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A SYSTEMATIC REVIEW AND META-ANALYSIS ON THE EFFICACY AND SAFETY OF MIRABEGRON 50 MG AND 100 MG VS. TOLTERODINE AND PLACEBO FOR OVERACTIVE BLADDER/STORAGE LUTS.

Hypothesis / aims of study

There is a need for different pharmacological compounds to treat overactive bladder (OAB)/storage LUTS in order to improve the ratio efficacy/side-effect and the compliance when compared to the standard of care, i.e. the antimuscarinics: mirabegron, a β_3 -adrenoceptor agonist, has been recently approved in this indication. Aim of our systematic review and meta-analysis is to assess the efficacy and safety of different dosage of mirabegron, in the treatment of OAB/storage LUTS.

Study design, materials and methods

A MEDLINE, EMBASE, Cochrane Library, and Science Citation Index Expanded Medline search was performed to identify all published randomized placebo-controled trials (RCTs) evaluating mirabegron for the treatment of OAB/storage LUTS. We evaluated the mean difference (MD) to assess the efficacy profile in terms of incontinence episodes/24h, number of micturitions/24h, voided volume per micturition. We also evaluated the different rate of treatment-emergent adverse events (TEAEs).

Results

Out of 491 retrieved articles, 8 RCTs were included in the present meta-analysis, evaluating a total of 10,239 participants. Mirabegron 50 mg (Mir50), mirabegron 100 mg (Mir100) and tolterodine 4 mg (Tol) were significantly associated with improvement of voiding outcomes when compared to placebo.

Regarding the number of incontinence episodes/24h, Mir100 did not provide greater efficacy than Mir50 (weighted mean difference [WMD]: 0.15; p=0.08) or Tol (WMD: -0.07; p=0.48). Moreover, Mir50 was statistically similar to Tol (WMD: -0.09; p=0.49). Likewise, we did not find any difference in the decrease in the number of micturitions/24h when comparing Mir100 vs. Mir50 or Tol (WMD: 0.03; p=0.70 and WMD: -0.08; p=0.39 respectively), or Mir50 vs. Tol (WMD: -0.11; p=0.12). The increasing of mean voided volume per micturition was similar among the 3 treatments.

Both Mir50 (OR: 0.94; p=0.32) and Mir100 (OR: 0.97; p=0.75) did not provide increased TEAEs vs placebo. Conversely, Tol was associated with a higher occurrence of TEAEs (OR: 1.38; p<0.0001).

Interpretation of results

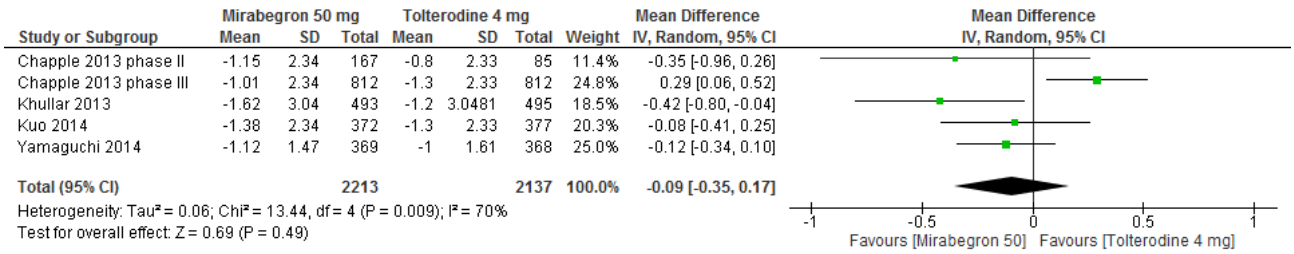
According to our meta-analysis Mirabegron can significantly improve the voiding outcomes at the investigated dosages. However, there were no statistically significant improvement when Mir50 was compared to Mir100. These results can be explained to pharmacokinetics effects, to the reaching of the drug's maximum effects, but β_3 -adrenoceptor are sensible to downregulation in chronic therapy, so an higher dosage of the drug can be necessary on long term treatment.

Tolterodine proved to be as effective as Mir50 and Mir100, but at the cost of an higher rate of TEAEs, because of the drug' mechanism of action and the receptors distribution. Muscarinic receptor are widely present in different organs and the drug pharmacokinetic does not provide a focused action on bladder, and that can explain the higher TEAEs rate. On the other hand, β_3 -adrenoceptor are located only in bladder and adipose tissue, allowing a higher selectiveness and reduced TEAEs compared to Tol.

Concluding message

Our meta-analysis showed that Mir100, Mir50 and Tol share the same efficacy profile. Mir100 and Mir50 share the same rate of TEAEs without any difference when compared with placebo. Conversely Tol was associated with an increase in TEAEs, potentially leading to treatment discontinuation.

Figure 1. Weighted mean difference for number of episodes of incontinence per 24h.



