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SCIENTIFIC INVESTIGATIONS

Efficacy of a novel oral appliance and the role of posture on nasal resistance in obstructive sleep apnea

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Study Objectives: High nasal resistance is associated with oral appliance treatment failure in obstructive sleep apnea (OSA). A novel oral appliance with a built-in oral airway has been shown to reduce pharyngeal pressure swings during sleep and may be efficacious in those with high nasal resistance. The role of posture and mandibular advancement on nasal resistance in OSA remains unclear. This study aimed to determine (1) the effects of posture and mandibular advancement on nasal resistance in OSA and (2) the efficacy of a new oral appliance device including in patients with high nasal resistance.

Methods: A total of 39 people with OSA (7 females, apnea-hypopnea index (AHI) (mean ± standard deviation) = 29 ± 21 events/h) completed split-night polysomnography with and without oral appliance (order randomized). Prior to sleep, participants were instrumented with a nasal mask, pneumotachograph, and a choanal pressure catheter for gold standard nasal resistance quantification seated, supine and lateral (with and without oral appliance, order randomized).

Results: Awake nasal resistance increased from seated, to supine, to lateral posture (median [interquartile range] = 1.8 [1.4, 2.7], 2.7 [1.7, 3.5], 3.4 [1.9, 4.6] cm H_2O/L/s, P < .001). Corresponding measures of nasal resistance did not change with mandibular advancement (2.3 [1.4, 3.5], 2.5 [1.8, 3.6], 3.5 [1.9, 4.8] cm H_2O/L/s, P = .388). The median AHI reduced by 47% with oral appliance therapy (29 ± 21 versus 18 ± 15 events/h, P = .002). Participants with high nasal resistance (> 3 cm H_2O/L/s) had similar reductions in AHI versus those with normal nasal resistance (61 [−8, 82] versus 40 [−5, 62] %, P = .244).

Conclusions: Nasal resistance changes with posture in people with OSA. A novel oral appliance with a built-in oral airway reduces OSA severity in people with OSA, including in those with high nasal resistance.

Clinical Trial Registration: Registry: ANZCTR; Title: Combination therapy for obstructive sleep apnoea; Identifier: ACTRN12617000492358; URL: https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=372279

Keywords: lung, mandibular advancement therapy, sleep-disordered breathing, upper airway physiology

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BRIEF SUMMARY

Current Knowledge/Study Rationale: High nasal resistance can contribute to obstructive sleep apnea (OSA) pathogenesis and is associated with poor continuous positive airway pressure and oral appliance treatment outcomes. The effects of both mandibular advancement and changes in posture on nasal resistance in OSA are incompletely understood.

Study Impact: Nasal resistance is posture dependent but is not altered with mandibular advancement in people with OSA during wakefulness. A novel oral appliance with a built-in oral airway reduces OSA severity including in patients with high nasal resistance and thus may be a therapeutically beneficial alternative to traditional OSA therapies for these patients.

INTRODUCTION

Obstructive sleep apnea (OSA) is a common disorder characterized by recurrent pauses in breathing during sleep. This results in sleep disruption and blood oxygen desaturations. Common symptoms of untreated OSA include excessive daytime sleepiness and impaired cognitive function. Other comorbidities include cardiovascular disease, hypertension,[1] and stroke.[2]

Continuous positive airway pressure (CPAP) is the gold standard treatment for OSA.[3,4] It is highly efficacious in reducing breathing disturbances during sleep and can improve daytime sleepiness, cognitive function, blood pressure, and quality-of-life outcomes.[5–9] Despite the health benefits of CPAP, only about half of all patients with OSA are adherent to CPAP therapy.[10] Many people complain that CPAP is cumbersome, is difficult to tolerate with high pressures, and there are issues with mask leak[10,11] that may have an adverse effect on adherence.

