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Effectiveness of tadalafil and tamsulosin combination in benign prostatic hyperplasia: A prospective cohort study at a tertiary care center

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ABSTRACT

Background: Benign prostatic hyperplasia (BPH) is one of the major causes of lower urinary tract symptoms (LUTS) in men. The uroselective tamsulosin helps in rapid reduction of prostate symptoms and its combination with Tadalafil, a phosphodiesterase inhibitor leads to synergistic benefit improving the LUTS of BPH. **Aims and Objectives:** This study was conducted with the aim to assess the effectiveness of synergistic effect of Tadalafil and Tamsulosin in improving the symptoms of BPH patients. **Materials and Methods:** A prospective cohort study was conducted among the patients admitted with LUTS due to BPH in the surgery ward of Annapoorna Medical College. A total of 100 patients were included in the study. The control group was administered 0.4 mg of tamsulosin and the study group was administered with combination of tadalafil 5 mg and tamsulosin 0.4 mg for 3 weeks and followed up at an interval of 3 weeks, 1 month, and 6 months. Paired t-test was used to compare the international prostate symptom score (IPSS) mean scores. **Results:** A total of 100 patients were included in the study. There was significant improvement in the post-voided volume of the study group in comparison to the control. The IPPS score of the study group at the baseline was 16.39 ± 4.89 which was decreased to a score of 11.42 ± 3.39 after the combination drug therapy with $P < 0.001$ which was statistically significant. **Conclusion:** The combination therapy of tamsulosin and tadalafil marked an improvement in the symptoms of BPH which can be noted with fall down of IPSS score after the therapy.

Key words: Benign prostatic hyperplasia; International prostate symptom score; Tadalafil; Tamsulosin

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INTRODUCTION

Benign prostatic hyperplasia (BPH) is a progressive disease that causes lower urinary tract symptoms (LUTS) which substantially affect quality of life (QoL) for many patients.[1] LUTS associated with BPH include storage or irritative (mainly including urinary frequency, urgency, and nocturia), voiding or obstructive (mainly including urinary hesitancy, straining, retention, and a decreased force of urination), and postmicturition symptoms, which can significantly and negatively affect the QoL of the elderly. More than 50% of men >50 years and over 80% of men >80 years old experience LUTS/BPH.[2] BPH is one of the common causes of LUTS in aging men. Voiding symptoms have been related to obstruction of the bladder outlet. Phosphodiesterase type 5 inhibitors (PDE5 – Is) cause relaxation of bladder neck and prostate by increasing nitric oxide in smooth muscle, facilitating voiding phase of micturition cycle. They also exert potent anti-inflammatory effects on prostate therefore reducing fibrosis and overgrowth. All these beneficial effects help in reducing symptoms

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due to prostatic enlargement.[3] The mechanism of action involves the PDE5 is induced increase in the level of the second messenger cyclic guanosine monophosphate, which promotes smooth muscle relaxation and induces penile erection. In theory, PDE5 is can increase the level of nitric oxide in smooth muscle, which in turn relaxes the smooth muscle of urinary organs (such as the bladder neck and the prostate) and ultimately relieves the symptoms of LUTS associated with BPH. Studies have shown that combination therapy with PDE5 is and alpha-blockers provided better outcomes than a-adrenergic blocker monotherapy.[4] Several meta-analyses have defined the efficacy and safety of PDE5 is alone or in combination with α1-blockers for the treatment of BPH-LUTS. Moreover, the combination therapy can significantly improve international prostate symptom score (IPSS) and maximal flow rate (Qmax).[5] Currently, the efficacy of PDE5 is on LUTS recovery has been well established, and tadalafil 5 mg once daily has been approved for the treatment of LUTS/BPH.[6]

With this background, the study was conducted to assess the effectiveness of the synergistic effect of tadalafil and tamsulosin in improving the symptoms of patients of BPH and their improvement in QoL.

Aims and objectives

This study was conducted with the aim to assess the effectiveness of synergistic effect of Tadalafil and Tamsulosin in improving the symptoms of BPH patients.

MATERIALS AND METHODS

Study design and study setting

A prospective cohort study was conducted among the patients with LUTS due to BPH admitted in the surgical ward of Annapoorna Medical College, Tamil Nadu, India. The study was conducted for a period of 1 year (December 2021–November 2022).

Study population

BPH patients presenting with LUTS to the surgery OPD and admitted in the surgical ward were included in our study.

Inclusion criteria

The patients diagnosed with LUTS due to BPH and those willing to consent were included in our study.

