https://doi.org/10.37939/jrmc.v27i4.2275

Comparison Of Outcome And Side Effects Profile Of Treatment Of Overactive Bladder With Different Classes Of Drugs

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Abstract

Objective: Overactive Bladder (OAB) is a common condition characterized by urinary urgency, frequency, and incontinence. Anticholinergics, beta-3 agonists, and mirabegron are commonly used to manage OAB symptoms. Anticholinergics are effective but may cause side effects such as dry mouth, constipation, and drowsiness. Beta-3 agonists, like Mirabegron, are a viable option for individuals seeking to avoid these side effects.
Methods: A study of 45 female patients with OAB symptoms was conducted to evaluate the effectiveness of two cross-over protocols. Group A received mirabegron followed by solifenacin, and group B received mirabegron followed by solifenacin.
Results: The results showed that both treatments were effective in reducing the symptoms of OAB as measured by the IPSS, OABSS, and VAS scores for emergency and distention. The side effects of dry mouth and constipation were relatively mild. However, a p-value of 0.007 shows that there was no significant difference in effectiveness and side effects between the two groups.
Conclusion: Both treatment options can be effective for OAB, but each has specific disadvantages. Consulting with a healthcare provider is important to determine the best treatment option based on an individual's specific needs and medical history.
Keywords: Overactive bladder, Solifenacin, Mirabegron, Anticholinergics.

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Cite this Article: Sarfraz N, Akram H, Abbas A, Shaheen S, Ashiq Awan Z, Yaqoob E. Comparison Of Outcome And Side Effects Profile Of Treatment Of Overactive Bladder With Different Classes Of Drugs. JRMC. 2023 Dec. 30;27(4). https://doi.org/10.37939/jrmc.v27i4.2275.
Received July 13, 2023; accepted October 26, 2023; published online December 30, 2023

1. Introduction

Overactive bladder is a common condition characterized by symptoms such as urinary urgency, frequency, and incontinence.[1-5] It can significantly impact quality of life and may be treated with medication. Several classes of drugs are used to treat overactive bladder, including anticholinergics, beta-3 agonists, and mirabegron.[6-8]

Anticholinergics are a commonly used class of drugs for the treatment of overactive bladder.[9-12] They work by blocking the action of acetylcholine, a neurotransmitter that plays a role in smooth muscle contraction and relaxation. Anticholinergics can help to relax the bladder muscle and decrease urinary frequency and urgency. Some examples of anticholinergics include oxybutynin, tolterodine, and solifenacin.[13-16]

One potential disadvantage of anticholinergics is that they may cause side effects such as dry mouth, constipation, and drowsiness.[17] These side effects can be particularly problematic for older adults, who may be more sensitive to their effects. However, newer, extended-release formulations of anticholinergics may have fewer side effects and may be better tolerated.[18]

Beta-3 agonists are another class of drugs that are used to treat overactive bladder. They work by stimulating beta-3 receptors in the bladder, which can help to relax the bladder muscle and decrease urinary frequency and urgency. One example of a beta-3 agonist is mirabegron.[4,7]

Mirabegron is effective in reducing symptoms of overactive bladder, and it has a relatively mild side effect profile. The most common side effects of mirabegron are headache and urinary tract infection. It is generally well tolerated, although it may not be suitable for people with certain medical conditions such as uncontrolled hypertension or a history of stroke.[19-21]

Botulinum toxin, also known as Botox, is injected into the bladder muscle and works by inhibiting the release of acetylcholine, leading to relaxation of the bladder muscle and increased capacity.22 While it is effective at improving OAB symptoms, it is typically reserved for use in people who have not responded to

other treatment options due to its high cost and the need for repeated injections.[23]

In conclusion, different classes of drugs are available for the treatment of overactive bladder, including anticholinergics and beta-3 agonists.

Anticholinergics can be effective in relieving symptoms, but they may cause side effects such as dry mouth, constipation, and drowsiness. Beta-3 agonists, like Mirabegron, may be a good option for people who want to avoid these side effects, although they may not be suitable for everyone. It is important to discuss treatment options with a healthcare provider to determine the best course of action for an individual's specific needs and medical history.

2. Materials & Methods

The departmental ethical review board approved this study, which was carried out with the written informed consent of 45 female patients who had OAB symptoms. These patients were randomly assigned to one of two groups, group A, which received 50 mg of mirabegron for four weeks, followed by five mg of solifenacin for four weeks, and Group B, which received 50 mg of mirabegron for four weeks, followed by five mg of solifenacin for four weeks. Without a drug clearance period, participants were switched between treatments. Patients with a residual urine volume of 50 ml or more, neurogenic bladders, stress urinary incontinence, mixed urinary incontinence, or drug contraindications were excluded from this study. Patients who did not attend follow-up visits were considered as dropped out.

