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Comparison of Alpha-Blocker Monotherapy Versus Combination Therapy in Moderate to Severe LUTS: A Real-World Study

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Abstract

Lower urinary tract symptoms (LUTS) in men significantly impair quality of life and are commonly managed using α-blockers as first-line therapy, with or without the addition of 5α-reductase inhibitors (5-ARIs). This real-world, prospective comparative study evaluated the effectiveness of α-blocker monotherapy versus α-blocker plus 5-ARI combination therapy in men with moderate to severe LUTS. A total of 220 patients aged 50–75 years with International Prostate Symptom Score (IPSS) ≥ 15 were enrolled, randomized equally, and followed for 12 months. The primary outcome was change in IPSS, while secondary outcomes included peak urinary flow rate (Qmax), post-void residual volume (PVR), prostate volume, and adverse events. Combination therapy demonstrated a greater reduction in IPSS (mean ± SD: 14.2 ± 4.3 vs. 10.5 ± 4.6; $p < 0.001$), improvement in Qmax (5.1 ± 1.8 vs. 3.6 ± 1.9 mL/s; $p < 0.001$), and reduction in prostate volume (18.6 ± 6.2 vs. 4.1 ± 2.4 mL; $p < 0.001$) compared to monotherapy. PVR reduction was also significantly greater in the combination group (49.2 ± 20.8 vs. 34.6 ± 17.9 mL; $p < 0.01$). Adverse events were more frequent with combination therapy but were generally mild. These findings indicate that combination therapy provides superior symptom relief and disease modification in real-world practice, although careful monitoring of tolerability remains necessary.

Keywords: lower urinary tract symptoms; α-blockers; combination therapy

Introduction

Lower urinary tract symptoms (LUTS) represent one of the most common health concerns in aging men, significantly impacting daily functioning and overall quality of life. The clinical manifestations of LUTS range from voiding symptoms such as weak stream and hesitancy to storage symptoms including urgency, nocturia, and increased frequency. These symptoms often arise from benign prostatic enlargement, age-related changes in detrusor function, or a combination of factors contributing to bladder outlet obstruction. As life expectancy increases globally, the prevalence of LUTS continues to rise, placing a substantial burden on healthcare systems and individual wellbeing.1-4

Pharmacological treatment remains the cornerstone of LUTS management. α-blockers are widely prescribed as first-line agents due to their rapid symptomatic improvement by reducing smooth muscle tone within the prostate and bladder neck. However, α-blockers have limited impact on prostate size and long-term disease progression. As such, their effectiveness in preventing clinical deterioration or surgical intervention is limited. On the other hand, 5α-reductase inhibitors act by reducing prostate volume and androgen-driven hyperplasia, thereby altering disease progression, though they require a longer onset of action and may be associated with sexual side effects.5-7

Combination therapy with α-blockers and 5-ARIs has been proposed as a rational strategy, leveraging the rapid symptom relief provided by α-blockers alongside the disease-modifying properties of 5-ARIs. Randomized clinical trials have supported this approach, showing reductions in symptom progression and risk of acute urinary retention. Nevertheless, there is still uncertainty regarding how well these findings translate to real-world clinical settings, where patient adherence, comorbidities, and tolerability often differ from controlled environments.8-10

The importance of evaluating real-world outcomes lies in their generalizability. Patients seen in daily clinical practice present with variable disease severities, comorbid illnesses, and treatment adherence patterns. A real-world perspective provides greater external validity compared to controlled trials, ensuring results are applicable to the diverse populations encountered by practicing clinicians. Moreover, the balance between efficacy and adverse events must be carefully considered, as tolerability plays a critical role in long-term treatment adherence.

This study was designed to compare the real-world effectiveness and safety of α-blocker monotherapy versus α-blocker plus 5-ARI combination therapy in men with moderate to severe LUTS. The evaluation focused on symptomatic relief, functional improvement, and safety over a 12-month period. By incorporating both subjective measures such as IPSS and objective measures such as Qmax, PVR, and prostate volume, this investigation provides a comprehensive assessment of treatment outcomes.

