Open Access
Journal of the Faculty of Medicine Baghdad
Print ISSN: 0041-9419, Online ISSN: 2410-8057
DOI: https://doi.org/10.32007/jfacmedbaghdad2451
Research Article

Mirabegron in the Management of Overactive Bladder Syndrome in Ghazi Al-Hariri Hospital

Hiba H. Razaq *[1], Mohammed B. Ismail[2], Mohamed E. Abdelrhman[3]

[1]*Department of Pharmacology, College of Medicine, University of Baghdad, Baghdad, Iraq.*
[2]*Department of Surgery, College of Medicine, University of Baghdad, Baghdad, Iraq.*
[3]*Department of Surgery, Faculty of Medicine, University of Gezira, Wadi Medani, Sudan.*

Received: Aug. 2024
Revised: Nov. 2024
Accepted: Jan. 2025
Published: April 2025

Abstract

Background: An individual's quality of life is adversely affected by overactive bladder (OAB) symptoms. The key element that characterizes OAB is urgency, which, together with nocturia and urge urinary incontinence, are considered the most irksome symptoms. The side effects of the anticholinergic medication have caused a significant number of patients to discontinue their treatment. More recently, there has been research conducted on the potential correlation between an anticholinergic burden and the development of dementia. The detrusor muscle has been demonstrated to relax as a result of the activation of β3 adrenoceptors, which in turn facilitated the development of the first β3 adrenoceptor agonist. Mirabegron is the initial medication in this category to receive approval for the treatment of an overactive bladder.
Objectives: To explore the effect of mirabegron on bladder capacity in patients with OAB.
Methods: A case series study was performed on 40 patients diagnosed with OAB from October 2023 to March 2024 in the Medical City Complex (Ghazi AL-Hariri Hospital) Urology Outpatient Clinic. These patients took a single dose of mirabegron 50 mg per day for four months and were assessed for the effect of this drug on the bladder capacity measurement, in milliliters, measured by ultrasound.
Result: Following treatment with Mirabegron, a statistically significant increase in bladder capacity was found from the baseline level after two and four months.
Conclusion: Mirabegron is an effective drug for the treatment of OAB, as it increases bladder capacity.
Keywords: β3-adrenergic receptors; Bladder capacity; Mirabegron; Overactive bladder; Urinary incontinence.

Introduction

In the absence of any other apparent pathology or urinary tract infection, overactive bladder (OAB) is defined by urinary urgency, which is typically accompanied by urinary frequency and nocturia, with or without urgency incontinence (1,2). It is a problem that has an increasing incidence and a clear impact on the quality of life of many Iraqi patients who suffer it and can lead them to significantly reduce their social activity and negatively condition their work. Treating such patient will alleviate their suffering, improving quality of life and productivity (3). OAB has been linked to symptoms characterized by involuntary contractions of the bladder muscle (4).

A complex of interactions between the central and peripheral nervous systems is responsible for the control of the bladder, while the micturition reflex is activated when the detrusor muscle is stretched. The bladder's sensory pathway is impacted by the pathological conditions of OAB syndrome, which contribute to the urge to urinate at a low bladder volume (5). Detrusor muscle relaxation is dependent on norepinephrine released from sympathetic nerves innervating the bladder to stimulate β3-adrenergic receptors (β3-ARs) (6). The β3 subtype in the human bladder facilitates the relaxation of the detrusor and the storage of urine. The human urinary bladder is the primary site of β3-adrenoceptor expression, with 97% of the total expressed as the β3 subtype and the remaining percentage expressed as the β1 and β2 subtypes (7). Acting on the β3-ARs, which are the most prevalent β-ARs in the human bladder, mirabegron specifically contributes to the neural regulation of the storage phase of micturition (8). The afferent activity in the bladder, during the process of filling, is a treatment worth trying to target an OAB, a filling disorder. Low-threshold, "in series"-coupled mechanoreceptive (Aδ) afferents are stimulated by bladder distension. The response to distention is diminished when bladder compliance is increased; therefore, bladder capacity increases, as greater filling volumes are required to recruit adequate afferent activity to initiate micturition. During the process of filling, spontaneous (autonomous) bladder activity is a factor in determining bladder compliance (9). A novel class of medications - the β3 -β3-adrenergic receptor agonists (β3 agonists) are applicable, in a similar manner, to patients with neurogenic and non-neurogenic detrusor hyperactivity. The adverse effect profile of ß3

