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ORIGINAL ARTICLE

Mirabegron versus darifenacin: which is the preferred first-line treatment for overactive bladder syndrome?

Mirabegrón versus darifenacina: ¿cuál se prefiere como tratamiento de primera línea en el síndrome de vejiga hiperactiva?

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Abstract

Objective: *Overactive bladder affects up to 32% of Latin Americans over 40.This study compares mirabegron and darifenacin in terms of safety and efficacy, as no similar studies exist in Colombia.* **Method:** *A retrospective study of 234 patients treated with mirabegron or darifenacin between January/2019 and April/2022. Data were analyzed using statistical tests, with significance set at $p < 0.05$.* **Results:** *Both drugs significantly reduced urination frequency, with no difference in patient-reported improvement. Women experienced more side effects, particularly with Darifenacin.* **Conclusions:** *Both treatments were effective, but Darifenacin had more side effects, leading to higher discontinuation rates for women.*

Keywords: *Overactive bladder. Mirabegron. Darifenacin.*

Resumen

Objetivo: *La vejiga hiperactiva afecta hasta el 32% de los latinoamericanos mayores de 40 años. Este estudio compara mirabegron y darifenacina en términos de seguridad y eficacia, ya que no existen estudios similares en Colombia.* **Método:** *Estudio retrospectivo de 234 pacientes tratados con mirabegron o darifenacina entre enero/2019 y abril/2022. Los datos se analizaron utilizando pruebas estadísticas, con una significancia establecida en $p < 0.05$.* **Resultados:** *Ambos medicamentos redujeron significativamente la frecuencia de micción, sin diferencias en la mejora reportada por los pacientes. Las mujeres experimentaron más efectos secundarios, principalmente con darifenacina.* **Conclusiones:** *Ambos tratamientos fueron efectivos, pero darifenacina tuvo más efectos secundarios, y más altas de suspención en mujeres.*

Palabras clave: *Vejiga hiperactiva. Mirabegron. Darifenacina.*

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Introduction

According to the International Continence Society, overactive bladder (OAB) is defined as urinary urgency, usually with urinary frequency and nocturia, with or without urgency urinary incontinence. Urinary tract infection must have been previously ruled out[1,2]. OAB is predominant in the African-American race and in the female sex[3-5]. It presents a 30% prevalence in patients > 60 years. In Latin America, the prevalence in women > 18 years old is 14%, and in women > 40 years is 32%[6].

The OAB treatment is a widely debated topic, in which multiple prospective studies have been carried out, allowing different treatments to be compared. Based on these studies, recommendations have changed over time, starting from the premise that a few decades ago, antimuscarinics were the treatment of choice for this pathology[7]. Since 2010, this has been a debated subject due to the appearance of new treatments such as B3 agonists[7]. Mirabegron, being a sympathomimetic, does not have the typical effects of antimuscarinics such as dry mouth, urinary retention, or constipation[8]. In terms of efficacy, in clinical trials conducted to date, mirabegron has shown similar efficacy to that of antimuscarinics, conducting the treatment based on the side effects and tolerability[8]. In the latest guidelines of the European Association of Urology, it is recommended to start antimuscarinic drugs or beta 3 agonists as an alternative to antimuscarinic drugs if they do not respond to conservative treatment (pelvic floor therapy and adjustment of voiding habits)[9].

Darifenacin is one of the few antimuscarinics that does not penetrate the central nervous system, since it does not cross the blood-brain barrier, as well as being a selective M3 receptor (present in the urinary tract). Thus, it is considered the antimuscarinic agent with fewer secondary effects of neural origin. About mirabegron, it is a B3 agonist that does not have penetrance into the central nervous system either, with mainly peripheral side effects such as arterial hypertension. When reviewing the literature, few studies have been found comparing mirabegron versus darifenacin, and none in the Colombian population. A comparative retrospective study was carried out in this population, facilitating the decision on first-line treatment in OAB syndrome (OABS).

