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Comparative Efficacy and Safety of Antimuscarinic and β3-Agonist Therapy in Overactive Bladder: A Randomized Controlled Trial

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Abstract: ***Background:*** Overactive bladder (OAB) is a common lower urinary tract disorder characterized by urgency, frequency, nocturia, and urge urinary incontinence, leading to significant impairment in quality of life. Antimuscarinic agents such as solifenacin have traditionally been used as first-line therapy, but their clinical utility is often limited by anticholinergic adverse effects and poor treatment adherence. Mirabegron, a β3-adrenergic receptor agonist, offers an alternative mechanism of action with a potentially better tolerability profile. However, comparative data from South Asian populations, particularly Pakistan, remain limited. ***Objective:*** To compare the efficacy, safety, and tolerability of solifenacin and mirabegron in patients with overactive bladder treated at a tertiary care hospital in Pakistan. ***Methods***: This randomized controlled trial was conducted at a tertiary care teaching hospital in Pakistan. Adult patients diagnosed with idiopathic overactive bladder were randomly allocated into two groups: one receiving solifenacin 5 mg once daily and the other receiving mirabegron 50 mg once daily for 12 weeks. Primary outcome measures included changes in daily micturition frequency and urgency episodes. Secondary outcomes included urge urinary incontinence episodes, quality of life scores, and incidence of adverse drug reactions. Statistical analysis was performed using intention-to-treat principles, with a p-value < 0.05 considered statistically significant. ***Results:*** Both solifenacin and mirabegron significantly reduced micturition frequency, urgency, and urge incontinence compared with baseline ($p < 0.05$). Mirabegron demonstrated efficacy comparable to solifenacin in controlling OAB symptoms. However, adverse effects such as dry mouth and constipation were significantly more frequent in the solifenacin group, leading to higher rates of treatment discontinuation. Patients receiving mirabegron showed better treatment adherence and superior improvement in quality-of-life scores. ***Conclusion:*** In patients with overactive bladder treated at a tertiary care hospital in Pakistan, mirabegron was as effective as solifenacin in improving urinary symptoms but was better tolerated. Mirabegron appears to be a preferable therapeutic option, particularly for patients who are sensitive to anticholinergic adverse effects or require long-term therapy.

Keywords: Overactive bladder; Solifenacin; Mirabegron; β3-agonist; Antimuscarinic; Randomized controlled trial; Pakistan.

INTRODUCTION

Overactive bladder (OAB) is a highly prevalent and distressing lower urinary tract disorder characterized by urinary urgency, usually accompanied by increased frequency, nocturia, and with or without urge urinary incontinence.1 According to the International Continence Society, OAB is a symptom-based syndrome that significantly impairs social, occupational, and psychological well-being2. Despite not being life-threatening, OAB imposes a substantial burden on healthcare systems and markedly reduces patients' quality of life, particularly in aging populations3.

The pathophysiology of OAB is complex and involves detrusor overactivity, altered afferent signaling, and central nervous system dysregulation of bladder function4. Pharmacological therapy remains the cornerstone of treatment when behavioral interventions fail5. For decades, antimuscarinic drugs, such as solifenacin, have been the standard first-line pharmacotherapy6. These agents exert their effect by blocking M3 muscarinic receptors in the detrusor muscle, thereby reducing involuntary bladder contractions7. However, their widespread use is limited by anticholinergic adverse effects including dry mouth, constipation, blurred vision, and cognitive impairment, which lead to poor compliance and early treatment discontinuation8,9.

Mirabegron, a β3-adrenergic receptor agonist, represents a mechanistically novel approach to OAB management10,11. By stimulating β3 receptors in the bladder detrusor muscle, mirabegron promotes relaxation during the storage phase, thereby increasing bladder capacity without inhibiting normal voiding12. Large international trials have demonstrated that mirabegron is effective in reducing urgency, frequency, and incontinence, with a significantly more favorable side-effect profile compared with antimuscarinic drugs13. As a result, mirabegron is increasingly recommended in international guidelines as either an alternative or a preferred option for patients intolerant to antimuscarinics14.