* *Corresponding author:* Heba.Razaq2206m@comed.uobaghdad.edu.iq

agonists is more favorable in comparison to that of antimuscarinics (10,11). Beta3-adrenergic agonists exhibit greater efficacy in inhibiting detrusor contractions induced by stimuli other than cholinergic agonists (12). One advantage of this class is the circumvention of anticholinergic adverse effects, including constipation and dry mouth (13).

Mirabegron operates differently from anticholinergic drugs due to its role in the relaxation of the detrusor muscles. The β3-AR agonists increase bladder capacity without affecting micturition pressure or residual volume, in contrast to the anticholinergic medications (14). Mullen et al. discovered that mirabegron was effective in treating patients' urinary symptoms of benign prostatic hyperplasia and overactive bladder, and side effects were reported infrequently (15). By ensuring low intravesical pressure during the bladder filling phase, when the urethral sphincter is closed, detrusor muscle relaxation is crucial for achieving bladder compliance. Adenylyl cyclase, which generates cyclic adenosine monophosphate (cAMP), is subsequently activated in response to β3-AR activation, resulting in bladder relaxation (16). Consequently, the activation of protein kinase A hinders the interaction between calcium-calmodulin and myosin/ actin by phosphorylating myosin light chain kinase. An intracellular component interaction further impedes Ca2+ sensitization. One plausible hypothesis for this phenomenon is the lack of calcium-calmodulin signaling or the inhibition of myosin light chain phosphatase (MLCP). By interacting directly with the system that phosphorylates myosin light chain kinase (MLCK) (17). This study highlights the potential efficacy of mirabegron in managing OAB among a selected Iraqi patient cohort, setting the stage for larger-scale studies to confirm these findings and further explore the therapeutic benefits and safety profile of Mirabegron in this population.

Patient &Methods

For ethical considerations, approval by the Research Ethics Committee of the University of Baghdad's College of Medicine under registration number (03-32) dated 21/12/2023. Patient's consent was obtained after explaining to the patient the purpose, procedures, and rights involved in participating in the study. All patients involved in this research acknowledged and consented to the form being included in this study protocol. In this case series follow-up study conducted from October 2023 to March 2024 at Ghazi Al-Hariri Hospital, 50 adult patients were initially recruited based on a clinical and urodynamic diagnosis of overactive bladder (OAB). Patients with untreated bladder outlet obstruction, untreated urinary tract infections, uncontrolled hypertension, pregnancy or lactation, severely impaired renal function (GFR < 15 ml/min/1.73 m²), previous failure of multiple OAB treatments, or severe hepatic impairment were excluded from the study. Each participating patient provided informed consent, and confidentiality of personal information was strictly maintained. The study design did not impose any gender restrictions. Ten patients who did not attend follow-up visits were excluded, resulting in a final sample of 40 patients.

These 40 patients were prescribed Mirabegron at a dose of 50 mg per day, a standard treatment for OAB. Baseline bladder capacity measurements were obtained using ultrasound, with the ellipsoid formula (depth × width × height × 0.52) employed to calculate bladder volume (18). Bladder capacity was re-measured during follow-up visits at two months (1st visit) and four months (2nd visit) after the baseline.

Patients were advised to monitor for potential side effects such as hypertensive crises, allergic reactions, or urine retention, and to report any occurrences to the urology department. Additionally, they were instructed to avoid diuretics, excessive fluid intake, anticholinergic drugs, and antihistamines during the study period. Three patients reported experiencing mild dyspepsia, which they associated with Mirabegron intake; however, these symptoms did not lead to discontinuation, as patients noted an improvement in their OAB symptoms.

