Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Urology

Efficacy of Tamsulosin Alone versus Tamsulosin Plus Tadalafil in Treatment of LUTS due to BPH: A Comparative Study

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DOI: 10.36347/sjams.2023.v11i07.029 | **Received:** 14.06.2023 | **Accepted:** 20.07.2023 | **Published:** 31.07.2023

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Abstract **Original Research Article**

Background: Lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH) and erectile dysfunction (ED) are common disorders whose prevalence increases with advancing age. Recent large-scale epidemiological studies reported a statistically significant association between these two conditions, independent of age and cardiovascular co-morbidities. Furthermore, a significant association between the increased severity of LUTS and the increased severity of ED has been confirmed. ***Objectives:*** The purpose of the study is to offer a clinical evaluation to verify the safety and efficacy of the combination of tamsulosin 0.4 mg/day plus tadalafil 5 mg/day vs. tamsulosin 0.4 mg/day alone to treat patients with LUTS due to BPH. ***Materials & Methods:*** This comparative study was conducted in the Department of Urology, Dhaka Medical College Hospital. The duration of this study was 1 year from April 2018 to March 2019. A total of 170 patients, with a history of symptomatic BPH who attended the Urology Outpatient Department, Dhaka Medical College Hospital, were selected as per inclusion and exclusion criteria. Of them, 85 patients were treated with tamsulosin 0.4mg/day in group A whereas 85 patients were treated with tamsulosin 0.4mg/day plus tadalafil 5mg/day in group B. The general medical condition of the patients was evaluated through history, physical examination. The size of the prostate and PVR were evaluated through ultra-sonogram, and Qmax was assessed with uroflowmetry. The outcome of the patient was assessed by IPSS, IPSS total, IPSS voiding subscore, IPSS storage subscore, IPSS nocturia questionnaire, QOL, International Index of Erectile Function (IIEF-5) questionnaire, Qmax, USG of KUBP with MCC with PVR. Follow-up will be recorded in 4 visits in screening, week 0 randomization, 6 and 12. ***Results:*** One hundred and forty patients completed the study. Improvements in IPSS score and IPSS-QOL were significant with both treatments but greater with the drug combination (p=0.0042 and p=0.0001 respectively) Both regimens similarly improved the Qmax and decreased the PVR volume from baseline with no significant differences between tamsulosin alone vs. tamsulosin and tadalafil (p=0.07 and p=0.51 respectively). The IIEF improved with tamsulosin plus tadalafil but not with tamsulosin alone (p=0.0001). Both treatments were well tolerated. ***Conclusions:*** Tamsulosin 0.4 mg/day plus tadalafil 5 mg/day was more effective than tamsulosin 0.4 mg/day alone to improve LUTS and erectile dysfunction and was also well tolerated.

Keywords: LUTS, BPH, ED, Tamsulosin, Tadalafil.

INTRODUCTION

Benign prostatic hyperplasia (BPH) is a pathologic process that is one of the important causes of lower urinary tract symptoms (LUTS) in ageing men, also described as "male LUTS." Histopathologically, BPH is characterized by an increased number of epithelial and stromal cells in the periurethral area of the prostate and is thus correctly referred to as hyperplasia and not hypertrophy [1]. BPH is prevalent in elderly men and often results in LUTS, i.e. urinary frequency, urgency, nocturia, intermittency, straining, incomplete emptying and a weak urinary stream. LUTS secondary to BPH (LUTS/BPH) increases with age and negatively impacts patients" quality of life".

Community-based and clinical data demonstrate a strong and consistent association between

LUTS and Erectile Dysfunction. Demonstrated a very strong relationship between age, LUTS severity, and ED. Braun *et al*., found that the prevalence of LUTS in men suffering from ED was more frequent than in men with normal erections, considering LUTS as an age-independent risk factor for the development of ED [2]. In addition to surgical interventions, medical therapies extensively investigated for LUTS and BPH include α-adrenergic blockers, 5α-reductase inhibitors, aromatase inhibitors and numerous plant extracts. Newer therapies include antimuscarinic drugs, β3-agonists, phosphodiesterase inhibitors (PDEIs), and several combinations of these agents [3]. Although efficacious, some therapies have the potential for side effects related to sexual dysfunction.