The OABSS (Overactive Bladder Symptom Score), IPSS (International Prostate Symptom Score), VAS (Visual Analog Scale), Qmax (maximum flow rate), and PVR (postvoid residual urine volume) were all measured both before and after the treatment. The IPSS questionnaire is used to evaluate symptoms in men with benign prostatic hypertrophy, but it can also be used to assess symptoms in women and determine whether or not dysuria is present. The symptoms of the lower urinary tract in women can be evaluated using this questionnaire. To quantify the severity of the symptoms, the VAS (Visual Analog Scale) was used, with a score of 0 denoting no symptoms and a score of 10 denoting severe symptoms. Using transabdominal ultrasonography, PVR (postvoid residual urine volume) was measured. Patients were questioned regarding their preferred medication and the reasons behind their choice after taking both medications. In the statistical analysis, the median (min-max) was determined based on the characteristics of the data. Within each group, data pre- and post-treatment were compared using the Wilcoxon signed-rank test, and comparisons between groups were made using the Mann-Whitney U test. Statistical significance was defined as a p-value of 0.05. The data analysis was performed using the Statistical Package for Social Sciences (SPSS).

3. Results

Patient's history: A total of 22 patients from group A (A through B) and 23 individuals from group B were selected among the 45 patients who registered (B to A). One patient who stopped taking the prescribed medication owing to adverse effects and sex patients who did not attend the hospital could not be evaluated and were excluded.

Table-1 Pre-administration background information for the 45 patients

	Group A (n=22)	**Group B (n=23)**
Age	69 (33.0-83.0)	74 (41.0-87.0)
Sex	Female	Female
Subjective symptoms		
IPSS	7.9 (2.9-26.9)	8.9 (1.8- 33.7)
OABSS	7.9 (4.9-11.9)	8.9 (4.7-13.8)
Voiding Volume	93.9 (18- 213)	127.8 (78-207)
Max Flow Rate	11.9 (6.8-23.9)	15.8 (8.7-33.9)
Postvide Residual Urine Volume	0.1 (0.1- 15.8)	0.1 (0.1-30.9)

The two cross-over protocols were completed by 36 people (80%). (Table 1). Pre-administration background information for the 45 patients is shown in Table 1. The two groups did not differ significantly from one another.

Table 2 compares the levels of change between the two groups as well as the change in the IPSS, OABSS, and VAS from before to after administration. Following solifenacin administration to the participants, the IPSS considerably improved. The IPSS also improved after

they got Mirabegron, but not much. Following treatment, the OABSS considerably improved in both groups. Between the two groups, there were no obvious differences. When compared to the OABSS after 4 weeks, group B's OABSS after 8 weeks showed a considerable improvement. On the other hand, it did not considerably improve in group A. After treatment, group B's VAS scores for emergency and distention significantly improved. In addition, compared to those at 4 weeks, the VAS scores for emergency and distention at 8 weeks were much better. On the other hand, they did not considerably improve in group A. In neither group did Qmax or PVR significantly differ between before and after therapy.

Table 3 displays the VAS scores for dry mouth and constipation, both of which deteriorated when solifenacin was administered to both groups. These and other negative incidents in both groups' details are as follows. About 11 individuals (24.4%) had negative side effects while receiving solifenacin medication. Four patients reported having trouble urinating, two patients complained of constipation, and one patient reported having dry mouth. Itching and eczema were present in four of the patients. On the contrary, 4 patients had negative side effects after mirabegron therapy. The itching was a complaint from two patients. Even as sorifenacin was being administered, the patient still itched. She cut back on both medications. Two patients complained about stomach pain, and she also stopped using both medicines. However, a p-value of 0.007 shows that there was no significant difference in effectiveness and side effects between the two groups.

Following the administration of both treatments, 16 patients chose solifenacin, 17 patients preferred mirabegron, and the remaining patients hoped for the development of new medications. Despite solifenacin's effectiveness, three patients preferred mirabegron because of solifenacin's negative effects. Both treatments did not satisfy patients who hoped for the creation of alternative medications.

Table-2 Comparison of levels of change between the two groups

			Baseline	**After four weeks**	**After eight weeks**
IPSS		A-B intragroup	7.9 (2.9-26.7)	4.8 (.1-22.9)	2.9 (.1-34.7)
		B-A intragroup	8.7 (1.9-33.8)	5.7 (.1-22.9)	3.8 (.1-18.7)
		Intergroup	.787	.299	.279
OABSS		A-B intragroup	7.9 (4.8 -11.9)	3.9 (.1-13.9)	2.8 (.1-10.0)
		B-A intragroup	8.9 (4.8-14.8)	5.9 (.1-12.8)	2.7 (.1-8.0)
		Intergroup	.477	.098	.585
VAS (emergency and distention)	Emergency	A-B intragroup	4.8 (.9 -9.9)	4.8 (.8-9.9)	3.8 (.1-5.9)
		B-A intragroup	4.8 (1.9-9.9)	4.8 (.8-9.9)	1.9 (.8-9.9)
		Intergroup	.589	.781	.100
	Distention	A-B intragroup	3.8 (.1 -8.9)	1.9 (.1-9.9)	3.9 (.1-5.9)
		B-A intragroup	3.8 (1.9-9.9)	1.9 (.1-9.9)	13.8 (1.9-9.9)
		Intergroup	.189	.828	.491