Statistical analysis

The data was analyzed using Statistical Package for Social Sciences (SPSS) version 22, and was presented as mean ± standard deviation. The paired t-test was used to compare the means of continuous variables. A P-value of less than 0.05 was considered significant.

Results

Of the 40 patients included in the study, 60% were females and 40% were males, with a mean age of 50.7±18.13 years. The mean height and weight were (163.7±8.39 cm and 77.3±12.10 Kg, respectively) as shown in Table 1.

Table 1: Demographic criteria for Patients with OAB receiving mirabegron

Variables		Mean	Std. Deviation
Age (years)		50.7	18.13
Height (centimeters)		163.7	8.39
Weight (Kilograms)		77.3	12.10
		Frequency	Percent
Gender	Female	24	60
	Male	16	40
Total		40	100

A notable and progressive increase in bladder capacity was noticed over time among the participants. Initially, the mean bladder capacity at baseline was 128.4 ml. After two months, this means capacity doubled, reaching approximately 251.6 ml. Four months after the baseline measurement, the mean bladder capacity had reached nearly three times the initial measurement, around 357.9 ml (Table 2.

Table 2: Mean±SD of bladder capacity in the study group throughout the study

Study time	Mean	Standard Deviation
At baseline time	128.4	45.37
After 2 months	251.6	64.10
After 4 months	357.9	68.00

The study observed a statistically significant change in bladder capacity after two months and four months of treatment, with a p-value of 0.001, (Table 3).

Table 3: Mean±SD Bladder capacity in the study group over the study period

Time of the measurement	Mean±SD Bladder Capacity (ml)	Paired t-test value	
Zero time	128.4±45.36	-16.063 (DF=39) *P* < 0.001	-17.585 (DF=39) *P* < 0.001
2 months	251.6±64.10		
4 months	357.9±68.00		

Discussion

The objective of this investigation was to assess the impact of Mirabegron on bladder capacity in patients with overactive bladders. The results after an 8–16 week period showed a significant increase in mean bladder capacity which suggests that Mirabegron may be effective in enhancing bladder capacity in patients with overactive bladder, providing potential therapeutic benefits in managing this condition. This observed improvement in bladder capacity is unlikely to be due to chance, supporting the efficacy of Mirabegron in this group over the given treatment duration.

The results of the current study revealed that after four months, there was a statistically significant increase in mean bladder capacity compared to the initial reading and to those made after two months. This result indicates that the observed increase in bladder capacity is highly unlikely to have occurred by chance alone, suggesting that the treatment or intervention had a measurable effect. A p-value of 0.001 is below the typical significance threshold of 0.05, reinforcing the robustness of this finding. Thus, it can be concluded that Mirabegron had a significant impact on bladder capacity over the course of four months. It highlights the impact of the treatment on bladder capacity, suggesting a reliable and clinically meaningful improvement.

Oral Mirabegron therapy over a 12-week period has been found to significantly enhance bladder capacity and alleviate subjective symptoms in patients newly diagnosed with overactive bladder (OAB), without worsening voiding symptoms. (19) A retrospective observational study of 16 patients treated with Mirabegron demonstrated a statistically significant increase in the bladder capacity ratio (actual bladder capacity divided by expected bladder capacity for age), improving from 0.57 to 0.97. This improvement underscores Mirabegron's effectiveness in increasing bladder capacity relative to age-specific expectations, offering a promising therapeutic option for managing OAB symptoms without compromising voiding function. (19).

According to the study of O'Kane et al, the maximum cystometric capacity of their total studied population experienced a statistically significant increase by week 24 as a result of the Mirabegron treatment (20). Nevertheless, additional clinical research has demonstrated that β3-adrenergic receptor stimulants, which are novel agents for OAB, are both relatively safe and effective (21,22,23).

