ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 14, Issue 2, 2021

Online - 2455-3891
Print - 0974-2441

Research Article

ASSESSMENT OF COMPARATIVE PATIENT SATISFACTION AND SIDE-EFFECTS ASSOCIATED WITH TAMSULOSIN VERSUS SILODOSIN THERAPY IN BENIGN PROSTATE HYPERPLASIA

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Received: 5 October 2020, Revised and Accepted: 2 December 2020

ABSTRACT

Objective: The aim of our study was to assess the comparative patient satisfaction and side-effects of the currently prescribed drugs – tamsulosin and silodosin for benign prostatic hyperplasia (BPH).

Methods: A prospective study was conducted in a total of 110 BPH patients from the Department of Urology for a period of 6 months. Fifty-five patients in each group received silodosin 8 mg or tamsulosin 0.4 mg once daily. Data were collected using a suitably designed pro forma and the patient satisfaction was assessed with patient's perception of study medication (PPSM) scale. International prostate symptom score (IPSS) was used for assessing the severity of symptoms.

Results: The current study found that the treatment had a significant effect on improving scores of PPSM and IPSS at which all changes were significant at $p<0.01$ (paired t-test). An independent t-test showed that silodosin group had a greater improvement in PPSM scores – PPSM total by 40.4%, PPSM global by 43.7%, and PPSM pain by 0.39% which was supported by corresponding decline in IPSS scores. The side effects reported for tamsulosin were headache (5.5%), dizziness (5.5%), dry mouth (3.6%), and postural hypotension (14.4%) and those reported for silodosin were myalgia (5.5%), dizziness (7.3%), diarrhea (1.8%), and postural hypotension (10.9%).

Conclusion: Patient satisfaction was improved by both the alpha blockers but silodosin showed a significantly greater increase in patient satisfaction than tamsulosin. Thus, silodosin is the better drug of choice.

Keywords: Benign prostate hyperplasia, International prostate symptom score, Patient perception of study medication, Silodosin, Tamsulosin.

 DOI: http://dx.doi.org/10.22159/ajpcr.2021v14i2.39931. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Benign prostatic hyperplasia (BPH) is the most common benign tumor in men and is responsible for urinary symptoms in majority of males over the age of 50 years [1]. It refers to the proliferation of smooth muscles and epithelial cells within the prostatic transition zone [2]. It is a complex disease and is often associated with lower urinary tract symptoms (LUTS) which includes nocturia, urgency, urinary frequency, urinary tract infections, and benign prostatic obstruction [3].

Prostatic hypertrophy is directly related to the aging process and to the hormonal activity. Within the prostate, testosterone is converted by 5 alpha-reductase to dihydrotestosterone and is responsible for stimulating growth factor that influence cell division leading to prostatic hyperplasia and enlargement [4]. LUTSs can be divided into irritative and obstructive symptoms. Irritative symptoms include frequency, urgency, nocturia, and obstructive symptoms include straining, intermittency, weak stream, and incomplete emptying [5].

The range of treatment options for the management of BPH includes watchful waiting, medical therapies, and surgical interventions [6]. Watchful waiting is recommended for patients with mild symptoms, medical treatment for patients with mild to moderate symptoms, and surgery for patients who failed medication/conservative management [7,8]. The widely used drugs for BPH are tamsulosin, silodosin, finasteride, and dutasteride [9].

Tamsulosin is a selective inhibitor of the α1A-adrenoceptor. Although the side-effect profile of tamsulosin is similar to other α1-adrenoceptor antagonists, it is normally well tolerated [10]. Silodosin has a high selectivity for α1A receptors which predominates in male bladder outflow tract and thus it helps to relax the muscles in the prostate and in the opening to the bladder [11,12].

Patient satisfaction is an important and commonly used indicator for measuring the quality of health care. Patient satisfaction affects clinical outcomes, patient retention, and medical malpractice claims [13].

The objective of this study was to assess the comparative patient satisfaction with tamsulosin and silodosin therapy in BPH. Many studies have been conducted about the safety and efficacy of drugs in BPH. However, only a few studies have been conducted in assessing humanistic outcomes.

METHODS

A prospective study was conducted among patients from the department of urology in a tertiary care hospital who were diagnosed with BPH. The study was for a period of 6 months from December 2018 to May 2019. A written informed consent as per ICMR Biomedical Research Guideline Format was taken from the BPH patients.

