

A PROSPECTIVE STUDY ON THE EFFICACY OF TADALAFIL IN PATIENTS WITH BENIGN PROSTATIC HYPERPLASIA**¹*Abhinand S., ¹Aadeesha A., ¹Keerthi Krishna R. R., ¹Reshma Raj B. L., ²P. S. Joy Jyothis and ¹John Wesley I.**¹Department of Pharmacy Practice, Sreekrishna College of Pharmacy and Research Centre, Thiruvananthapuram, Kerala.²Cosmopolitan Hospital, Thiruvananthapuram, Kerala.***Corresponding Author: Abhinand S.**

Department of Pharmacy Practice, Sreekrishna College of Pharmacy and Research Centre, Thiruvananthapuram, Kerala.

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ABSTRACT

Background: Benign prostatic hyperplasia (BPH) is the most common problem in aged men and is responsible for the majority of urinary symptoms in males over the age of 50 years. **Aim:** Aim of this study is to assess the efficacy of Tadalafil 5mg OD in BPH patients. **Materials and Method:** The efficacy of Tadalafil was assessed in 62 patients using International prostate symptom score questionnaire and USG, then the patients was asked to review after one months of drug therapy. **Results and Discussion:** Tadalafil 5mg OD has significant effect on IPSS and USG before and after the treatment. **Conclusion:** Tadalafil 5mg OD is found to be clinically significant in improving LUTS secondary to BPH and there was significant improvement in IPSS and USG after the treatment.

KEYWORDS: Benign prostatic hyperplasia (BPH), Lower urinary tract symptoms (LUTS), Tadalafil, International Prostate symptom Score (IPSS), Ultra sonography (USG), Erectile dysfunction (ED).

INTRODUCTION

Benign prostatic hyperplasia (BPH) is one of the most common benign tumour in men and is responsible for majority of urinary symptoms in males over the age of 50 years. Autopsy studies have revealed the histological presence of BPH in 50% of males aged 51–60 years, increasing to 90% in those over 85. By the age of 80 years, virtually all men exhibit one or more of the symptoms associated with BPH.^[1] The etiology of BPH include obstruction of the bladder neck caused by an enlarged prostate gland, excessive stimulation of α -adrenergic receptors in the smooth muscle of the prostate, urethra, and bladder neck or irritability of hypertrophied detrusor muscle as a result of long-standing bladder outlet obstruction.^[3]

Drug treatment goals for benign prostatic hyperplasia include relieving obstructive and irritative voiding symptoms, preventing complications of disease, and reducing the need for surgical intervention. Single-drug treatment with an α -adrenergic antagonist like Doxazosin, Prazosin is preferred for patients with moderate symptoms of benign prostatic hyperplasia. Single-drug treatment with a 5 α -reductase inhibitor like Dutasteride, Finasteride should be reserved for patients with significantly enlarged prostates of at least 40g.^[1,14] These drugs are clinically effective in treating BPH but have certain side effects like sexual dysfunction, dizziness, hypotension, headache.

Several studies reported that ED and BPH are associated epidemiologically and can have common pathophysiological pathway, since then PDE-5 inhibitors like Sildenafil, Tadalafil, Vardenafil have received increased attention for treating BPH.^[2,8] Tadalafil is initially given for ED and found to be effective in BPH with ED.^[6] The mechanism of action of long acting PDE -5 inhibitor Tadalafil in the treatment of men with LUTS secondary to BPH is believed to be associated with stimulation of increased activity of NO or CGMP pathway via inhibition of PDE- 5 isoenzymes in different tissues of the lower urinary tract. This results in smooth muscle relaxation in the bladder, urethra, prostate and supporting vasculature, Increased blood perfusion to the pelvic area and modulation of sensory stimuli from this area.^[4,7] The objective of present study is to assess the efficacy of Tadalafil 5mg- OD in patients with BPH.

MATERIALS AND METHODS

The present study was conducted for a period of 6 months after getting clearance from the Institutional Human Ethical committee. It was carried out in 62 patients in the Urology department of a tertiary care hospital. All the details regarding the patient was kept in confidentiality.

Inclusion criteria

- Patients who were willing to participate in the study.
- International Prostate Symptom Score of ≥ 8
- Peak urine Flow Rate <15 ml/sec.

