Randomized, double-blind placebo controlled trial of the once daily antimuscarinic agent solifenacin succinate in patients with overactive bladder
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Study Type: POEM

Purpose: Assess the efficacy, safety and tolerability of solifenacin once daily in patients with overactive bladder (OAB).

Study Duration: 12 weeks

Trial Design: double-blinded, placebo-controlled, modified intention-to-treat, multicenter (84 sites multinational)

Drug: solifenacin 5 mg + 1 placebo vs solifenacin 10 mg + 1 placebo vs 2 placebo tablets

Patients: 907 patients, mean age ~56, ~82% female, 74 kg, 98% white, ~35% had been treated before, mean number of micturitions per 24 hours is ~12

Inclusion: men and women > 18 years, OAB symptoms for > 3 months, 2 week placebo washout determined the patients, they had to report an average micturition frequency of 8 times or more per 24 hours and at least 3 episodes of urgency during a 3-day diary period

Exclusion: published previously

Outcomes:
Primary end point: micturition times per 24 hours
Secondary measures: urgency episodes, incontinence and sleep interruption, micturition volume, pad use

1. Are the results valid?
   * randomized? yes
   * double-blinded? yes
   * were groups similar? yes
   * allocation concealment? Not mentioned
   * all patients accounted for? yes

2. What were the results:
   Outcomes
   - Solifenacin reduced the number of micturitions by one per 24 hours for either dose.
   - One less incontinence episode every 3 days.
   - Only the 10 mg dose reduced mean nightly nocturia episodes, equivalent to one less micturition every 5 nights.
   - Micturition volume increase from 10.7 ml in placebo group to 36 ml in the solifenacin group
   - The effect was achieved by 4 weeks.

Adverse Event

<table>
<thead>
<tr>
<th>Adverse events</th>
<th>Placebo</th>
<th>5 mg solifenacin</th>
<th>10 mg solifenacin</th>
<th>ARI</th>
<th>NNH Placebo vs 10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry mouth</td>
<td>2.3%</td>
<td>7.7%</td>
<td>23.1%</td>
<td>20.8%</td>
<td>5</td>
</tr>
<tr>
<td>Constipation</td>
<td>2%</td>
<td>3.7%</td>
<td>9.1%</td>
<td>7.1%</td>
<td>14</td>
</tr>
<tr>
<td>Blurred vision</td>
<td>2.3%</td>
<td>4%</td>
<td>5.9%</td>
<td>3.6%</td>
<td>28</td>
</tr>
</tbody>
</table>

3. Will the results help me?
   - Most side effects were mild to moderate in severity.
   - The side effects are similar to other antimuscarinic agents.
   - The efficacy difference between the 5 mg and 10 mg dose does not warrant the difference in the rate of dry mouth (8% vs 23%).

Conclusion: In this trial, solifenacin was marginally effective for the treatment of OAB. The mean number of micturitions per day was reduced by one, there was one less incontinence episode every 3 days and one less nocturia episode every 5 nights. Allow 4 weeks of use before assessing efficacy. Side effect rates are similar to the other antimuscarinic agents. The 5 mg dose offers a lower incidence of dry mouth than the 10 mg dose with similar efficacy. For every patient placed on solifenacin, it would cost approximately $100 a month to reduce the number of micturitions by one per day.