Mirabegron and Solifenacin in the Treatment of Overactive Bladder

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Abstract

Overactive bladder is a condition where the bladder muscles contract before the bladder is full, causing the urge to urinate. The standard first line medication for overactive bladder is solifenacin, and mirabegron serves as an alternative option. Solifenacin is an antimuscarinic medication that is associated with a wide range of undesirable side effects. Therefore, this review analyzes the use of a combination of solifenacin and mirabegron, compared to monotherapy with solifenacin, for symptom management in patients suffering from moderate to severe overactive bladder.

Introduction

Overactive Bladder

Overview:
- Condition involves involuntary leakage of urine
- Consists of stress urinary incontinence, overflow incontinence and urge incontinence
- Affects 17% of adults in the United States and Europe

Symptoms:
- Urinary urgency, urinary frequency, nocturia
- Can significantly reduce quality of life, leading to higher levels of anxiety and depression, reduced general health status and poorer sleep quality

Treatment:
- Conservative treatment includes weight loss, fluid reduction, bladder training, pelvic floor muscle exercises or electrical stimulation of the posterior tibial nerve.
- Pharmacologic treatment with antimuscarinics, beta- adrenergic agonists, OnabotulinumtoxinA or intravaginal estrogen
- First line: Solifenacin, an antimuscarinic drug, and mirabegron, a beta- adrenergic agonist

Methods

Performed in November 2019 using:
- PubMed
- Academic Search Ultimate
- Google Scholar

Search terms: “urinary incontinence” AND “mirabegron” AND “solifenacin”

Inclusion Criteria:
1. Publish date within last 5 years
2. Randomized control trial or clinical trial

Exclusion Criteria:
1. Systematic review or meta-analysis
2. Studies involving trials with animals and not humans
3. Studies involving humans outside of adult age range

Table 1: Comparison of study designs for Mirabegron and Solifenacin vs. Monotherapy

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Total N</th>
<th>Population Demographic</th>
<th>Age range</th>
<th>Length of Dx at Baseline</th>
<th>Duration of Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>RCT</td>
<td>1306</td>
<td>867 F 439 M</td>
<td>18 or older</td>
<td>≥3 months</td>
<td>12 weeks</td>
<td>solifenacin, mirabegron or placebo</td>
</tr>
<tr>
<td>2</td>
<td>RCT</td>
<td>1887</td>
<td>1434 F 452 M</td>
<td>18 or older</td>
<td>≥3 months</td>
<td>12 weeks</td>
<td>solifenacin 5 mg</td>
</tr>
<tr>
<td>3</td>
<td>RCT</td>
<td>2174</td>
<td>1757 F 353 M</td>
<td>18 or older</td>
<td>≥3 months</td>
<td>16 weeks</td>
<td>solifenacin 5 mg, solifenacin 10 mg</td>
</tr>
<tr>
<td>4</td>
<td>RCT</td>
<td>1829</td>
<td>1463 F 366 M</td>
<td>19-66 years old</td>
<td>≥3 months</td>
<td>112 months</td>
<td>mirabegron, solifenacin, or placebo</td>
</tr>
<tr>
<td>5</td>
<td>RCT</td>
<td>3527</td>
<td>2716 F 811 M</td>
<td>18 or older</td>
<td>NA</td>
<td>18 weeks</td>
<td>mirabegron, solifenacin, or placebo</td>
</tr>
<tr>
<td>6</td>
<td>RCT</td>
<td>239</td>
<td>NA</td>
<td>Average age: 71.2</td>
<td>≥3 months</td>
<td>6 weeks</td>
<td>solifenacin, mirabegron or placebo</td>
</tr>
<tr>
<td>7</td>
<td>RCT</td>
<td>2174</td>
<td>NA</td>
<td>18 or older</td>
<td>≥3 months</td>
<td>12 weeks</td>
<td>solifenacin 5 mg, solifenacin 10 mg</td>
</tr>
</tbody>
</table>

Results

4. RCT of 2174 participants designed to test the efficacy of mirabegron and solifenacin in combination compared to the effectiveness of monotherapy with solifenacin in the treatment of overactive bladder.

Discussion

6/7 studies found the greatest reduction of symptoms with solifenacin and mirabegron when compared to solifenacin only, mirabegron only, or placebo.

Strengths:
- All studies based on randomized control trial with a double-blind study design + prevents research outcomes from being affected by placebo effect or observer bias
- 6/7 studies required participants to have symptoms of overactive bladder for at least 3 months
- Recruitment methods

Limitations:
- Small sample sizes
- Short study durations with no long term follow up

Future Research:
- Studies showing efficacy and tolerability for a longer duration and larger population is needed to improve the validity of the results

Conclusion

Since only one study conducted to this date has taken place over 12 months, more follow up research should be conducted to evaluate the long-term efficacy and tolerability of the combination of mirabegron and solifenacin in the treatment of overactive bladder.

In addition, future studies should aim to include a greater number of male participants, since majority of the studies discussed above consisted of mainly female participants. The prevalence of the condition is similar in both males and females, and therefore studies should look at the effectiveness of treatment regimen equally across both sexes. Trials with a larger sample size, with different racial groups, cultural groups, and co-morbidities should also be conducted. Although some of these seven studies had areas with weakness, the results from the studies as a whole may support the use of solifenacin and mirabegron together to treat overactive bladder that does not respond to monotherapy. Future research is warranted.
References:


