BETTER SLEEP, BETTER HEALTH and a BETTER LIFE

ASX Release

New clinical trial data demonstrates the Oventus Sleep Treatment Platform delivers significantly improved treatment outcomes for OSA sufferers

Key points:

- **Oventus to present new clinical data from four separate studies at the Sleep Down Under 2018 conference this week**
- **170 patients have now been studied in Oventus clinical trials, with outcomes consistently showing that the Sleep Treatment Platform can treat more than 75% of obstructive sleep apnoea patients across the full spectrum of disease severity**

Brisbane, Australia 18th October 2018: Oventus Medical Ltd (ASX: OVN) is pleased to announce that new clinical data from four separate studies on its Sleep Treatment Platform will be presented at Sleep DownUnder, the 30th annual meeting of sleep specialists, taking place in Brisbane between 17th -20th October.

Clinical work across multiple trials, through which 170 patients have been treated, shows Oventus' devices successfully treat more than 75% of patients without the need for Continuous Positive Airway Pressure (CPAP), the standard of care treatment for sleep apnoea.

In keeping with earlier studies, key highlights included:

- Patients with nasal obstruction who would normally struggle with treatment were found to benefit owing to the Oventus O_2Vent's airway technology, which acts as a second nose, enabling the patient to breathe freely overnight
- Patients that had failed prior lines of therapy were shown to have benefit from Oventus airway technology
- Addition of the Oventus PEEP (positive end expiratory pressure) valve technology (which will be called ExVent™ once on market) to the O_2Vent airway duck bill delivered a 30% ($p<0.01$) increase in efficacy
- Addition of the Oventus oro-nasal PEEP Valve (which will be called ONEPAP™ once on market) increased O_2Vent efficacy by 50% ($p<0.01$)
- Oventus airway technology improved treatment outcomes for CPAP users by reducing pressure requirements by 40-50% ($p<0.001$) and eliminating the need for full face masks

A new finding from a physiologic study predicting response to Oventus Airway Technology showed improved treatment outcomes for female patients ($p<0.02$.)

"We have seen a dramatic improvement in our patients in clinical trials," said Dr Chris Hart, CEO of Oventus.

"The technology in these devices eliminates the need for full face masks and greatly improves treatments for the majority. We have been consistently delighted with the results."

Sleep Down Under is the scientific meeting of the Australasian Sleep Association (ASA) and Australasian Sleep Technologists Association (ASTA). The event brings together expert sleep clinicians and scientists to share the latest advancements and innovations in the world of sleep research and clinical practice.

Copies of the posters are attached with this announcement. Further information on Oventus O_2Vent appliances can be found on our website: http://oventus.com.au/how-it-works/.

—ENDS—

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About Oventus

Oventus is a Brisbane based medical device company that is commercialising a unique treatment platform for the treatment of sleep apnoea and snoring. Unlike other oral appliances or CPAP interfaces, the Oventus devices have a unique and patented airway within the treatment platform that allows air to flow to the back of the mouth unobstructed while maintaining an oral seal and stable jaw position, bypassing multiple obstructions from the nose, soft palate and tongue, reducing airway collapsibility and managing mouth breathing while maintain a stable airway with or without nasal CPAP. They are particularly designed for the many people that have nasal obstructions and consequently tend to mainly breathe through their mouth. While it may seem counterintuitive, this technology actually manages mouth breathing by converting it to device breathing and normalising ventilation. The O_2Vent™ is designed to allow nasal breathing when the nose is unobstructed, but when obstruction is present, breathing is supplemented via the airways in the appliance.

According to a report published by the Sleep Health Foundation Australia, an estimated 1.5 million Australians suffer with sleep disorders and more than half of these suffer with obstructive sleep apnoea.[1]

Continuous positive airway pressure (CPAP) is the most definitive medical therapy for obstructive sleep apnoea, however many patients have difficulty tolerating CPAP[2]. Oral appliances have emerged as an alternative to CPAP for obstructive sleep apnoea treatment.[3]

[1] *Deloitte Access Economics. Reawakening Australia: the economic cost of sleep disorders in Australia, 2010. Canberra, Australia.*

[2] *Beecroft, et al. Oral continuous positive airway pressure for sleep apnea; effectiveness, patient preference, and adherence. Chest 124:2200–2208, 2003*

[3] *Sutherland et al. Oral appliance treatment for obstructive sleep apnea: An updated Journal of Clinical Sleep Medicine. February 2014.*

AIRWAY OPEN-AIRWAY CLOSED:

THE EFFECT OF MANDIBULAR ADVANCEMENT THERAPY FOR OBSTRUCTIVE SLEEP APNOEA WITH AND WITHOUT A NOVEL IN-BUILT AIRWAY.

Lavery D[1], Szollosi I[2], Moldavtsev J[3], McCloy K[4], Hart C[2]

1. National Dental Care 2. Oventus Medical 3. Bite Dental 4. McCloy Dental

INTRODUCTION

CPAP is the first-line treatment for obstructive sleep apnoea (OSA). However, it is often poorly tolerated with adherence rates of ≤50%. Mandibular advancement devices (MAD) are a viable alternative for mild to moderate OSA or for patients who are CPAP intolerant.

In addition to mandibular advancement, the O_2Vent MAD incorporates a novel in-built airway to circumvent nasopharyngeal obstruction.

AIMS

To determine the effects of the built-in airway on treatment response and to identify responders.

METHODS

Level 1 attended PSG was performed to determine baseline OSA severity.

Two devices were manufactured for each participant, one with airway open (AO) and one with airway closed (AC).

Following randomisation to either AO-AC or AC-AO sequence, MAD fitting, titration and acclimatisation occurred under dental supervision.

Once subjective symptoms were managed or maximal level of titration was achieved for at least 2 weeks, PSG was repeated with the device in situ. Crossover to the second arm occurred ensuring the alternate device was worn at the same level of advancement for at least 2 weeks before the final PSG assessment. Nasal resistance was assessed using anterior rhinomanometry prior to each PSG.

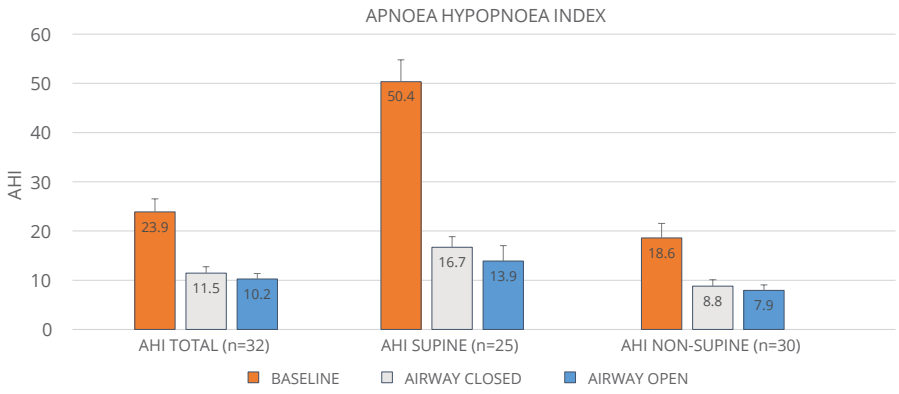
Treatment response was assessed as AHI < 10 as well as ≥ 50% reduction in AHI from baseline.

RESULTS

32 participants (20 Male) mean+/-SD age 56.1+/-9.7 years, BMI 30.4+/-5.0 kg/m² completed the study. Mean level of advancement was 10.9+/-2.2 mm.

Baseline AHI 23.9+-/15.0 events/hr decreased with AC to 11.5+/-7.3 ($p<0.001$) and AO to 10.2+/-6.3 ($p<0.001$), despite a significant increase in supine sleep from baseline 21.1+/-24.1% to AC 32.0+/-23.6% and AO 34.6+/-27.1% (both $p<0.01$). From baseline, the average reduction in AHI Total was 52% with AC and 57% with AO. Larger reductions in AHI were observed during supine sleep, with average reductions in AHI Supine of 56% with AC and 68% with AO for participants who had supine (n= 25) and non-supine sleep (n=30) in all 3 conditions (Figure 1).

FIGURE 1: TOTAL, SUPINE AND NON-SUPINE AHI AT BASELINE, AIRWAY CLOSED AND AIRWAY OPEN



The overall response rate as defined by AHI < 10 was 56% for AC and 62% for AO; response rate as defined by ≥ 50% reduction from baseline was 47% for AC and 56% for AO; response rate meeting both criteria was 41% for both AC and AO (Table 1 Overall response rate).

