

SAFETY AND EFFICACY OF MIRABEGRON ADD-ON TREATMENT TO SOLIFENACIN IN OAB SUBJECTS IN COMPARISON TO SOLIFENCIN MONOTHERAPY: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

Hypothesis / aims of study

Antimuscarinic (AM) agents are the mainstay of oral pharmacotherapy for overactive bladder (OAB), but persistence with treatment is limited by insufficient efficacy and AM-associated adverse events. The approval of the b3-adrenoceptor agonist mirabegron has added a new class of pharmacotherapy for OAB. Multiple randomized controlled trials (RCTs) and meta-analysis have demonstrated efficacy and safety of mirabegron (25 mg and 50 mg) in comparison to placebo. mirabegron showed better reductions in micturition and incontinence episode frequency, with an incidence of AEs similar to placebo.

Most recently published data from RCTs reported safety and efficacy of combinations of solifenacin/mirabegron compared with solifenacin 5mg and 10mg monotherapy. The aim of the current study is to synthesize evidence from published RCTs comparing the evaluating combinations of solifenacin and mirabegron versus solifenacin alone in the treatment of overactive bladder.

Study design, materials and methods

We searched PubMed, Web of Science and Cochrane CENTRAL databases for RCTs measured mirabegron 50mg with solifenacin 5mg or 10mg combination versus solifenacin alone in OAB patients. Data were extracted and analysed using RevMan version 5.3 for windows. Changes in number of micturition/24 hours were pooled as mean difference (MD between combination and solifenacin group) in a fixed effect model using inverse variance (IV) method. Complications were pooled as relative risk (RR) in a fixed effect model using Mantel Haenzel (M-H) method. Heterogeneity was assessed by visual inspection of the forest plots and measured by I-square and Chi-square tests.

Results

Three RCTs with a total of 2603 patients (combination group n=922, solifenacin 5mg n= 855, and solifenacin 10mg n= 826) were included in this meta-analysis. Compared with solifenacin 5mg, the overall effect estimate favoured combination group in term of frequency of micturition /24 hours (MD -0.46, 95% CI [-0.68, -0.25], p <0.0001), and in comparison with higher dose of solifenacin 10mg (MD -0.46, 95% CI [-0.67, -0.24], p <0.0001). No significant heterogeneity was detected (I²=0%, p =0.5). Other efficacy data as volume void per micturition, urgency episodes /24 hours and urgency incontinence episodes could not be pooled due to incompletely reported data. For complications, the pooled effects were: (1) sum of adverse events (RR 1.06, 95% CI [0.83, 1.36] p = 0.62); (2) dry mouth (RR 0.60, 95% CI [0.35, 1.02], p =0.06); (3) hypertension (RR 2.79, 95% CI [1.15, 6.77], p = 0.02); and (4) cardio vascular disorders other than hypertension (RR 0.90, 95% CI [0.73, 1.10], p = 0.29).

Interpretation of results

The presented meta-analysis shows that mirabegron/solifenacin combination improved micturition/24 hours compared solifenacin 5mg or 10mg monotherapy. Combination shows similar incidence of adverse events as dry mouth and cardiovascular events other than hypertension. Increase in risk of developing hypertension was noted

Concluding message

Mirabegron 'add-on' therapy to solifenacin offers a safe option for cases of overactive bladder resistant to solifenacin monotherapy ,however caution is needed in hypertensive patients and monitoring of blood pressure is required. Further well-deigned RCTs are needed to evaluate efficacy and safety of mirabegron 'add-on' therapy to solifenacin and other anticholinergics.

References

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Disclosures

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