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ORIGINAL RESEARCH ARTICLE

A Comparative Study of the Combination Treatment of Tamsulosin and Dutasteride with Monotherapy of Tamsulosin in Lower Urinary Tract Symptoms Due to Benign Prostatic Hyperplasia

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ABSTRACT

Introduction: Benign prostatic hyperplasia (BPH) is a common condition in aging men, often leading to lower urinary tract symptoms (LUTS), such as increased frequency, urgency, and weak urine flow. These symptoms negatively impact quality of life and, if untreated, can lead to complications like acute urinary retention, bladder stones, and renal failure. Medical management, including alpha-blockers like tamsulosin and 5-alpha reductase inhibitors like dutasteride, is an effective approach for symptom relief. This study aims to compare the clinical effectiveness of combination therapy (tamsulosin and dutasteride) with tamsulosin monotherapy in alleviating LUTS due to BPH. It also aims to assess the reduction in prostate volume, post-void residual volume, and improvement in peak urinary flow rate.

Material and methods: A study was conducted on 200 male patients aged 50 to 80 years with obstructive LUTS. Patients were randomized into two groups: monotherapy with tamsulosin 0.4 mg/day or combination therapy with tamsulosin 0.4 mg/day and dutasteride 0.5 mg/day for 3 months. Patients were followed fortnightly, and pre-and post-treatment assessments were done.

Results: The study found that both combination therapy with tamsulosin and dutasteride and monotherapy with tamsulosin helped in the improvement of lower urinary tract symptoms (LUTS) in patients with benign prostatic hyperplasia (BPH). Post-treatment, both groups showed significant improvements in AUA scores, prostate volume, and post-void residual volume and peak urinary flow rate. In comparing combination and monotherapy, combination therapy was more effective than monotherapy.

Conclusion: Both combination and monotherapy are effective in reducing LUTS due to BPH, but combination therapy is more effective than monotherapy in comparison between the two, though further long-term studies are required to assess the sustainability of these improvements.

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INTRODUCTION

Benign prostatic hyperplasia (BPH) is a prevalent condition among aging men, often leading to lower urinary tract symptoms (LUTS), such as increased frequency, urgency, weak urine flow, and nocturia.[1] As men age, the risk of BPH-related symptoms rises, with about 40% of men over 60 experiencing moderate to severe LUTS. If left untreated, BPH can cause complications such as urinary tract infections (UTIs), bladder stones, acute urinary retention (AUR), and renal failure.[2] Managing BPH often begins with medical treatment, including the use of α1-adrenergic antagonists like tamsulosin, which helps relax the smooth muscles of the bladder, neck and prostate to improve urinary flow. Another treatment option involves 5-alpha reductase inhibitors like dutasteride, which reduces prostate size by inhibiting the conversion of testosterone to dihydrotestosterone, further improving urinary flow.[3]

For men with moderate to severe LUTS, a combination therapy of tamsulosin and dutasteride may offer enhanced symptom relief compared to tamsulosin monotherapy. While tamsulosin works to alleviate muscle-related obstruction, dutasteride helps reduce the overall size of the prostate, providing a dual mechanism for improving urinary symptoms. However, both therapies carry potential side effects, including asthenia, headaches, dizziness, and postural hypotension, which affect a small percentage of patients.[4,5]

This article aims to evaluate and compare the clinical effectiveness of combination therapy with tamsulosin and dutasteride versus monotherapy with tamsulosin

in managing LUTS due to BPH. The findings may help identify the most effective treatment approach, considering both symptom relief and the minimization of adverse effects, ultimately guiding treatment decisions for better patient outcomes.

