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Original Article

A Comparative Analysis of Mirabegron versus Tolterodine for the Management of Irritative Symptoms Caused by Ureteral Stents

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ABSTRACT

Background: The use of ureteral stents is a common practice in the management of urinary tract obstruction. However, the presence of a stent often leads to irritative lower urinary tract symptoms (LUTS), significantly impacting the patient's quality of life. Traditional management with anticholinergics is limited by side effects, whereas beta 3 agonists like Mirabegron offer a potentially more tolerable alternative.

Objective: To compare the efficacy and tolerability of Mirabegron versus Tolterodine in the management of irritative symptoms associated with ureteral stents.

Methods: This prospective randomized controlled trial was conducted at the Department of Urology and Renal Transplant, Institute of Kidney Diseases, Hayatabad Medical Complex, Peshawar, from January 2019 to August 2020. A total of 104 patients who had undergone ureteral stent placement were randomized into two groups: Mirabegron (52 patients) and Tolterodine (52 patients). Inclusion criteria included individuals aged 18 years or older without prior LUTS history. The primary outcome measured was the change in the International Prostate Symptom Score (IPSS) Irritative score from baseline to post-treatment. Data analysis was conducted using SPSS version 25, with paired and unpaired t-tests for within and between-group comparisons, respectively.

Results: The mean age in the Mirabegron group was 29.44 ± 6.25 years, and 28.23 ± 5.97 years in the Tolterodine group. Pre-treatment IPSS Irritative scores were 9.19 ± 3.72 for Mirabegron and 9.88 ± 3.5 for Tolterodine. Post-treatment, scores reduced to 3.27 ± 1.34 in the Mirabegron group and 4.13 ± 1.47 in the Tolterodine group. The change in IPSS Irritative score was 5.92 ± 2.46 for Mirabegron and 5.75 ± 2.10 for Tolterodine, with no significant difference between groups ($p > 0.05$).

Conclusion: Mirabegron is as effective as Tolterodine in reducing irritative LUTS in patients with ureteral stents, with a comparable side effect profile. These findings support Mirabegron as a viable alternative for patients experiencing LUTS due to ureteral stents.

Keywords: Ureteral stents, Mirabegron, Tolterodine, Irritative urinary symptoms, Lower urinary tract symptoms, Beta 3 agonists, Anticholinergics, Randomized controlled trial, IPSS score.

INTRODUCTION

Ureteral stents are frequently employed in both open and endoscopic interventions of the urinary tract, a practice that, despite its widespread application, is associated with a range of morbidities that significantly detract from patient quality of life. The advent of the ureteral stent, with a conceptual foundation laid by Joaquin Albarrano in the early 20th century, marked a pivotal advancement in urological interventions (1, 2). Over the years, efforts to refine the design and composition of these stents have been relentless, aimed at reducing the morbidity associated with their use. Despite these advancements, the insertion of ureteral stents often results in a spectrum of lower urinary tract symptoms (LUTS) such as increased urination frequency, urgency, urge incontinence, and discomfort in the suprapubic area and flank pain, phenomena that not only impair patient comfort but also necessitate additional medical management (1). These symptoms are principally attributed to the mechanical irritation of the bladder trigone and the reflux of urine through the stent, prompting strategies to mitigate such effects through adjustments in stent diameter, precise positioning, and optimization of length (4-6).

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Notwithstanding the aforementioned mechanical modifications, the management of stent-related discomfort often requires pharmacological intervention, with a range of medications including non-steroidal anti-inflammatory drugs (NSAIDs), alpha blockers, anticholinergics, and β3 agonists being employed. Anticholinergics, traditionally the mainstay for managing such symptoms, are increasingly being supplanted by beta 3 agonists due to the latter's more favorable side effect profile. Mirabegron, a beta 3 agonist, has gained prominence since its approval in 2012 for the management of overactive bladder, demonstrating superior efficacy over placebo in alleviating irritative bladder symptoms (7-9). However, the phenomenon of "forgotten stents," a serious complication, underscores the importance of ongoing innovation in stent technology, including the exploration of biodegradable alternatives to prevent such occurrences (3).