Exclusion criteria

Patients of BPH with cardiac comorbidities, those who are on beta-blocker therapy, and patients who are known hypertensives and on hypertensive medication were excluded from our study.

Sample size and sampling method

The patients presenting to the OPD were grouped as the study group (50 patients) and control group (50 patients). The patients were assigned into the study and control based on serial numbers/OPD numbers: odd numbers in the study group and even numbers in the control group.

Study tools and data collection

A pro forma was used to collect the data from the study participants. It consisted of the patient's demographic details, clinical history, clinical examination, routine blood and urine investigations, ultrasound KUB (for assessing the pre-void and post-volume) and the IPSS. IPSS is most widely used and valid instrument to measure subjective severity of symptoms and symptom progression. It consists of seven accurately adjusted questions which include common urinary symptoms such as irritative (frequency, urgency, and nocturia) and obstructive (hesitancy, incomplete emptying, intermittency, and weak stream). Each question on the IPSS can yield 0–5 points, producing a total symptom score that can range from 0 to 35. Patients with IPSS scores of 8, 8–19, and 19–35, will be considered to have mild, moderate, and severe symptoms, respectively.[7]

A written informed consent was obtained from the study participants. The study group was administered with tadalafil 5 mg and tamsulosin 0.4 mg for a period of three 3 weeks, and followed up for a period of 6 months. The control group was administered with tamsulosin 0.4 mg for 3 weeks and followed up for the same period. The prostate volume of all the patients was estimated using ultrasound KUB. The IPSS score was recorded at the end of 3 weeks of the drug therapy. They were then followed up after 1 month and 6 months for assessing the IPSS score. Patients' severity of symptoms and response to treatment were assessed using the IPSS score.

Ethical consideration

Ethical clearance was obtained from the Institutional Ethics Committee (AMC/IEC. Proc no.13/2021). Data were collected after explaining the purpose of the study and taking informed consent from the patients willing to participate in the study.

Statistical analysis

Data were entered in Microsoft Excel and analyzed using IBM SPSS version 21.0. Descriptive statistics were analyzed in the form of proportions, means, and standard deviation. Paired t-test was used to compare the IPSS mean scores.

RESULTS

A total of 100 patients were included in the study. The mean age of the study participants was 55±10.5 years. Nearly half

of the participants belonged to the age group of 51–60 years. Table 1 shows that there was an improvement in the post-voided volume of the study group as compared to the control.

Table 2 shows the proportion of patients having LUTS associated with BPH in the study group.

Table 3 shows the proportion of patients having LUTS associated with BPH in the control group.

The IPPS score of the study group at the baseline was 16.39±4.89 which was decreased to a score of 11.42±3.39 after the combination drug therapy which was statistically significant with $p < 0.05$. This is shown in Table 4.

DISCUSSION

Our study found that the BPH associated LUTS were improved after the combination therapy of tamsulosin and tadalafil. In a study conducted by Singh et al.,[8] by comparing the results of treatment with tamsulosin or tadalafil monotherapies against tamsulosin and tadalafil combination therapy, end point IPSS scores decreased by 10.7, 6.8, 11.7 points for tamsulosin group, tadalafil group, combination group. Our study correlates with this study in respect to the end point IPSS scores where there is significant reduction in scores with combination therapy. The clinical improvement in IPSS-total score with tadalafil and tamsulosin was seen in approximately 70% of the patients in our study. This is the clinical response criteria as per the AUA guidelines which suggests a >3 point decrease in total IPSS score from the baseline is indicative of a clinically meaningful improvement and this change is also consistent with that observed in other published tamsulosin and tadalafil studies.[9] Combination of daily tadalafil 5 mg and tamsulosin 0.4 mg showed an improvement of LUTS relief when compared to monotherapy with both the single drugs.[10] This finding was consistent with the finding in our study. The mean changes in total IPSS was −9.46 for tadalafil 5 mg, respectively, which indicated superiority in LUTS improvement.[11] This was similar with the findings in our study where there was improvement in the IPSS score in the patients who received the combination therapy. The combination of tamsulosin and tadalafil

Table 1: Prostate volume of the BPH patients with lower urinary tract symptoms

Post void residue (ML)	Study group (%)	Control group (%)
45–50	7.14	6.12
51–55	23.46	14.28
56–60	18.36	10.20
61–65	2.4	13.26
>66	0.0	7.14