Tadalafil is a phosphodiesterase type 5 (PDE5) inhibitor (PDE5-I) widely approved for the treatment of ED. Several placebo-controlled studies in men with LUTS/BPH have demonstrated improvements in International Prostate Symptom Scores (IPSS) with tadalafil. Compared with the other PDE5-I, tadalafil is unique in its longest half-life amounting to 17.5 hours, where drug efficacy potentially lasts up to 36 h. No untoward concern of increased morbidity has been reported with its long half-life [4].

There is basic scientific evidence that LUTS/ BPH and ED share the same pathophysiology [5]. Likewise, some studies support the role of PDE 4 and 5 inhibitors in LUTS/BPH based on the presence of PDE isoenzymes 4 and 5 in human prostatic tissue [6]. Tadalafil was recently approved in the United States for the treatment of symptoms of BPH (LUTS/BPH) and the treatment of coexisting ED.

PDEIs and α-blockers in combination reduce adrenergic tone in the prostate, bladder neck, and cavernosal smooth muscle tissue in organ bath studies [7], leading researchers to consider combining PDEIs and α-adrenergic blocker medication in man. Considering the high incidence of ED and BPH in ageing men, the same pathophysiology and probability to treat both disorders with the same treatment (alpha-blockers and/or PDE5i) in improving the symptoms of LUTS. Therefore, analyzing the current evidence was necessary to determine the relative outcome and safety of combination therapy with tamsulosin and tadalafil for LUTS/BPH. Patient in Bangladesh, α-blocker tamsulosin 0.4 mg once daily is given as a first-line treatment for LUTS/BPH. So tamsulosin 0.4 mg once daily was included as an active control.

It is expected that combined therapy will improve patients symptoms and quality of life in comparison to monotherapy. But to establish the combination therapy as an effective one, documentation and thorough research are required. We will aim to assess the safety and efficacy of tamsulosin 0.4 mg/day versus tamsulosin 0.4 mg/day plus tadalafil 5 mg/day in patients with LUTS/BPH. So, our target is to evaluate the effectiveness of a combination involving tamsulosin and tadalafil at their conventional dose.

OBJECTIVES

General Objectives

- To determine the outcome of tamsulosin plus tadalafil in comparison to tamsulosin alone in patients with symptomatic BPH.

Specific Objectives

- To observe the improvement of clinical manifestation of symptomatic BPH following tamsulosin 0.4mg or tamsulosin 0.4mg plus tadalafil 5 mg therapy by IPSS.
- To assess changes of uroflowmetry & post voidal residual volume.
- To evaluate the concomitant improvement of associated erectile dysfunction with symptomatic BPH by IIEF5 score.
- To compare the outcome of tamsulosin with tamsulosin plus tadalafil in patients with symptomatic BPH by IPSS score, IPSS voiding subscore, IPSS storage subscore, IPSS nocturia questionnaire, IPSS Quality of Life, Q max, Post voidal residual urine.

MATERIALS AND METHODS

This quasi-experimental study took place at the Department of Urology at Dhaka Medical College Hospital. The study duration was one year, from April 2018 to March 2019. A total of 170 patients with symptomatic benign prostatic hyperplasia (BPH) who visited the urology outpatient department at DMCH were included in the study. Male patients aged 50 years or older with a history of lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) for at least 6 months. The collection was conducted through face-to-face interviews, questionnaires, and gathering investigation data at the Outpatient Department of Urology in Dhaka Medical College Hospital. Participants were selected based on specific inclusion and exclusion criteria, and they agreed not to use any BPH medications other than those provided in the study.

Inclusion Criteria

- Men ages ≥50 years old,
- Clinical diagnosis of BPH by medical history and physical examination (including digital rectal examination),
- IPSS ≥12 points at baseline,
- Total serum Prostatic Specific Antigen (PSA) ≤4.0 ng/ mL,
- Qmax >5 mL/s and <15 mL/s with minimum voided volume of >125 mL at screening,

- Willing and able to give written informed consent, and comply with study procedures.