Material and methods

A retrospective observational study was carried out in patients with OAB without treatment started. About 3013 medical records of patients with OAB diagnosis from two institutions were reviewed between January 2019 and April 2022. Only patients starting on mirabegron or darifenacin as first-line treatment were included. All patients with incomplete data, combined treatments, or previous treatments were excluded. Having received previous pelvic floor therapy was not an exclusion criteria.

The U Mann-Whitney test was obtained to compare the quantitative variables, and the χ^2 for the qualitative ones, considering a significant difference of $p < 0.05$. To establish the difference between daytime and nighttime urinary frequency before and after treatment, differencing between darifenacin and mirabegron, the Student's t-test tool was used. Data were tabulated and calculated using the Statistical Package for the Social Sciences 28. Objective results decreased daytime and nighttime frequency, and subjective results were about the patient-reported improvement after starting medication. In addition, a subanalysis by age and sex was performed.

Results

A total of 234 patients who received mirabegron (66%) or darifenacin (33%) as initial treatment were included. There were no demographic differences in terms of age, sex, comorbidities, or the presence or absence of uninhibited contractions in urodynamics (Table 1).

There was no statistically significant difference related to the subjective improvement referred by the patient. When performing the analysis by subgroups regarding sex and age, there was also no difference in subjective improvement (Table 2).

A significant decrease in overall daytime voiding frequency was evidenced, including darifenacin or mirabegron, finding a difference in daytime frequency of 2.6 urinations per day (95% confidence interval [CI]: 1.5-3.6; p = 0.0001). When discriminating between mirabegron and darifenacin, it was found that mirabegron presented a significant difference in terms of the daytime frequency change, before and after treatment, decreasing 2.87 urinations per day (95% CI: 1.76-3.97; p = 0.0001). On the other hand, darifenacin did not show a statistically significant difference with a decrease of 1.25 micturitions per day (95% CI: 1.8-4.3; p = 0.39).

About nocturnal urination frequency, it also presented a significant global decrease in the number of nocturnal micturitions before and after the medication (1.1 micturitions with 95% CI: 0.7-1.51; p = 0.0001); Alone treatment with darifenacin did not present a significant

Table 1. Demographic data according to treatment

Demographic data	Total, n = 234 (%)	Darifenacin, n = 78 (%)	Mirabegron, n = 156 (%)	p
Age	68 ± 19	69 ± 22	67 ± 17	0.61
Sex				0.578
Female	129 (55.1)	41 (52.6)	88 (56.4)	
Male	105 (44.9)	37 (47.4)	68 (43.6)	
Comorbidities				
Neurological disease	22 (9.4)	8 (10.3)	14 (9.0)	0.756
Obesity	25 (10.7)	10 (12.8)	15 (9.6)	0.454
Arterial hypertension	96 (41)	32 (41)	64 (41)	1.000
Radiotherapy	9 (3.9)	1 (1.3)	8 (5.1)	0.149
Pelvic surgery	40 (17.1)	15 (19.2)	25 (16)	0.539
Oncological disease	32 (13.7)	8 (10.3)	24 (15.4)	0.282
Coronary disease	30 (12.8)	11 (14.1)	19 (12.2)	0.678
Overactive detrusor in urodynamics	34 (14.5)	9 (11.5)	25 (16)	0.359

Table 2. Subjective improvement assessed, after starting darifenacin versus mirabegron

Outcomes	Total, n = 234 (%)	Darifenacin, n = 78 (%)	Mirabegron, n = 156 (%)	p
Subjective improvement	157 (67.1)	48 (61.5)	109 (69.9)	0.31
Daytime voiding frequency				
Onset	8 ± 4.5	7.5 ± 5	8 ± 4	0.61
Post treatment	6 ± 4	6 ± 5	6 ± 4	0.21
Nocturnal voiding frequency				
Onset	3 ± 2.5	2 ± 4	3 ± 2	0.49
Post treatment	2 ± 2	2 ± 2	2 ± 2	0.43