Inclusion criteria

- BPH patients who were willing to participate in the study from outpatient setting
- Age greater than 50 years
- IPSS ≤23 who lacks absolute indication of surgical intervention.

Exclusion criteria

- Serum prostate specific antigen level >20 ngml/suspected prostatic malignancy
- Post void residual urine of >200 ml

- History of lower urinary tract malignancy/pelvic surgery
- Neurological conditions causing bladder dysfunction, hepatorenal insufficiency.

All information was collected using a suitably designed pro forma and direct interview with patients using questionnaires – patient's perception of study medication (PPSM) and international prostate symptom score (IPSS). All the scales were translated into local language (Malayalam) and the patients were requested to fill them.

Patients were provided with a copy of informed consent form and a patient information sheet. The patients were grouped into two, where one group receive silodosin 8 mg once daily and the other group receive tamsulosin 0.4 mg once daily.

PPSM questionnaire is a 12-item questionnaire designed to quantify patients' satisfaction with the effect of treatment by focusing on specific changes experienced by patients during the study period in 4 areas – control of urinary symptoms, strength of urinary stream, 2 aspects of pain of urination, effect on usual activities, and with a single item asking about overall satisfaction. There is also a final item asking about whether the respondent would ask again their doctor for this medication [11]. The patient satisfaction on treatment with tamsulosin and silodosin was assessed using PPSM at first and second review.

IPSS is a symptom severity assessing tool which comprise of eight questions. Based on IPSS, patients were categorized into mildly symptomatic (score 0–7), moderately symptomatic (score 8–19), and severely symptomatic (score 20–35). IPSS was assessed at the first and second visits. IPSS includes questions regarding incomplete emptying, frequency intermittency, urgency, weak stream, straining, and nocturia [1]. At the end of the study, all the parameters and scores were compared from baseline to end of study.

For data entry, we used the software Microsoft excel and all the analysis were carried out with the help of statistical software SPSS V.22 for WINDOWS. For the analysis of improvement in scores within the group, paired t-test was used and for between group comparisons, independent sample t-test was applied.

RESULTS

In our study, we analyzed the data collected from 110 patients with Benign Prostate Hyperplasia at urology department. Fifty-five patients in each group received silodosin 8 mg or tamsulosin 0.4 mg once daily. Out of the total sample size of 120, there were 10 dropouts as they were unable to come for follow-up or opted for surgical intervention. This study aimed to assess the comparative patient satisfaction and side-effects of the two currently prescribed drugs – tamsulosin and silodosin for BPH. The comparison of improvement in scores before and after therapy was assessed statistically with paired t-test and independent t-test. A calculated $p<0.05$ was considered to be statistically significant.

Demographic details of patients

The distribution of total patients based on age from both groups has been shown in Table 1.

From Table 1, it was observed that out of 110 patients 22 (20%) were below 60 years of age, 58 (52.7%) were in between 61 and 70 years, 23 (20.9%) were in between 71–80 years, and 7 (6.4%) were above 80 years of age. We found that more than 50% of patients who attended the urology OPD were of age group 61–70 years.

Symptomatic distribution of BPH patients

The symptomatic distribution of BPH patients was assessed using I-PSS and is shown in Table 2. We observed that about 12.7% of patients were mildly symptomatic, 68.2% of patients were moderately symptomatic, and 19.1% of patients were severely symptomatic. Thus, we inferred that more than half of the patients who attended urology OP were moderately symptomatic.

Table 1: Frequency and percentage distribution of total no. of patients based on age

Age (years)	Frequency	Percentage
≤60	22	20
61–70	58	52.7
71–80	23	20.9
>80	7	6.4
Total	110	100

Table 2: Symptomatic distribution of BPH patients

Symptom severity	Frequency	Percentage
Mildly symptomatic	14	12.7
Moderately symptomatic	75	68.2
Severely symptomatic	21	19.1

Side-effect profile of tamsulosin and silodosin

The side-effect profile of tamsulosin and silodosin reported by the patients is shown in the following Figs. 1 and 2, respectively.

Fig. 1 shows that in tamsulosin group, the reported side effects were headache in 3 out of 55 (5.5%), dizziness in 3 out of 55 (5.5%), dry mouth in 2 out of 55 (3.6%), and postural hypotension in 8 out of 55 (14.4%) patients, respectively, and those reported in silodosin were myalgia in 3 out of 55 (5.5%), dizziness in 4 out of 55 (7.3%), diarrhea in 1 out of 55 (1.8%), and postural hypotension in 6 out of 55 (10.9%) patients (Fig. 2). It was evident that the most common side effect of tamsulosin and silodosin was postural hypotension.

