ORIGINAL RESEARCH PAPER

General Surgery

MIRABEGRON AND SILODOSIN COMBINATION THERAPY: A NEW STRATEGY FOR IMPROVING QUALITY OF LIFE IN PATIENTS WITH BENIGN PROSTATIC HYPERPLASIA AND STORAGE SYMPTOMS

KEY WORDS: Benign prostatic hyperplasia, silodosin, mirabegron, storage symptoms, alpha-blockers, beta-3 adrenergic agonists, combination therapy.

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ABSTRACT

Introduction: Benign prostatic hyperplasia (BPH) affects a substantial portion of the aging male population, particularly those over 50, causing non-cancerous enlargement of the prostate gland and leading to lower urinary tract symptoms (LUTS). These symptoms are often divided into obstructive (voiding) and storage (irritative) categories. While alpha-blockers such as silodosin are commonly used to manage BPH, they primarily alleviate voiding symptoms and may be inadequate in resolving persistent storage symptoms. Mirabegron, a beta-3 adrenergic agonist, has shown promise in treating overactive bladder (OAB), which overlaps with BPH storage symptoms. This study evaluates the efficacy of combining mirabegron with silodosin in patients with persistent storage symptoms despite silodosin monotherapy. **Materials and Methods:** This prospective, randomized study was conducted from January 2021 to August 2022 at Shri Atal Bihari Vajpayee Medical College and Research Institute, Bangalore. We included 92 patients diagnosed with BPH and persistent storage symptoms after two weeks of silodosin treatment. Participants were randomized into two groups: Group A (45 patients) continued with silodosin 8 mg, while Group B (47 patients) received an additional 25 mg of mirabegron along with silodosin. Assessments were performed at baseline and after an 8-week follow-up, focusing on parameters such as International Prostate Symptom Score (IPSS), IPSS storage subscore, quality of life (QoL), maximum flow rate (Qmax), post-void residual urine (PVRU), and prostate-specific antigen (PSA) levels. Statistical analyses were conducted using paired t-tests, with a p-value <0.05 considered significant. **Results:** Baseline characteristics were similar between groups, with no significant differences in age, PSA levels, prostate volume, or symptom scores. After 8 weeks, Group B showed significant improvements compared to Group A. Total IPSS decreased from 21.0±8.4 to 18.3±6.9 (p=0.04) in the mirabegron add-on group, while IPSS storage subscore improved from 8.7±4.9 to 6.5±2.9 (p=0.002). QoL also enhanced from 3.9±2.0 to 3.0±1.7 (p=0.006). Minimal adverse effects were reported, with a slightly higher incidence of dry mouth and constipation in the mirabegron group. **Discussion:** The addition of mirabegron to silodosin significantly improved symptom control in patients with persistent storage symptoms. This combination therapy effectively addresses both obstructive and irritative components of BPH, providing a more comprehensive treatment approach. The results support the potential of mirabegron as an adjunct therapy, aligning with previous studies on combination therapies for BPH. The minimal adverse effects observed suggest that the benefits of combination therapy outweigh the risks. **Conclusion:** Mirabegron as an add-on to silodosin presents a viable option for managing persistent storage symptoms in BPH patients who do not respond adequately to monotherapy. Further research is warranted to confirm the long-term benefits and safety of this combination therapy.

INTRODUCTION:

Benign prostatic hyperplasia (BPH) commonly affects men over 50, causing non-cancerous prostate enlargement and lower urinary tract symptoms (LUTS), including storage symptoms (frequency, urgency, nocturia) that harm quality of life [1].

Silodosin, an alpha-1A blocker, improves urine flow by relaxing prostate/bladder neck muscles but often fails to fully relieve storage symptoms [2,3]. Up to 40% of patients on alpha-blockers still experience persistent urgency/frequency, worsening their quality of life [4,5].

Mirabegron, a beta-3 agonist, reduces overactive bladder symptoms by relaxing the detrusor muscle and may complement silodosin for residual storage symptoms [6,7]. However, limited evidence exists on their combined use in BPH [8].

This combination therapy could improve symptom control, enhance patient outcomes, and influence treatment guidelines. Further research is needed to confirm its efficacy and safety [9]

MATERIALS & METHODS.

Study Design & Setting: This prospective randomized study (Jan 2021–Aug 2022) at Shri Atal Bihari Vajpayee Medical College, Bangalore, followed ethical guidelines (Declaration of Helsinki). It included 92 BPH patients with persistent storage symptoms after 2 weeks of silodosin monotherapy.

Groups & Intervention:

- **Group A (n=45):** Continued silodosin 8 mg alone.
- **Group B (n=47):** Received silodosin 8 mg + mirabegron 25 mg. Both groups were followed for 8 weeks.

