Atomoxetine plus Oxybutynin for Symptomatic Snoring and Airflow Limitation

Nicole Calianese[1], Ali Azarbarzin[1], Lauren B Hess[1], Daniel Vena[1], Laura Gell[1], Dwayne Mann[2], Luigi Taranto-Montemurro[1], Suzanne M. Bertisch[1], Scott A Sands[1*]

[1]Division of Sleep and Circadian Disorders, Brigham and Women's Hospital and Harvard Medical School, Boston, MA.
[2]School of Information Technology and Electrical Engineering, The University of Queensland, Brisbane, Australia.

Rationale: Sleep disordered breathing severity is incompletely characterized by the apnea hypopnea index (AHI). Although typically viewed as a milder disease, snoring and flow limitation can yield major deficits in sleep health for both patients and their bed partners. Here we tested whether a combination of noradrenergic and antimuscarinic agents that improve upper airway dilator muscle function improves snoring loudness, flow limitation severity, and patient- and partner-reported outcomes.

Methods: Patients with loud habitual snoring participated in a randomized-controlled double-blind crossover study of 10 nights of atomoxetine-plus-oxybutynin at bedtime at 1) full doses (80/5 mg respectively) and 2) half doses (40/2.5 mg) versus placebo. For the first 3 nights, patients were administered no more than half doses (run-in). Baseline polysomnography with tracheal sound recordings established the presence of snoring (mean loudness >75 dB) and absence of moderate-to-severe sleep apnea (AHI <15/hr). Mixed models compared full and half doses to placebo in snoring loudness (primary outcome), adjusting for baseline and time effects (intention-to-treat analysis). Secondary outcomes included flow-limitation severity and Snoring Evaluation Scales.

Results: 15 patients were randomized and 13 completed all three treatment periods. Snoring loudness was reduced with full dose (−9.3[−19.6,−2.9] dB; effect[95%CI]) and half dose (−9.0[−17.8,−3.2] dB) versus placebo (mean 102.2 dB), equivalent to a two-thirds reduction in snoring amplitude (pressure). Flow-limitation severity was also significantly reduced (both doses). The Snoring *Bed-Partner* Evaluation Scale (range 0–16) was reduced with the half dose (−2.8[−5.3,−0.4] points; placebo mean = 10.1 points) but not the full dose (−1.7 [−4.1,0.6]). In exploratory analyses: *Self-*Evaluation scores were lowered with both doses (1.9-2.1 points) exclusively in those with bothersome snoring at baseline (N=7/15). Apnea-hypopnea index (4% desaturation) was reduced with both doses (5.5-5.9 events/hr; placebo mean = 11.7 events/hr).

Conclusions: In patients with loud habitual snoring without moderate-to-severe sleep apnea, atomoxetine-plus-oxybutynin at half and full doses improves snoring and flow limitation. A half-dose intervention may also improve bed partner-reported symptoms.