

## SAFETY, EFFICACY, AND REDUCTION OF DRY MOUTH SIDE EFFECT IN OAB / UUI PATIENTS RECEIVING COMBINATION THERAPY OF TOLTERODINE AND PILOCARPINE

### Hypothesis / aims of study

Patients with overactive bladder (OAB) and urge urinary incontinence (UUI) treated with oral muscarinic antagonists, such as oxybutynin or tolterodine, report dry mouth as the most common side effect. Independent studies have also noted the poor long-term patient compliance with anti-muscarinic therapy, and this is believed to be largely due to dry mouth. In addition, dry mouth is often observed to be a dose-dependent side effect in clinical practice, frequently limiting the use of high doses of anti-muscarinic agents as a means to obtain greater efficacy in bladder control. The purpose of this small study was to examine the potential of oral pilocarpine, a short-acting muscarinic agonist and salivary stimulant, as means of reducing or eliminating the dry mouth side effect in subjects with OAB and UUI receiving tolterodine treatment. The safety and efficacy of standard doses of tolterodine given in combination with pilocarpine was assessed.

### Study design, materials and methods

Seven subjects (5 female, 2 male) with OAB and UUI were studied at two clinics. All subjects had voiding symptoms that were controlled with 2mg tolterodine immediate release (Detrol®) tablets during a baseline period of at least 8 weeks. Voiding symptoms were recorded using standard 3-day diaries at the end of the baseline period. Dry mouth severity, and other related symptoms, were also assessed by using 100mm visual analog scales (VAS) in these 3-day diaries. All subjects demonstrated < 11 voids per day and < 2 incontinence episodes per day during the baseline period. They were then administered a daily regimen of 10mg pilocarpine immediate release (Salagen®) tablets, approximately 20 minutes after their usual dose of tolterodine, for a period of 4 weeks. Voiding symptoms, dry mouth, and other related symptoms, were then re-evaluated with 3-day diaries at the end of this period. Patient safety was monitored throughout the study.

### Results

An average improvement in dry mouth symptom scores of over 25mm (measured by 100mm VAS) was observed in seven subjects, when given the tolterodine and pilocarpine combination therapy for four weeks, as compared to tolterodine alone. Patients also noted benefits from the combination therapy in other related symptoms, such as general mouth comfort, speaking ability, and sleep quality. Pilocarpine did not appear to interfere with the efficacy of tolterodine, in terms of control of voiding symptoms. Blood pressure and heart rate of subjects on combination therapy were unchanged, relative to the baseline period of tolterodine monotherapy. No significant safety issues were observed in this study.

### Interpretation of results

Data from this small study suggests potential benefits in treating OAB and UUI through the use of the muscarinic antagonist tolterodine, and the subsequent administration (20 minutes later) of the muscarinic agonist pilocarpine. The most common side effect of tolterodine therapy, dry mouth, was reduced or eliminated in this patient group.

### Concluding message

Larger and more significant studies of tolterodine and pilocarpine combination therapy for the treatment of OAB and UUI, with rigorous placebo and active controls, are suggested for the future.

### Disclosures

**Funding:** TheraVida, Inc. **Clinical Trial:** Yes **Public Registry:** No **RCT:** No **Subjects:** HUMAN **Ethics not Req'd:** This human clinical study examined patients receiving two drugs previously approved by US FDA (tolterodine and pilocarpine), that were administered within dose ranges previously approved by US FDA. **Helsinki:** Yes **Informed Consent:** Yes