Exclusion Criteria

- Total serum PSA >4 ng/mL,
- History or evidence of prostate cancer,
- Previous prostatic surgery or other invasive procedures to treat BPH,
- Post-void residual volume (PVR) >250 mL (suprapubic ultrasound) at screening,
- History of acute urinary retention (AUR) within 3 months before the screening visit,
- Any causes other than BPH, which may in the judgement of the investigator, result in urinary symptoms or changes in flow rate (i.e., neurogenic bladder, bladder neck contracture, urethral stricture, bladder malignancy, acute or chronic prostatitis, or acute or chronic urinary tract infections),
- Use of any 5-alpha-reductase inhibitor or use of phytotherapy within the past 6 months of a screening visit,
- Use of any alpha adrenoreceptor blockers within 2 weeks of a screening visit, use of any PDE5i within 2 weeks of a screening visit,
- Certain cardiovascular diseases, for example, unstable angina, recent myocardial infarction, or poorly controlled blood pressure;
- Clinically significant renal or hepatic insufficiency;
- Recent history of stroke or spinal cord injury;
- Current treatment with nitrates, cancer chemotherapy, antiandrogens, or a potent cytochrome P450 3A4 inhibitor;
- Uncontrolled diabetes (glycosylated HbA1c greater than 9%).

Group Allocation

The patients were divided into two groups. One group received treatment with tamsulosin plus tadalafil, while the other group received treatment with tamsulosin alone. The allocation of patients to the treatment groups was done based on the study protocol.

Assessments

The patients underwent various assessments to evaluate their medical condition. These included ultrasounds to measure the size of the prostate and post-void residual (PVR), as well as uroflowmetry to assess the maximum urinary flow rate (Qmax).

Outcome Measures

The primary outcome measure was the International Prostate Symptom Score (IPSS), which was used to assess the severity of lower urinary tract symptoms (LUTS). Secondary outcome measures included IPSS subscores (voiding and storage), IPSS nocturia questionnaire with quality of life (QOL) assessment, International Index of Erectile Function (IIEF-5) questionnaire, and uroflowmetry findings. Follow-up visits were scheduled during the 6th and 12th weeks of the study. During these visits, IPSS, QOL, IIEF-5, uroflowmetry, and ultrasounds of the kidneys, ureters, bladder, and prostate (KUBP) with PVR were performed to track the patient's progress and assess treatment outcomes. At each visit, patients were asked about any adverse effects experienced or any worsening of LUTS. Any adverse effects were recorded and taken into consideration in the analysis.

Statistical Analysis

Compared the efficacy of tamsulosin alone versus tamsulosin plus tadalafil in treating lower urinary tract symptoms (LUTS) caused by benign prostatic hyperplasia (BPH). Various statistical methods, such as t-tests, chi-square tests, and regression analysis, were likely employed to assess treatment outcomes and determine the significance of differences between the two treatment groups.

Ethical Consideration

Before the commencement of the study, the respective authority approved the research protocol. Proper permission was taken from the department and institution concerned for the study. All the patients included in this study were informed about the nature, risks and benefits of the study. No data was collected without the permission of the patient. Participation in this research is fully voluntary. The respondents remained entirely free to withdraw their participation at any stage or any time of the study. Informed written consent was taken from each patient. Confidentiality was assured and anonymity was maintained. No participant was identified in any report or publication of the study.

RESULTS

The study was intended to determine the efficacy of tamsulosin plus tadalafil in comparison to tamsulosin alone in patients with symptomatic BPH. A total of 170 cases of symptomatic BPH were selected by the inclusion and exclusion criteria. Cases were allocated to Group A (Patients treated with tamsulosin alone) and Group B (Patients treated with tamsulosin plus tadalafil). The outcome variables were IPSS, IPSS-QOL, IIEF, and PVR in Ultrasonography of KUBP and Qmax in uroflowmetry. The findings derived from data analysis were presented below.