TABLE 1: OVERALL RESPONSE RATE

	AHI Total (n=32)		
	≤ 10 N (%)	**≥50% reduction N (%)**	**Both Criteria Met N (%)**
Closed	18 (56%)	15 (47%)	13 (41%)
Open	20 (62%)	18 (56%)	13 (41%)

Of the 17 non-responders to AC, using a ≥ 50% reduction in AHI from baseline, AO resulted in approximately 20% reduction in mean residual AHI ($p<0.04$) (Figure 2) and a further 6/17 (35%) were classified as responders.

AIRWAY OPEN-AIRWAY CLOSED:

THE EFFECT OF MANDIBULAR ADVANCEMENT THERAPY FOR OBSTRUCTIVE SLEEP APNOEA WITH AND WITHOUT A NOVEL IN-BUILT AIRWAY.

FIGURE 2

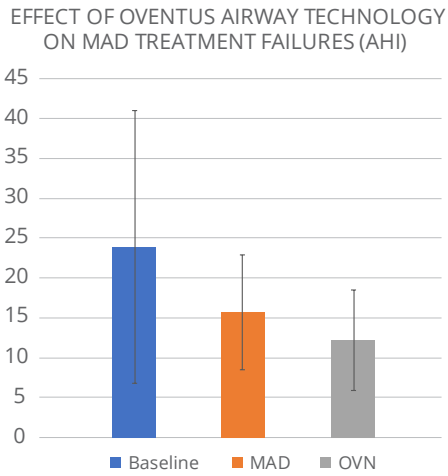
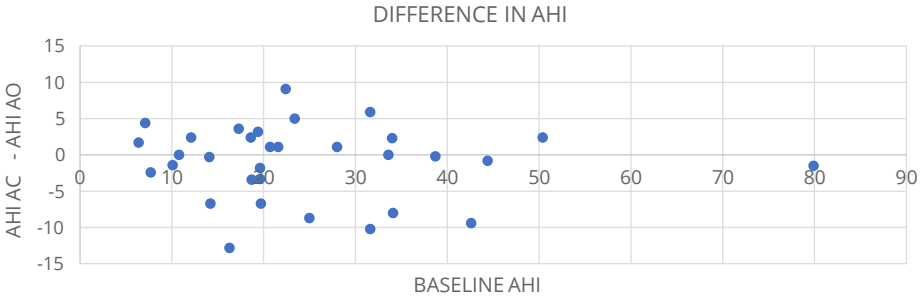


TABLE 2: RESPONSE RATE IN SUPINE AND NON-SUPINE SLEEP

	AHI Supine					AHI Non-Supine				
	N	≤ 10 N (%)	N	≥50% reduction N (%)	Both Criteria Met N (%)	N	≤ 10 N (%)	N	≥50% reduction N (%)	Both Criteria Met N (%)
Closed	30	11 (37%)	26	19 (73%)	10 (38%)	31	22 (71%)	31	14 (45%)	13 (42%)
Open	29	12 (41%)	25	20 (80%)	12 (48%)	31	23 (74%)	31	15 (48%)	10 (32%)

Whilst the mean reduction in AHI and response rate with AC and AO was similar, there was considerable individual variability in response to AC and AO. Approximately half of the participants had a greater reduction in AHI Total with AC and half with AO – see Figure 3. Those with a negative AHI AC – AHI AO on the graph had a greater reduction in AHI with AO. 2/32 participants had > 5 events per hour reduction in AHI with AC compared to AO, whilst 7/32 participants had > 5 events per hour reduction in AHI with AO compared to AC (Figure 3).

FIGURE 3



Additionally, there was a moderate negative correlation between inspiratory nasal resistance and AHI with AO (r=-0.48, p =0.028). Preference data was gathered on 27 patients, of which 63% participants indicated a preference for AO 15% had no preference and 22% preferred AC at the conclusion of the study.

SUMMARY

The results suggest that, on the whole, treatment response is similar with and without a MAD airway. However, individual variability exists in treatment response. Approximately 50% of participants had a lower AHI with AO compared to AC. Whilst the other 50% had a lower AHI with AC, it appears that when a significant differential response occurred i.e. difference > 5 events per hour in AHI, it occurred more frequently favouring AO. Patients that failed to respond on MAD treatment with AC and those with higher inspiratory nasal resistance tended to respond more favourably to AO.

CONCLUSION

Approximately 50% of patients prescribed MAD treatment may receive a greater treatment response from inclusion of a MAD airway. Further studies are required to understand the pathophysiology behind the individual variability and to determine predictors of response.

