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EFFICACY AND SAFETY OF MIRABEGRON AS AN ADD-ON THERAPY IN PATIENTS WITH NEUROGENIC DETRUSOR OVERACTIVITY RESISTANT TO MONOTHERAPY WITH ANTIMUSCARINICS: INITIAL EXPERIENCE.

Hypothesis / aims of study

Neurogenic detrusor overactivity (NDO), characterized by symptoms of urgency, urinary frequency and nocturia, with or without urgency incontinence, is a common finding in neurologic patients with brain and suprasacral lessions or diseases. Antimuscarinic therapy is the recommended first-line medical treatment of NDO. Unfortunately insufficient response and side effects (dry mouth, constipation) are reported from patients and reduce patient's compliance and adherence to antimuscarinic therapy. As a second line treatment, injection of onabotulinumtoxin into the detrusor is recommended. Although it is a minimally invasive procedure, some patients do not wish to undergo this procedure due to the increase risk of urinary retention and infection.
B3- adrenergic receptors, which are abundant in bladder smooth muscle, promote detrusor relaxation and urine storage. Mirabegron is a selective β3-adrenergic receptor agonist, approved for the treatment of idiopathic detrusor overactivity (IDO) , overactive bladder symptoms (OAB) and urge incontinence [1]. Also, Mirabegron has been used in the treatment of NDO in patients with spinal cord injuries [2].
In this original study, based on the pre-mentioned data, we evaluate the potential efficacy and safety of Mirabegron, as an add-on to antimuscarinics therapy, in patients with neurogenic detrusor overactivity resistant to monotherapy with antimuscarinics.

Study design, materials and methods

This is a single centre, prospective study. Patients with symptoms of NDO refractory or not well treated with antimuscarinics received 50 mg as an add-on therapy to the "most efficient" previously received antimuscarinic. Patients refused to undergo onabotulinumtoxin intradetrusor injection. Patients were informed for the off-label use of the drug, as well as for the efficacy and safety [1] of the drug in patients suffering from IDO and OAB. Patients were evaluated with a 3-day bladder diary (urine volume per void or catheterization, micturition or catheterization number /24h, number of urgency incontinence episodes/24h and severity of urgency) before and 4 weeks after the administration of Mirabegron. Urgency was rated on a 5-point categorical scale (0, no urgency; 1, mild urgency; 2, moderate urgency; 3, severe urgency; and 4, urgency incontinence). Furthermore maximum flow rate (Qmax), post void residual urine (PVR), side effects, blood pressure and heart rate were assessed. Also patients were assessed with the simple question "are you satisfied with the combination therapy" at the follow-up visit. Contraindications were uncontrolled arterial hypertension and known allergy to Mirabegron.

Results

Nineteen patients [32- 57 years old, 11 women-8 men, Multiple Sclerosis (MS) n=9, suprasacral Spinal Cord Injuries (SCI) n=6 and cerebral strokes n=4] with NDO and urge incontinence resistant to antimuscarinics received Mirabegron 50 mg/24h as an add-on therapy to antimuscarinics for a period of at least 4 weeks.
Seven out of nine patients with MS and three out of four patients with cerebral strokes reported significant reduction of micturition frequency/24h (mean 6.7 vs 11.6, $p<0.05$), number of urgency incontinence episodes/24h (mean 0.9 vs 2.7, $p<0.05$) and significant increase of urine volume/void (mean 255 ml vs 195 ml). Eleven out of thirteen patients (one of them without having improvement in micturition frequency, incontinence and volume/void) with MS and cerebral strokes reported reduction of urgency severity. These patients were satisfied and they wished to continue with combination therapy. Three out of six patients with suprasacral SCI mentioned reduction of urgency incontinence episodes/24h (mean 1.3 vs 3.3, $p<0.05$), reduction of the catheterization/24h (4.3 vs 5.7, $p<0.05$) and increase of the urine volume/catheterization (mean 325 ml vs 240 ml, $p<0.05$). These patients reported reduction of urgency severity or lower limb spasticity and they were satisfied with the treatment. There were no significant changes in Qmax and PVR. Combination therapy with antimuscarinic and Mirabegron was well tolerated and there weren't any serious side effects which resulted in discontinuation of the therapy. At 4 weeks 14/19 patients were satisfied and they wished to continue with the combination therapy.

Interpretation of results

The efficacy of Mirabegron as an add-on therapy was proved by reducing urgency and frequency, and increasing voided volume. We noticed significant improvements in all clinical parameters, especially in patients with Multiple Sclerosis and Cerebral strokes. Safety was also evaluated without any adverse effects. Most of the patients were satisfied and they wish to continue with the combination therapy.

Concluding message

Mirabegron was efficient and well tolerated as an add-on therapy in patients with neurogenic detrusor overactivity resistant to monotherapy with antimuscarinics, who do not wish to receive onabotilinum toxin A. Due to the limited number of patients and the retrospective nature of the study, prospective, placebo-controlled studies are necessary for more definitive conclusions.

References

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