Table 1: Age distribution

Group	Age	Number of Patients (n)
A	59.87 ± 4.6 years	85
B	60.24 ± 3.92 years	85

The age differences between the two groups were not statistically significant (p = 0.56).

Table 2: Pre-Treatment Assessments

Assessment	Group A (Mean ± SD)	Group B (Mean ± SD)	p-value
IPSS	21.22 ± 1.5	21.02 ± 1.5	0.90
IPSS-QOL	4.57 ± 0.56	4.56 ± 0.52	0.90
Erectile Function (IIEF)	14.94 ± 0.80	15.14 ± 0.75	0.09
Maximum flow rate (Qmax)	10.12 ± 0.79	9.97 ± 0.80	0.22
Post voidal residual (PVR)	58.31 ± 4.68	58.6 ± 5.1	0.69

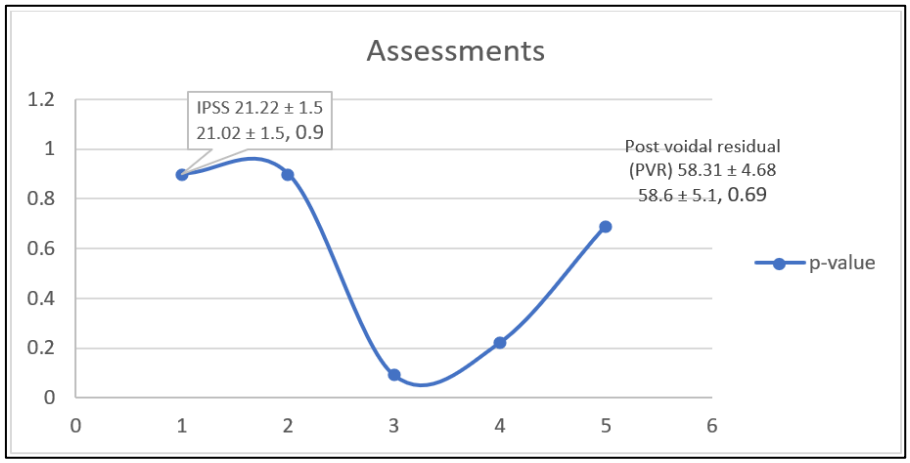

Figure 1: Periodically re Evaluations

Table 3: Post Treatment Assessment at the 6th week of treatment

Assessment	Group A (Mean ± SD)	Group B (Mean ± SD)	p-value
IPSS	18.47 ± 1.21	17.30 ± 0.77	0.0001
IPSS-QOL	3.41 ± 0.49	3.21 ± 0.41	0.004
Erectile Function (IIEF)	15.25 ± 0.74	19.14 ± 0.63	0.0001
Maximum flow rate (Qmax)	11.65 ± 0.64	11.68 ± 0.72	0.77
Post voidal residual (PVR)	41.89 ± 3.95	42.82 ± 3.1	0.08

Table 4: Post Treatment Assessment at the 12th week of treatment

Assessment	Group A (Mean ± SD)	Group B (Mean ± SD)	p-value
IPSS	10.43 ± 5.30	8.31 ± 3.10	0.0042
IPSS-QOL	1.88 ± 1.03	1.04 ± 0.61	0.0001
Erectile Function (IIEF)	15.27 ± 1.99	22.65 ± 0.87	0.0001
Maximum flow rate (Qmax)	13.35 ± 0.66	13.54 ± 0.60	0.07
Post voidal residual (PVR)	24.13 ± 1.44	23.97 ± 1.46	0.51

Table 5: Adverse events during the treatment

Adverse events	Tamsulosin plus Tadalafil (n=85)	Tamsulosin (n=85)
Headache	12	0
Postural hypotension	5	6
Dizziness	2	0
Ejaculation disorder	1	2
Dyspepsia	6	0
Altered Vision	0	0
Diarrhoea	1	2

Data were analyzed using Student's t-test, and the level of significance was set at < 0.05.