Abstract ID Number P119

Poster Presentation: ASA Sleep DownUnder, Brisbane.
Saturday October 20, 2018 – 11.24am to 11.30am

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Combination therapy with CPAP plus MAS reduces CPAP therapeutic requirements in incomplete MAS responders

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Introduction

CPAP therapy
- First line treatment for OSA
- Highly efficacious but is often poorly tolerated

MAS therapy
- Common alternative to CPAP therapy
- Higher adherence vs. CPAP but efficacy varies and is difficult to predict

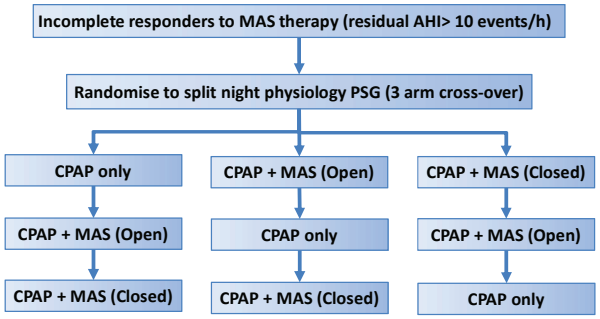
Combination therapy (CPAP + MAS)
- A potential therapeutic solution for:
  - Incomplete responders to MAS therapy alone
  - Patients who cannot tolerate high pressure levels with CPAP including oronasal mask users
- Combination therapy in OSA has been minimally studied

Aims

To compare pharyngeal pressure (Pepi) swings and therapeutic CPAP requirements when CPAP is combined with MAS therapy versus CPAP therapy alone in incomplete MAS responders

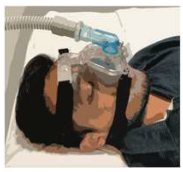
Methods ACTRN#: 12617000492358

Study design



- CPAP titrations were conducted during NREM supine sleep

CPAP only

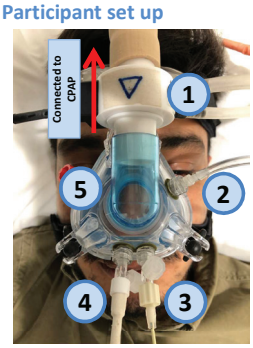


CPAP + MAS (airway open)

CPAP + MAS (airway closed)

Oventus O_2 Vent T
- Novel MAS device with a built in oral airway was used

Participant set up



CPAP titration set up
1. Pneumotachograph
2. Mask pressure
3. Epiglottic pressure catheter (Pepi)
4. End tidal CO_2
5. Nasal mask

Results

16 incomplete responders to MAS therapy (residual AHI: 13-63 events/h, average % of maximum mandibular advancement: 83 %) [13 males, 3 females, age: 31-65 years, BMI: 22 – 38 kg/m^2]

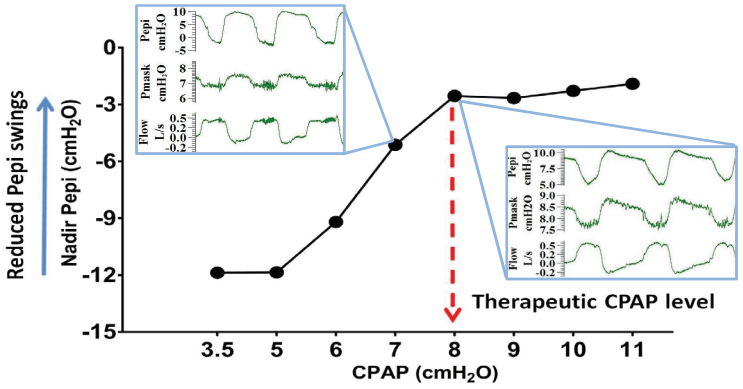


Figure 1: Therapeutic CPAP level was objectively defined as the pressure at which there were no respiratory events or flow limitation and where pharyngeal pressure swings were stabilised to near wakefulness levels as shown in this individual example