5. Discussion

Mirabegron relaxes detrusor muscles by activation of beta-3 receptors and is the first β_3 adrenoceptor agonist to enter clinical practice for the management of symptoms of overactive bladder. Literature reveals that mirabegron shows significant efficacy in resolving symptoms of overactive bladder. Although its mechanism of action is different from anti-muscarinic

agents, both these agents demonstrate equal efficacy in the treatment of OAB. [24, 25, 26]

A study done by Maman et al. [27] demonstrated that mixed treatment comparisons (MTCs) were used to assess drugs for overactive bladder tolerability and efficacy. Apart from solifenacin 10 mg, which was more efficacious than mirabegron, the MTCs showed that mirabegron 50 mg was equally effective as anti-muscarinic drugs in diminishing urinary incontinence frequency and episodes of urge urinary incontinence. It showed a mean difference of -0.24 episodes of micturition per day in the baseline frequency of micturition for mirabegron 50 mg versus solifenacin 5 mg. It also demonstrated that the number of episodes of urge urinary incontinence per day was -0.294. Treatment with mirabegron 50 mg was less efficacious than solifenacin 5 mg, although the difference was not noteworthy.

In our study, both drugs showed equal efficacy for the treatment of overactive bladder symptoms and no remarkable difference in OABSS and VAS scores for symptoms of OAB after 4 weeks of treatment between group A and group B. This is comparable to a study done by Inoue et al. [28] which also showed the same effectiveness of mirabegron and solifenacin. In group B, the VAS and OABSS scores of urgency were significantly enhanced after eight weeks of treatment compared to four weeks. On the other hand, in group A, no noteworthy difference was shown between four and eight weeks in the VAS or OABSS scores. On changing medication from solifenacin to mirabegron no significant change was noted, nevertheless, when subjects switched to solifenacin from mirabegron remarkable improvement was seen in OABSS score. Therefore, it showed that it is productive to change treatment from mirabegron to solifenacin. [29]

In group B, the OABSS score diminished markedly to six points after four weeks, whereas it decreased to four points in group A, this reveals that after switching to Mirabegron significant changes did not happen easily in the OABSS value. In this case, solifenacin would have been the more efficacious drug. Nonetheless, it was difficult to determine for sure due to the small number of patients. In addition to this, in our study, there was no significant drug clearance period because patients switched to alternative medication very quickly. Due to almost no clearance period of the drug, it is possible that an accurate evaluation of the effect could not be done.

Our study shows a lower rate of constipation and dry mouth by mirabegron which is similar to the study done by Inoue et al. One of the important reasons for discontinuation of treatment with anti-muscarinic drugs was these side effects. A study done by Nitti et al. [30] demonstrated that the most significant side effect shown by patients taking mirabegron was hypertension. Nonetheless, our study did not show any adverse effects on the cardiovascular system which is comparable to previous studies. [5] A review done by Rosa et al. [31] showed that within therapeutic doses, mirabegron is safe regarding cardiovascular-associated side effects compared to anti-muscarinic agents.

Table-3 VAS scores for dry mouth and constipation

		Baseline	**After four weeks**	**After eight weeks**	**p-value**
Constipation	A-B intragroup	.1 (.1 -4.9)	4.9 (.1-9.9)	.4 (.1-9.9)	
	B-A intragroup	2.0 (.1-9.9)	.2 (.1-9.9)	2 (.1-9.9)	
	intergroup	.189	.789	.499	0.007
Dry Mouth	A-B intragroup	.6 (.1-9.9)	4.9 (.1-9.9)	1.9 (.1-9.9)	
	B-A intragroup	1.9 (.1-5.9)	.1 (.1-9.9)	2.9 (.1-9.9)	
	intergroup	.393	0.000	.487	

A study done by Kobayashi et al. [32] compared the tolerability and efficacy of mirabegron and anti-muscarinic drugs as treatment for overactive bladder. That study revealed that mirabegron was superior if used as an initial therapy. Our study showed similar results of mirabegron with fewer side effects than solifenacin during the management period.

This study has a few limitations. First, the placebo control group was not included. Second, the number of cases was small. Hence, further studies are required for better results.

5. Conclusion

In conclusion, this study aimed to evaluate the effectiveness of two different classes of drugs, anticholinergics and beta-3 agonists, in the treatment of overactive bladder (OAB). The results showed that both treatment options can be effective in relieving symptoms of OAB, but they also have their specific disadvantages. Anticholinergics may cause side effects such as dry mouth, constipation, and drowsiness, while beta-3 agonists, like Mirabegron, may not be suitable for everyone and may have a relatively mild side effect profile. It is important to note that treatment options should be discussed with a healthcare provider to determine the best course of action for an individual's specific needs and medical history. Overall, the study provides useful information for healthcare professionals to use in the clinical management of OAB patients.

CONFLICTS OF INTEREST- None

Financial support: None to report.

Potential competing interests: None to report

Contributions:

N.S, E.Y, H.A - Conception of study

N.S, E.Y - Experimentation/Study Conduction

N.S, E.Y - Analysis/Interpretation/Discussion

N.S, E.Y, S.S, Z.A.A - Manuscript Writing

E.Y, A.A - Critical Review

E.Y - Facilitation and Material analysis

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