MATERIAL AND METHODS

This study included 200 male patients aged 50 to 80 years, presenting with obstructive lower urinary tract symptoms (LUTS). Randomization was conducted using a lottery system, where patients were assigned to either monotherapy or combination therapy groups based on the lottery draw. Patients with obstructive LUTS symptoms within the age range of 50 to 80 years were included in the study. Patients were excluded if they had any of the following conditions: A history of urinary retention requiring catheterization, suspected or confirmed prostatic carcinoma, and definite neurological lesions affecting the brain or spinal cord. Associated urinary bladder pathology such as stones, malignancy, or diverticulum. Patients were assigned to one of the following treatment groups: Monotherapy group: Tamsulosin 0.4 mg/day for 3 months. Combination therapy group: Dutasteride 0.5 mg/day and tamsulosin 0.4 mg/day for 3 months. Patients were evaluated before being included and after the completion of the study, CBC, KFT, and PSA were evaluated. Subjective evaluation was done using the AUA symptom scoring index. Objective evaluation was done using ultrasound whole abdomen to confirm the diagnosis, assess pre and post-treatment prostate volume and post-void residual volume, and rule out any associated bladder or urinary tract pathology. Uroflowmetry was done pre and post-treatment to measure peak urinary flow rate. Cystoscopy was done to support the diagnosis, assess prostate size and rule out any associated bladder pathology. All patients underwent pre-treatment evaluations and were followed up fortnightly for 3 months to monitor treatment compliance and assess their progress. Post-treatment evaluations were conducted to compare outcomes.

RESULTS

Table 1 highlights the improvements in AUA scores following both combination therapy and monotherapy. Post-treatment, a substantial shift from severe to mild cases was observed, with a significant *p-value* of < 0.0001, demonstrating the effectiveness of both treatments in reducing lower urinary tract symptoms.

On comparing mean post treatment scores of combination and monotherapy, combination therapy was more effective than monotherapy (Table 2). Table 3 presents the significant reduction in prostate volume after both combination therapy and monotherapy.

A noticeable shift to lower prostate volume categories was observed post-treatment in both groups, with a *p-value* < 0.0001, indicating the efficacy of both treatments in reducing prostate size. In comparing combination therapy and monotherapy, combination therapy was more effective than monotherapy in reducing prostate volume (Table 4).

Table 5 presents the reduction in post-void residual volume after both combination therapy and monotherapy, with a *p-value* < 0.0001, indicating the effectiveness of both therapies.

Table 6 shows a comparison of the mean pre and post-treatment residual volume of combination and monotherapy and *p-value* of post treatment score.

Table 7 presents the improvement in peak urinary flow rate following both combination therapy and monotherapy, indicating the efficacy of both treatment approaches in enhancing urinary flow.

Table 1: AUA scores in pre- and post-treatment patients under combination therapy and monotherapy

AUA category	*Pre-treatment patients*	*Post-treatment patients*	*p-value*	*AUA category*	*Pre-treatment patients*	*Post-treatment patients*	*p-value*
Combination therapy				Monotherapy			
Mild	0 (0%)	48 (48%)	< 0.0001	Mild	0 (0%)	39 (39%)	< 0.0001
Moderate	64 (64%)	39 (39%)		Moderate	65 (65%)	40 (40%)	
Severe	36 (36%)	13 (13%)		Severe	35 (35%)	21 (21%)	
Total patients	100 (100%)	100 (100%)		Total patients	100 (100%)	100 (100%)	
Mean AUA score ± Standard Deviation	17.71 ± 6.10	10.31 ± 6.02		Mean AUA Score ± Standard Deviation	17.78 ± 5.95	12.30 ± 7.25	

Table 2: Comparing mean pre and post treatment AUA score of combination and monotherapy and *p-value* of post treatment score

Mean AUA score ± Standard deviation	*Pre-treatment*	*Post-treatment*	*p-value*
Combination therapy (Group1)	17.71 ± 6.10	10.31 ± 6.02	0.03
Monotherapy (Group2)	17.78 ± 5.95	12.30 ± 7.25	

Table 3: Prostate volume in pre-treatment and post-treatment patients under combination and monotherapy

Prostate volume (cc)	*Pre-treatment (Patients)*	*Post-treatment (Patients)*	*p-value*	*Prostate volume (cc)*	*Pre-treatment (Patients)*	*Post-treatment (Patients)*	*p-value*
Combination therapy				Monotherapy			
< 25	0	27	< 0.0001	< 25	0	24	< 0.0001
25–50	11	40		25–50	12	33	
50–75	44	16		50–75	43	31	
75–100	34	14		75–100	38	10	
> 100	11	3		> 100	7	2	
Total	100	100		Total	100	100	
Mean Prostate Volume ± Standard Deviation	77.48 ± 19.74	37.40 ± 23.41		Mean Prostate Volume ± Standard Deviation	77.46 ± 19.42	46.86 ± 22.68	

Table 4: Comparison of mean pre and post-treatment prostate volume of combination and monotherapy and *p-value* of post-treatment score.