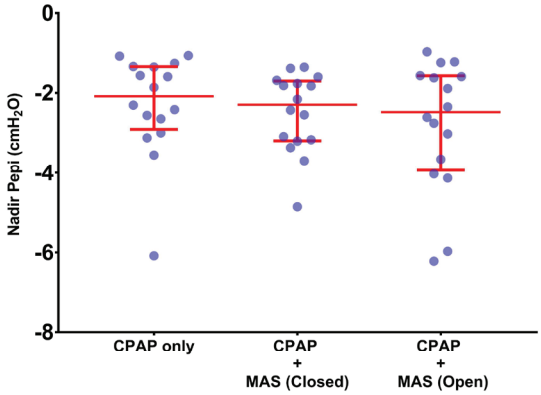


Figure 2: As per study design, pharyngeal pressure swings were successfully normalised to CPAP only levels (near wakefulness levels) with combination therapy (CPAP + MAS) with oral airway opened and closed) RM ANOVA p= 0.144

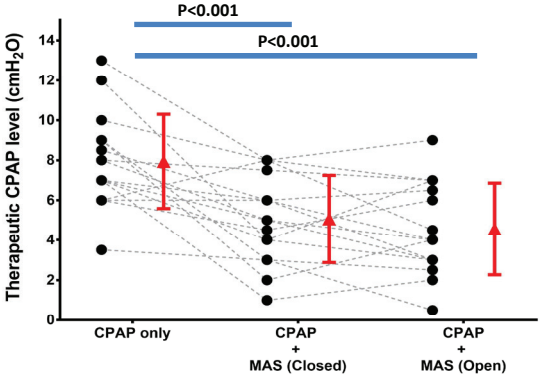


Figure 3: Combined CPAP plus mandibular advancement splint (MAS) therapy reduces the CPAP requirements required to eliminate OSA by ~35-45%

Conclusion

- Combination therapy (CPAP + MAS) can normalise pharyngeal pressure swings with ~35-45% lower CPAP requirements than CPAP alone
- This may be a therapeutic option for patients who are incomplete responders to MAS therapy alone and those who can not tolerate CPAP due to high pressure requirements

Acknowledgements

- This study was supported by a Cooperative Research Centre Project grant from the Australian Government in collaboration with academia and industry (Industry partner: Oventus Medical)
- DJE is supported by a NHMRC of Australia Senior Research Fellowship (1116942)

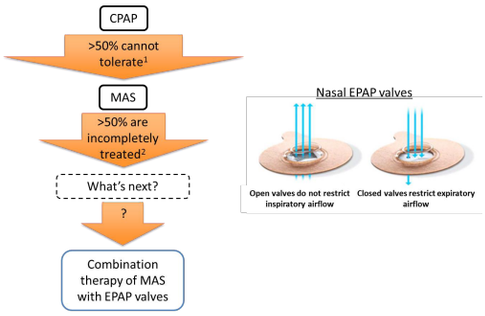
Combination therapy with mandibular advancement and expiratory positive airway pressure (EPAP) reduces OSA severity

Victor Lai[1,2], Benjamin Tong[1,2], Carolin Tran[1], Andrea Ricciardeiello[1], Michelle Donegan[1], Nicholas Murray[3], Jayne Carberry[1,2] and Danny Eckert[1,2]

1. Neuroscience Research Australia (NeuRA), 2. School of Medical Sciences, UNSW, 3. Prince of Wales Hospital.

Background

- Current challenges in OSA treatment leave many patients who are incompletely treated at risk of adverse health outcomes
- EPAP valves (restricts expiratory airflow to build up upper airway pressure) may complement mandibular advancement splint (MAS) therapy to prevent upper airway collapse
- No studies have explored the efficacy of this simple and potentially beneficial combination therapy



Research Question

Does combination therapy with MAS plus oral ± nasal EPAP reduce OSA severity in incomplete responders to MAS therapy alone?

Methods

Participants

- OSA (baseline AHI > 10 events/hr)
- Recommended by physician for MAS therapy
- Incomplete response to MAS (O2VentT™, Oventus) therapy (residual AHI > 5 events/hr) during 1st split-night PSG

Current study

- 2nd split-night PSG
- Participants wore MAS + an oral EPAP valve for half the night & MAS + oral and nasal EPAP (Provent™) valves for the other half (order randomised).