Patient satisfaction between tamsulosin and silodosin groups

The patient satisfaction between the tamsulosin and silodosin groups using PPSM questionnaire is shown on the following table:

From Table 3, we observed that silodosin made comparatively more patient satisfaction than tamsulosin – PPSM total ($t=8.22$, $p<0.01$), PPSM global ($t=8.14$, $p<0.01$), and PPSM pain ($t=0.029$, $p>0.01$). For silodosin group, the satisfaction levels of PPSM were – PPSM total – 39.41±13.27, PPSM global – 37.15±13.62, and of PPSM pain – 68.47±28.86. However, for tamsulosin group, the values were – 23.48±5.59 for PPSM total, 20.91±5.87 for PPSM global, and 68.20±34.97, respectively. We found that there was more significant reduction on PPSM total by 40.4%, PPSM global by 43.7%, and PPSM pain by 0.39% in silodosin group than that of tamsulosin group.

Severity of symptoms between tamsulosin and silodosin groups

The severity of symptoms between tamsulosin and silodosin groups was analyzed using independent t-test and is shown on the following table:

From Table 4, independent t-test showed that the percentage improvement in patient symptom status differed significantly between groups on IPSS ($t=3.83$, $p>0.05$). Silodosin group reported a higher level of percentage improvement in patient symptom status (IPSS 38.39±17.53) by 23.7% as compared to tamsulosin group (IPSS 50.24±15.14).

DISCUSSION

BPH is the most common benign tumor in men and is responsible for LUTS. LUTS increases with age in an overall prevalence greater than 50% in men of 50 years or older and was associated with a significant negative impact on patient's quality of life (QoL) as postulated by Mahajan [14]. From our study, we found that about 52.7% of BPH patients attending the urology OP belonged to an age group of 61–70 years.

In the current study, we observed that more than half that is 68.2% were moderately symptomatic. A study by Nageratnam and Latheef in a