Against this background, the present study is positioned to evaluate the comparative efficacy of Mirabegron and tolterodine, an anticholinergic agent, in the management of irritative lower urinary tract symptoms associated with ureteral stent placement. By focusing on these two therapeutic agents, the study aims to illuminate the potential benefits of newer pharmacological strategies over traditional treatments, thereby offering insights into optimizing patient care in the context of ureteral stent-related morbidity. This comparative analysis seeks not only to address the symptomatic relief afforded by these medications but also to consider their tolerability and overall impact on patient well-being, factors that are critical in the holistic management of patients undergoing urinary tract interventions.

MATERIAL AND METHODS

The study was conducted at the Department of Urology and Renal Transplant, Institute of Kidney Diseases, Hayatabad Medical Complex, Peshawar, over a period spanning from January 2019 to August 2020. This research was designed as a prospective randomized controlled trial to assess the comparative efficacy of Mirabegron and Tolterodine in managing irritative lower urinary tract symptoms (LUTS) in patients with ureteral stents. A total of 104 patients met the inclusion criteria and were enrolled in the study. These criteria included individuals aged 18 years or older who had no prior history of LUTS, had recently undergone either retrograde or antegrade ureteral stent placement, and did not present with concurrent urinary tract pathologies such as tumors, stones, neurogenic bladder disorders, or outlet abnormalities that predispose to LUTS.

Participants were systematically randomized into two groups, with group A (52 patients) receiving Mirabegron and group B (52 patients) administered Tolterodine, ensuring an equitable distribution of subjects for a valid comparison of treatment outcomes. Initial evaluation involved detailed history-taking and physical examination, from which demographic details and baseline scores on the International Prostate Symptom Score (IPSS) Irritative scale were meticulously recorded. Follow-up assessments captured subsequent IPSS Irritative scores after treatment administration, facilitating the evaluation of each drug's impact on alleviating stent-related symptoms.

The ethical considerations of this study were scrupulously observed in accordance with the Declaration of Helsinki. Ethical approval was obtained from the institutional review board (IRB) of Hayatabad Medical Complex Peshawar prior to the commencement of the study. Participants were informed about the purpose of the research, the procedures involved, and their right to withdraw at any point without any consequences. Informed consent was obtained from all participants, ensuring that they were fully aware of their involvement and the study's objectives.

Data collected from the study were analyzed using SPSS version 25. The analysis employed paired t-tests to compare mean changes in IPSS Irritative scores within each group, to determine the internal efficacy of the treatments. Furthermore, unpaired t-tests were utilized to compare the mean changes between the groups, providing a comparative evaluation of Mirabegron and Tolterodine's effectiveness in managing irritative symptoms. The level of statistical significance was predetermined at $p < 0.05$, ensuring that the findings were both statistically and clinically relevant.

RESULTS

In the comparative study assessing the efficacy of Mirabegron versus Tolterodine in managing irritative symptoms caused by ureteral stents, a detailed analysis of demographic and clinical outcomes was conducted. The gender distribution across the two groups showed a balanced representation, with the Mirabegron group comprising 27 males (51.92%) and 25 females (48.08%), while the Tolterodine group included 25 males (48.08%) and 27 females (51.92%). This near-equal gender distribution underscores the study's inclusive nature and the applicability of its findings across both sexes, highlighting that the treatment effects were evaluated across a diverse patient pool (Table 1).

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Regarding the age of participants, the Mirabegron group had a mean age of 29.44 years (SD ± 6.25), slightly higher than the Tolterodine group, which had a mean age of 28.23 years (SD ± 5.97). These figures suggest a young adult cohort was predominantly studied, reflecting the potential for these findings to influence the management of younger patients with ureteral stents. Despite the slight difference in mean ages, the statistical analysis revealed no significant age disparity between the two groups (Table 1), indicating that age did not influence the treatment outcomes.

The clinical effectiveness of both treatments was primarily evaluated using the change in the International Prostate Symptom Score (IPSS) irritative scores, both before and after the intervention. Initially, the Mirabegron group presented with a mean pre-treatment IPSS irritative score of 9.19 (SD ± 3.72), and the Tolterodine group with a slightly higher mean score of 9.88 (SD ± 3.5). Following treatment, the mean post-treatment IPSS irritative scores were observed to decrease in both groups, to 3.27 (SD ± 1.34) in the Mirabegron group and to 4.13 (SD ± 1.47) in the Tolterodine group (Table 1). This reduction in scores signifies a clinically relevant alleviation of irritative symptoms in patients following treatment with either drug.