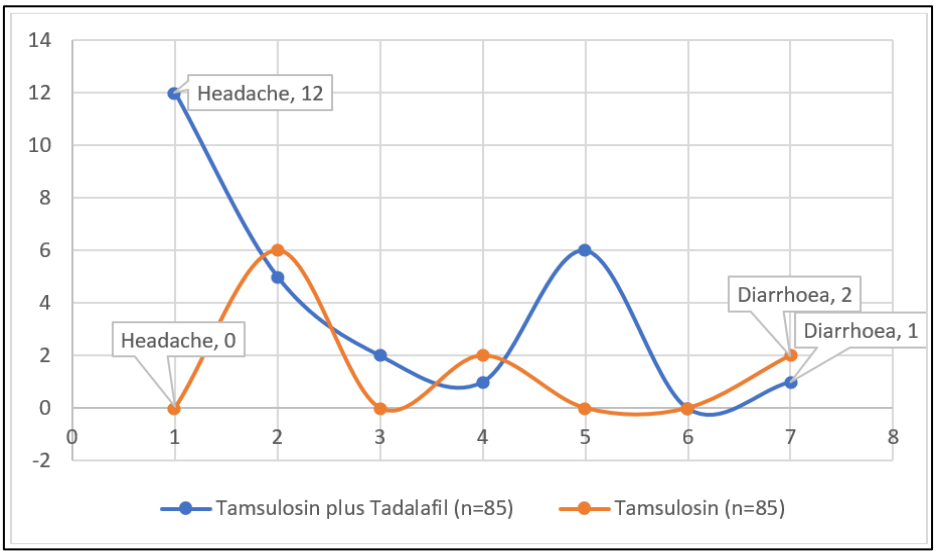

Figure 2: Severe reactions to the treatment

The findings demonstrate that both treatment groups exhibited similar baseline characteristics, as indicated by the non-significant age differences (p = 0.56). However, when comparing the efficacy of the two treatments, the combination therapy showed more promising results in alleviating urinary symptoms at both the 6th and 12th weeks of treatment. In the 6th week, patients in the tamsulosin plus tadalafil group reported significantly lower IPSS scores (p = 0.0001) and improved IPSS-QOL (p = 0.004) compared to those treated with tamsulosin alone. Additionally, the combination therapy demonstrated a significant improvement in erectile function (p = 0.0001) compared to tamsulosin alone. However, the maximum flow rate of urine and post-void residual urine did not show any significant difference between the two treatment groups at both time points.

By the 12th week, the tamsulosin plus tadalafil group continued to exhibit better outcomes in terms of IPSS (p = 0.0042), IPSS-QOL (p = 0.0001), and erectile function (p = 0.0001). Notably, the combination therapy resulted in a more substantial improvement in these parameters. Overall, the study suggests that combining tadalafil with tamsulosin may offer superior benefits in terms of improving urinary symptoms and erectile function in patients compared to tamsulosin monotherapy. However, it is important to acknowledge that more extensive studies with larger sample sizes and longer follow-up periods are necessary to corroborate these findings and establish the treatment's long-term safety and efficacy.

DISCUSSION

Lower urinary tract symptoms (LUTS) and benign prostatic hyperplasia (BPH), as well as erectile dysfunction (ED), are common conditions among ageing men [8]. Alpha-blockers, including tamsulosin, are frequently used to manage LUTS and BPH, while phosphodiesterase 5 inhibitors (PDE5i), such as tadalafil, are prescribed for ED [9]. Given the close association between LUTS and ED, there has been an increase in the concurrent administration of these medications.