Mirabegron induces relaxation of the detrusor muscle; however, the precise cellular mechanism responsible for this effect is still unknown. There is a substantial body of evidence that suggests an alternative mechanism by which β-ARs can activate large-conductance Ca2+-activated K+ (BKCa) channels. This phenomenon has been observed in a variety of species, including humans (17).

Mirabegron in clinical trials was generally well tolerated, with a profile that was generally comparable to that of a placebo for a period of up to 52 weeks (24,25).

Limitation Sample size & time limit.

Conclusion

The notable improvement in bladder capacity among the study group emphasizes Mirabegron's efficacy and suggests substantial potential for improving the quality of life for individuals affected by this condition. These findings not only highlight the therapeutic promise of Mirabegron but also pave the way for innovative approaches to OAB management. This hospital-based study, may serve as a foundation for future, larger and longer-term studies to further elucidate the benefits of Mirabegron for OAB patients.

Authors' declaration

We confirm that all figures and tables presented in the manuscript are our original work.

Ethical Approval: Ethical approval for this study was obtained from the University of Baghdad, College of Medicine. All participants provided written informed consent before sample collection. The study protocol, subject information sheet, and consent form were reviewed and approved by a local ethics committee according to document number (03-32) on 25/12/2023.

Conflicts of Interest: None
Funding: Non

Authors' contribution

Study conception & design: (Hiba H Razaq, Mohammed B. Ismail). Literature search: (Hiba H. Razaq). Data acquisition: (Hiba H. Razaq). Data analysis & interpretation: (Hiba H. Razaq). Manuscript preparation: (Hiba H. Razaq). Manuscript editing & review: (Mohammed Bassil Ismail & Mohamed E. Abdelrhman).

References

1. Hutchinson A, Nesbitt A, Joshi A, Clubb A, Perera M. Overactive bladder syndrome Management and treatment options. Aust J Gen Pract. 2020;49(9):593-8. https://doi.org/10.31128/AJGP-11-19-5142.

2. Scarneciu I, Lupu S, Bratu O, Teodorescu A, Maxim L, Brinza A, et al. Overactive bladder: A review and update. Exp Ther Med. 2021;22(6):1–8. https://doi.org/10.3892/etm.2021.10879.

