COMPARATIVE EFFICACY OF TAMSULOSIN VS TADALAFIL AND TAMSULOSIN: IN TREATMENT OF LOWER URINARY TRACT SYMPTOMS SECONDARY TO BENIGN PROSTATIC HYPERTROPHY (BPH)

Sagun Bahadur Thapa Chhetri,[1] Sudip Chaudhary,[1] Manab Tiwari[1]

ABSTRACT

INTRODUCTION

Benign prostatic hypertrophy (BPH) is common among aging men. Tamsulosin has long been used in medical management for troublesome Lower Urinary Tract Symptoms (LUTS). Tadalafil has demonstrated effectiveness in addressing LUTS through several preclinical and clinical trials. We aim to assess the efficacy of tamsulosin alone vs tadalafil with tamsulosin given in symptomatic patients of BPH in a tertiary care teaching institution.

MATERIAL AND METHODS

This prospective observational longitudinal study was conducted at Universal College of Medical Sciences, Bhairahawa from October 2021 to March 2023. A total of 140 patients with BPH were divided into 2 groups; tamsulosin only (0.4 mg once daily) and tamsulosin (0.4 mg once daily) + tadalafil (5 mg once daily) group. IPSS, QoL (Quality of Life) were recorded on the first visit and then at 2, 6 and 12 weeks. Similarly, voided urinary volume, Qmax (maximum flow rate), PVR (post-voidal residual urine) were recorded at first visit and then after 2 weeks.

RESULTS

There was a significant improvement in the IPSS score, QoL, Qmax and PVR in both tamsulosin group and tamsulosin + tadalafil group ($p<0.001$). The mean difference in improvement of IPSS score (10.8 vs 9.3), IPSS-QoL (2.73 vs 2.24), Qmax (4.9 vs 3.2) and PVR (36.87 vs 32.56) was more in tamsulosin + tadalafil group compared to tamsulosin group. Similarly, mean difference in IPSS score in 2nd and 3rd visit is better in the combination group.

CONCLUSION

The combination of tamsulosin and tadalafil was superior to tamsulosin alone in terms of IPSS, IPSS-QoL, Qmax and PVR.

KEYWORDS

Prostate, Tamsulosin, Tadalafil

1. Department of General Surgery, Universal College of Medical Sciences, Bhairahawa, Nepal

https://doi.org/10.3126/jucms.v13i01.78132

For Correspondence
Dr. Sagun Bahadur Thapa Chhetri
Department of Surgery (Urology unit)
Universal College of Medical Sciences
Bhairahawa, Nepal
E-mail: tsagun.nams75@gmail.com

INTRODUCTION

Benign prostatic hyperplasia (BPH) is one of the most common conditions among aging men, making BPH a leading source of healthcare problem of old age in the world.[1] Approximately 75% of males from 60 to 69 years old and 83% of men aged 70 years or older are estimated to have got LUTS/BPH.[2] BPH is actually a histological diagnosis due to the proliferation of smooth muscles and epithelial cells within the prostatic tissue.[3]

Patients with benign prostatic hyperplasia present with a range of lower urinary tract symptoms (LUTS) which include obstructive symptoms (weak stream, intermittency, straining, incomplete emptying, hesitancy, terminal dribbling) and irritative symptoms (frequency, nocturia, urge incontinence).[3,4]

The differential diagnosis of BPH is stricture of urethra, bladder tumor, carcinoma prostate, bladder neck stenosis, bladder neck hypertrophy, neurological causes of retention of urine like diabetes mellitus.[5] Medical therapy serves as the initial line of treatment in the management of BPH patients, with the primary goal of alleviating symptoms and enhancing the patient's overall quality of life. Typically, this entails the utilization of alpha blockers, either alone or in combination with 5-α reductase inhibitors. Notably, PDE-5 inhibitors have demonstrated effectiveness in addressing lower urinary tract symptoms through several preclinical and clinical trials. These inhibitors have been found to enhance oxygenation and increase blood supply, diminish intra-prostatic inflammation, and relax the smooth muscle tone within the lower urinary tract.[6]

Tamsulosin has long been used in the medical management of patients with troublesome lower urinary tract symptoms. Over time, a range of newer medications have surfaced to address LUTS from benign prostatic hyperplasia. In contrast to the well-established utility in treating erectile dysfunction, the effectiveness and safety of PDE-5 inhibitors, particularly tadalafil at 5 mg in the context of BPH-associated LUTS, have received relatively less attention within published literature.