Several studies have compared the effectiveness of tamsulosin alone versus tamsulosin in combination with tadalafil for the treatment of LUTS in BPH. One such study conducted by Bechara *et al.*, demonstrated significant improvements in the International Prostate Symptom Score (IPSS) and IPSS-Quality of Life (IPSS-QOL) with both treatment approaches, but the combination therapy showed greater efficacy [10]. Both treatment regimens similarly improved maximum flow rate (Qmax) and reduced post-void residual (PVR) volume compared to baseline (P < 0.001), with no significant differences observed between tamsulosin alone and tamsulosin plus tadalafil (P > 0.05). However, the International Index of Erectile Function (IIEF) score significantly improved with tamsulosin plus tadalafil (P < 0.001), whereas tamsulosin alone did not yield significant improvements (P > 0.05).

The current study aimed to compare the effectiveness of tamsulosin alone versus tamsulosin in combination with tadalafil in patients with symptomatic benign prostatic hyperplasia (BPH). A total of 170 patients meeting the inclusion and exclusion criteria were divided into two groups. Group A received tamsulosin alone, while Group B received a combination of tamsulosin and tadalafil. The study analyzed and compiled the results of treatment outcomes, including age, urinary symptoms, erectile

function, maximum flow rate of urine (Qmax), and post-void residual urine, for comparison between the two groups. The average age of patients in Group A was 59.87 (± 4.6) years, and in Group B, it was 60.24 (± 3.92) years, showing no statistically significant difference (p = 0.56). This age range was consistent with previous studies conducted [10], which also assessed the efficacy of tamsulosin and tadalafil combinations in patients with BPH.

Regarding urinary symptoms measured by the International Prostate Symptom Score (IPSS), both groups showed similar pre-treatment mean values (21.22 ± 1.5 for Group A and 21.02 ± 1.5 for Group B), with no significant difference between the two (p = 0.90). The same trend was observed for IPSS-Quality of Life (IPSS-QOL), where there was no significant difference between the two groups (p = 0.904). Similarly, no significant difference was found for erectile function as measured by the International Index of Erectile Function (IIEF) between Group A and Group B (p = 0.09). The pre-treatment maximum flow rate of urine (Qmax) and post-void residual urine values were also comparable between the two groups, with no significant differences observed (p = 0.22 for Qmax and p = 0.69 for post-void residual urine).

These findings align with the study conducted by Bechara *et al.,* [10], which reported no significant differences in IPSS, IPSS-QOL, IIEF, Qmax, and post-void residual urine between the two groups at the pre-treatment stage. In 6th week of follow up the IPSS was calculated, in group A mean IPSS was 18.47 (± 1.21) and in group B it was 17.30 (± 0.77). In both groups, IPSS was reduced but in group B it was reduced more. And there is a significant difference in IPSS value between the two groups (p=0.0001). At the 12th week of follow up the IPSS in group A and group B was 10.43 (± 5.30) and 8.31 (±3.10), the difference of which is significant (p=0.0042). Bechara *et al.,* (2008) compared the efficacy of tamsulosin versus tamsulosin plus tadalafil in the treatment of LUTS. They found that both tadalafil plus tamsulosin and tamsulosin alone significantly improved the IPSS from baseline (p< 0.001), the combination being better than tamsulosin alone (p<0.05). Singh *et al*. have done a prospective randomized study among 133 men complaining of LUTS, a significant decrease in IPSS score was observed in monotherapy of tamsulosin (50.90%, p< 0.05) and with combined therapy of tamsulosin and tadalafil (53.90%, p< 0.05) [11]. Tamsulosin monotherapy and combination regimen both were significantly good (P< 0.05), whereas the combination regimen may not be statistically significant but better than the tamsulosin regimen (P=0.147).

IPSS-QOL score was measured in the 6th week of treatment in group A and group B where there is a significant decrease of mean value in both groups (3.41 ± 0.49 and 3.21 ± 0.41 respectively) but in the combination group, it is more significant (P=0.004). At the 12th week of treatment, the mean QOL score in group A and group B was 1.88 (± 1.03) and 1.04 (± 0.61) respectively which is statistically significant (P=0.0001). Bechara *et al.,* [10] also showed that there is a statistically significant improvement in the QOL score in the combination drug group and it is comparable to our study. IIEF score in group A and group B in the 6th week of treatment was 15.25 ± 0.74 and 19.14 ± 0.63, and in the 12th week of treatment was 15.25 ± 1.99 and 22.65 ± 0.87. There is much improvement in IIEF score in the combination drug group (P=0.0001 and P=0.0001). Similar study found the combination drug group is more effective.