Assessments:

Baseline And Post-treatment Evaluations Included:

- **Clinical Parameters:** Age, PSA, prostate volume (TPV).
- **Symptom Scores:** IPSS, IPSS storage subscore, QoL.
- **Urodynamics:** Qmax, post-void residual (PVRU).

Exclusion Criteria:

- Recent use of 5-alpha reductase inhibitors/ antimuscarinics.

- Obstructive LUTS dominance, PVRU >100 mL.
- Renal dysfunction, diabetes, orthostatic hypotension.

Statistical Analysis:
- Paired t-test for comparisons.
- Significance threshold: $p < 0.05$

RESULTS

Table-1: Baseline Characteristics Of Patient In Both The Groups.

Characteristics	Group A (Silodosin only, n=45)	Group B (Mirabegron Add-on, n=47)	p-value
Age (years)	68.2±7.2	66.5±7.8	0.19
PSA (ng/ml)	2.3±2.5	1.9±1.8	0.29
TPV (ml)	32.5±11.0	29.3±9.5	0.07
Total IPSS	18.7±6.5	21.0±8.4	0.08
IPSS storage	9.3±3.7	8.7±4.9	0.43
QoL	4.2±1.3	3.9±2.0	0.31
Q-Max	14.3±6.8	15.6±7.0	0.28
PVRU (ml)	21.9±19.5	28.3±23.0	0.08

Table-2 Baseline & endpoint characteristics evaluation between groups and statistical significance

Characteristics	Group A (Silodosin only, n-65)		p-value	Group B (Mirabegron Add-on, n-65)		p-value
	Baseline	Endpoint		Baseline	Endpoint	
Total IPSS	18.7±6.5	17.3±7.9	0.27	21.0±8.4	18.3±6.9	0.04
IPSS storage	9.3±3.7	8.9±5.0	0.60	8.7±4.9	6.5±2.9	0.002
QoL	4.2±1.3	3.8±2.0	0.17	3.9±2.0	3.0±1.7	0.006
Q-Max	14.3±6.8	13.7±8.1	0.64	15.6±7.0	17.5±7.2	0.12
PVRU (ml)	21.9±19.5	18.6±13.7	0.26	28.3±23.0	30.5±18.9	0.55

Minimal adverse effects were reported in both groups. In the Mirabegron add-on group, 6.4% (3 out of 47) experienced dry mouth and constipation, whereas in the Silodosin-only group, 4.4% (2 out of 45) reported a stuffy nose. No participants discontinued medication during the study.

The study indicated that after eight weeks, the Mirabegron add-on therapy led to significant improvements in total IPSS, IPSS storage, and QoL in Group B. Total IPSS decreased from 21.0±8.4 to 18.3±6.9 (p=0.04), IPSS storage reduced from 8.7±4.9 to 6.5±2.9 (p=0.002), and QoL improved from 3.9±2.0 to 3.0±1.7 (p=0.006).

DISCUSSION:

This study aimed to evaluate the efficacy of adding Mirabegron to Silodosin therapy in patients with benign prostatic hyperplasia (BPH) who continued to experience storage symptoms despite two weeks of Silodosin monotherapy.

Key Results:
- **Mirabegron add-on group** showed significant improvements ($p < 0.05$) in:
- **Total IPSS** (21.0 → 18.3)
- **IPSS storage subscore** (8.7 → 6.5)
- **QoL** (3.9 → 3.0)
- **Mechanistic synergy:** Silodosin (alpha-1A blocker) relieves obstruction, while Mirabegron (beta-3 agonist) improves bladder storage.
- **Safety:** Minimal side effects (e.g., dry mouth, constipation).

Clinical Relevance:
- Supports **combination therapy** for refractory storage symptoms.
- Aligns with prior studies (e.g., Kaplan et al. [12]).

Limitations:
- Small sample size (n=92), short follow-up (8 weeks).
- Excluded high-risk patients (e.g., diabetes, PVRU >100 mL).

Future Directions:
- Larger, longer-term trials to confirm efficacy/safety.
- Research on predictive factors for treatment response.

CONCLUSION

In conclusion, the addition of Mirabegron to Silodosin therapy significantly improves symptom control in patients with BPH who experience persistent storage symptoms. This combination therapy offers a viable option for patients not adequately managed by monotherapy and warrants further investigation to confirm its long-term benefits and safety.

MEsh Terms: Benign Prostatic Hyperplasia, Silodosin, Mirabegron, Urinary Bladder, Overactive, Adrenergic beta-3 Receptor Agonists, Alpha-1 Adrenergic Blockers, Drug Therapy Combination.

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