- Patients of age group greater than 50 yrs.

Exclusion criteria

- Patients with raised Serum Prostate Specific Antigen level(>20ng/ml)/ suspected prostatic malignancy.
- Post Void Residual Urine of >200ml.
- Patients who received recent 5 alpha reductase inhibitors.
- History of lower urinary tract malignancy /pelvic surgery.
- Neurological conditions causing bladder dysfunction, hepato-renal insufficiency.

Study Procedure

A written informed consent was taken in prescribed format from the patients diagnosed with BPH satisfying the inclusion and exclusion criteria. All information relevant to study was collected from case records and direct interview with patients. Data was collected by using a suitably designed proforma. The efficacy of Tadalafil (5mg, OD) was assessed using Ultrasound scan and International Prostate Symptom Score questionnaire and the patients were asked to review after one month of drug therapy.

Based on International Prostate Symptom Score, Patients were categorized into mildly symptomatic (score 0 -7), moderately symptomatic (score 8-19) and severely symptomatic (score 20-35) International Prostate Symptom Score was evaluated after the drug therapy, IPSS parameters includes incomplete emptying,

frequency, intermittency, urgency, weak stream, straining, nocturia and USG was also evaluated which includes prostate volume and residual volume. At the end of the study all the parameters and scores were compared from base line to end of the study.

Statistical Analysis

For data entry we had used the software Microsoft excel and the change in IPSS and USG was plotted using Paired T- Test.

The data regarding personal information and different parameters of IPSS questionnaire and USG before and after intervention were collected and calculated using basic descriptive statistics such as mean, standard deviation, frequency and percentages.

The effectiveness of treatment was statistically assessed using paired T test. A calculated p-value less than 0.05 is considered to be statistically significant. The details given are as follows.

RESULTS

62 patients having LUTS due to BPH diagnosed by physicians were enrolled in the study. The study was done in the urology department of a tertiary care hospital in south kerala. Patients between the age of 50-80 were enrolled in the study. Out of 62 patients 35 patients had BPH with Erectile dysfunction and 27 patients had BPH without Erectile dysfunction.

Effectiveness of treatment Based on IPSS

Table 1: Based on IPSS.

VARIABLE	TEST	MEAN	STANDARD DEVIATION	PERCENTAGE CHANGE	t value	P value
IPSS	BEFORE	25.3	4.01	54.1%	32.1	0.00
	AFTER	11.48	2.78			

From table-1 paired t-test showed that treatment has significant effect on IPSS. That is, before treatment, mean of total IPSS was 25.3 with standard deviation 4.01 and after the treatment it significantly reduced to a mean

11.48 with standard deviation 2.78, showed that symptoms were reduced significantly.

The graphical representation of total IPSS before and after treatment is shown in figure.1

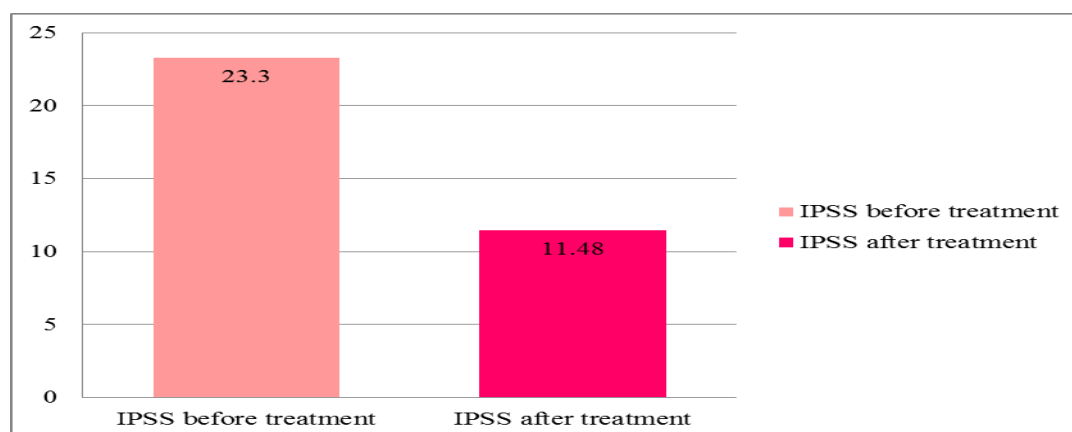


FIGURE-1.