Table 3. Adverse events and drug suspension cause

Demographic data	Total, n = 234 (%)	Darifenacin, n = 78 (%)	Mirabegron, n = 156 (%)	p
Treatment suspension causes				
Arterial hypertension	4 (1.7)	2 (2.6)	2 (1.3)	0.476
Headache	5 (2.1)	4 (5.1)	1 (0.6)	0.025
Dry mouth	5 (2.2)	3 (3.9)	2 (1.3)	0.195
Dry skin	1 (0.4)	1 (1.3)	0	0.151
Constipation	4 (1.7)	4 (5.1)	0	0.004
Rash	1 (0.4)	0	1 (0.6)	0.48
Blurry vision	1 (0.4)	1 (1.3)	0	0.16
Drowsiness	1 (0.4)	1 (1.3)	0	0.16
Edema	1 (0.4)	0	1 (0.6)	0.48
Adverse event	15 (6.4)	10 (12.8)	5 (3.2)	0.005
Treatment suspension	16 (6.8)	10 (12.8)	6 (3.8)	0.010

decrease (0.54 urinations with 95% CI: –0.49-1.57; p = 0.28), unlike mirabegron, which presented a decrease of 1.25 nocturnal urinations (95% CI: 0.8-1.6; p = 0.0001), being statistically significant (Table 3).

Mirabegron was less discontinued than darifenacin (3.8% vs. 12.8% p = 0.01) with fewer adverse events (3.2% vs. 12.8% p = 0.005). Women presented a greater number of side effects (10.1 vs. 1.9% p = 0.011) and tended to quit treatment (10.1 vs. 2.9% p = 0.03) in comparison with men, with a statistically significant difference. When performing the analysis according to age (greater or younger than 65 years), no significant difference was found in terms of secondary events and suspension.

Discussion

"Overactive detrusor" term differs from OAB in that the first is a urodynamic parameter, whereas the latter is a combination of signs and symptoms. Therefore, an overactive detrusor can be one of the many causes of OABS. Among the etiologies of this syndrome, it is found mucosa inflammation, chronic outlet tract obstruction, and idiopathic or neurogenic hyperactive detrusor due to neurological pathologies (Parkinson's, cerebrovascular disease, transverse myelitis, or spinal cord lesions)[1-10]. Both, antimuscarinics and B3 adrenergics have been studied and their formulation has been widely applied as first-line drugs in the treatment of OABS, regardless of an overactive detrusor or not[10]; Patients with this syndrome are more likely to suffer from depression and anxiety, making extremely important to know the effectiveness and safety of the different medications, choosing the best option according to each case[11]. In this order, the main purpose of this study was to compare two first-line drugs (mirabegron vs. darifenacin) with different mechanisms of action and with little penetration into the central nervous system.

Since then, mirabegron (B3 agonist) has been compared with different antimuscarinics such as tolterodine, imidafine, and solifenacin[12-16]. However, all of these antimuscarinics have penetrance into the central nervous system and can produce neurological effects such as dizziness, drowsiness, blurred vision, or cognitive defects, which may condition their suspension[17]. The effectiveness of mirabegron has approached 70% with 50 mg daily compared to 59% with placebo[18].

Besides, darifenacin and trospium do not cross the blood-brain barrier, presenting fewer neuronal effects[19,20]. In addition, darifenacin is the most selective for M3, showing fewer adverse effects on the cardiovascular system (M2 receptors) and the nervous system (M1)[20]. Solifenacin has been shown to be more effective than the rest of the antimuscarinics but with greater adverse effects since it is not M3 selective[21], Its use is contraindicated in patients with angle-closure glaucoma.

On the other hand, mirabegron is a sympathomimetic B3 adrenergic agonist that produces relaxation of the longitudinal detrusor under the influence of norepinephrine. This does not have the typical effects of anticholinergics; however, they can present hypertension, nasopharyngitis, and headaches[22]. In terms of efficacy, in clinical trials carried out to date, mirabegron has shown similar efficacy to antimuscarinic drugs.