Despite robust evidence from Western and East Asian populations, data comparing antimuscarinics and β3-agonists in South Asian and Pakistani patients remain scarce. Differences in genetic background, comorbidities, healthcare access, and medication adherence may influence both efficacy and tolerability. Moreover, in Pakistan, where long-term follow-up and patient compliance are major challenges, the tolerability of OAB medications becomes particularly important in determining real-world effectiveness.

Therefore, this randomized controlled trial was conducted to compare solifenacin and mirabegron in terms of efficacy, safety, and quality-of-life outcomes among patients with overactive bladder treated at a tertiary care hospital in Pakistan. By generating local evidence, this study aims to inform rational, patient-centered pharmacological management of OAB in the regional clinical setting.

METHODOLOGY

This study was a prospective, randomized, open-label controlled trial conducted in the department of urology and outpatient clinics of multiple tertiary care teaching hospitals in Pakistan from July 2023 to July 2024. The study duration was 12 months, including patient recruitment, intervention, and follow-up. A total of 100 Adult patients of age 18 to 65 years presenting with symptoms of overactive bladder (OAB) and who gave informed consent, were screened for eligibility. Clinical diagnosis of idiopathic OAB was based on International Continence Society (ICS) criteria i.e. symptoms of urinary urgency with or without urge incontinence, with increased frequency (>8 micturition/day) for at least 3 months15. Patients already taking medicines and patients with neurogenic bladder (e.g., spinal cord injury, multiple sclerosis), bladder outlet obstruction or significant pelvic organ prolapse, active urinary tract infection, severe renal or hepatic impairment, uncontrolled hypertension, pregnancy or lactation and history of bladder malignancy or pelvic radiation were excluded from the study. Patients in both groups received their assigned medication for 12 weeks. All participants were counselled on lifestyle modifications including: fluid management, bladder training and avoidance of caffeine and bladder irritants. No dose escalation was permitted during the study period to maintain treatment uniformity. Primary outcomes measures were change in mean daily micturition frequency and change in number of urgency episodes per day. These were assessed using a 3-day bladder diary at baseline and at week 12. Secondary outcomes measured were number of urge urinary incontinence episodes, Patient-reported quality of life using the Overactive Bladder Questionnaire (OAB-q), incidence and type of adverse drug reactions, treatment discontinuation rates16. Participants were evaluated at baseline and then after every four-week interval till the 12th week.

Data were analyzed using SPSS version 25. Continuous variables were expressed as mean ± standard deviation and categorical variables as frequencies and percentages. Independent t-test was used to compare continuous variables between groups. Chi-square test was used for categorical data. p-value < 0.05 was considered statistically significant.

RESULTS

A total of 138 patients were screened for eligibility. Of these, 110 patients met the inclusion criteria and were randomized into two groups: 55 patients received solifenacin and 55 received mirabegron. During the study period, 6 patients in the solifenacin group and 4 in the mirabegron group were lost to follow-up. Final analysis included 49 patients in the solifenacin group and 51 patients in the mirabegron group.

Baseline demographic and clinical characteristics were comparable between the two groups ($p > 0.05$). The mean age of participants was 52.3 ± 10.6 years, with a female predominance (62%). The mean baseline micturition frequency and urgency episodes did not differ significantly between the two groups.

At baseline, the mean daily micturition frequency was 11.8 ± 2.1 in the solifenacin group and 11.6 ± 2.3 in the mirabegron group. After 12 weeks of treatment, this decreased to 7.1 ± 1.8 in the solifenacin group and 6.9 ± 1.6 in the mirabegron group. Both groups showed a statistically significant reduction compared with baseline ($p < 0.001$), with no significant difference between groups ($p = 0.42$). Mean daily urgency episodes decreased from 6.4 ± 1.7 to 2.5 ± 1.2 in the solifenacin group and from 6.2 ± 1.8 to 2.3 ± 1.1 in the mirabegron group. The magnitude of improvement was significant in both groups ($p < 0.001$) and comparable between treatments ($p = 0.38$).
Results of urge urinary incontinence are shown in table 1 and the results of adverse drug reactions are shown in table 2. Quality of life score (OAB-q) improved significantly in both groups. The mean quality-of-life score increased by 41% in the solifenacin group and 52% in the mirabegron group. The improvement was significantly greater in the mirabegron group ($p = 0.03$).