Table 2: Distribution of lower urinary tract symptoms of the study group

Frequency	Lower urinary tract symptoms																							
	Frequency of micturition			Urgency of micturition			Presence of Nocturia			Straining during micturition			Presence of Weak stream			Intermittency micturition			Incomplete emptying		
	VISIT			VISIT			VISIT			VISIT			VISIT			VISIT			VISIT		
	I (%)	II (%)	III (%)	I (%)	II (%)	III (%)	I (%)	II (%)	III (%)	I (%)	II (%)	III (%)	I (%)	II (%)	III (%)	I (%)	II (%)	III (%)	I (%)	II (%)	III (%)
Not at all	4.8	6.12	6.12	5.10	6.12	6.12	6.12	7.14	7.14	4.8	6.12	6.12	6.12	6.12	6.12	4.8	6.12	6.12	4.8	6.12	6.12
<1 time	12.24	16.32	1632	10.20	16.32	16.32	14.28	16.32	16.32	12.24	16.32	16.32	12.24	16.32	16.32	12.24	16.32	16.32	12.24	16.32	16.32
About half the time	14.28	1632	1632	15.30	16.32	16.32	15.30	16.32	16.32	14.28	16.32	16.32	15.30	16.32	16.32	14.28	16.32	16.32	14.28	16.32	16.32
More than half times	14.28	12.24	12.24	10.20	12.24	12.24	10.20%	11.22	11.22	14.28	12.24	12.24	10.30	12.24	12.24	14.28	12.24	12.24	14.28	12.24	12.24
Almost always	6.12	—	—	10.20	—	—	5.10	—	—	6.12	—	—	7.14	—	—	6.12	—	—	6.12	—	—

Table 3: Distribution of lower urinary tract symptoms of the control group

Frequency	Lower urinary tract symptoms																					
	Frequency of micturition			Urgency of micturition			Presence of Nocturia			Straining during micturition			Presence of Weak stream			Intermittency micturition			Incomplete emptying		
	Visit			Visit			Visit			Visit			Visit			Visit			Visit		
	I (%)	II (%)	III (%)	I (%)	II (%)	III (%)	I (%)	II (%)	III (%)	I (%)	II (%)	III (%)	I (%)	II (%)	III (%)	I (%)	II (%)	III (%)	I (%)	II (%)	III (%)
Not at all	6.12	7.14	7.14	7.14	8.16	9.18	6.12	7.14	7.14	7.14	8.16	9.18	6.12	7.14	7.14	6.12	7.14	7.14	7.14	8.16	9.18
<1 time	12.24	13.26	13.26	12.24	16.32	16.32	12.24	13.26	13.26	12.24	16.32	16.32	12.24	13.26	13.26	12.24	13.26	13.26	12.24	16.32	16.32
About half the time	14.28	16.32	16.32	14.28	16.32	18.36	14.28	16.32	16.32	14.28	16.32	18.36	14.28	16.32	16.32	14.28	18.36	18.36	14.28	16.32	18.36
More than half times	14.28	12.24	12.24	14.28	10.20	7.14	14.28	12.24	12.24	14.28	10.20	7.14	14.28	12.24	12.24	14.28	12.24	12.24	14.28	10.20	7.14
Almost always	6.12	2.4	2.4	3.6	—	—	6.12	2.4	2.4	3.6	—	—	6.12	—	—	6.12	—	—	3.6	—	—

Table 4: Comparison of IPPS score before and after the therapy

Patients' group	Baseline score	After study score	Improvement (%)
IPSS study	16.39±4.89	11.42±3.39	16
IPSS control	10.39±3.94	9.90±3.34	2

produced significantly better improvements in LUTS, QoL, erectile function and Q_{max} compared to monotherapy with tamsulosin, without an increase in adverse effects.[12] Similarly, in our study there was improvement in LUTS with the combination therapy.

Limitations of the study

One of the limitation of our study could be the lesser number of study participants.

CONCLUSION

Frequency and nocturia were the common symptoms noted in BPH patients. The combination therapy of tamsulosin and tadalafil marked an improvement in symptoms of BPH which can be noted with fall down of IPSS score after the therapy. Post void residue was improved in most of the patients.

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SS- Definition of intellectual content, literature survey, prepared first draft of manuscript, implementation of study protocol, data collection, data analysis and manuscript preparation; **PT-** Concept, design, clinical protocol, manuscript preparation, editing, and manuscript revision and submission of article; **RTR-** Design of study, statistical analysis and interpretation editing and manuscript revision; **LS-** Design of study, statistical analysis and interpretation, editing and manuscript revision.

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