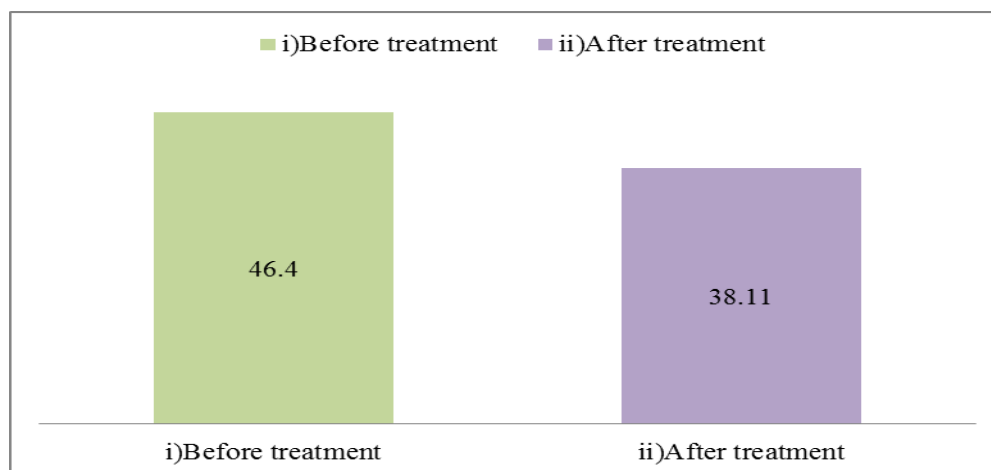
Effectiveness of treatment based on USG-Prostate volume**Table 2: Based on Prostate volume.**

Variable	Test	Mean	Standard Deviation (SD)	Percentage change	t value	p value
USG (prostate volume)	Before	46.4	5.61	21.7%	44.24	0.00
	After	38.11	5.12			

From table 2, it was found to produce significant reduction in prostate volume after the treatment, that is, before the treatment, mean of prostate volume was 46.4 with standard deviation 5.61 and after the treatment,

there was significant reduction to a mean of 38.11 with SD 5.12.

The graphical representation of mean of USG prostate volume before and after treatment is shown in figure 2.

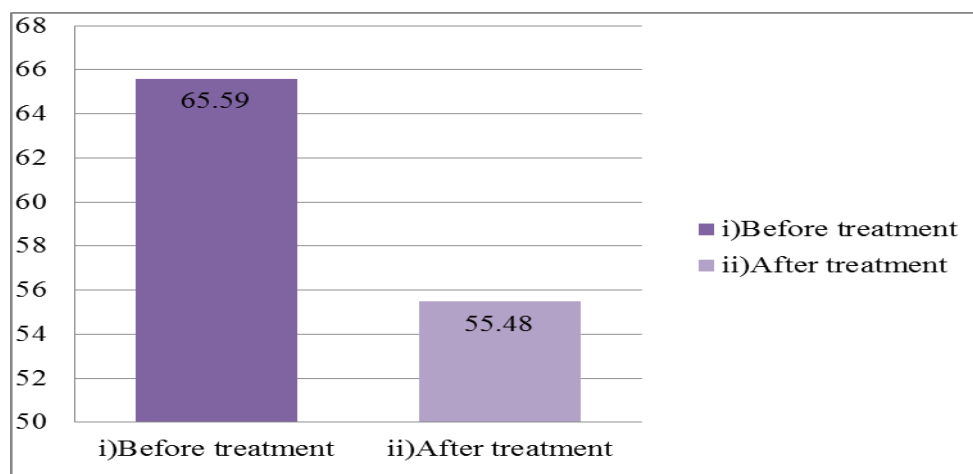
**FIGURE- 2.****Effectiveness of treatment based on USG-Residual volume****Table 3: Based on Residual volume.**

Variable	Test	Mean	Standard Deviation	Percentage change	t value	p value
USG (residual volume)	Before	65.59	6.61	18 %	45.82	0.00
	After	55.48	5.72			

From the table 3, it shows a reduction in residual volume to a clinically significant level, that is, before treatment, the mean of residual volume was 65.59 with standard deviation 6.61 and it was reduced to a mean of 55.48

with standard deviation 5.72 which shows efficacy with the treatment.