In 6th week of treatment, the Maximum flow rate of urine (Qmax) was measured in both groups and the mean Qmax in group A was 11.65 (± 0.64) ml/sec and in group B was 11.68 (± 0.72) ml/sec. There is no significant difference of change in Qmax between the two groups (p=0.77). In the 12th week the mean Qmax in group A was 13.35 (± 0.66) ml/sec and in group, B was 13.54 (± 0.60) ml/sec, and there is no statistically significant changes in Qmax value between the two group (P=0.07). Singh *et al*. compared the efficacy of tamsulosin and tadalafil versus tamsulosin or tadalafil alone in patients with LUTS due to BPH, they found that there is no statistically significant difference between the monotherapy and combination drug group (p=0.307), which is comparable to my study [11].

In our study, we have found that there is no significant improvement in the post-void residue in both groups. In the 6th week of follow-up, we found mean PVR in group A was 41.89 (± 3.95) ml and in group, B was 42.82 (± 3.1) ml, the difference of which is not statistically significant (P= 0.089). In the 12th week, we found mean PVR in group A was 24.13 (± 1.44) and in group B was 23.97 (± 1.46), the difference of which is also not statistically significant (P= 0.51). Bechara *et al.,* found that the combination of tamsulosin and tadalafil did not produce significant changes in PVR when compared with alpha-blocker monotherapy, which is similar to our study [10].

There were no severe adverse events in any of the active treatment groups. There were no clinically significant changes in laboratory measurements or vital signs. Twelve patients complained of headaches in the tamsulosin plus tadalafil group. Five patients from the tamsulosin plus tadalafil group and six patients from the tamsulosin group complained of postural hypotension. Other side effects include dizziness, ejaculation disorder, dyspepsia, and diarrhea which were not so significant. Seven patients in the tamsulosin plus tadalafil group discontinued the study for severe headache and for postural hypotension, four patients from group A and two patients from group B

discontinued the study. A total of thirty patients discontinued the treatment (17.64%) out of which seventeen patients dropped out because of the adverse effect of drugs and thirteen patients for noncompliance.

CONCLUSION

The 6-week combination therapy of tamsulosin 0.4 mg/day and tadalafil 5 mg/day proved more effective and well-tolerated than tamsulosin alone in treating lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH) and erectile dysfunction (ED). Further large-scale, randomized, placebo-controlled studies are required to assess the long-term safety and efficacy of these agents in symptomatic BPH management, with or without ED.

Limitations

The study's duration was standard for assessing lower urinary tract symptoms (LUTS) and benign prostatic hyperplasia (BPH) outcomes. However, the longer-term effects of tadalafil and its impact on disease progression were not investigated. Future studies with extended follow-up periods are needed to understand the sustained efficacy and potential disease-modifying effects of tadalafil.

Prostate size not considered: The study did not include an assessment of prostate size as a variable. Prostate size is an important factor in BPH management and may influence the efficacy of drugs in improving LUTS/BPH. Future research should take prostate size into account to determine its impact on treatment outcomes.

Lack of long-term side effect analysis: While short-term tolerability was assessed, the study did not examine the long-term side effects of the treatment groups. Understanding the potential adverse effects over an extended period is crucial for ensuring the safety profile of these drugs. Future studies should investigate the long-term side effects to provide a comprehensive understanding of the risks associated with these treatment approaches.

RECOMMENDATION

Combination therapy: The combination of tamsulosin and tadalafil can be recommended as a safe and effective treatment option for patients with symptomatic benign prostatic hyperplasia (BPH) and lower urinary tract symptoms (LUTS). This combination therapy has been shown to improve symptoms and enhance the quality of life compared to tamsulosin monotherapy.