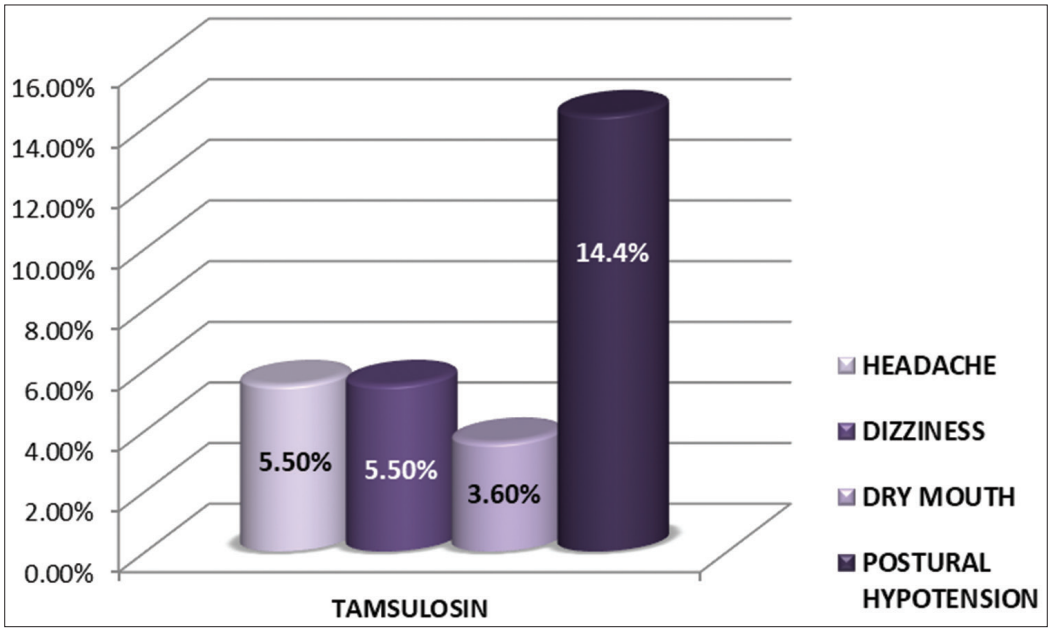

Fig. 1: Percentage distribution of side effects in tamsulosin group

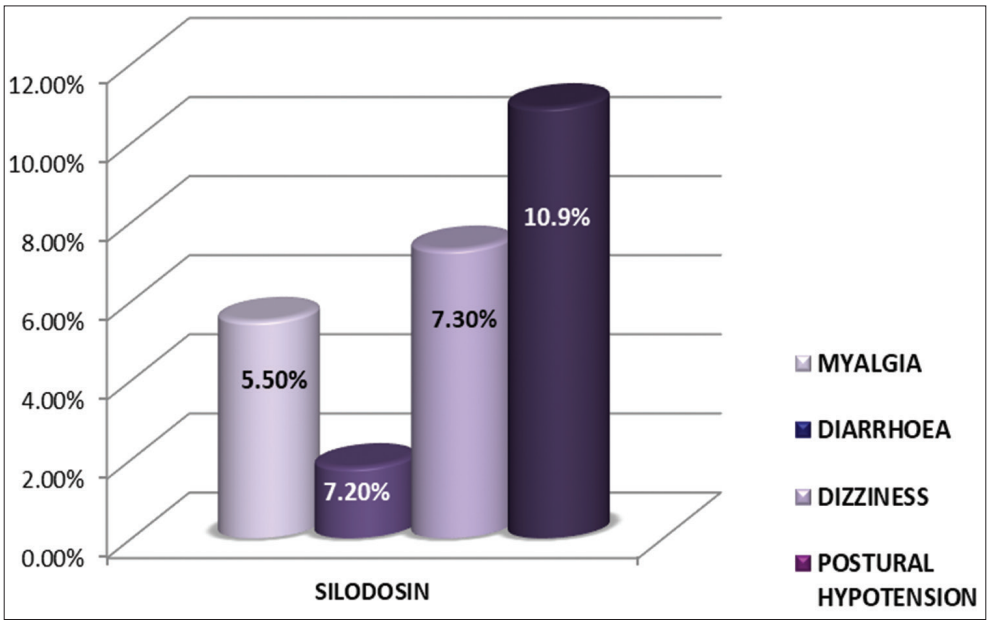

Fig. 2: Percentage distribution of side effects in silodosin group

Table 3: Effect of treatment on PPSM between tamsulosin 0.4 mg and silodosin 8 mg (independent t-test)

Parameter	Group	Mean	S.D	Percentage improvement	t	p-value
PPSM total	Silodosin	39.41	13.27	40.4	8.22	0.000*
	Tamsulosin	23.48	5.59			
PPSM global	Silodosin	37.15	13.62	43.7	8.14	0.000*
	Tamsulosin	20.91	5.87			
PPSM pain	Silodosin	6.84	2.88	0.39	0.03	0.381^{NS}
	Tamsulosin	6.57	3.49			

*Significant at 1%. ^{NS}: Not significant

hospital at Andhra Pradesh also showed that most of the BPH patients were moderately symptomatic [15].

In our study, the side effects reported by BPH patients in tamsulosin group were headache (5.5%), dizziness (5.5%), dry mouth (3.6%), and postural hypotension (14.4%) and those reported in silodosin group were myalgia (5.5%), dizziness (7.3%), diarrhea (1.8%), and postural hypotension (10.9%). From this, it was evident that the most common side effect of tamsulosin and silodosin was postural hypotension. A study conducted by Rossi and Roumeguère showed that the most

