Comparative study of tamsulosin versus tadalafil in benign prostatic hyperplasia patients with lower urinary tract symptoms. A prospective randomized study

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Abstract

Introduction: Benign prostatic hyperplasia (BPH) is one of the common causes of lower urinary tract symptoms (LUTS) in aging men. Men with LUTS have a higher incidence of erectile dysfunction (ED), and LUTS themselves represent an independent risk factor for ED, triggering a significant negative impact on quality of life.

Materials and Methods: A total of 92 patients were randomly assigned to two groups. Groups I and II had 45 and 47 patients, two patients from Group I and three patients from Group II did not follow and were excluded from the study. Patients in Group I received 0.4 mg of tamsulosin and Group II patients received 5 mg tadalafil. Patients were assessed at baseline, 3 months, and at 6 months after receiving treatment. Treatment efficacy was measured by a change in Qmax, post void residual urine (PVR), International Prostate Symptom Score (IPSS), and Sexual Health Inventory for Men (SHIM) score at 3 months and 6 months.

Results: Baseline parameters between the two groups were similar. Mean Qmax improved by 7 ml/s at 3 months to 9.44 ml/s at 6 months in Group I versus 4.73 ml/s at 3 months to 6.46 ml/s at 6 months in Group II (P = 0.739). Mean PVRU decreased by 35.53 ml at 3 months to 47.23 ml at 6 months in Group I versus 44.98 at 3 months to 58.28 ml at 6 months in Group II (P = 0.102). IPSS score improved by 4.24 points at 3 months to 7.22 points at 6 months in Group I versus 4 points at 3 months to 5.02 points at 6 months in Group II (P = 0.336). SHIM score improved by 0.7 points 16.2 at 3 months to 6.3 points at 6 months (P < 0.001).

Conclusion: When both groups were compared, tadalafil showed statistically similar improvements in Qmax, PVRU, and IPSS score, but statistically significant improvement was observed with tadalafil in SHIM score compared with tamsulosin in treating LUTS secondary to BPH. Our study provides evidence that once daily tadalafil 5 mg is well tolerated and can be considered for the treatment of LUTS secondary to BPH especially in patient with ED.

Keywords: Benign hypertrophy of prostate, lower urinary tract symptoms, tadalafil, tamsulosin

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INTRODUCTION

Benign prostatic hyperplasia (BPH) is one of the common cause of lower urinary tract symptoms (LUTS) in aging men. Voiding symptoms have been related to obstruction of the bladder outlet. However, it is well recognized that voiding symptoms may or may not correlate with underlying pathophysiology. Erectile dysfunction (ED) and LUTS are interrelated. Men with LUTS have a higher incidence of ED, and LUTS themselves represent an independent risk factor for ED, resulting in significant negative impact on quality of life. The pathophysiology of LUTS secondary to BPH and ED are not completely understood, even though several determinants are shared by these two clinical entities. The current standard of care in men with symptomatic LUTS secondary to BPH is treatment with 5-alpha-reductase inhibitors either alone or in combination with alpha-blockers and transurethral surgery is reserved for those who have failed medical therapy.

Phosphodiesterase type 5 inhibitors (PDE5-Is) were approved for the treatment of ED, but they have been also found highly effective in blunting LUTS in men with or without ED. PDE5-Is causes relaxation of bladder neck and prostate by increasing nitric oxide in smooth muscle, facilitating voiding phase of micturation cycle. They also exert potent anti-inflammatory effects on prostate therefore reducing fibrosis and overgrowth. All these beneficial effects help in reducing symptoms due to prostatic enlargement.

We carried out a prospective Comparative study, with the aim to compare the efficacy and safety of daily administration tamsulosin 0.4 mg versus tadalafil 5 mg.

MATERIALS AND METHODS

This study was a prospective comparative randomised study conducted in the Department of Urology SKIMS Srinagar J AND K India between August 2018 and July 2020.