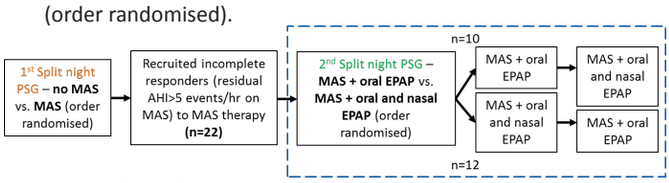


Figure 1. *Study design. Dashed box around current study.*

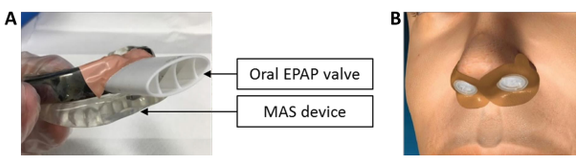


Figure 2. A: *MAS with oral EPAP valve attached .* ***B:*** *Nasal EPAP valves*

Analysis

- PSG data scored (2012 AASM criteria) for the following conditions: **1) No MAS, 2) MAS, 3) MAS + oral EPAP valve, 4) MAS + oral and nasal EPAP valves.**

Results

1. MAS + oral EPAP reduces OSA severity from no MAS and MAS. Nasal EPAP further reduces OSA severity.

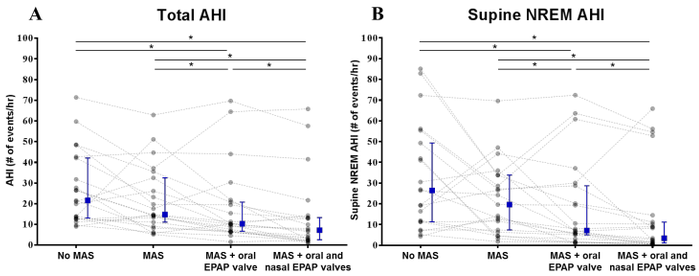


Figure 3. *Group median (blue boxes) and individual data (dotted lines) for total AHI (**A**) and supine NREM AHI (**B**).*

2. Up to ~60% of participants who were incomplete responders to MAS alone had treatment success with combination therapy.

Treatment success	MAS	MAS + oral EPAP valve	MAS + oral and nasal EPAP valves
AHI	% of participants	% of participants	% of participants
< 10 events/hr	23 (5/22)	45 (10/22)	59 (13/22)
< 5 events/hr	0 (0/22)	9 (2/22)	41 (9/22)

3. Sleep efficiency was reduced with MAS + oral and nasal EPAP.

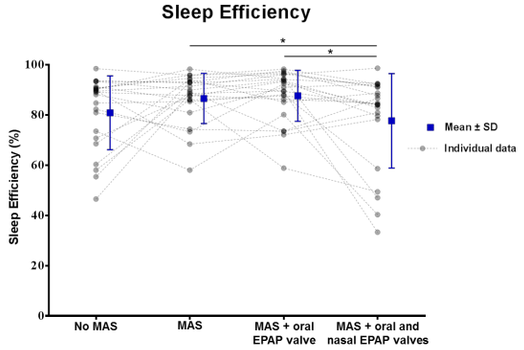


Figure 4. *Group and individual data for sleep efficiency. Sleep efficiency was calculated as the total sleep time/total time in bed (%).*

Conclusions

- Combination therapy with MAS plus EPAP **reduces OSA severity to therapeutic levels** for a substantial proportion of incomplete responders to MAS therapy
- A caveat was that 23% (5/22) had a substantial reduction in sleep efficacy with MAS plus oro-nasal (but not oral) EPAP
- Future objectives are to assess **long term adherence and efficacy** and **identify predictors** to facilitate and tailor treatment for each individual patient

Support

This study was funded by a Cooperative Research Centre Project Grant, a joint Government, Academia and Industry collaboration (Industry partner: Oventus Medical).

Predictors of Response to a Novel Mandibular Advancement Device (Oventus O_2Vent T) in Patients with OSA

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[1] Centre for Sleep Science, School of Human Sciences, The University of Western Australia; [2] West Australian Sleep Disorders Research Institute, Sir Charles Gairdner Hospital; [3] Absolute Dental, West Perth; [4] QV1 Dental, Perth; [5] Oventus Medical Ltd.