Meek et al. performed a meta-analysis comparing the risk of constipation by the administration of anticholinergics, showing that tolterodine (OR 1.36, 95% CI = 1.01-1.85) and darifenacin (OR 1.93, 95% CI = 1.40-2.66) gets on less constipation. On the other hand, trospium (OR 2.93, 95% CI = 2.00-4.28) and solifenacin produce greater constipation (OR 3.02, 95% CI = 2.37-3.84)[23]. In another meta-analysis conducted by Cochrane, they conclude that solifenacin is more effective than tolterodine, with a lower risk of dry mouth. Within the reported data, two crossover trials were presented comparing oxybutynin and darifenacin, having the same effectiveness.

In the SOLIDAR study published in 2012, the efficacy and safety profile of darifenacin was compared with solifenacin. There was no significant difference in the reduction of OAB symptoms with overactive detrusor between the two groups; however, solifenacin showed a greater increase in quality of life compared to darifenacin. Adverse effects in both groups were similar (constipation, blurred vision, headache, dizziness, insomnia, concentration, and memory problems) with the exception of dry mouth, which was higher with darifenacin[24].

The BLOSSOM clinical trial also compared tolterodine versus placebo versus mirabegron (100/150 mg) in a period of 4 weeks[25]. Voiding frequency and incontinence frequency were significantly decreased in both mirabegron groups compared to placebo; however, there was no significant difference between tolterodine and placebo. About drug suspension due to adverse effects, 1.5% was discontinued in the placebo group, 4.6% in the mirabegron 100 mg group, 7.7% in the mirabegron 150 mg group, and 3.1% in the tolterodine group. More adverse effects were observed in the mirabegron 150 mg group, consisting of palpitations, vertigo, blurred vision, dry mouth, nausea, dizziness, rash, and fatigue[25].

The SCORPIO trial was carried out in 27 countries of Europe and in Australia, a double-blind, randomized controlled phase 3 study, where the efficacy of mirabegron (50, 100 mg) versus placebo and tolterodine 4 mg versus placebo was evaluated for 12 weeks[26]. A greater reduction in urination and incontinence episodes was found in 12% of patients compared to placebo[26]. When comparing tolterodine with placebo, there was no significant difference in the reduction of voiding episodes per day, but there was a significant difference in the reduction of incontinence episodes. In this study, tolterodine is not directly compared with mirabegron[26]. The ARIES study (USA and Canada) followed a similar

methodology to the SCORPIO study for 12 weeks, where mirabegron 50/100 mg was compared versus placebo. However, this study did not compare tolterodine versus placebo. Likewise, it showed a significant decrease in micturition frequency and incontinence in both groups of mirabegron versus placebo. The JAPAN and ASIA study, carried out more recently, shows the same results, evidencing a significant decrease in micturition frequency and incontinence with mirabegron than with placebo. However, there is no significant decrease in these parameters with tolterodine[27,28].

The TAURUS study (Europe, Australia, South Africa, USA, and Canada) is the continuation of the SCORPIO and ARIES study, whose main outcome was to evaluate the safety profile of mirabegron compared to placebo and tolterodine for 12 months[29]. The incidence of adverse effects was similar in the mirabegron 50 mg/100 mg and tolterodine groups (59.7% vs. 61.3% vs. 62.6%, respectively)[29,30]. Most of them were mild-to-moderate adverse effects, including hypertension, headache, dry mouth, or constipation. Of these, the only significant difference between the groups was the incidence of dry mouth, with a higher presentation in the tolterodine group. The rise in systolic blood pressure was only 0.2 and 0.4 mmHg in the mirabegron 50 mg and 100 mg groups, respectively. The drug discontinuation was similar in the three groups (6.4% vs. 5.9% vs. 6.0%). Major adverse events were similar in the three groups. A higher incidence of cardiac arrhythmias and episodes of urinary retention was found with tolterodine.

Following this, few studies have been carried out comparing antimuscarinics with mirabegron in monotherapy or as an enhancement to anticholinergic therapy. In 2016, the BESIDE study was carried out, in which solifenacin was compared versus mirabegron is associated with solifenacin. The results showed superiority of the combination of mirabegron 50 mg associated with solifenacin 5 mg over the administration of solifenacin 5 mg in monotherapy. In addition, the non-inferiority of this combination is shown with solifenacin 10 mg in monotherapy.