The graphical representation of USG residual volume before and after treatment is shown in figure 3.

**FIGURE 3.**

DISCUSSION

Benign Prostatic Hyperplasia (BPH) was one of the most common benign tumour in men and is responsible for urinary symptoms in males over the age of 50 years.^[3] LUTS increases with age with overall prevalence of greater than 50% in men 50 years or older and are associated with a significant negative impact on patient's QOL.^[2]

Konstantinos Hatzimouratidis^[6] have postulated that there is an epidemiological data link between ED and BPH associated lower urinary tract symptoms and these are two highly prevalent conditions in aging men, assuming common pathophysiological pathways.

One theory focuses on the mechanism of the accumulation of intracellular prostatic and bladder smooth muscle cyclic guanosine monophosphate following PDE5 inhibition, which may decrease tension in the smooth muscle of the prostatic stroma and capsule. This muscle relaxation results in bladder neck opening and improved voiding function and it decreases detrusor muscle activity in the bladder body and neck.^[10]

Statistically significant improvement in IPSS from baseline were observed with tadalafil doses of 2.5, 5, 10 and 20 mg at all post randomization visit (4, 8 and 12 weeks) compared to placebo in a study done by Roehrborn C.G et al. In that study IPSS change from baseline in patients with mild-moderate symptoms was -4.3+/- 4.94, whereas this change was -6.2+/-6.71 in patients with severe symptoms was 7.3+/- 6.71 and -8.4 +/- 6.36 with tadalafil dose of 10 and 20 mg respectively.^[10]

Dr. Puneet Mahajan et al postulated that the tadalafil 5mg resulted in clinically meaningful and statistically significant improvement in LUTS secondary to BPH. Tadalafil improved IPSS, Qmax, PURV and quality of life index. Statistically significant improvement of IIEF score (mean change; 3.735+/-1.082) at 12 weeks was observed. In this study, showed that tadalafil seems to be promising treatment option for patients with LUTS secondary to BPH and associated ED.^[2]

In our study, the magnitude of improvement in IPSS (Mean+/-SD) from baseline (25.3+/-4.01) to the end point (11.48+/-2.73) was statistically significant. The effect of tadalafil on USG Prostate Volume before and after the treatment was statistically significant with a mean from 46.4 to 38.11. The effect of tadalafil on USG Residual Volume before and after treatment was statistically significant with a change in mean from 65.59 to 55.48. This shows significant reduction in prostate size after the treatment. In our study, we also found, out of 62 patients, 35 patients had erectile dysfunction (56.5%). That is, majority of patients had the problem of erectile dysfunction. 30 patients (48.4%) had the history of UTI, indicating majority having history of UTI. In terms of demographic details, we found that, majority of

patients are alcoholic (66.1%) compared to smokers (43.5%). On comparing both IPSS and USG, there was more improvement in IPSS (25.3 to 11.48) when compared to USG. Thus the symptomatic relief was more with the tadalafil when compared to other parameters. Another advantage is that, this single drug can be used for to treat two conditions simultaneously (LUTS and ED). Another advantage is that, the sexual and ejaculatory dysfunction caused by other drugs like alpha adrenergic agonist and 5 α - reductase inhibitors can be replaced with tadalafil.

CONCLUSION

Tadalafil (5mg OD) was found to be clinically significant in improving LUTS secondary to BPH and there was a significant improvement in the IPSS and USG after the treatment. In our study the results shows that there was more significant improvement in the IPSS when compared to USG – Prostate volume and residual volume. Thus we can conclude that the symptomatic relief with Tadalafil after treatment is much more better than its effect in prostate volume and residual volume. Tadalafil 5mg OD is the only drug available to treat LUTS and ED conditions simultaneously. The sexual dysfunction and ejaculatory dysfunction caused by α -adrenergic agonist and 5 α - reductase inhibitors can be avoided with Tadalafil.

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