Further research: To strengthen the evidence base and provide more comprehensive information, large-scale multicentric studies are needed. These studies should involve a broader patient population and assess the long-term effectiveness, safety, and tolerability of the combination therapy. Additionally, investigating the impact of combination therapy on disease progression and evaluating its potential benefits for specific subgroups, such as patients with varying prostate sizes, would be valuable.

Drug management: Proper drug management strategies should be implemented when using the combination of tamsulosin and tadalafil. This includes careful patient selection, dosage adjustment based on individual needs, monitoring for potential side effects, and regular follow-up to assess treatment response.

REFERENCES

1. Roehrborn, C. G. (2012). Benign prostatic hyperplasia. *Campbell-Walsh Urology*, 2570-2610.
2. Braun, M. H., Sommer, F., Haupt, G., Mathers, M. J., Reifenrath, B., & Engelmann, U. H. (2003). Lower urinary tract symptoms and erectile dysfunction: co-morbidity or typical "Aging Male" symptoms? Results of the "Cologne Male Survey". *European urology*, *44*(5), 588-594.
3. McVary, K. T., Monnig, W., Camps, J. L., Young, J. M., Tseng, L. J., & Van Den Ende, G. (2007). Sildenafil citrate improves erectile function and urinary symptoms in men with erectile dysfunction and lower urinary tract symptoms associated with benign prostatic hyperplasia: a randomized, double-blind trial. *The Journal of urology*, *177*(3), 1071-1077.
4. Goldfischer, E., Kowalczyk, J. J., Clark, W. R., Brady, E., Shane, M. A., Dgetluck, N., & Klise, S. R. (2012). Hemodynamic effects of once-daily tadalafil in men with signs and symptoms of benign prostatic hyperplasia on concomitant α1-adrenergic antagonist therapy: results of a multicenter randomized, double-blind, placebo-controlled trial. *Urology*, *79*(4), 875-882.
5. Khan, M. A., Thompson, C. S., Dashwood, M. R., Mumtaz, F. H., Morgan, R. J., & Mikhailidis, D. P. (2003). Endothelin-1 and nitric oxide in the pathogenesis of urinary tract disorders secondary to bladder outlet obstruction. *Current Vascular Pharmacology*, *1*(1), 27-31.
6. ÜCKERT, S., KÜTHE, A., Jonas, U. D. O., & Stief, C. G. (2001). Characterization and functional relevance of cyclic nucleotide phosphodiesterase isoenzymes of the human prostate. *The Journal of urology*, *166*(6), 2484-2490.
7. Oger, S., Behr-Roussel, D., Gorny, D., Lecoz, O., Lebret, T., Denoux, Y., ... & Giuliano, F. (2009). Combination of doxazosin and sildenafil exerts an additive relaxing effect compared with each compound alone on human cavernosal and prostatic tissue. *The Journal of Sexual Medicine*, *6*(3), 836-847.
8. Berry, S. J., Coffey, D. S., Walsh, P. C., & Ewing, L. L. (1984). The development of human benign

prostatic hyperplasia with age. *The Journal of urology*, *132*(3), 474-479.

9. Emberton, M., Zinner, N., Michel, M. C., Gittelman, M., Chung, M. K., & Madersbacher, S. (2007). Managing the progression of lower urinary tract symptoms/benign prostatic hyperplasia: therapeutic options for the man at risk. *BJU international*, *100*(2), 249-253.
10. Bechara, A., Romano, S., Casabé, A., Haime, S., Dedola, P., Hernández, C., & Rey, H. (2008). Comparative efficacy assessment of tamsulosin vs. tamsulosin plus tadalafil in the treatment of LUTS/BPH. Pilot study. *The journal of sexual medicine*, *5*(9), 2170-2178.
11. Singh, D. V., Mete, U. K., Mandal, A. K., & Singh, S. K. (2014). A comparative randomized prospective study to evaluate efficacy and safety of combination of tamsulosin and tadalafil vs. tamsulosin or tadalafil alone in patients with lower urinary tract symptoms due to benign prostatic hyperplasia. *The journal of sexual medicine*, *11*(1), 187-196.