

THE EFFICACY OF MIRABEGRON AS THE SECOND LINE THERAPY OF OAB AFTER THE FIRST LINE THERAPY USING ANTI-MUSCARINIC AGENTS

Hypothesis / aims of study

Anti-muscarinic agents remain the first line treatment of overactive bladder (OAB). However, some patients have a suboptimal response to anti-muscarinic agents or the unfavorable compliance by their adverse events is often a critical problem. Mirabegron (YM178, Astellas Parma Inc. Tokyo, Japan), selective β_3 -adrenoceptor agonist, is now commercially available to be considered an attractive alternative to anti-muscarinic agents (1). Recent phase III studies demonstrated favorable efficacy of mirabegron for patients with OAB as the first line therapy (2). However, the efficacy of mirabegron as the second line therapy after refractory to or discontinuation of anti-muscarinic agents remains unknown. The aim of this study was to assess the efficacy and tolerability of once-daily mirabegron as the second line therapy of OAB patients after refractory to or discontinuation of anti-muscarinic agents.

Study design, materials and methods

This study was conducted with the approval of the institutional ethical committee. Patients in out patient clinic (15 female and 4 male) who had continuously complaining of OAB symptoms after refractory to anti-muscarinic agents or discontinuation of anti-muscarinic agents due to the adverse events, were enrolled in this study. Patients were received once daily mirabegron 25mg or 50mg. The 3-days frequency volume chart was assessed before and after the treatment. The severity of OAB symptoms and the bother specific to each OAB symptom were assessed using 2 questionnaires the OAB symptom score (OABSS) and the visual analogue scale (VAS) questionnaires for each OABSS (OABSS-VAS), respectively. A 10-cm line scale of VAS was used to assess the patient's bother specific to each of the 4 questions on the OABSS. The patients self-reported a rate of their bother or satisfaction specific to each of the OAB symptom to make a check in the 10 cm line from "delighted" at the left end of the line to "terrible" at the right end of the line (3). For clinical simplicity of use, the OABSS and OABSS-VAS were printed on one single sheet, with the former on the front and the latter on the back, facilitating quick self-assessment in the out-patient clinic. Before the treatment, all patients had detailed consent of possible adverse events including cardiovascular events, hypertension, dry mouth, headache, nasopharyngitis, urinary tract infection, and constipation (1,2), and were asked to report any adverse events. All patients with any present or past history of hypertension or cardiovascular diseases were asked to monitor daily measurement of blood pressure to be reported in each out-patient clinic.

Results

Total 19 patients (15 female and 4 male, median age 77 years) were enrolled. The demographic data was shown in Figure 1. Among the 19 patients, 18 (95%) patients had urgency incontinence and 1 (5%) patient had continence. Most of the patients (14/19, 74%) were refractory to anti-muscarinic agents with experience of three or greater time's exchange of anti-muscarinic drugs. Median treatment time period was 8 weeks, ranged 4-28 weeks.

The score of OABSS-urinary incontinence ($p=0.021$) demonstrated significant improvement after mirabegron treatment (Figure 2a). Total of OABSS score also demonstrated significant improvement ($p=0.014$). The rate of VAS for urgency showed significant ($p=0.038$) improvement (Figure 2b). The assessment of bladder diary revealed improvement in number of incontinence episode in 24 hours (from 4.8 times to 3.1 times), number of micturition in 24 hours (from 10.3 times to 9.4 times), and increase of average voided urine volume (from 146 ml to 154 ml). All patients had good compliance with mirabegron during the study period. There were no patient-reported adverse events, and no requirement of additional treatment for cardiovascular disease.

Interpretation of results

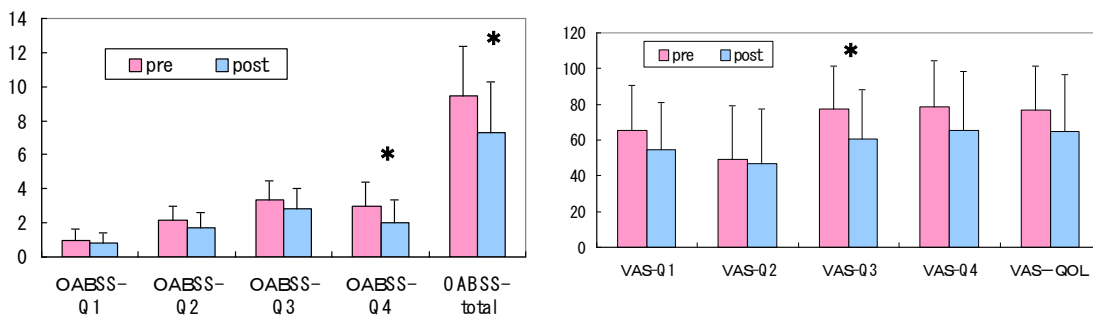
Refractory or poor compliance to anti-muscarinic agents is critical problem for clinical management of OAB. In this short-time study using mirabegron as the second line treatment of OAB after the first line therapy using anti-muscarinic agents, no obvious adverse events were observed, and significant improvement in severity of OAB-symptom as well as in patient's perception of treatment-related satisfaction were observed.

Fig.1 Demographic data of patients

Sex female : 15 male : 4
OAB wet : 18 dry : 1
Pre treatment 1 kind of anti-muscarinic agent : 5
3 kinds of anti-muscarinic agents : 3
4 kinds of anti-muscarinic agents : 11
Dose of mirabegron (per day) 25mg: 4 50mg: 15
Treatment period (median) 8weeks (4-18 weeks)

Fig.2 The change of OABSS and OABSS-VAS after treatment

a Score of OABSS questionnaire b Rate of VAS mesure



*: P<0.05

Concluding message

This study suggests that oral daily mirabegron could be effective and safe as the second line treatment for OAB patients who have experienced refractory or unfavorable compliance to anti-muscarinic agents. Longer-follow-up study with larger number of cohort is clearly needed.

References

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Disclosures

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