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ANTIMUSCARINIC THERAPY FOR OVERACTIVE BLADDER SYNDROME: POSSIBLE BENEFITS OF SWITCHING TO SOLIFENACIN

Hypothesis / aims of study
Clinicians will often try a number of options to treat patients' overactive bladder (OAB) symptoms, while looking for a balance between treatment efficacy and tolerability. Antimuscarinic agents are the mainstay of treatment in OAB, but patients' adherence to medication remains poor. In order to investigate the effects of switching antimuscarinic therapy, we performed a subanalysis of patients who switched from placebo, tolterodine or solifenacin fixed dose treatment to a flexible dosing regimen with solifenacin.

Study design, materials and methods
After 12-weeks of randomized, double-blind treatment with either 5 mg solifenacin once-daily (od), 10 mg solifenacin od, placebo or 2 mg tolterodine twice daily, patients were given the option of entering a 40-week open-label extension study. They initially received solifenacin 5 mg for the first 4 weeks, which could then be increased to the 10 mg dose if it was considered by the investigator and the patient that their response to treatment could possibly be improved, in the absence of any moderate to severe side effects. Subsequently, patients were again given the option to increase (from 5 mg) or decrease (from 10 mg) their solifenacin dose at weeks 16 and 28 of the extension study, as they (in discussion with the investigator) deemed necessary. As all patients received solifenacin during the extension study, only descriptive statistics are presented.

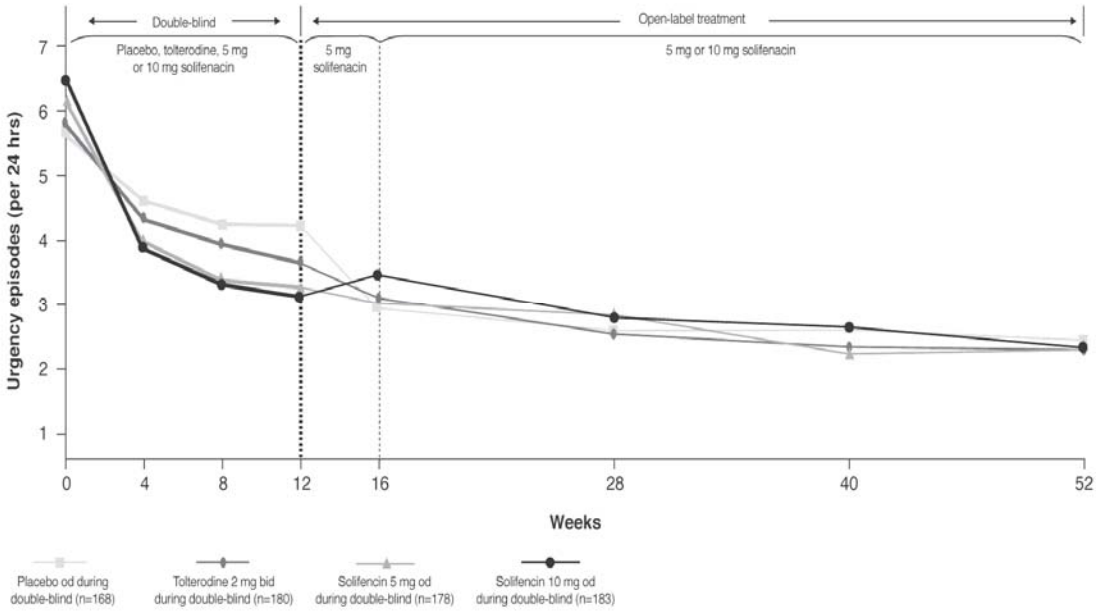
Results
On entering the extension study, all groups experienced improvements in symptoms (urgency, incontinence and micturition frequency) beyond those realised with the previous treatments, except for those originally receiving 10 mg solifenacin. This group experienced a transient increase in symptoms from the time their solifenacin dose was reduced until initiation of the flexible dosing regimen. Patients randomized to receive placebo and tolterodine experienced reductions in incontinence episodes from baseline of 39% and 56%, respectively, after 12 weeks of double-blind treatment, which increased to reductions of 60% and 62% after 4 weeks of open-label treatment with 5 mg solifenacin. The improvements seen in these groups after switching to the flexible dosing regimen of solifenacin were sustained over the 40 weeks of the open-label extension period, with incremental improvements up to the end of the open-label phase. Changes in episodes of urgency over time are graphically illustrated in the figure. The most common adverse events were dry mouth, constipation and blurred vision during the double-blind and open-label extension studies, all expected side effects of antimuscarinic agents. Discontinuations due to adverse events were low for both the double-blind and open-label phases, with discontinuations due to adverse events being seen in 6.0% of patients during the 40 weeks of open-label flexible dosing with solifenacin.

Interpretation of results
The results of the sub-analysis do suggest that switching subjects to solifenacin treatment affords improvements in major OAB symptoms, including incontinence, urgency episodes, and micturition frequency, and that these improvements are sustained. The benefits observed by open-label solifenacin treatment, which went beyond the improvements realised in the double-blind phase, are likely to be due to the effect of active medication, not the change in blinding. The justification for this is the increase in symptoms for those patients previously randomised to 10 mg solifenacin dose when their solifenacin dose was reduced to 5 mg, despite the fact that these individuals were never aware of what treatment they had previously received. In addition to experiencing improvements in symptoms, switching to solifenacin was not associated with any significant changes in tolerability.

Concluding message

Solifenacin seems to represent a favourable option for patients who require a change in their medication for OAB, as solifenacin treatment appears to confer additional (and sustained) clinical benefits to patients, without compromising safety or tolerability.

Figure: Change in mean number of urgency episodes over time



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