However, few studies comparing directly darifenacin with mirabegron were found. In 2014, Maman and associates combined the results of different studies evaluating the efficacy of antimuscarinic drugs with placebo and compared them with the results of Mirabegron versus placebo. In this way, possible results of hypothetical direct comparison studies between B3 adrenergic and antimuscarinic drugs were simulated[31]. It was found that there would be no statistically significant difference between mirabegron compared to tolterodine, darifenacin, fesoterodine, oxybutynin, solifenacin 5 mg, and trospium. However, solifenacin 10 mg was the only one showing possibly greater efficacy than mirabegron[31].

The only prospective study carried out in 2020 by Bhangu et al. analyzed 60 patients with mirabegron and 60 patients with darifenacin, finding that darifenacin had comparable results to mirabegron, with a slightly greater improvement in symptoms than mirabegron. The improvement in voiding frequency at 4 weeks was 63% for mirabegron and 91% for darifenacin ($p = 0.001$); however, at 12 weeks, 90% of patients improved with mirabegron and 98% improved with darifenacin, without significant differences. These results differ from our study, where comparable results were found but with a significant decrease in daytime and nighttime urinary frequency[32].

On the other hand, Vasudeva et al. conducted a randomized clinical trial comparing these two drugs in the neurogenic bladder and stroke population, finding comparable effectiveness and safety. In both medications, there was a significant decrease when comparing pre- and post-treatment symptoms, such as incontinence, nocturia, and micturition frequency. However, there was no significant difference between the two drugs in terms of these parameters[33].

In our study, we did a retrospective comparison of efficacy and side effects between mirabegron and darifenacin as first-line treatment in patients with OAB. Both groups presented similar demographic characteristics with no significant difference in terms of age, sex, comorbidities, or presence of hyperactive destructor in urodynamics. As previously mentioned in studies, there was no significant difference between mirabegron and antimuscarinic in terms of subjective symptom improvement, even when performing a subanalysis by gender and age. However, in terms of daytime and nighttime micturition frequency, a significant difference was seen when comparing the pre- and post-treatment frequency with mirabegron. This difference was not significant for darifenacin. However, it is important to highlight that the number of patients included in mirabegron´s group was double than of darifenacin, which could have affected the result. Now, when comparing daytime and nighttime micturition frequencies, both pre- and post-treatments were comparable.

In terms of safety, darifenacin showed a worse safety profile than mirabegron, with a higher rate of adverse events and suspension, with a significant difference. Constipation and headache were the secondary events presented in the darifenacin group, with a significant difference when compared to mirabegron. This differs

from what has been reported in the literature, given that headache and hypertension were the most frequent events with mirabegron. No comparative studies of this medication with mirabegron were found. As expected, no differences were found in neurological side events. Women presented a greater number of side effects and discontinuation of treatment than men, without a difference when discriminating by age (greater or younger than 65 years).

One of this study's limitations is its retrospective nature, with a difference between the number of patients in each group, doubling the number of cases treated with mirabegron. The results were based on subjective aspects recorded by the specialist in clinical history. Given that urodynamics are not routinely performed in clinical practice before and after the start of treatment in OAB, it was not possible to use this parameter to compare both drugs.

Conclusion

The subjective improvement between mirabegron and darifenacin is comparable; however, a significant decrease in daytime and nighttime micturition frequency was observed in mirabegron related to darifenacin. In addition, darifenacin showed a higher rate of secondary events and drug discontinuation, with constipation prevailing in this group. Constipation and headache were the secondary events with a significant difference between both groups, favoring the patients treated with mirabegron. Based on the above, the door is opened to carry out a prospective comparison that allows a more objective analysis of the symptomatic and urodynamic parameters in the Colombian population, including a larger number of patients.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments on humans or animals were performed for this research.

