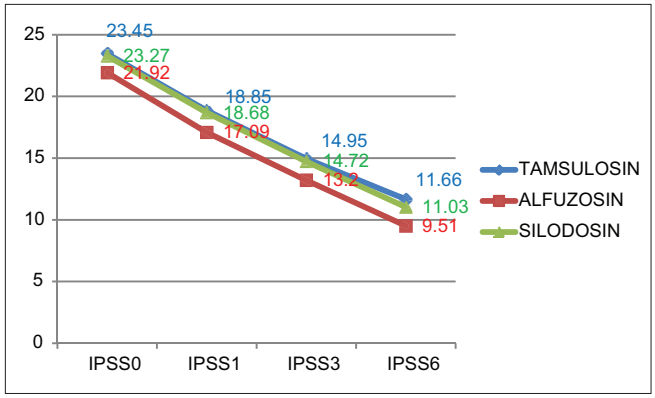

Fig. 3: Comparison of international prostate symptom score among three groups

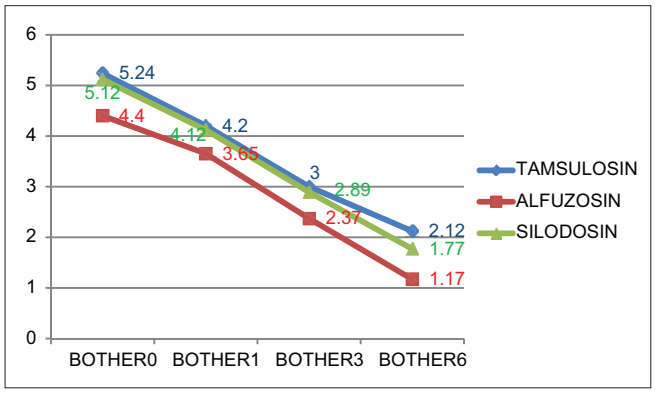

Fig. 4: Comparison of bother score among three groups

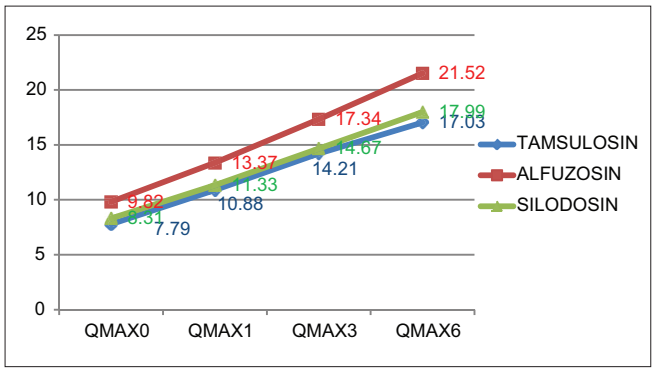

Fig. 5: Comparison of Qmax among three groups

12 weeks in all the three drugs and the maximum improvement was seen in silodosin group [6].

The mean bother score was increasing in each follow-up visit for all the three drugs and the maximum improvement was seen with alfuzosin. Jardin *et al.* reported the first large-scale, multicentric, randomized, and placebo-controlled trial demonstrating that alfuzosin was safe and effective for the treatment of BPH [12]. A long-term open-label extension study showed that the effectiveness of alfuzosin was durable up to 30 months [13].

In the study by Manjunatha *et al.*, there was a slight decline in the mean Qmax observed between the 4th and 12th week in all the three study groups. The improvement in Qmax was modest with alfuzosin and tamsulosin and minimal with silodosin [1]. In the study by Manohar *et al.*, the mean Qmax score was also improving in follow-up visits at 1 week, 4 weeks, and 12 weeks in all the three drugs and the maximum improvement was seen in silodosin group [6].

ADR like asthenia in tamsulosin group (one patient) and hypotension in silodosin group (one patient) were noted. There was only one episode of these ADR, and hence, neither the drug was stopped nor the dose of drug was changed. The patients recovered within few hours and it was uneventful. In the study by Manjunatha *et al.*, upper respiratory tract infection was the most common adverse event (n=14, 10, and 14 with alfuzosin, tamsulosin, and silodosin, respectively) followed by dizziness (n=13, 09, and 10 with alfuzosin, tamsulosin, and silodosin, respectively) in all the three groups. Two patients with alfuzosin and three patients with tamsulosin had a significant QTc prolongation (>45 ms). The incidence of ejaculatory dysfunction was highest with silodosin (n=9) [1]. In the study by Manohar *et al.*, dizziness was the most common side effects in all of the three groups. Abnormal ejaculation, insomnia, and syncope were observed only in this silodosin group. Fatigue was observed in groups tamsulosin and alfuzosin. Headache was observed only in six patients in alfuzosin group at 1 and 12 weeks [6].

CONCLUSION

The values of IPSS and bother score among tamsulosin, alfuzosin, and silodosin were found to be progressively decreasing from the baseline which indicated improvement at each follow-up visits. Maximum improvement was seen with alfuzosin. When comparing the peak urine flow rate Qmax, all the three drugs were showing improvement from the baseline and the maximum improvement was seen with alfuzosin. One patient in tamsulosin group developed asthenia and one patient in silodosin group developed hypotension during this study.

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AUTHOR'S CONTRIBUTION

Dr. Aparna R: Design, data collection, data analysis. Dr. Syam Sreedharan: Provided guidance and data review. Dr. Fredrick Paul: Guidance and data review. Dr. Harisankar K N: Guidance and data review. Dr. Brighty Mathew: Data collection and review.

CONFLICTS OF INTEREST

The authors confirm that this article content has no conflicts of interest.

FINANCIAL COMMITMENTS

None.

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