Mean prostate volume ± Standard deviation	*Pre-treatment*	*Post-treatment*	*p-value*
Combination therapy (Group1)	77.48 ± 19.74	37.40 ± 23.41	0.0039
Monotherapy (Group2)	77.46 ± 19.42	46.86 ± 22.68	

Table 5: Post-void residual volume in pre-treatment and post-treatment patients under combination and monotherapy

Residual volume (mL)	*Pre-treatment patients*	*Post-treatment patients*	*p-value*	*Residual volume (mL)*	*Pre-treatment (Patients)*	*Post-treatment (Patients)*	*p-value*
Combination therapy				*Mono therapy*			
< 50	0	28		< 50	0	24	
50–100	14	40		50–100	13	32	
100–150	46	15		100–150	46	31	
150–200	32	15		150–200	38	13	
> 200	8	2	< 0.0001	> 200	3	0	< 0.0001
Total	100	100		Total	100	100	
Mean residual volume ± Standard deviation	145.94 ± 38.34	68.71 ± 48.55		Mean residual volume ± Standard deviation	148.36 ± 35.55	92.67 ± 45.90	

Table 6: Pre and post-treatment residual volume of combination and monotherapy and p-value of post-treatment score.

Mean residual volume ± Standard deviation	*Pre-treatment*	*Post-treatment*	*p-value*
Combination therapy (Group1)	145.94 ± 38.34	68.71 ± 48.55	0.004
Monotherapy (Group2)	148.36 ± 35.55	92.67 ± 45.90	

DISCUSSION

The present study found that combination therapy of tamsulosin and dutasteride significantly improved AUA scores in patients with benign prostatic hyperplasia (BPH). A shift from severe to mild symptoms was observed in 48% of combination therapy patients compared to 39% in the monotherapy group. Zhou *et al*. conducted a meta-analysis that included five studies including 4348 patients, which confirmed the superiority of combination treatment of tamsulosin with dutasteride on comparison with tamsulosin monotherapy (mean difference [MD], −1.43; 95% confidence interval

Table 7: Peak urinary flow rate in pre-treatment and post-treatment patients under combination therapy and monotherapy

Peak flow rate (mL)	*Pre-treatment (Patients)*	*Post-treatment (Patients)*	*p-value*	*Peak flow rate (mL)*	*Pre-treatment (Patients)*	*Post-treatment (Patients)*	*p-value*
Combination therapy				Monotherapy			
0–5	8	1		0–5	7	0	
5.1–10	31	14		5.1–10	32	14	
10.1–15	51	18		10.1–15	45	29	
15.1–20	10	41		15.1–20	16	33	
> 20	0	26	< 0.0001	> 20	0	24	< 0.0001
Total	100	100		Total	100	100	
Mean peak flow rate ± Standard Deviation	10.09 ± 3.73	18.84 ± 6.95		Mean peak flow rate ± Standard deviation	10.77 ± 4.04	16.97 ± 6.31	

Table 8: Mean pre and post-treatment peak flow rate of combination and monotherapy and p-value of post-treatment score.

Mean peak flow rate ± Standard deviation	*Pre-treatment*	*Post-treatment*	*p-value*
Combination therapy (Group1)	10.09 ± 3.73	18.84 ± 6.95	0.04
Monotherapy (Group2)	10.77 ± 4.04	16.97 ± 6.31	

[CI], − 2.20 to − 0.66; $p = 0.0003$).[6] Haque *et al*. (2018) conducted a 4-week, single-blind, placebo, run-in which was followed by a 2-year double-blind, randomized controlled trial in men aged ≥50 years with symptomatic benign prostatic hyperplasia depicting better clinical response in combination group in comparison with the monotherapy group.[7] Behnam *et al*. conducted a meta-analysis including six studies and 6647 patients and reported significant improvement in the combination therapy group compared to the tamsulosin group (mean difference [MD]=-2.59, %95 confidence interval [CI]: -4.20 to -0.99; $p = 0.002$)[8] Osama *et al*. reviewed six randomized controlled trials involving comparison of combination therapy with monotherapy using ARAs and 5-αRIs and found that combination group had significantly greater effects in relieving symptoms.[9]

These studies confirm the greater efficacy of combination therapy in improving LUTS and reducing symptom severity when compared to monotherapy.