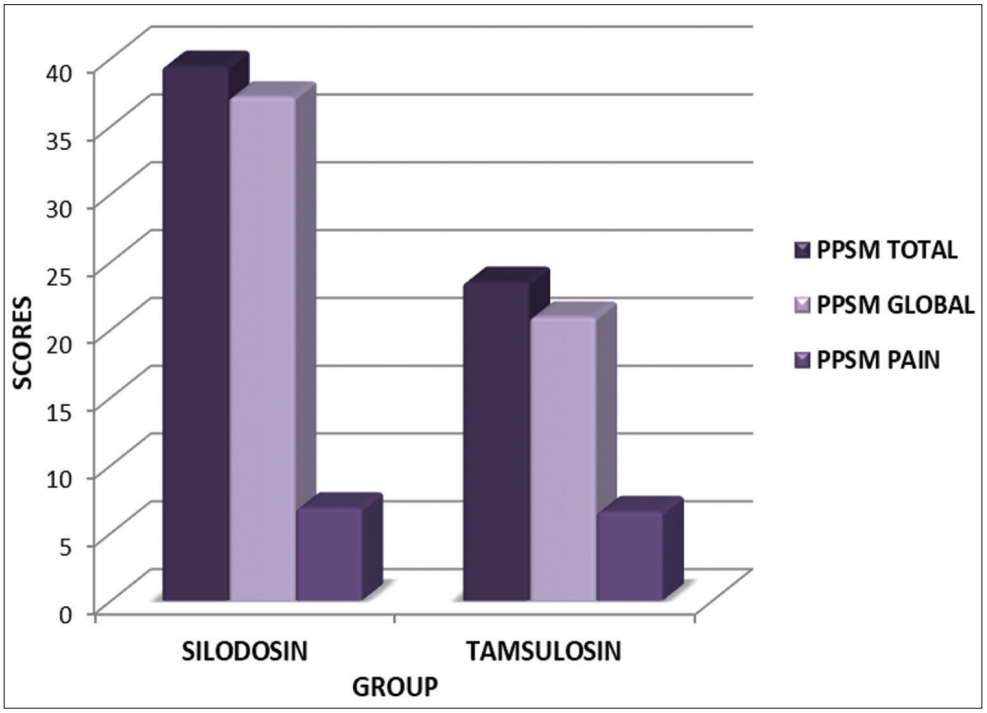

Fig. 3: Diagrammatic representation of effect of treatment on patient's perception of study medication scores between tamsulosin 0.4 mg and silodosin 8 mg

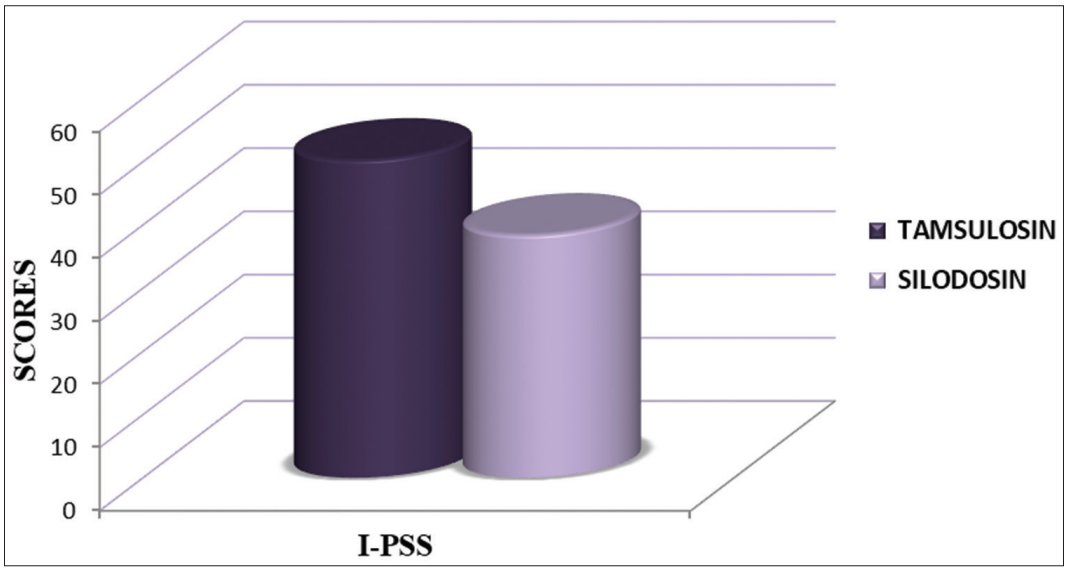

Fig. 4: Diagrammatic representation of effect of treatment on international prostate symptom score between tamsulosin 0.4 mg and silodosin 8 mg

Table 4: Effect of treatment on IPSS between silodosin group 8 mg and tamsulosin groups 0.4 mg (independent t-test)

Scale	Group	Mean	S.D	Percentage improvement	t	p-value
IPSS	Silodosin	38.39	17.53	23.5%	3.83	0.034*
	Tamsulosin	50.24	15.14			

*Significant at 5%

commonly reported adverse reaction of silodosin and tamsulosin were retrograde ejaculation and orthostatic hypotension [16]. Although clinical trials have reported side effects like abnormal ejaculation with tamsulosin [17,18] and silodosin, no such reports were observed in the current study [19]. This could be due to the reluctant attitude or embarrassment of the study population in regard of reporting the same.

Patient satisfaction with treatment, which includes patients' evaluations of the process and outcome of their treatment experience, is increasingly being evaluated in clinical trials and disease-management programs [20]. Measuring satisfaction with medication provides important outcome information from the patient's perspective as to their experience with the therapy and their willingness to ask their physician for the treatment [21].