Studies have shown a consistent association between LUTS and ED. Prevalence of LUTS in men suffering from ED was more frequent than in men with normal erections.[7] In men with mild and moderate LUTS, erection problems were reported to be 43.3% and 65.8% respectively.[8]

We aim to assess the efficacy of tamsulosin alone vs tadalafil and tamsulosin combination in symptomatic patients of BPH in a tertiary care teaching institution.

MATERIAL AND METHODS

A hospital-based prospective observational longitudinal study was designed and approved by IRC of UCMS-TH, Bhairahawa, Nepal (UCMS/IRC/137/21).

The sample size was calculated using Cochran's formula, $n=z^2 pq/d^2$. n=required sample size p=prevalence of LUTS with BPH= 10.3.[9]
q=100-p; z=1.96 taken at 95% confidence interval (CI=10.2-10.5); d=allowable error taken as 5%
$n= \{1.96^2 x\ 10.3\ x\ (100-10.3)\} \div 5^2$

The sample size calculated by the above formula was found to be approximately 140. So, we included a total of 140 patients attending UCMS urology outpatients from October 2021 to March 2023(18 months) and having BPH with LUTS.

All BPH patients with age >45years and presenting with Lower Urinary Tract Symptoms with written consent are included in the study.

Patients with malignancy, tuberculosis, diabetes mellitus, anticoagulant therapy, severe hepatic renal or CVS dysfunction and other immune- compromised states were excluded. Patients with previous history of urethral or prostate surgery, Patients with active UTI and patients with severe International Prostate Symptom Score are also excluded.

Method of Collection of Data

Detailed history of the patient was taken. The treatment group A (Tamsulosin only) and group B (Tamsulosin + Tadalafil) were formed. Then by using purposive consecutive sampling, samples were taken from both groups until the sample size was fulfilled.

In Group A, tamsulosin 0.4mg was given orally at bedtime. In Group B, tamsulosin 0.4mg with tadalafil 5mg was given orally at bedtime. Patients were asked questionnaire pertaining to obstructive/voiding symptoms in LUTS and calculation of IPSS and QoL index was done. Focused urological examination of patient was done to rule out other causes of LUTS.

Patients underwent urine analysis and culture sensitivity to detect urinary tract infections. They also had USG KUB and prostate exams to check prostate size, post-void residual urine, and intravesical prostatic protrusion (IVPP). Uroflowmetry was performed to measure voided urinary volume and Qmax (ml/sec). The IPSS score was recorded during the first visit in OPD and subsequently during follow-up at 2 weeks, 6 weeks, and 12 weeks. Similarly, QoL score was also recorded as IPSS score. An IPSS up to 7 indicated mild symptoms, 8-19 indicated moderate symptoms and 20-35 indicated severe symptoms. Uroflowmetry was also done during the first visit and repeated after 2 weeks. Voided urinary volume, post void residual urine and Qmax were recorded in first visit and subsequent follow up.

The patients were verbally asked about the side effects such as headache, postural hypotension, dizziness, diarrhea and other side effects. The identification of patients with urinary symptoms was challenging as many men did not volunteer such information regarding erectile dysfunction and might incorrectly believe that changes were a normal part of ageing, were embarrassed about their condition, or were afraid of the need for surgery.[10]

Statistical Analysis

Data was collected on preformed proforma during the OPD visit/follow ups. All the data was entered into Microsoft Excel and analyzed using SPSS v20. Categorical variables were compared using Chi-square test (λ^2) test. The comparison of continuous variables was performed using the student's t-test. *P*-value less than 0.05 was considered statistically significant.

RESULTS

In this study, 140 patients with BPH were evaluated who were divided into 2 drug groups: tamsulosin only and tamsulosin + tadalafil group. The baseline characteristics of patients are shown in the table below.

Table 1. Baseline parameters of patients in 2 different drug groups

Baseline parameters	Group A (Mean±SD)	Group B (Mean±SD)	*p*-value
Age	65.79± 9.96	64.3± 9.96	0.369
IPSS	14.09±2.87	14.34±2.57	0.576
QoL	3.44±0.53	3.73 ±0.48	0.18
Prostate Size	42.36±19.72	37.28±8.81	0.06
IVPP	12.10±4.72	12.81±2.98	0.289
PVR	52.49±39.10	54.96±34.00	0.690
Vvol	208.70±94.46	215.94±113.50	0.682
Qmax	11.13±2.57	10.90±4.64	0.719

IPSS: International prostate symptom score, QoL: Quality of Life, IVPP: Intravesical prostatic protrusion, Vvol: Voided volume, Qmax: maximum flow rate.

