Tolterodine, a new antimuscarinic agent: as effective but better tolerated than oxybutynin in patients with an overactive bladder


Study Type: POE
Purpose: To compare the safety and efficacy of tolterodine with that of oxybutynin.
Study Duration: 12 weeks
Patients: 293 patients, mean age ~58 yrs, 75% female, 25% male, mean micturitions/day ~12, ~75% with incontinence episodes or ~3 incontinent episodes per day, all had a history of symptoms > 6 mths and more than half for > 5 yrs, ~ 30% had undergone some type of surgery, more of those in the placebo group had previous drug therapy (p<.05)
Trial Design: Double-blinded, randomized, placebo-controlled, multicenter (42 centers in UK, Ireland and Sweden), 2:2:1 randomization to tolterodine 2 mg bid, or oxybutynin 5 mg tid, or placebo for 12 weeks, dose could be titrated
Inclusion: > 18 yrs, Community dwelling, at least 1 urge incontinence episodes per day on NO medicine, increase frequency of micturition (>8/day)
Exclusion: stress incontinence, detrusor hyper-reflexia, hepatic or renal disorders, recurrent UTI’s, those receiving bladder training, pregnancy, lactation, catheter
Outcome Events: frequency of micturitions in 24 hours, number of incontinent episodes, volume per micturition, patient subjective assessment of symptoms

1. Are the results valid?
   * randomized? yes
   * double-blinded? yes
   * were groups similar? yes
   * all patients accounted for? yes

2. What were the results?
   1. frequency of micturitions in 24 hours - reduced 2-3 micturitions per day (p< .01 for both drugs vs placebo, P = NS between the two drugs)
   2. number of incontinent episodes - reduced by ~1.5 incontinent episodes per day (p< .01 for both drugs vs placebo, P = NS between the two drugs)
   3. volume per micturition - increased by ~50 ml per micturition (p< .01 for both drugs vs placebo, P = NS between the two drugs)

Subjective analysis
   * 47% of placebo, 50% of tolterodine, 49% of oxybutynin perceived an improvement of their bladder symptoms
   * lots of trend data

<table>
<thead>
<tr>
<th>Safety</th>
<th>Placebo</th>
<th>Tolterodine</th>
<th>Oxybutynin</th>
<th>P value (vs placebo)</th>
<th>NNH (TvsP)</th>
<th>NNH (OvsP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>dry mouth</td>
<td>21%</td>
<td>50%</td>
<td>86%</td>
<td>0.001</td>
<td>3</td>
<td>1.5</td>
</tr>
<tr>
<td>dyspepsia</td>
<td>5%</td>
<td>9%</td>
<td>23%</td>
<td>0.01</td>
<td>NS</td>
<td>6</td>
</tr>
<tr>
<td>nausea</td>
<td>11%</td>
<td>3%</td>
<td>6%</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td># &gt; 1 adverse rxn</td>
<td>81%</td>
<td>89%</td>
<td>97%</td>
<td>0.001</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td>withdrawals</td>
<td>12%</td>
<td>8%</td>
<td>17%</td>
<td>?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3. Will the results help me?
   * tolterodine and oxybutynin was statistically equivalent
   * dry mouth with oxybutynin occurs in at least 50% and half of these will discontinue therapy
   * high placebo response rate, may be due to diary reporting, close monitoring or reduced fluid intake, this could be functioning as bladder training
   * no difference in subjective rating scale, the authors claim lack of an accepted rating scale, but thought it to be surprising
   * tolterodine was better tolerated but there was no dose titration for oxybutynin, patients started on full dose (32% needed a dose reduction, 8% in the tolterodine group)