Confidentiality of data. The authors declare that they have followed their center's protocols on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

References

1. Abrams P. Describing bladder storage function: overactive bladder syndrome and detrusor overactivity. Urology. 2003;62:28-37.
2. Ulmsten U, Griffiths D, Victor A, Fall M, Abrams P, Rosier P, et al. The standardisation of terminology in lower urinary tract function: report from the standardisation sub-committee of the International Continence Society. Urology. 2003;61:37-49.
3. Nitti VW, Auerbach S, Martin N, Calhoun A, Lee M, Herschorn S. Results of a randomized phase III trial of mirabegron in patients with overactive bladder. J Urol. 2013;189:1388-95.
4. Irwin DE, Milsom I, Hunskaar S, Reilly K, Kopp Z, Herschorn S, et al. Population-based survey of urinary incontinence, overactive bladder, and other lower urinary tract symptoms in five countries: results of the EPIC study. Eur Urol. 2006;50:1306-14.
5. Stewart WF, Van Rooyen JB, Cundiff GW, Abrams P, Herzog AR, Corey R, et al. Prevalence and burden of overactive bladder in the United States. World J Urol. 2003;20:327-36.
6. Patiño G, Sanchez C, Iregui JD, Fernández N. Guía vejiga hiperactiva no neurogénica en adultos. Urol Colomb. 2016;25:62.e1-15.
7. Kosilov K, Loparev S, Ivanovskaya M, Kosilova L. A randomized, controlled trial of effectiveness and safety of management of OAB symptoms in elderly men and women with standard-dosed combination of solifenacin and mirabegron. Arch Gerontol Geriatr. 2015;61:212-6.
8. Marcelissen T, Koeveringe G. Mirabegron versus antimuscarinics in the treatment of overactive bladder: the final answer? Eur Urol. 2018;74:334-5.
9. Harding C, Lapitan M, Arlandis S, Bo K. EAU guidelines on management of non-neurogenic female lower urinary tract symptoms. Eur Urol. 2022; 10-104.
10. Vo A, Kielb SJ. Female voiding dysfunction and urinary incontinence. Med Clin North Am. 2018;102:313-24.
11. Coyne KS, Sexton CC, Kopp ZS, Ebel-Bitoun C, Milsom I, Chapple C. The impact of overactive bladder on mental health, work productivity and health-related quality of life in the UK and Sweden: results from EpiLUTS. BJU Int. 2011;108:1459-11.
12. Drake MJ, Chapple C, Esen AA, Athanasiou S, Cambronero J, Mitcheson D, et al. Efficacy and safety of mirabegron add-on therapy to solifenacin in incontinent overactive bladder. Eur Urol. 2016;70:136-45.
13. Otsuka A, Kageyama S, Suzuki T, Matsumoto R, Nagae H, Kitagawa M, et al. Comparison of mirabegron and imidafenacin for efficacy and safety in Japanese female patients with overactive bladder: a randomized controlled trial (COMFORT study). Int J Urol. 2016;23:1016-23.
14. Torimoto K, Matsushita C, Yamada A, Goto D, Matsumoto Y, Hosokawa Y, et al. Clinical efficacy and safety of mirabegron and imidafenacin in women with overactive bladder: a randomized crossover study (the MICRO study). Neurourol Urodyn. 2017;36:1097-103.
15. Chapple CR, Amarenco G, Lõpez Aramburu MA, Everaert K, Liehne J, Lucas M, et al. A proof-of-concept study: mirabegron, a new therapy for overactive bladder. Neurourol Urodyn. 2013;32:1116-22.
16. Chapple CR, Dvorak V, Radziszewski P, Van Kerrebroeck P, Jacques Wyndaele J, Bosman B, et al. A phase II dose-ranging study of mirabegron in patients with overactive bladder. Int Urogynecol J. 2013; 24:1447-58.
17. Chapple CR, Khullar V, Gabriel Z, Muston D, Bitoun CE, Weinstein D. The effects of antimuscarinic treatments in overactive bladder: an update of a systematic review and meta-analysis. Eur Urol. 2008;54:543-62.
18. Herschorn S, Barkin J, Castro-Diaz D, Frankel JM, Espuna-Pons M, Gousse AE, et al. A phase III, randomized, double-blind, parallel-group, placebo-controlled, multicentre study to assess the efficacy and safety of the β3 adrenoceptor agonist, mirabegron, in patients with symptoms of overactive bladder. Urology. 2013;82:313-20.
19. Paquette A, Gou P, Tannenbaum C. Systematic review and meta-analysis: do clinical trials testing antimuscarinic agents for overactive bladder adequately measure central nervous system adverse events? J Am Geriatr Soc. 2011;59:1332-9.
20. Zinner N, Tuttle J, Marks L. Efficacy and tolerability of darifenacin, a muscarinic M3 selective receptor antagonist (M3 SRA), compared with oxybutynin in the treatment of patients with overactive bladder. World J Urol. 2005;23:248-52.