Inclusion criteria
• Male patient with age >40 years and diagnosed with symptomatic benign prostate hyperplasia.

Exclusion criteria
• Patient already on alpha-blockers
• Haematuria
• Chronic kidney disease
• Bilateral hydro-ureteronephrosis
• Bladder calculi
• Bladder diverticula.

A total of 92 patients were randomly assigned to two groups using a computer-based method. Groups I and II had 45 and 47 patients, respectively. Two patients from Group I and three patients from Group II did not follow and were excluded from the study. Patients in Group I received 0.4 mg of tamsulosin and Group II patients received 5 mg tadalafil. Patients were advised to take drugs at bedtime.

All patients were properly evaluated before enrolling them for study. Detailed history, general physical examination with abdominal examination, examination of external genitalia and digital rectal examination was done in each case. Neurological examination was done to exclude any neurological deficit.

Investigations done include urine analysis, urine culture, baseline investigations including renal function tests, abdominal ultrasound, serum prostate-specific antigen, and uroflowmetry.

All patients were explained about the International Prostate Symptom Score (IPSS) and the IPSS scoring sheet was provided to quantify the severity of LUTS and Sexual Health Inventory for Men (SHIM) scoring to access ED. SHIM score signifies sexual health of patients, five questions were asked in each patient, and each question carries a score of 1–5. Score varies from 5 to 25. Score 22–25 meaning no ED, 17–21 mild ED, 12–16 mild to moderate ED, 8–11 moderate ED, and 5–7 severe ED.

Patients were assessed at baseline, 3 months, and at 6 months after receiving treatment. Treatment efficacy was measured by a change in Qmax, post void residual urine (PVR), IPSS score, and SHIM score at 3 months and 6 months.

Data analysis
Data was analysed using SPSS ver. 15.0 software. Student's t-test, and univariate logistic regression analysis were used for statistical assessment of results and a value of $P < 0.05$ was considered statistically significant.

RESULTS

Baseline parameters of patients in Group I and Group II

1. Age: Mean age of patients in group 1 was 60.4 SD8.74 with range from 42–78 years and in group II Mean age of patients was 62.66 SD8.89 With range from 42–80 years.
2. Prostate size: The mean prostate size of patients in Group I was 35.32 (Sd 9.79) with a range from 16 to 50
and in Group II, the mean prostate size was 32.20 (SD: 9.26) with a range from 18 to 48

3. Post voidal residual urine (PVRU): Mean PVRU of patients in Group I was 64.76 (SD 45.84) with a range from 15 to 200, while in patients in Group II, the mean PVRU was 78.5 (SD: 55.02), with a range from 0 to 220

4. Qmax: The mean Qmax of patients in Group I was 11.44 (SD 4.49) with a range from 2.9 to 22.1, while in patients in Group II, the mean Qmax was 12.46 (SD 4.54) with a range from 3.9 to 23.1

5. IPSS score: The mean IPSS SCORE of patients in Group I was 16.84 (SD: 4.88) with a range from 4 to 25, while in Group II, the mean IPSS score was 15.62 (SD 4.78) with a range from 3 to 21

6. SHIM Score: The mean Shim score of patients in Group I was 15.5 (SD: 5.12) with a range from 8 to 25, while in patients in Group II, the mean SHIM score was 15.8 (SD 4.89) with a range from 7 to 25.

Parameters of patients in Group I and Group II at 3 months after receiving tamsulosin 0.4 mg in Group I and tadalafil 5 mg in Group II [Table 2]

1. Post voidal residual urine (PVRU): Mean PVRU at 3 months of patients in Group I was 29.22 (SD: 10.82) with a range from 0 to 71 and in Group II, mean PVRU at 3 months was 33.52 (SD: 13.94) with a range from 0 to 80.