3. Ismail MB, Abdullhussein WQ. Efficacy and safety of sacral neuromodulation in treatment of refractory overactive bladder. Indian J Forensic Med Toxicol. 2021;15(1):1315-21. https://doi.org/10.37506/ijfmt.v15i1.13597.
4. Abbas IK, Rajab NA, Hussein AA. Formulation and in-vitro evaluation of darifenacin hydrobromide as buccal films. Iraqi J Pharm Sci. 2019;28(2):83-94. https://doi.org/10.31351/vol28iss2pp83-94.
5. Leron E, Weintraub AY, Mastrolia SA, Schwarzman P. Overactive Bladder Syndrome: Evaluation and Management. Curr Urol. 2018;11(3):117-25. https://doi.org/10.1159/000447205.
6. Sam P, Nassereddin A, LaGrange CA. Anatomy, Abdomen and Pelvis: Bladder Detrusor Muscle. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 https://www.ncbi.nlm.nih.gov/books/NBK482181/.
7. Kennelly M, Wielage R, Shortino D, Thomas E, Mudd PN Jr. Long-term efficacy and safety of vibegron versus mirabegron and anticholinergics for overactive bladder: a systematic review and network meta-analysis. Drugs Context. 2022. https://doi.org/10.7573/dic.2022-4-2.
8. Maggiore ULR, Cardozo L, Ferrero S, Sileo F, Cola A, Torella M, et al. Mirabegron in the treatment of overactive bladder. Expert Opin Pharmacother. 2014;15(6):873-87. https://doi.org/10.1517/14656566.2014.898752.
9. Andersson KE. New developments in the management of overactive bladder: Focus on mirabegron and onabotulinumtoxinA. Ther Clin Risk Manag. 2013;9(1):161-70. https://doi.org/10.2147/TCRM.S33052.
10. Kim JK, De Jesus MJ, Lee MJ, Dos Santos J, Dy JS, Ming JM, et al. β3-Adrenoceptor Agonist for the Treatment of Bladder Dysfunction in Children: A Systematic Review and Meta-Analysis. J Urol. 2022;207(3):524-33. https://doi.org/10.1097/JU.0000000000002361.
11. Huang CK, Lin CC, Lin ATL. Effectiveness of antimuscarinics and a beta-3 adrenoceptor agonist in patients with overactive bladder in a real-world setting. Sci Rep. 2020;10(1):1-7. https://doi.org/10.1038/s41598-020-68170-4.
12. Krhut J, Skugarevská B, Míka D, Lund L, Zvara P. Clinical Utility of β3-Adrenoreceptor Agonists for the Treatment of Overactive Bladder: A Review of the Evidence and Current Recommendations. Res Reports Urol. 2022; 14:167-75. https://doi.org/10.2147/RRU.S309144.
13. Raju R, Linder BJ. Evaluation and Treatment of Overactive Bladder in Women. Mayo Clin Proc. 2020;95(2):370-7. https://doi.org/10.1016/j.mayocp.2019.11.024.
14. Sartori LGF, Nunes BM, Farah D, Oliveira LM De, Novoa CCT, Sartori MGF, et al. Mirabegron and Anticholinergics in the Treatment of Overactive Bladder Syndrome: A Meta-analysis. Rev Bras Ginecol e Obstet. 2022;45(6):337-46. https://doi.org/10.1055/s-0043-1770093.
15. Mullen GR and Kaplan SA. Efficacy and Safety of Mirabegron in Men with Overactive Bladder Symptoms and Benign Prostatic Hyperplasia. Curr. Urol. Rep. 2021; 22 (1), 5. https://doi.org/10.1007/s11934-020-01017-7.
16. Kwon J, Kim DY, Cho KJ, Hashimoto M, Matsuoka K, Kamijo T. Pathophysiology of Overactive Bladder and Pharmacologic Treatments Including β3-Adrenoceptor Agonists -Basic Research Perspectives. Int Neurourol J. 2024 Feb;28(Suppl 1):12-33. Epub 2024 https://doi.org/10.5213/inj.2448002.001,
17. Almallah R and a Almukhtar H. Mirabegron-Induced Smooth Muscle Relaxation: Review of the Suggested Mechanisms. IJPhr 2023;20:195-200. https://doi.org/10.33899/iphr.2023.142851.1057.
18. Schallom M, Prentice D, Sona C, Vyers K, Arroyo C, Wessman B, et al. Accuracy of measuring bladder volumes with ultrasound and bladder scanning. Am J Crit Care. 2020;29(6):458-67. https://doi.org/10.4037/ajcc2020741.
19. Kim SC, Park M, Chae C, Yoon JH, Kwon T, Park S. Efficacy and tolerability of mirabegron compared with solifenacin for children with idiopathic overactive bladder: A preliminary study. Investig Clin Urol. 2021 May;62(3):317-323. https://doi.org/10.4111/icu.20200380.
20. O'kane M, Robinson D, Cardozo L, Wagg A, Abrams P. Mirabegron in the Management of Overactive Bladder Syndrome. Int J Womens Health. 2022;14:1337-50. https://doi.org/10.2147/IJWH.S372597.
21. Makhani A, Thake M, Gibson W. Mirabegron in the treatment of overactive bladder: Safety and efficacy in the very elderly patient. Clin. Interv. Aging 2020, 15, 575-581. https://doi.org/10.2147/CIA.S174402.
22. Wagg A, Staskin D, Engel E, Herschorn S, Kristy R.M, Schermer CR. Efficacy, safety, and tolerability of mirabegron in patients aged 65 yr with overactive bladder wet: A phase IV, double-blind, randomised, placebo-controlled study (PILLAR). Eur. Urol. 2020, 77, 211-220. https://doi.org/10.1016/j.eururo.2019.10.002.
23. Krebs J, Pannek J, Rademacher F, Wöllner J. Real-World Effects of Mirabegron in Patients with Chronic Neurogenic Detrusor Overactivity - A Retrospective Cohort Study. Res Rep Urol. 2020 May 22;12:187-192. https://doi.org/10.2147/RRU.S253713.
24. Heintjes EM, Bezemer ID, Prieto-Alhambra D, Smits E, Booth HP, Dedman D, et al. Evaluating the effectiveness of an additional risk minimization measure to reduce the risk of prescribing mirabegron to patients with severe uncontrolled hypertension in four european countries. Clin Epidemiol. 2020;12:423–33. https://doi.org/10.2147/CLEP.S242065.
25. Makhani A, Thake M, Gibson W. Mirabegron in the Treatment of Overactive Bladder: Safety and Efficacy in the Very Elderly Patient. Clin Interv Aging. 2020 Apr 23;15:575-581. https://doi.org/10.2147/CIA.S174402/.

