

CLINICAL EVALUATION OF THE EFFICACY, SAFETY, AND DRY MOUTH SIDE EFFECT PROFILE OF OXYBUTYNYN AND PILOCARPINE COMBINATION THERAPY, IN SUBJECTS WITH OAB AND UUI VOIDING DYSFUNCTION

Hypothesis / aims of study

Anti-muscarinic agents such as oxybutynin, solifenacin, tolterodine, or fesoterodine, as first-line therapies for overactive bladder (OAB) and urge urinary incontinence (UUI), frequently produce significant dry mouth side effects in patients. Dry mouth side effects have been known to negatively affect patient tolerability of these medications, thereby limiting the dosing that can be used and reducing long-term patient compliance. A cross-over design study was completed in 40 subjects with OAB and UUI, to examine whether concomitant administration of pilocarpine would reverse the dry mouth side effect caused by oxybutynin therapy, without adversely impacting patient safety or efficacy in bladder control.

Study design, materials and methods

67 female subjects were initially enrolled into a lead-in period of the study, where 5mg or 10mg oxybutynin immediate release was administered BID for 4 to 8 weeks, to establish baseline control of voiding symptoms. Standard 3-day diaries were used at the end of this baseline period to assess micturitions, incontinence, and urge frequency and severity. Dry mouth severity, and other related symptoms, were also assessed by using 100mm visual analog scales (VAS) in these 3-day diaries. 43 subjects with micturition frequency < 13 per day and incontinence frequency ≤ 1 per day were then randomized to either continue with oxybutynin monotherapy, or to receive a regimen of oxybutynin plus 5mg or 10mg pilocarpine immediate release administered 30 minutes later. At the end of 2 weeks, another set of 3-day diaries were collected. Subjects were then crossed-over to receive the opposite regimen for 2 more weeks, and then a final set of 3-day diaries were collected. A total of 40 subjects completed the study.

Results

No significant safety issues were observed during any period of this study. The addition of pilocarpine in combination, administered 30 minutes after a daily regimen of oxybutynin, demonstrated a statistically significant reduction in dry mouth symptom scores (mean improvement of > 21mm on the 100mm VAS). Subjects also noted an improvement in their quality of sleep, when taking the combination regimen. Subjects did not demonstrate a loss of control over any of their voiding symptoms (micturitions, incontinence, and urge frequency and severity). Efficacious bladder control with oxybutynin therapy was maintained throughout this study, even with the concomitant presence of pilocarpine.

Interpretation of results

Pilocarpine (a muscarinic agonist) was able to effectively reduce or eliminate the dry mouth side effects associated with oxybutynin (a muscarinic antagonist) when administered at a proper relative dose and with a 30 minute time delay. Efficacy of this combination therapy was equivalent to that of oxybutynin alone.

Concluding message

Future clinical studies of oxybutynin and pilocarpine combination therapy should be conducted, to further validate the potential patient benefit of this combination drug regimen in the treatment of OAB and UUI.

Disclosures

Funding: TheraVida, Inc. **Clinical Trial:** Yes **Public Registry:** No **RCT:** No **Subjects:** HUMAN **Ethics Committee:** Coast Independent Review Board **Helsinki:** Yes **Informed Consent:** Yes