2. Qmax: Mean Qmax at 3 months of patients in Group I was 18.44 (SD 3.80) with a range from 9.6 to 23.2 and in Group II, mean Qmax at 3 months was 17.19 (SD: 3.54) with a range from 9.8 to 22.8

3. IPSS SCORE: Mean IPSS score at 3 months of patients in Group I was 12.60 (SD: 3.14) with a range from 4 to 18 and in Group II, mean IPSS score at 3 months was 11.62 (SD: 3.64) with a range from 3 to 17.

4. SHIM SCORE: Mean SHIM score at 3 months of patients in Group I was 16.2 (SD: 4.12) with a range from 7 to 25 and in group II, mean SHIM score at 3 months was 21.9 (SD: 4.89) with a range from 12 to 25.

Parameters of patients in Group I and Group II at 6 months after receiving tamsulosin 0.4 mg in Group I and tadalafil 5 mg in Group II [Table 3]

1. Post voidal residual urine (PVRU): Mean PVRU at 6 months of patients in Group I was 17.52 (SD: 6.94) with a range from 0 to 52. and in Group II, mean PVRU at 6 months was 20.22 (SD 7.82) with a range from 0 to 60

2. Qmax: Mean Qmax at 6 months of patients in Group I was 20.88 (SD 3.38) with a range from 12.5 to 24.6 and in Group II, mean Qmax at 6 months was 18.92 (SD: 3.44) with a range from 13.2 to 25.5

3. IPSS SCORE: Mean IPSS score at 6 months of patients in Group I was 9.62 (SD: 3.84) with a range from 3 to 13, and in Group II, the mean IPSS score at 6 months was 10.6 (SD: 3.54) with a range from 3 to 15

4. SHIM SCORE: Mean SHIM score at 6 months of patients in Group I was 16.3 (SD: 5.31) with a range from 8 to 22 and in Group II, the mean SHIM score at 6 months was 22.1 (SD: 4.93) with a range from 14 to 25.

DISCUSSION

The role of medical therapy in prostatomegaly with LUTS has been supported by the certain limitations of prostatectomy, which include significant early and late complications of the surgical procedure and significant re-treatment rate.[9] Treatment of symptomatic BPH

Table 1: Baseline parameters of patients in Group I and Group II

| Patient parameters | Group I (tamsulosin 0.4 mg) | Group II (tadalafil 5 mg) | P |
|--------------------|-----------------------------|---------------------------|---|
| Age (years)        | 60.40 8.74 42-78            | 62.66 8.89 42-80          | 0.202 |
| Prostate size (g)  | 35.32 9.79 16-50            | 32.20 9.26 18-48          | 0.284 |
| PVRU (ml)          | 64.76 45.84 15-200          | 78.55 50.02 0-220         | 0.152 |
| Qmax (ml/s)        | 11.44 4.49 2.9-22.1     | 12.46 4.54 3.9-23.1       | 0.248 |
| IPSS score         | 16.84 4.88 4-25            | 15.62 4.78 3-21           | 0.186 |
| SHIM score         | 15.5 5.12 8-25             | 15.8 4.89 7-25            | 0.395 |

PVRU: Postvoidal Residual Urine, IPSS: International Prostate Symptom Score, SHIM: Sexual Health Inventory for Men, SD: Standard deviation

Table 2: Parameters of patients in Group I and Group II at 3 months

| Patient parameters | Group I (tamsulosin 0.4 mg) | Group II (tadalafil 5 mg) | P |
|--------------------|-----------------------------|---------------------------|---|
| PVRU               | 29.22 10.82 0-71            | 33.52 13.94 0-80          | 0.139 |
| Qmax               | 18.44 3.8 9.6-23.2          | 17.19 3.54 9.8-22.8       | 0.142 |
| IPSS score         | 12.5 4.12 3-13             | 16.2 4.12 7-25            | 0.236 |
| SHIM score         | 9.62 3.84 3-13             | 9.62 3.84 3-13            | 0.336 |

PVRU: Postvoidal Residual Urine, IPSS: International Prostate Symptom Score, SHIM: Sexual Health Inventory for Men, SD: Standard deviation