Table 1 Demographic and Study Characteristics

Variable	Mirabegron Group	Tolterodine Group	p-value
Gender			>0.05
- Male	27 (51.92%)	25 (48.08%)	
- Female	25 (48.08%)	27 (51.92%)	
Age in years (Mean ± SD)	29.44 ± 6.25	28.23 ± 5.97	>0.05
Pre-treatment IPSS Irritative Score (Mean ± SD)	9.19 ± 3.72	9.88 ± 3.5	>0.05
Post-treatment IPSS Irritative Score (Mean ± SD)	3.27 ± 1.34	4.13 ± 1.47	>0.05
Change in IPSS Irritative Score (Mean ± SD)	5.92 ± 2.46	5.75 ± 2.10	>0.05

The magnitude of change in the IPSS irritative scores further elucidates the treatments' impact. The Mirabegron group experienced a mean reduction of 5.92 (SD ± 2.46) in their scores, compared to a mean reduction of 5.75 (SD ± 2.10) in the Tolterodine group. These results highlight that both medications were effective in reducing irritative symptoms associated with ureteral stents, with Mirabegron showing a marginally higher but not statistically significant improvement over Tolterodine (Table 1).

DISCUSSION

In the realm of managing irritative bladder symptoms, anticholinergic medications have long been the cornerstone of treatment, albeit their utility is frequently marred by adverse effects that compromise patient tolerability. This has paved the way for the exploration of beta 3 agonists like Mirabegron, which, as evidenced in our study, has demonstrated efficacy on par with Tolterodine, a traditional anticholinergic, in mitigating symptoms such as frequency and urgency. This finding echoes the research conducted by Thiagamoorthy G et al. and Batista JE et al., which similarly reported the effectiveness of Mirabegron in symptom amelioration (10, 11). Despite Mirabegron's efficacy, it is noteworthy that it is not devoid of side effects, with Sacco E et al. documenting occurrences of hypertension, urinary tract infections, and nasopharyngitis at rates comparable to those associated with Tolterodine (12). However, our study participants did not report these adverse effects, a phenomenon that is in concordance with the broader literature (13).

The study at hand found that both Mirabegron and Tolterodine were well-tolerated by patients, with no instances of medication discontinuation observed within the treatment duration, which lasted up to three months. Literature supports the notion that beta 3 agonists exhibit superior tolerability and adherence compared to anticholinergics, a finding that aligns with our observations of comparable adherence rates for both medications, likely owing to the short treatment duration (14). However, it is postulated that the adverse effects associated with anticholinergics may become more pronounced over longer treatment periods, potentially leading to decreased tolerance and subsequent noncompliance or discontinuation.

Anticholinergics, despite their long-standing use, have an established safety profile across a wide age range, including pediatric and geriatric populations (15). On the other hand, beta 3 agonists are relatively new, and data concerning their safety in these particular demographics, especially pediatrics, remain sparse, although recent studies have begun to bridge this gap (16). Despite our study's focus on individuals aged 18 to 40 years, existing evidence suggests that Mirabegron is well-tolerated across various age groups, reinforcing its safety profile (17,18).

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Our investigation underlined the significant efficacy of both Mirabegron and Tolterodine in alleviating symptoms of frequency, urgency, and urge incontinence, a finding that is in harmony with existing literature (19,20). The strengths of our study include a robust methodological design and the application of well-established measures for symptom evaluation. However, limitations are present, including a relatively small sample size and the study's short duration, which may not fully capture long-term adherence patterns or the potential emergence of adverse effects over time. Moreover, the study's demographic was somewhat narrow, focusing on a younger adult population, which might limit the generalizability of the findings to older age groups or those with comorbid conditions.

CONCLUSION

In conclusion, our study posits that Mirabegron, with its comparable efficacy to Tolterodine and a favorable side effect profile, emerges as a viable alternative for the management of irritative symptoms in patients with ureteral stents. Nevertheless, it is imperative to advocate for further research, incorporating larger sample sizes and extended follow-up periods, to validate these findings. Future studies should also aim to explore the cost-effectiveness, adherence, and tolerance over prolonged treatment durations, offering a comprehensive perspective on the clinical utility of Mirabegron in this context.

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