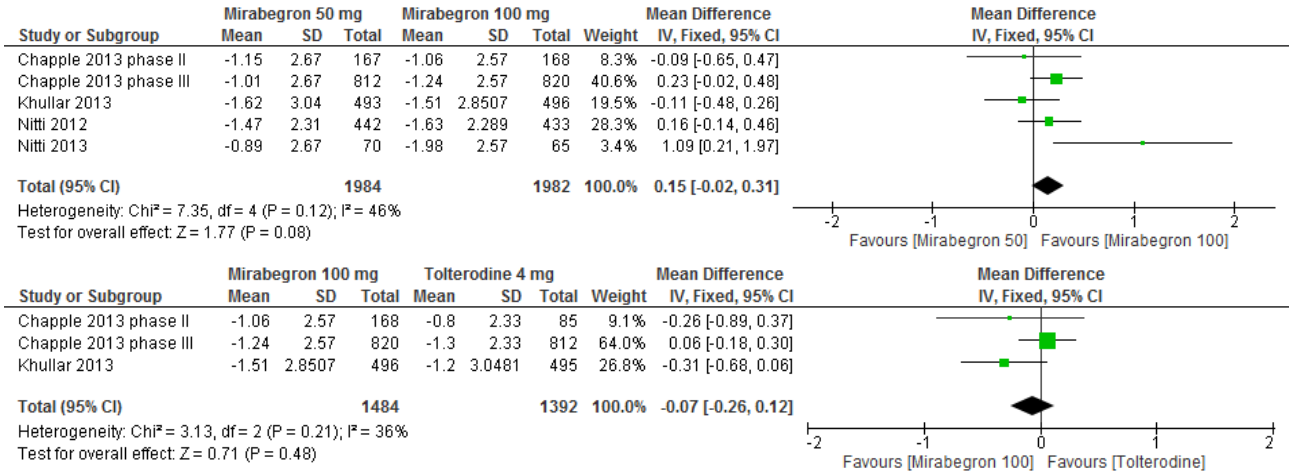
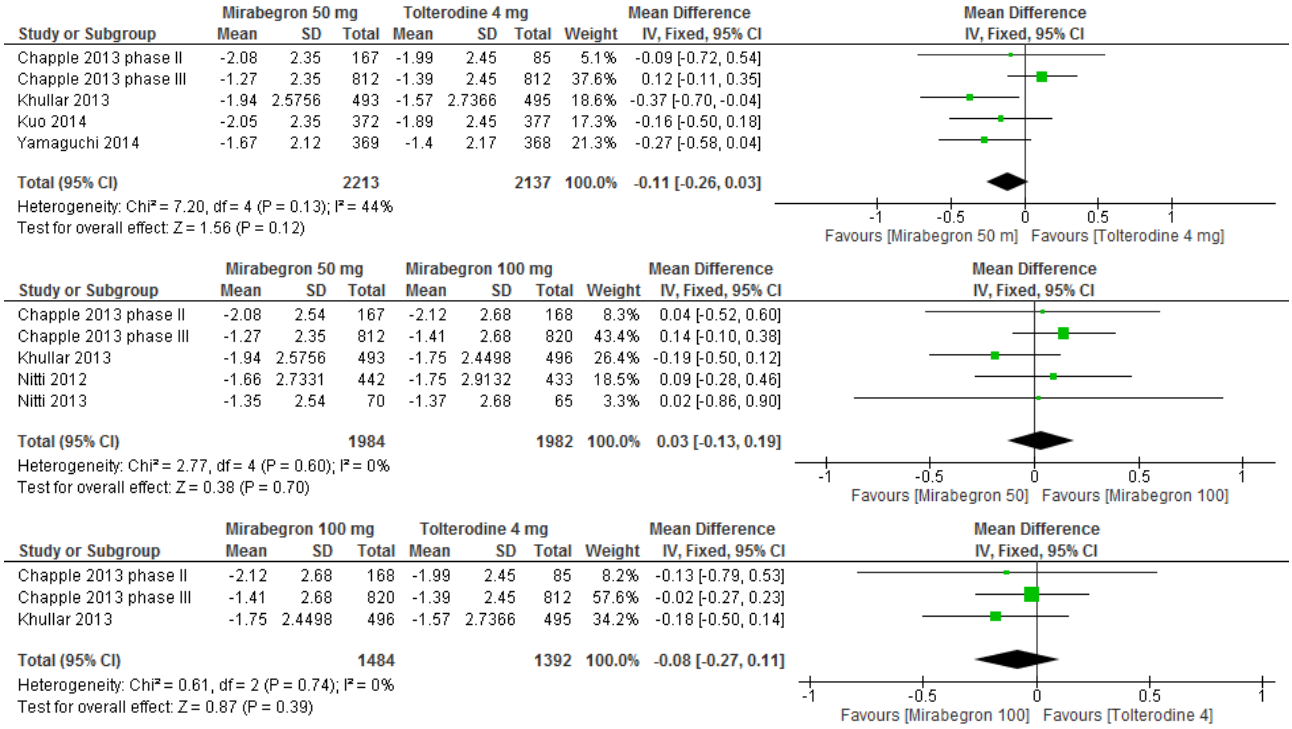


Figure 2. Weighted mean difference in the mean number of micturitions per 24 h.



Disclosures

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