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A SYSTEMATIC REVIEW AND META-ANALYSIS COMPARING OF MIRABEGRON IN TWO DIFFERENT DOSAGE (50 MG VS 100 MG) VS. TOLTERODINE 4 MG IN REDUCING OVERACTIVE BLADDER SYMPTOMS/STORAGE LUTS.

Hypothesis / aims of study

Overactive bladder (OAB)/storage LUTS, a multifactorial and common condition, affecting 30–40% of the population >75 yr of age, is characterized by nocturnal micturition and urgency episodes, with a consequent worsening of quality of life.

The hypothesis that we wanted to verify with this systematic review and meta-analysis is the assessment of mirabegron efficacy, a β_3 -adrenoceptor agonist, in two different dosages in the reduction of urgency and nocturia episodes.

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 controlled clinical trials (RCTs) evaluating mirabegron for the treatment of OAB/storage LUTS, in reducing the number of nocturia and urgency episodes.

Results

The search extracted 491 studies from the relevant databases. After a thorough evaluation of each study, 8 RCTs were identified. Mirabegron 50 mg (Mir50), mirabegron 100 mg (Mir100) and tolterodine 4 mg (Tol) were all significantly associated with the reduction of urgency episodes when compared to placebo.

Mir50 showed greater efficacy versus placebo in the reduction of nocturia episodes (weighted mean difference [WMD]: -0.13; p=0.003) and versus Tol (WMD= -0.07; p=0.03). Conversely, Tol was not associated with a significant reduction of nocturia episodes compared to placebo (WMD: -0.05; p=0.36). Furthermore, Mir100 was not statistically superior to Mir50 for nocturnal episodes (WMD: -0.07;p=0.17).

When assessing the reduction of urgency episodes, Mir50 was statistically better than placebo (WMD: -0.53; p<0.00001) but not than Tol (WMD: -0.02; p=0.85), which was associated with greater efficacy than placebo (WMD: -0.29; p=0.01). Mir100 was statistically similar to Mir50 (WMD: 0.0; p=1.00) and Tol (WMD: -0.29; p=0.52).

Figure 1. Weighted mean difference for nocturia.