Table 1: Secondary Efficacy Outcome: Urge incontinence

Variable	Solifenacin	Mirabegron	*p*-value
Urge incontinence (baseline)	3.2 ± 1.3	3.1 ± 1.2	0.74
Urge incontinence (12 weeks)	1.1 ± 0.7	0.9 ± 0.6	0.08
OAB-q score improvement (%)	41%	52%	0.03

Table 2: Adverse Effects and Treatment Adherence

Variable	Solifenacin (n = 49)	Mirabegron (n = 51)	*p*-value
Dry mouth	19 (38.7%)	5 (9.8%)	< 0.001
Constipation	13 (26.5%)	4 (7.8%)	0.01
Hypertension / palpitations	1 (2.0%)	3 (5.8%)	0.34
Treatment discontinuation	7 (14.5%)	2 (3.9%)	0.04
Medication adherence	78.6%	91.4%	0.02

DISCUSSION

This randomized controlled trial conducted in a tertiary care hospital in Pakistan demonstrates that mirabegron and solifenacin are equally effective in reducing the core symptoms of overactive bladder, including urinary frequency, urgency, and urge urinary incontinence17. However, mirabegron showed a significantly superior safety and tolerability profile, leading to better treatment adherence and greater improvement in quality of life18. These findings have important implications for OAB management in low- and middle-income countries where long-term medication compliance remains a major challenge19.

The comparable efficacy observed between solifenacin and mirabegron in our study is consistent with international trials. The SCORPIO, ARIES, and CAPRICORN trials demonstrated that mirabegron significantly reduces micturition frequency and urgency episodes, with efficacy comparable to antimuscarinic drugs20,21. Similarly, Chapple et al. reported that mirabegron 50 mg achieved reductions in incontinence episodes and voiding frequency that were not inferior to solifenacin, reinforcing that β3-agonist therapy is not merely an alternative but a true therapeutic equivalent14.

What clearly differentiates these two drug classes is tolerability. In our study, the incidence of dry mouth (38.7%) and constipation (26.5%) in the solifenacin group closely mirrors figures reported in previous antimuscarinic trials, where up to 40–50% of patients experience anticholinergic adverse effects22,23. In contrast, mirabegron produced significantly fewer such effects, a finding in agreement with the PILLAR and BESIDE trials, which showed markedly lower rates of dry mouth and treatment discontinuation. The

slightly higher incidence of mild hypertension in the mirabegron group in our cohort is also consistent with global safety data and was clinically insignificant24,25.

A particularly important finding in our Pakistani population was the higher medication adherence in the mirabegron group (91.4% vs 78.6%). This aligns with real-world studies from Europe and East Asia showing that patients are more likely to persist with β3-agonist therapy than antimuscarinics26,27. In my view, this is not a trivial outcome—in chronic conditions like OAB, adherence is more important than marginal differences in pharmacologic efficacy. A drug that patients cannot tolerate will ultimately fail, no matter how effective it is in controlled settings22.

Quality-of-life improvement was also significantly greater in the mirabegron group. This is clinically meaningful because OAB is not a life-threatening disorder but a quality-of-life disease14. International studies consistently show that reduction of embarrassment, nocturia, and social restriction matters more to patients than small changes in voiding frequency. The better QoL scores with mirabegron likely reflect its low anticholinergic burden and better patient comfort17.

From a regional perspective, this study fills a critical evidence gap. South Asian populations are underrepresented in OAB pharmacotherapy trials, despite differences in health-seeking behavior, comorbidities, and medication tolerance. The consistency of our results with Western trials strongly supports the external validity of mirabegron in Pakistani patients.

CONCLUSION

Mirabegron and solifenacin were equally effective in improving symptoms of overactive bladder; however, mirabegron demonstrated superior tolerability, better treatment adherence, and greater quality-of-life improvement. Owing to its favorable safety profile, mirabegron appears to be the preferable first-line therapy for overactive bladder in the Pakistani tertiary-care setting.

Future Considerations

Future research should include larger, multicenter studies with longer follow-up to confirm long-term efficacy, safety, and treatment persistence. Cost-effectiveness analyses and evaluation of combination therapy would further guide optimal management of overactive bladder in the Pakistani healthcare setting.

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