Table 3: Parameters of patients in group I and group II at 6 months

| Patient parameters | Group I (tamsulosin 0.4 mg) | Group II (tadalafil 5 mg) | P |
|--------------------|-----------------------------|---------------------------|---|
| PVRU               | 17.52 6.94 0-52             | 20.22 7.82 0-60           | 0.739 |
| Qmax               | 20.88 3.38 12.5-24.6        | 18.92 3.44 13.2-25.5      | 0.102 |
| IPSS score         | 16.3 5.31 8-22              | 22.1 4.93 14-25           | 0.336 |

PVRU: Postvoidal Residual Urine, IPSS: International Prostate Symptom Score, SHIM: Sexual Health Inventory for Men, SD: Standard deviation
has evolved from surgical therapy to medical therapy. Depending on weight of prostate either combination therapy with 5α-reductase inhibitors with α-adrenergic antagonists or alpha-blocker alone is used in clinical practice guidelines. Several long-term studies such as MTOPS and ComBAT have demonstrated the superiority of combination therapy over monotherapy in preventing disease progression.\[10,11\]

α-adrenergic blockers use in the treatment of LUTS is based on the hypothesis that LUTS due to bladder outlet obstruction is mediated by α1 adrenoceptors associated with prostatic smooth muscle,\[12\] since smooth muscles are dominant constituents of BPH, accounting for around 40% of the area density of the hyperplastic prostate,\[13\] signifying the role of α-blockers in BHP.

The rationale for the use of PDEIs in the treatment of LUTS and BPH was based on data showing the frequent occurrence of both ED and LUTS in men as they age. This raised the possibility of a common underlying mechanism contributing to both processes, which, in turn, raised the possibility of new treatment options that might affect both processes. The pathophysiologic link between these conditions is not yet clear. It is likely that there is an overlap between the roles of each of these candidate mechanisms, and an ultimate effect leading to smooth muscle relaxation in the prostate bladder neck or erectile tissues appears to be crucial.

We conducted this study to compare the efficacy of tamsulosin and tadalafil in men with BHP with LUTS by measuring a change in Qmax, PVR (post void residual urine), IPSS score, and SHIM score at 3 months and 6 months after receiving tamsulosin 0.4 mg in Group I and tadalafil 5 mg in Group II with respect to baseline score in these two groups.

In our study, tamsulosin 0.4 mg was found to improve Qmax, PVR, and IPSS score more than tadalafil 5 mg, but the difference was statistically insignificant. Pogula et al., Abrams et al., and Lepor et al. stated in their studies that patients treated with tamsulosin experienced a greater increase in peak urinary flow\[14,17\].

In our study, almost all patients with BHP with LUTS had some degree of ED (mild to severe). We found that patients taking tadalafil 5 mg had statistically significant improvement in overall SHIM score compared to patients taking tamsulosin 0.4 mg. Vedamurthy Reddy Pogula et al.\[14\] reported patient taking tadalafil 5 mg had an increase in mean SHIM score at 3 months compared to tamsulosin 0.4 mg. Lee et al.\[18\] observed that after 12 weeks of tadalafil treatment, IIEF-5 scores had increased from baseline by 47.8%. Sebastianelli et al.\[19\] reported in their study that from baseline to 12 week, all the subjects showed a significant improvement of International Index of Erectile Function (IIEF), but tadalafil achieved the same improvements of IIEF when compared to combination alpha-blocker and tadalafil.

CONCLUSION

When both groups were compared, tadalafil showed statistically similar improvements in Qmax, PVRU, and IPSS score, but statistically significant improvement was observed with tadalafil in SHIM score compared with tamsulosin in treating LUTS secondary to BPH. Our study provides evidence that once-daily tadalafil 5 mg is well tolerated and can be considered for the treatment of LUTS secondary to BPH, especially in patients with ED.

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Conflicts of interest
There are no conflicts of interest.

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