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PRELIMINARY EFFICACY OF A NOVEL ITERATIVE DEVICE AND MATERIAL

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Introduction: Launching a new device design or use of a new material with optimistic expectations should always be undertaken with caution and an ounce of skepticism. When this novel device and material was first described in an IRB Abstract derivative report at the AASM, it was under the umbrella of a patient and provider preference survey. In April 2020, the broader availability post FDA clearance is providing strong early indications of excellent efficacy.
Methods: An analysis of data from four treatment centers using this novel device and material was undertaken. Patients were to be included if they had a diagnosis of mild, moderate, or severe OSA confirmed by a physician, and an AHI score >5 and a follow up study resulting in treatment success or failure. Results would be grouped as Complete Success = AHI <5, Clinical Success = 50% reduction and <10. All patients were to be treated with the Novel ProSomnus EVO Iterative advancement device.
Results: 55 total consecutive patients were treated at four centers for dental sleep medicine. 37 male and 18 female patients with an average age of 53.3 ranging from 30 to 78 with pre and post data were included and treated with a ProSomnus EVO. The initial AHIs ranged from 6.0 to 116.0 with an average of AHI pretreatment of 26.4 (15 mild, 23 moderate and 17 severe). Follow up testing for this group revealed an average overall reduction in AHI of 75%, from 26.4 to 6.6. Overall, 62% resolved to below an AHI of 5 (100% of mild, 65% of moderate and 24% of severe patients). Similarly, 85% resolved to below an AHI of 10 and a 50% reduction (100% of mild, 96% of moderate and 59% of severe patients)
Conclusion: This novel interactive device and material combination appear, after early analysis, appear to yield significantly better results that previous data has demonstrated. The literature suggests that legacy oral appliance efficacies range from 50%-62% and other AADSM poster/abstracts have reported similar precision milled, control cure PMMA appliances in the 74% - 76% range. These results suggest a need for further investigation of exceptional efficacy for this device design and material.
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PREDICTORS OF RESIDUAL SLEEP APNEA IN OSA PATIENTS ON PAP

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Introduction: Positive airway pressure (PAP) is the first line therapy for patients with obstructive sleep apnea (OSA). However, clinical OSA may have multiple disease drivers beyond upper airway collapse, such as high loop gain and a low arousal threshold. The burden of residual sleep apnea in patients treated with PAP and it's predictors remained to be fully defined.
Methods: Adult patients who were diagnosed with OSA through a split-night polysomnography (PSG) in the AASM accredited sleep center at the Beth Israel Deaconess Medical Center, Harvard Medical School and followed using the EncoreAnywhereTM system were prospectively included. Monthly visual/manual scoring of residual events was done. The ratio of patients with residual sleep apnea (defined as a manually-scored respiratory event index (REI) ≥ 15 times/hour in the 3rd month and 12th month were calculated. A linear regression model was used to explore the predictors of residual sleep apnea on PAP.
Results: One hundred and ninety five patients were included. In the 3rd month, there were 166 patients still on PAP. There were 74 (44.58%) with a residual AHI ≥ 15 times/h. In the 12th month, there were 93 patients still on PAP and 41 (44.09%) had residual AHI ≥ 15. In the short term, treatment CAHI (β= 0.511, SE=0.123, p=0.001), age (β= 0.123, SE=0.054, p=0.025), and hypertension (β= 3.627, SE=1.536, p=0.019) were the predictors for residual sleep apnea. In the long term, treatment CAHI (β= 0.598, SE=0.163, p=0.001), male gender (β= -5.117, SE=2.005, p=0.013) and baseline mean arousal duration (β= -0.601, SE=0.184, p=0.002) were predictors for residual sleep apnea.
Conclusion: There was a high percentage of patients with OSA on PAP who have residual sleep apnea. Treatment CAHI is a strong predictor, and may reflect high loop gain effects.
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EFFECTS OF ATOMOXETINE PLUS A HYPNOTIC ON OBSTRUCTIVE SLEEP APNEA (OSA) SEVERITY IN PATIENTS WITH A MODERATELY COLLAPSIBLE PHARYNGEAL AIRWAY

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Introduction: The combination of atomoxetine and oxybutynin has demonstrated efficacy in the treatment of OSA. Oxybutynin may play a role as an upper airway dilator muscle activator and/or a hypnotic to improve sleep quality. We assessed the effectiveness of atomoxetine when combined with one of two hypnotics. Trazodone is a known hypnotic with possible effects on pharyngeal muscle activity. The other is lemborexant, an orexin antagonist. The effects of both combinations were assessed in patients with OSA and a moderately collapsible pharyngeal airway.
Methods: Recruited patients were 18 – 65 years of age, with an AHI 4 (4% desaturation criteria) of 10 – 55 and a BMI < 40 kg/m2. Each had to have a moderately collapsible pharyngeal airway using previously defined criteria based on the average percent desaturation during obstructive events (< 8%) and the ratio of hypopneas to total events (> 50%). After a qualifying PSG, each patient spent three nights in the sleep laboratory with approximately one week between studies. Nights were randomized to placebo, atomoxetine 80 mg plus trazodone 100 mg, and atomoxetine 80 mg plus lemborexant 10 mg. Primary outcomes were AHI 4 and the sleep apnea specific hypoxic burden (HB), the area under the SpO2 curve associated with disordered breathing events.
Results: Fifteen patients completed the trial (median [interquartile range] age was 52 [48-55] and BMI was 33.6 [30 – 35.1] kg/m2. Atomoxetine plus trazodone showed a strong trend for AHI 4 reduction from placebo (from 18.2 [11.8 – 31.3] to 7.4 [5.4 – 16.1] events/h, p=0.064), a significant reduction in HB from placebo (from 48.2 [31.2 – 79.6] to 18.7 [14.9 – 43.5] % min/h) and a trend for a reduction in HB with atomoxetine plus lemborexant (from 34.1 [12.1 – 128.8] to 18.7 [14.9 – 43.5] % min/h, p=0.055). There was no change in total sleep time or arousal index between treatment arms. Mild adverse events were reported on atomoxetine plus trazodone (2/15 sinusitis, 1/15 heartburn).