How to Cite

Razaq HH, Ismail MB, Abdelrhman ME. Mirabegron in the Management of Overactive Bladder Syndrome in Ghazi Al-Hariri Hospital. J Fac Med Baghdad. 2025;67(1). Available from: https://iqjmc.uobaghdad.edu.iq/index.php/19JFacMedBaghdad36/article/view/2451

تأثير ميرابيغرون على سعة المثانة في العراق للمرضى الذين يعانون من فرط نشاط المثانة

هبه حميد رزاق[1]، محمد باسل اسماعيل[2]، محمد عبدالرحمن[2]
[1] فرع علم الادوية ، كلية الطب، جامعة بغداد، بغداد، العراق.
[2] فرع الجراحة،كلية الطب، جامعة بغداد، بغداد، العراق.
[3] فرع الجراحة، كلية الطب، جامعة الجزيرة، وادي مدني، السودان

خلفية:
تتأثر نوعية حياة الأفراد سلبا بأعراض فرط نشاط المثانة OAB تسببت الآثار الجانبية للأدوية المضادة للكولين في توقف عدد كبير من المرضى عن علاجهم. في الآونة الأخيرة ، أجريت أبحاث حول العلاقة المحتملة بين عبء مضادات الكولين وتطور الخرف. وقد ثبت أن عضلة النافصة تسترخي نتيجة لتنشيط مستقبلات الأدرينالين β3 ، والتي بدورها سهلت تطوير أول ناهض لمستقبلات الأدرينالين β3. Mirabegron هو الدواء الأولي في هذه الفئة للحصول على الموافقة لعلاج فرط نشاط المثانة.
الهدف من الدراسة: تقدير تأثير ميرابيغرون على سعة المثانة لدى مرضى OAB.
الطريقه : تمت الدراسة في مدينة الطب (مستشفى غازي الحريري) عيادة المسالك البولية الخارجية ، دراسة مستقبلية ل 40 مريضا تم تشخيص إصابتهم ب OAB.: أخذ هؤلاء المرضى جرعة واحدة من ميرابيغرون 50 ملغ يوميا لمدة 4 أشهر وتم تقييمهم لتأثير هذا الدواء على قياس سعة المثانة بالملليلتر الذي تم قياسه بواسطة الموجات فوق الصوتية.
الإستنتاج: أظهر التحقيق أن هناك زيادة ذات دلالة إحصائية ثابتة عن خط الأساس بعد 2 و 4 أشهر في سعة المثانة بعد العلاج بالميرابيغرون (القيمة Mirabegron دواء فعال لعلاج OAB من خلال زيادة سعة المثانة.
الكلمة الرئيسية: فرط نشاط المثانة (OAB)، مستقبلات β3 الأدرينالية (β3-ARs)، ميرابيغرون ، سعة المثانة.