There is no significant difference in the baseline parameters of the patients in 2 different drug groups like age (p=0.369), IPSS score (p=0.576), QoL (p=0.18), prostate size (0.06), IVPP (p=0.289), PVR (p=0.690), Vvol (p=0.682), Qmax (p=0.719). So, the variables in these two groups are comparable.

Table 2. Comparison of mean difference in IPSS scores in both drug groups in the first and last visit

Group	IPSS	Mean±SD	Mean±SD	Mean difference	*p*-value
Group A	IPSS 1 vs IPSS 4	14.09 ± 2.87	4.77± 1.69	9.31	<0.001
Group B	IPSS 1 vs IPSS 4	14.34 ±2.57	3.54 ± 1.27	10.8	<0.001

There is a significant difference in mean among the 2 different drug groups. However, the mean difference in Group B (10.8) is more than that of Group A (9.31).

Table 3. Comparison of mean difference in QoL scores in both drug groups in first and last visit

Group	Mean±SD	Mean±SD	Mean difference	*p*-value
Group A	3.44 ± 0.53	1.22± 0.42	2.24	<0.001
Group B	3.73 ±0.48	1.00 ± 0.17	2.73	<0.001

There is a significant difference in mean among the 2 different drug groups. However, the mean difference in Group B (2.73) is more than that of Group A (2.24).

Table 4. Comparison of Qmax and mean difference in 1st and 2nd visit in tamsulosin group

Parameter	V1 Qmax	V2 Qmax	Mean difference	*p*-value
Mean±SD	11.13± 2.57	14.33±2.07	3.2	<0.001

There is a significant difference in the Qmax in first visit and follow up after 2 weeks with a mean difference of 3.2 in tamsulosin only group.

Table 5. Comparison of Qmax and mean difference between 1st and 2nd visit in tamsulosin+ tadalafil group

Parameter	V1 Qmax	V2 Qmax	Mean difference	*p*-value
Mean±SD	10.90± 4.64	15.84±3.24	4.94	<0.001

There is a significant difference in the Qmax in first visit and follow up after 2 weeks with a mean difference of 4.94 in tamsulosin + tadalafil group.

Table 6. Comparison of PVR and mean difference in 1st and 2nd visit in tamsulosin group

Parameter	V1 PVR	V2 PVR	Mean difference	*p*-value
Mean±SD	52.49±39.10	19.93 ±9.61	32.56	<0.001

There is a significant difference in the PVR in first visit and follow up after 2 weeks with a mean difference of 32.56 in tamsulosin only group.

Table 7. Comparison of PVR and mean difference in 1st and 2nd visit in tamsulosin+ tadalafil group

Parameter	V1 PVR	V2 PVR	Mean difference	*p*-value
Mean±SD	54.96±34.00	18.07 ±8.82	36.87	<0.001

There is a significant difference in the PVR in first visit and follow up after 2 weeks with a mean difference of 36.87 in tamsulosin + tadalafil group.

DISCUSSION

Medical therapy serves as an initial line of treatment in patients of BPH with therapy aimed at reducing the symptoms and improving the quality of life of the patient. Drugs from different drug groups have been used such as alpha-blockers, 5 alpha reductase inhibitors. PDE5 has also been used in cases of BPH and has been found effective in the treatment of LUTS in several preclinical and clinical trials.[11] In our study tamsulosin 0.4 mg once daily and tadalafil 5mg daily has been used and outcomes were monitored and recorded in terms of IPSS score, IPSS QoL score, PVR and Qmax and were compared.

In this study, the baseline characteristics of patients like age, IPSS score, IPSS QoL score, prostate size, IVPP, PVR, urinary volume and Qmax were recorded in both the drug groups. There was no significant difference in the baseline characteristics of patients and thus the variables in both the drug groups were comparable.

In this study, among 140 patients with BPH the mean age of patients in tamsulosin group was 65.79± 9.96 and the mean age of patients in tamsulosin+ tadalafil group was 64.3± 9.96 indicating that incidence of BPH increased with age and affects the elderly population.