The present study found that combination therapy with tamsulosin and dutasteride significantly reduced prostate volume compared to tamsulosin monotherapy. Post-treatment, 27% of patients in the combination group had a prostate volume less than 25 cc, compared to 24% in the monotherapy group. Zhou *et al*. confirmed the superiority of the combination treatment of tamsulosin with dutasteride compared with tamsulosin monotherapy in reducing prostate volume (MD, − 10.13; 95% CI, − 12.38 to − 7.88; $p < 0.00001$).[6] Haque *et al*. showed significant prostate volume reduction at months 12 and 24 ($p < 0.001$), depicting better clinical response in the combination group in comparison with the monotherapy group.[7] Nandana *et al*., conducted a study to measure the improvement of prostate volume after treatment with tamsulosin and dutasteride as a combination drug in BPH patients. The average prostate volume pre-therapy was 51.71 cc with the lowest volume was 25 cc and the highest volume 118 cc. The average prostate volume post-therapy was 42.38 cc with the lowest volume was 22 cc and the highest 92 cc. The ratio of prostate volume more than 40 cc at pre-therapy was 50%, and after therapy, was decreased to 40%, depicting a significant difference in comparison of pre and post-therapy prostate volume.[10] Behnam *et al*. reported significant reduction in prostate volume in the combination therapy group compared to the tamsulosin group (MD=-10.13, %95 CI: -12.38 to -7.88; $p < 0.05$).[8]

These results match the findings of the present study, confirming the superiority of combination therapy in reducing prostate size.

The present study found that combination therapy with tamsulosin and dutasteride significantly reduced post-void residual (PVR) volume compared to tamsulosin monotherapy. In the combination group, 28% of patients achieved a PVR volume of less than 50 mL post-treatment, compared to 24% in the monotherapy group. The mean residual volume in the combination group decreased from 145.94 ± 38.34 to 68.71 ± 48.55 mL, while in the monotherapy group, it decreased from 148.36 ± 35.55 to 92.67 ± 45.90 mL. Zhou *et al*. (2019) confirmed the superiority of the combination treatment of tamsulosin with dutasteride over tamsulosin monotherapy in decreasing post-void residual volume (MD, − 3.85; 95% CI, − 4.95 to − 2.76; $p < 0.00001$).[6] Haque *et al*. depicted better post-void residual volume reduction in the combination group in comparison with the monotherapy group.[7] Osama *et al*. found that the combination group had significantly greater effects in reducing post-void residual volume in comparison to monotherapy.[9]

These studies reinforce the current findings that combination therapy is more effective in reducing PVR volume than monotherapy.

The present study found that combination therapy with tamsulosin and dutasteride significantly improved peak urinary flow rate in comparison to tamsulosin monotherapy. In the combination therapy group, 26% of patients achieved a flow rate greater than 20 mL/s post-treatment, while 24% of patients in the monotherapy group reached similar levels. The mean peak flow rate increased from 10.09 ± 3.73 to 18.84 ± 6.95 mL/s in the combination group and from 10.77 ± 4.04 to 16.97 ± 6.31 mL/s in the monotherapy group. Zhou *et al*. confirmed the superiority of the combination treatment of tamsulosin with dutasteride compared with tamsulosin monotherapy in increasing peak urine flow rate (MD, 1.05; 95% CI, 0.82 to 1.29; $p < 0.00001$).[6] Haque *et al*. depicted more increase in peak urinary flow rate in the combination group in comparison with the monotherapy group.[7] Behnam *et al*. reported significant improvement in peak urinary flow rate in the combination therapy group compared to the tamsulosin group (MD=1.05, %95 CI: 0.82 to 1.29; p <0.05), confirming the effectiveness of combination treatment in improving urinary flow.[8]

CONCLUSION

Based on both existing literature and the current research, medical interventions for BPH have proven effective in alleviating symptoms and slowing disease progression while reducing the risk of complications like acute urinary retention and the need for surgery. Both combination and monotherapy have demonstrated their effectiveness as a medical treatment for BPH but on comparing between the two, combination therapy is more effective. However, the present study's three-month duration limits long-term conclusions. Uncertainty remains regarding the duration of pharmacotherapy necessary to achieve sustained improvement and whether symptom relief will persist once treatment is stopped or if patients will regress, requiring alternative interventions. While pharmacotherapy may not offer a permanent solution to BPH, it plays a crucial and effective role for patients who either decline invasive procedures or are unsuitable candidates for surgery due to high risk.

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