Conclusion: In OSA patients with a moderately collapsible upper airway, the combination of atomoxetine plus trazodone yielded clinically meaningful improvements in measures of sleep disordered breathing and oxygenation while atomoxetine plus lemborexant produced smaller effects.
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COMPARISON OF CLINICAL PATHWAYS FOR UPPER AIRWAY STIMULATION MANAGEMENT: IN-LABORATORY TITRATION POLYSOMNOGRAPHY VERSUS HOME-BASED EFFICACY SLEEP TESTING

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Introduction: Upper airway stimulation (UAS) therapy is an alternative treatment option for select CPAP-intolerant patients with obstructive sleep apnea. Current standard-of-care management uses in-laboratory polysomnography for titration of UAS stimulation amplitude (tPSG) after 3 months of patient self-titration at home. This home monitoring study was designed to evaluate whether tPSG or efficacy home sleep test (eHST) with tPSG by exception for eHST non-responders would have non-inferior apnea-hypopnea index (AHI) outcomes.
Methods: Enrolled patients underwent UAS implantation as part of regular clinical care and were randomized at the activation visit 1:1 between tPSG or eHST for the 3-month post-activation visit. If eHST results were suboptimal (AHI > 15 events/h or < 50% reduction from baseline AHI) patients underwent tPSG titration at 5 months. Both groups had 2-night eHSTs at 6 months post-activation. The primary endpoint was 6-month AHI equivalence between arms (defined as ± 15 events/h). Secondary endpoints were equivalence of Epworth Sleepiness Score (ESS; ± 2), oxygen desaturation index (ODI; ± 15 events/h), and nightly UAS device usage (± 0.5 h).
Results: The study randomized 60 patients from August 2020 through September 2021, who were primarily middle aged (57 ± 10 years), male (67%), Caucasian (98%), and overweight (BMI 29 ± 3 kg/m2), with severe OSA (AHI 35 ± 16). Eleven patients withdrew from the study early. As of December 2021, 41 and 36 patients have completed 3- and 6-month follow-up visits, respectively. Six-month visit AHI, ESS, ODI, and device usage data between arms is currently blinded and is expected to be complete by Q2 2021 prior to SLEEP 2022.
Conclusion: If the study demonstrates equivalent 6-month AHI, ESS, ODI, and usage outcomes, the use of eHST to ascertain therapy efficacy prior to tPSG could be a non-inferior alternative management option to tPSG.
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PRECLINICAL PHARMACOLOGY OF SOLRIAMFETOL: POTENTIAL MECHANISMS FOR WAKE PROMOTION

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Introduction: Solriamfetol is a wake-promoting agent (WPA) approved for the treatment of excessive daytime sleepiness associated with narcolepsy and obstructive sleep apnea. The wake-promoting mechanism of solriamfetol may result from dopamine and norepinephrine reuptake inhibition. Preclinical pharmacology studies were conducted to further elucidate the molecular targets activated by solriamfetol and compare them to that of known WPAs and traditional stimulants.
Methods: In vitro binding and functional studies were conducted in a panel of cell lines or membrane preparations expressing transmembrane receptors and monoamine transporters to measure the activity of solriamfetol, comparator WPAs, and traditional stimulants. Electrophysiology studies were conducted in slice preparations from mouse ventral tegmental area (VTA). Studies to measure locomotor activity and wake-promoting effects were conducted in mice.
Results: In vitro functional studies showed agonist activity of solriamfetol at human, mouse, and rat TAAR1 receptors. hTAAR1 EC50 values (10–16 µM) were within the clinically observed therapeutic solriamfetol plasma concentration range and overlapped with the observed DAT/NET inhibitory potencies of solriamfetol in vitro. TAAR1 agonist activity was unique to solriamfetol; neither the WPA modafinil nor the DAT/NET inhibitor bupropion had TAAR1 agonist activity. Solriamfetol (1–10 µM) dose-dependently inhibited the firing frequency of dopaminergic VTA neurons in mouse brain slices, similar to known TAAR1 agonists; however, these effects were inhibited by a D2 antagonist, suggesting a DAT-mediated effect. Unlike traditional stimulants, solriamfetol did not increase locomotor activity in naive mice, but inhibited the increase in locomotor activity in DAT knockout mice.
Conclusion: Preclinical studies have identified agonist activity at the TAAR1 receptor and, possibly, lower potency agonist activity at 5-HT1A receptors as potential pharmacological targets for solriamfetol, in addition to its activity as a DAT/NET inhibitor. Given the current understanding of TAAR1 agonists as modulators of monoamine transmission with potential wake-promoting effects in multiple preclinical species, agonist activity at the hTAAR1 receptor may represent an additional pharmacological target underlying the wake-promoting effects for solriamfetol, in addition to its DNRI activity.
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CLUSTER ANALYSIS FOR IDENTIFYING GOOD CPAP ADHERENCE USING THE PSG PARAMETERS AND PATIENT CHARACTERISTICS

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Introduction: CPAP is the standard treatment for obstructive sleep apnea (OSA). One of the important clinical issues to be solved is poor CPAP adherence. A growing body of studies has identified predictive factors for CPAP adherence including AHI, BMI, age, gender, symptoms, etc. When our sleep physicians prescribe CPAP, we would consider these known factors in multiple ways. One may want to know factors' combinations rather than each factor. In this case, cluster analysis might be useful since it is a