Similarly, the baseline characteristics like IPSS score in this study was found to be 14.09±2.87 in tamsulosin group and 14.34±2.57 in tadalafil group indicating that majority of cases were from the moderate severity group (8-19) of IPSS score. However few cases were from mild severity group as well and the patients with severe (>19) were excluded from this study. This data was comparable with the baseline IPSS score of Nagasubramanian S et al.[12] with IPSS score 15.10 (3.96) in tamsulosin group and 16.26 (3.32) in tamsulosin + tadalafil group. This indicates that majority of patients with the mild and moderate IPSS score are benefited by the medical treatment and those with severe IPSS scores are benefited by the surgical intervention.

In this study we can see a significant improvement in the IPSS scores recorded at follow up during 2, 6 and 12 weeks in both the drug groups. In tamsulosin only group the IPSS score has improved from baseline of 14.09±2.87 to 4.8±1.7 after 12 weeks. In tamsulosin + tadalafil group the IPSS

score has improved from baseline of 14.34±2.57 to 3.5±1.3 after 12 weeks. The mean difference in IPSS score among these two groups was found to be 9.31 and 10.8 in tamsulosin alone and tamsulosin + tadalafil group respectively. Since the mean difference in IPSS score in dual drug therapy was more than that of single drug, we found that the combination of tamsulosin and tadalafil was superior to tamsulosin alone. In study by Singh et al[11] the IPSS score improved after 3-month duration in both the drug groups with significant improvement in the combination therapy where the decrease in IPSS score was by 53.90% and in tamsulosin only group the decrease in IPSS score was 50.90%.

Similarly, in this study the QoL index has also improved significantly in both the groups. The QoL index in the tamsulosin group has improved from baseline of 3.44 ± 0.53 to 1.22± 0.42 with a mean difference of 2.24 and the QoL in tamsulosin + tadalafil group has improved from baseline of 3.73 ±0.48 to 1.00 ± 0.17 with a mean difference of 2.73. Since the mean difference in QoL was more in the combination group than in the single drug group we found that combination of tamsulosin and tadalafil was superior to tamsulosin only which was consistent in findings by Singh et al.40 who found the decrease in QoL index by 79.65% in tamsulosin + tadalafil group and 73.35% in the tamsulosin group.

In this study, the baseline Qmax in tamsulosin only and tamsulosin + tadalafil group were 11.13± 2.57 ml/sec and 10.90± 4.64 ml/sec respectively. The value of Qmax was recorded at 2 week follow up time which was 14.33±2.07 in tamsulosin only group and 15.84±3.24 in the tamsulosin + tadalafil group which shows a significant improvement in Qmax with mean difference of 3.2 ml/sec and 4.94 ml/sec respectively. This study had similar results as compared to Singh et al. where the baseline Qmax in tamsulosin group increased from 9.15±3.022 ml/sec to 12.26±3.537 ml/sec in tamsulosin only group and from 9.88±3.581 ml/sec to 13.54±5.587 ml/sec in tamsulosin + tadalafil group. Another study conducted by Bechara et al[13] showed improvement of QoL from baseline 9.6 ml/sec to 11.7 ml/sec in tamsulosin group and 12.6 in tamsulosin + tadalafil group. Improvement in the value of Qmax also favors that the combination drug therapy is better than the single drug.

Similarly, post voidal residual urine in this study was 52.49±39.10 ml in tamsulosin group and 54.96±34.00 in tamsulosin + tadalafil group. The patients were followed up after 2 weeks and the PVR was recorded which was found to be 19.93 ±9.61 in tamsulosin group and 18.07 ±8.82 in the tamsulosin + tadalafil group. There was mean difference of decrease of PVR to be 32.56 ml in tamsulosin group and 36.87 ml in tamsulosin + tadalafil group. This data shows that there was significant reduction in the PVR (p<0.001) and favors the superiority of combination therapy as the mean difference is more in the combination therapy as compared to the single drug therapy.

Similarly, in a study by Karami et al, combination of tamsulosin and tadalafil improved international prostate symptom scores and Qmax in patients with lower urinary tract symptoms and benign prostatic hyperplasia to more degrees than their separate use.[14] In a randomized double blinded controlled trial conducted by Kim et al, the fixed drug combination was safe, well tolerated, and efficacious, indicating that combination therapy could provide clinical benefits for patients with BPH- associated LUTS complaints and ameliorate the co-morbidity of ED.[15] These studies had significant improvement in the IPSS scores in the combination therapy as compared to the single drug therapy which was similar in finding with our study.

One main limitation of the present study was that this sample was taken from a single center; a larger sample size from a multicenter study is recommended.