21. Madhuvrata P, Ellis G, Herbison GP, Cody JD, Hay-Smith EJ. Which anticholinergic drug for overactive bladder symptoms in adults. Cochrane Database Syst Rev. 2012;1:CD005429.
22. Turpen HC, Zimmern PE. Mirabegron: a new option in treating overactive bladder. J Am Acad Physician Assist. 2015;28:16, 18.
23. Meek PD, Evang SD, Tadrous M, Roux-Lirange D, Triller DM, Gumustop B. Overactive bladder drugs and constipation: a meta-analysis of randomized, placebo-controlled trials. Dig Dis Sci. 2011;56:7-18.
24. But I, Goldstajn MS, Oreskovi ć S. Comparison of two selective muscarinic receptor antagonists (Solifenacin and Darifenacin) in women with overactive bladder-the SOLIDAR study. Coll Antropol. 2012;36:1347-53.
25. Thiagamoorthy G, Kotes S, Zacchè M, Cardozo L. The efficacy and tolerability of mirabegron, a β3 adrenoceptor agonist, in patients with symptoms of overactive bladder. Ther Adv Urol. 2016;8:38-46.
26. Khullar V, Amarenco G, Angulo JC, Cambronero J, Høye K, Milsom I, et al. Efficacy and tolerability of mirabegron, a β3-adrenoceptor agonist, in patients with overactive bladder: results from a randomised European-Australian phase 3 trial. Eur Urol. 2013;63:283-95.
27. Yamaguchi O, Marui E, Kakizaki H, Homma Y, Igawa Y, Takeda M, et al. Phase III, randomised, double-blind, placebo-controlled study of the β 3 -adrenoceptor agonist mirabegron, 50 mg once daily, in Japanese patients with overactive bladder. BJU Int. 2014;113:951-60.
28. Kuo HC, Lee KS, Na Y, Sood R, Nakaji S, Kubota Y, et al. Results of a randomized, double-blind, parallel-group, placebo- and active-controlled, multicenter study of mirabegron, a β3-adrenoceptor agonist, in patients with overactive bladder in Asia. Neurourol Urodyn. 2015;34:685-92.
29. Dorrepaal C, Drogendijk T, Chapple CR, Martin N, Kaplan SA, Cummings J, et al. Randomized double-blind, active-controlled phase 3 study to assess 12-month safety and efficacy of mirabegron, a β3-adrenoceptor agonist, in overactive bladder. Eur Urol. 2012;63:296-305.
30. Angulo JC, Khullar V, Nitti VW, Siddiqui E. Evidencia disponible acerca del uso del agonista 3-adrenoceptor selectivo mirabegrón para el tratamiento de la vejiga hiperactiva. Actas Urol Esp. 2013;37:640-51.
31. Maman K, Aballea S, Nazir J, Desroziers K, Neine ME, Siddiqui E, et al. Comparative efficacy and safety of medical treatments for the management of overactive bladder: a systematic literature review and mixed treatment comparison. Eur Urol. 2014;65:755-65.
32. Bhangu GS, Kaur KP, Bansal D, Bansal R. Comparison of efficacy of mirabegron and darifenacin in overactive bladder- a prospective study. Int Surg J. 2020;8:196.
33. Vasudeva P, Kumar A, Yadav S, Kumar N, Chaudhry N, Prasad V, et al. Neurological safety and efficacy of darifenacin and mirabegron for the treatment of overactive bladder in patients with history of cerebrovascular accident: a prospective study. Neurourol Urodyn. 2021;40:2041-7.