In our study, on the comparative patient satisfaction with silodosin versus tamsulosin therapy using PPSM showed that within the silodosin group, there was statistically significant change from 1st

review (PPSM total [somewhat satisfied], PPSM global [satisfied], PPSM pain [satisfied]) to "very satisfied" in 2nd review. Similarly, it was proven that all the PPSM parameters had a statistically significant change in 2nd review for tamsulosin group. This showed that both drugs were comparable of making the patient satisfied. On the comparison between the tamsulosin versus silodosin groups, we found that silodosin group showed a great statistically significant change in PPSM total and PPSM global than the tamsulosin group. However, no other similar studies were conducted for the same category of drugs – silodosin and tamsulosin.

A study by Montorsi *et al*. confirmed the efficacy of silodosin in treating BPH patients with moderate/severe LUTS in a real-life setting and this conclusion was similar to our study – silodosin was the drug which made patients 40.4% more satisfied than tamsulosin [19].

A study by Barkin *et al*. assessing the patient satisfaction using the PPSM questionnaire showed that a significantly higher proportion of BPH patients was satisfied with and would request dutasteride and tamsulosin combination therapy than with monotherapy [22]. Our study analyzed the comparative patient satisfaction with tamsulosin and silodosin, and we found that monotherapy with silodosin had more satisfaction than monotherapy with tamsulosin.

A study conducted by Pontari stated that pain is rarely reported in connection with BPH, where it is a feature of prostatitis, which is common in older men and can often be confused with BPH [23,24]. A study conducted by Litwin *et al*. concluded that men have more pain during urination with prostatitis than BPH [25]. From our study, we found that there was not any significant difference in percentage improvement of satisfaction of PPSM pain.

The reduction in symptom severity measured using I-PSS confirmed both drugs had a positive impact on patients. While comparing between the groups, we found that silodosin showed greater statistically significant change in symptom severity (I-PSS) by 23.5% than tamsulosin. A study by Pande *et al*. and Jung *et al*. stated that silodosin decreases symptom score in an appreciable number than tamsulosin [26,27]. In contrast, a study conducted by Patil *et al.* postulated that tamsulosin showed statistically significant improvement in both QoL and I-PSS than silodosin [28]. A study conducted by Yokoyama *et al*. stated that both the drugs showed comparable efficacy in decreasing the symptom score [29].

From our study, the comparative patient satisfaction with tamsulosin versus silodosin therapy showed that silodosin was the drug which satisfied patients on a higher margin by 40.4% and the most common reported side effect for both drugs was postural hypotension.

One limitation of the study was the absence of a placebo arm due to ethical considerations of the institution. Moreover, each drug had already shown superiority over placebo in clinical trials. The patients' response to the QoL and particularly to the PPSM questionnaire might have potentially influenced by the suggestive nature of the questions. The consistent effects observed across all questionnaires and the symptom measures (I-PSS) strengthened the confidence in the study results, even without a placebo arm. About a quarter of patients had received prior α-blocker therapy, which might also have an impact on treatment.

CONCLUSION

BPH is known to be a bothersome disease in elderly men, mostly between 61 and 70 years of age. On assessing the symptomatic distribution of patients, it was inferred that most of the out-patients who consulted the urology OP were moderately symptomatic and the most common reported side effect for both drugs was postural hypotension. Assessment of patient satisfaction is a mode of measuring humanistic outcomes of the treatment in general and particularly must be applied for the currently prescribed drugs – silodosin and tamsulosin. From the analysis of our observations, we concluded that the level of satisfaction was higher in those patients who were prescribed with silodosin than those with tamsulosin. Thus, it is essential that we cover both clinical and humanistic outcomes in the clinical practice.

ACKNOWLEDGMENT

Authors would like to thank Dr. J.S Joy Jyothis, Hon. Senior consultant, Department of Urology, who helped us in collecting the data for this study.

AUTHORS' CONTRIBUTIONS

Vineeth Jayakumar was involved in the planning of the study and preparation of data collection forms. Ashlin Treesa Johnson collected and organized the data. Pritty Anna Varghese analyzed the collected data and prepared the report of study. Karthik Vijayan was involved in writing, reviewing, and editing of the manuscript.

CONFLICTS OF INTEREST

The authors declared no conflicts of interest related to this study.

AUTHORS' FUNDING

The authors declared that there was no source of funding.

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