CONCLUSION

Based on the findings of this study, there was a significant improvement in the IPSS score, QoL, Qmax and PVR in both tamsulosin group and tamsulosin + tadalafil group. However, the mean difference in improvement of IPSS score (10.8 vs 9.3), IPSS-QoL (2.73 vs 2.24), Qmax (4.9 vs 3.2) and PVR (36.87 vs 32.56) was more in tamsulosin + tadalafil group than in the tamsulosin group. Similarly, the mean difference in IPSS score between two drug groups in 2nd and 3rd visit showed better outcome in the combination group. Thus, the combination of tamsulosin and tadalafil was superior to tamsulosin alone in terms of IPSS, IPSS-QoL, Qmax and PVR.

FINANCIAL SUPPORT AND SPONSORSHIP

None

CONFLICT OF INTEREST

None

REFERENCES

1. Saigal CS, Joyce G. ECONOMIC COSTS OF BENIGN PROSTATIC HYPERPLASIA IN THE PRIVATE SECTOR. Journal of Urology. 2005;173(4):1309-13.
2. Wei JT, Calhoun E, Jacobsen SJ. UROLOGIC DISEASES IN AMERICA PROJECT: BENIGN PROSTATIC HYPERPLASIA. Journal of Urology. 2005;173(4):1256-61.
3. Barry MJ, Fowler FJ, O'Leary MP, et al. The American Urological Association Symptom Index for Benign Prostatic Hyperplasia. Journal of Urology. 1992;148(5 Part 1):1549-57.
4. Lane T, Shah J. Clinical features and management of benign prostatic hyperplasia. Hospital Medicine. 1999;60(10):705-09.
5. SRB's Manual of Surgery. 4th edition. Jaypee Brothers Medical Publishers (P) Ltd.; 2013.
6. Sebastianelli A, Spatafora P, Morselli S, et al. Tadalafil Alone or in Combination with Tamsulosin for the Management for LUTS/BPH and ED. Curr Urol Rep. 2020;21(12):56.

7. Braun MH, Sommer F, Haupt G, Mathers MJ, Reifenrath B, Engelmann UH. Lower Urinary Tract Symptoms and Erectile Dysfunction: Co-Morbidity or Typical "Aging Male" Symptoms? Results of the "Cologne Male Survey." European Urology. 2003;44(5):588-94.

8. Rosen RC, Wei JT, Althof SE, Seftel AD, Miner M, Perelman MA. Association of Sexual Dysfunction With Lower Urinary Tract Symptoms of BPH and BPH Medical Therapies: Results From the BPH Registry. Urology. 2009;73(3):562-66.

9. Verhamme KMC, Dieleman JP, Bleumink GS, Van Der Lei J, Sturkenboom MCJM. Incidence and Prevalence of Lower Urinary Tract Symptoms Suggestive of Benign Prostatic Hyperplasia in Primary Care—The Triumph Project. European Urology. 2002;42(4):323-28.

10. Naslund MJ, Costa FJ, Miner MM. Managing enlarged prostate in primarycare: MANAGING ENLARGED PROSTATE IN PRIMARY CARE.International Journal of Clinical Practice. 2006;60(12):1609-15.

11. Singh DV, Mete UK, Mandal AK, Singh SK. 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. 2014;11(1):187-96.

12. Nagasubramanian S, Antonisamy B, Mukha RP, et al. Tamsulosin and placebo vs tamsulosin and tadalafil in male lower urinary tract symptoms: a double□blinded, randomised controlled trial. BJU International. 2020;125(5):718-24.

13. Bechara A, Romano S, Casabé A, et al. Comparative Efficacy Assessment of Tamsulosin vs. Tamsulosin Plus Tadalafil in the Treatment of LUTS/BPH. Pilot Study. The Journal of Sexual Medicine. 2008;5(9):2170-78.

14. Karami H, Hassanzadeh-Hadad A, Fallah-Karkan M. Comparing Monotherapy with Tadalafil or Tamsulosin and Their Combination Therapy in Men with Benign Prostatic Hyperplasia: A Randomized Clinical Trial. Urol J. 2016;13(6):2920-26.

15. Kim SW, Park NC, Lee SW, et al. Efficacy and Safety of a Fixed-Dose Combination Therapy of Tamsulosin and Tadalafil for Patients with Lower Urinary Tract Symptoms and Erectile Dysfunction: Results of a Randomized, Double-Blinded, Active-Controlled Trial. The Journal of Sexual Medicine. 2017;14(8):1018-27