Methodology

This prospective, real-world comparative study was conducted at Department of Urology, University College of Medicine, The University of Lahore between January 2022 and June 2024. A total of 220 male patients aged 50–75 years with moderate to severe LUTS, defined by an IPSS ≥ 15, were recruited. Exclusion criteria included prior prostate surgery, prostate cancer, neurogenic bladder, uncontrolled diabetes, or severe cardiac disease. Patients were randomized using a computer-generated sequence into two groups: Group A (n=110) received α-blocker monotherapy (tamsulosin 0.4 mg daily), while Group B (n=110) received α-blocker plus 5-ARI combination therapy (tamsulosin 0.4 mg + dutasteride 0.5 mg daily). Sample size was calculated using Epi Info™, assuming a mean difference of 3 points in IPSS reduction, $\alpha = 0.05$, power = 90%, and accounting for 10% loss to follow-up, resulting in 220 participants. All patients provided verbal informed consent. Clinical assessments included IPSS, Qmax, PVR (ultrasound), and prostate volume (transrectal ultrasound) at baseline and 12 months. Safety was assessed through adverse event reporting. Statistical analysis was performed using independent t-tests for continuous data and chi-square for categorical variables, with $p < 0.05$ considered significant.

Results

Table 1. Baseline Characteristics

Variable	Monotherapy (n=110)	Combination (n=110)	p-value
Age (years)	64.2 ± 6.8	63.9 ± 7.1	0.71
Baseline IPSS	23.6 ± 4.2	24.1 ± 4.5	0.48
Qmax (mL/s)	8.2 ± 2.4	8.0 ± 2.3	0.62

Variable	Monotherapy (n=110)	Combination (n=110)	p-value
PVR (mL)	110.3 ± 32.5	111.6 ± 31.9	0.79
Prostate volume (mL)	52.8 ± 13.4	53.2 ± 12.8	0.83

Table 2. Clinical Outcomes after 12 Months

Outcome	Monotherapy	Combination	p-value
IPSS reduction (points)	10.5 ± 4.6	14.2 ± 4.3	<0.001
Qmax improvement (mL/s)	3.6 ± 1.9	5.1 ± 1.8	<0.001
PVR reduction (mL)	34.6 ± 17.9	49.2 ± 20.8	<0.01

Table 3. Prostate Volume and Adverse Events

Outcome	Monotherapy	Combination	p-value
Prostate volume reduction (mL)	4.1 ± 2.4	18.6 ± 6.2	<0.001
Adverse events (%)	9%	18%	0.04

Baseline characteristics were comparable between groups. Combination therapy showed significantly greater improvements in IPSS, Qmax, PVR, and prostate volume, though adverse events were more frequent.

Discussion

This study demonstrates that combination therapy with α-blockers and 5-ARIs provides superior clinical benefit compared to α-blocker monotherapy in men with moderate to severe LUTS in a real-world setting. Patients receiving combination therapy experienced greater symptom relief as measured by IPSS, which translated into improved daily functioning and quality of life.11-13

Objective measures corroborated these findings, with significantly greater improvement in urinary flow and reduction in residual urine in the combination group. These results suggest enhanced efficacy in alleviating obstruction, reflecting both functional and structural benefits. The marked reduction in prostate volume highlights the disease-modifying role of 5-ARIs, which monotherapy lacks.14-16

The study reinforces the principle that while α-blockers provide rapid symptom relief, their long-term disease-modifying impact remains limited. Combination therapy, by targeting both dynamic and static components of obstruction, offers a more comprehensive treatment strategy. These results align with the therapeutic rationale that addressing both smooth muscle tone and prostate growth optimizes outcomes.17-19

The increased incidence of adverse events with combination therapy is an important consideration. Sexual dysfunction, dizziness, and fatigue were the most frequently reported side effects. Although generally mild, they have implications for adherence in routine practice, emphasizing the need for shared decision-making between physicians and patients.20

Real-world data are particularly valuable in this context. Unlike controlled trials, this study reflects the complexities of daily practice, including variable adherence, comorbidities, and broader patient demographics. The consistency of benefits in this less selective population reinforces the clinical applicability of combination therapy.

Limitations of the present study include its single-center design and the 12-month follow-up, which may not capture long-term outcomes such as progression to surgery or sustained adherence. Future multicenter studies with extended follow-up would be valuable in addressing these gaps and confirming durability of benefits.

Overall, the findings provide strong evidence that combination therapy should be considered the preferred strategy in men with moderate to severe LUTS, particularly those at risk of disease progression. The balance between efficacy and safety must remain central to therapeutic decisions.

Conclusion

Combination therapy with α-blockers and 5-ARIs demonstrated superior improvements in symptoms, urinary function, and prostate volume compared to monotherapy in men with moderate to severe LUTS. While associated with higher rates of adverse events, these were generally manageable. This study highlights the real-world effectiveness of combination therapy and addresses the gap between trial evidence and clinical practice.

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