Background

- The efficacy of mandibular advancement device (MAD) therapy for obstructive sleep apnoea (OSA) tends to be reduced in patients with high nasal resistance
- The Oventus O_2Vent T is a novel MAD which permits oral breathing and may therefore be efficacious in people with high nasal resistance (NR)

Aims

- Examine the efficacy of the O_2Vent T with oral breathing route CLOSED and OPEN for the treatment of OSA
- Identify responders and non-responders to the O_2Vent T and investigate predictors of response
- Assess the relationship between NR and effect of the O_2Vent T (oral route CLOSED and OPEN) on OSA severity

Methods

Participants

- Participants were recruited from those already using a MAD for treatment of OSA

Protocol

- Participants underwent three polysomnography (PSG) studies:
  - PSG #1 established BASELINE OSA severity (total AHI, apnoea hypopnea index) without an OA
  - PSG #2 established the optimal level of advancement of the O_2Vent T with the oral route OPEN
  - PSG #3 established OSA severity with the oral route CLOSED vs OPEN (half night under each condition, order randomised) at the optimal level of advancement (or as close to it as tolerated)

Instrumentation/Analysis

- For all PSG studies participants wore a full face mask which was partitioned into nasal and oral sections and each connected to pneumotachographs to measure nasal and oral flow
- For PSG #1 and #3, a catheter was inserted via the nares to measure pressure at the retro-palatal (RP), retro-glossal (RG), hypo-pharyngeal (HP) and oesophageal regions
- Nasal resistance at a flow of 0.1l.sec^{-1} was determined (from the relationship between upper airway (UA) pressures & nasal flow) during wakeful supine nasal breathing in the evening prior to and morning following PSG #1 and #3
- Site of airway collapse was identified from divergence in UA and oesophageal pressures when airflow was reduced/absent during sleep
- PSGs were scored according to AASM 2012 criteria with oral flow used to differentiate apnoeas and hypopnoeas
- Responders to the O_2Vent T were those with AHI (CLOSED) and/or AHI (OPEN) <50% AHI (BASELINE)

Results

- Data from 22 participants (6 female); mean age 55±10 years; BMI 28.2±3.2kg.m^{-2} are available
- Compared to BASELINE, mean AHI at PSG #3 decreased by 38.2±34.0 and 43.3±31.2% with device airway CLOSED and OPEN respectively (Fig 1)
- Ten participants responded to device airway CLOSED and 9 responded to device airway OPEN

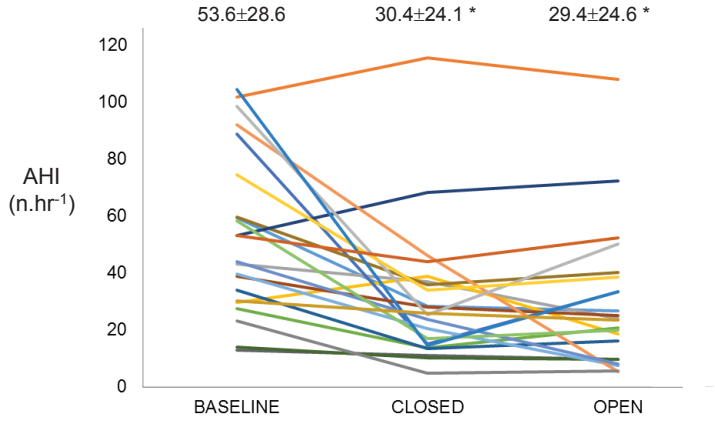

Figure 1. *AHI in BASELINE, CLOSED and OPEN conditions in all participants (n=22). Mean ± SD shown above each condition. * p<0.05 vs BASELINE*

- Supine AHI decreased more from BASELINE to PSG#3 in those with lower mean supine NR at BASELINE when device airway was CLOSED (r^2 = 0.54; p<0.01) and OPEN (r^2=0.21; p= 0.09)
- Responders to device airway CLOSED had a greater hip circumference (106±7 vs 100±3; p<0.02) and tended to have more severe OSA than non-responders (66±3 vs 43±23; p=0.06)
- Responders to device airway OPEN (n=9) tended to be female (n=5; p=0.02) and have a smaller neck circumference (36.2±2.6 vs 40.1±2.8cm) and hip:waist ratio (0.9±0.1vs1.0±0.1)
- UA collapse/narrowing at BASELINE was not different between responders (n=6 RP; n=1 nasal) and non-responders (n=9 RP; n=2 nasal) of device airway OPEN (p=0.89)
- Seven participants responded to both device airway CLOSED and OPEN

Conclusions

- On average, the Oventus O_2Vent T reduced AHI by approximately 40% in OSA patients; equally in the open and closed position, and more so in those with lower NR
- Access to an oral breathing route in a MAD may be most effective in sub-groups who are female, with smaller neck circumference and lower waist:hip ratio

Disclosure: This study was sponsored by Oventus Medical Ltd.