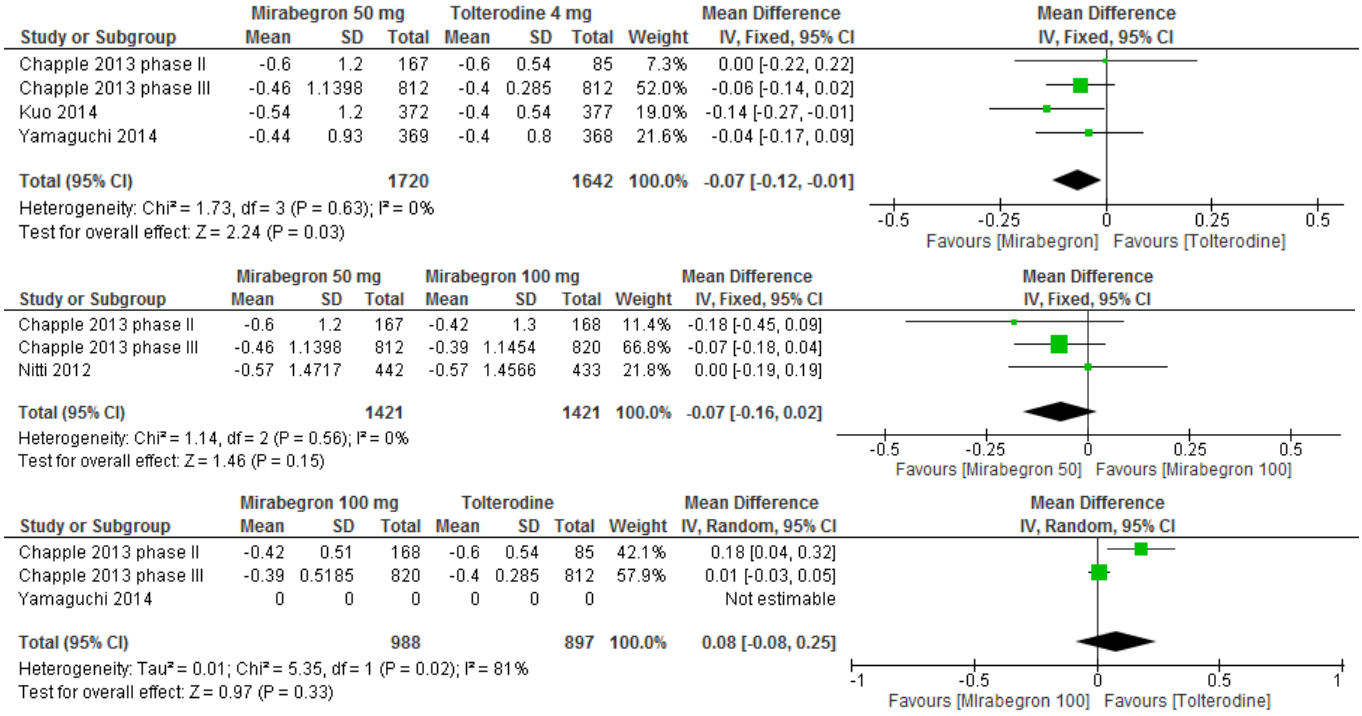
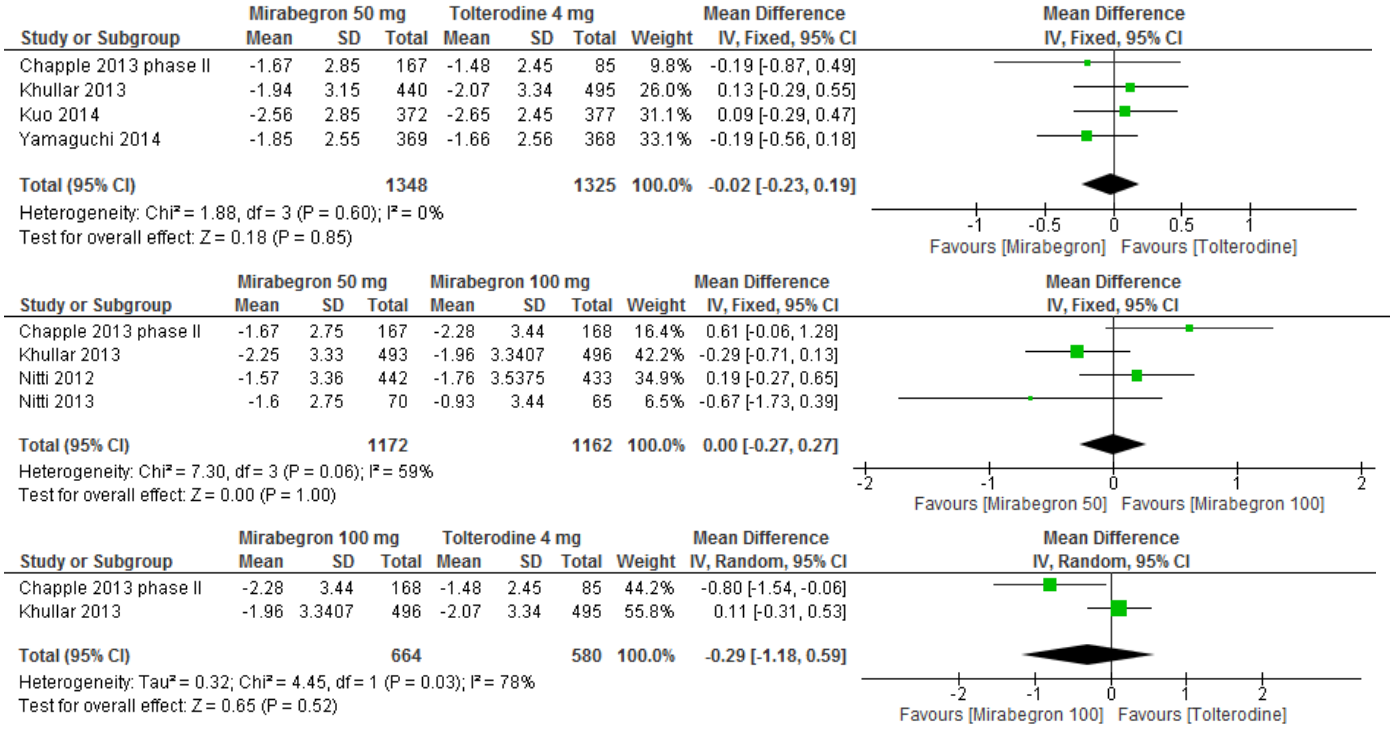


Figure 2. Weighted mean difference for urgency.



Interpretation of results

The efficacy of Mirabegron presents a statistically stronger evidence than Tol in reducing nocturia episodes. Every investigated dosage bring to the same conclusion. An explanation of this effect can be found in the different target of the drugs and the consequently different effect. Muscarinic receptors are not related to nocturia at the investigated dosage, but higher dosage can bring more adverse effects. At present time β_3 -adrenoceptor agonist have the advance to reduce nocturia episodes compared to other drugs.

Results showed that on urgency Mir50 and Tol have the same outcomes, so both β_3 -adrenoceptor receptors and muscarinic receptors can act on urgency.

The same effectiveness of both Mir50 and Mir100 on meta-analysis can be explained from the drug's pharmacokinetic or the consequent regulation of the receptor or the reaching of the maximum drug efficacy.

Concluding message

No statistical differences were found among Mir50 and Tol in reducing urgency episodes while Mir50 demonstrated a significant evidence in reducing nocturia. Mir100 did not show a greater efficacy in reducing the investigated LUTS (urgency and nocturia) if compared with Mir50.

Disclosures

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