Oral appliance devices are used as an alternative therapy to CPAP. Oral appliances work via protrusion of the mandible, which can increase pharyngeal airway caliber through an increase in the lateral dimensions.[12,13] Oral appliance devices are typically well tolerated, with one study reporting adherence of 83% after 1 year of treatment.[14] However, efficacy varies,

with only approximately 50% of patients achieving complete resolution of OSA (apnea-hypopnea index [AHI] < 5 events/h).[15] Successful treatment outcomes with oral appliance therapy for OSA are challenging to predict. Sex, OSA severity, subtypes of OSA (position-dependent OSA, rapid eye movement [REM], or non-rapid eye movement [NREM] predominant OSA), age, body mass index, craniofacial structure, and nasal resistance are factors that have been identified as contributors to treatment success.[16–20]

High nasal resistance is recognized as a risk factor for OSA.[21] Several studies have shown that high nasal resistance contributes to increased OSA severity.[22–24] Additionally, patients with OSA and high nasal resistance tend to be intolerant of CPAP and oral appliance therapy.[17,25] Nasal resistance is body position-dependent with increases from seated to the supine position in healthy individuals and those with rhinitis.[26] A similar effect has also been observed in people with OSA.[17,27] However, one study did not find a positional effect of nasal resistance in OSA.[28] The effects of lateral body position on nasal resistance in OSA is unknown. In addition, the role of mandibular advancement on nasal resistance in OSA has been minimally studied. Two studies demonstrated a reduction in nasal resistance in healthy individuals at different levels of mandibular advancement while seated.[29,30] In contrast, Zeng and colleagues found no change in seated nasal resistance with mandibular advancement at therapeutic levels in people with OSA in both responders and nonresponders to mandibular advancement therapy.[17] The same study showed an increase in nasal resistance with mandibular advancement in the supine position in nonresponders.[17]

A novel oral appliance with a built-in oral airway, which can allow for oral breathing without mouth opening and consequent mandible retraction, may be a suitable therapeutic option for patients with OSA and nasal obstruction. An initial monoblock prototype device was shown to reduce OSA severity by an average of 60%, with adherence of 80% in patients with and without nasal obstruction assessed by self-report.[31] A more recent pilot study investigated a two-piece titratable oral appliance with a built-in oral airway and found that pharyngeal pressure swings were reduced when the device oral airway was open.[32] However, efficacy data for this newer two-piece oral appliance device are not yet available.

Accordingly, the goals of this study were to determine (1) the effect of body posture and mandibular advancement on nasal resistance in OSA and (2) the efficacy of a novel oral appliance with a built-in oral airway in patients with OSA, including those with high nasal resistance. We hypothesized that nasal resistance would vary with posture and mandibular advancement in people with OSA and that the oral appliance would reduce OSA severity including in people with high nasal resistance.

METHODS

Participants

Thirty-nine participants with OSA were recruited from the Prince of Wales Hospital sleep clinic and local private sleep clinics. Participants were documented to have OSA (AHI > 10 events/h). Untreated and CPAP intolerant participants were included in the study. All participants were recommended for oral appliance therapy by their treating sleep physician. Participants were excluded if oral appliance therapy was contraindicated by the study dentist (periodontal disease, insufficient teeth for device retention or a strong gag reflex), central sleep apnea was diagnosed (> 5 events/h), intellectual or mental impairment was present that rendered them unable to provide informed consent, or they were pregnant or nursing mothers or taking medications known to affect sleep or breathing. All participants provided written informed consent prior to enrolment. The study was approved by the South Eastern Sydney Local Health District Human Research Ethics Committee and the protocol was preregistered on the Australian New Zealand Clinical Trials Registry (ACTRN12617000492358, Part A).

Protocol

Dental visits

Initially, participants with a referral for oral appliance therapy from their treating sleep physician were scheduled for a dental assessment with a dentist experienced in fitting oral appliance devices. During the visit, dental impressions were taken and the maximum tolerable level of mandibular advancement was determined. Participants were then scheduled for a follow-up dental visit for fitting and initial titration of the oral appliance. A novel custom-made oral appliance device (O_2Vent T, Oventus Medical, Indooroopilly, Queensland, Australia) was used (**Figure 1**). The device is a two-piece titratable oral appliance that fits on the lower and upper teeth. A built-in hollow core on the maxillary piece enables oral breathing through the device while maintaining mandibular advancement as well as lip seal around the device opening. This allows air to be delivered directly to the oropharynx through the device without mouth opening, which tends to cause mandibular retraction and airway narrowing.

Oral appliance therapy commenced at approximately 50% to 60% of each participant's maximal mandibular advancement range, followed by an 8- to 12-week acclimatization period. During this time, the oral appliance was incrementally advanced to at least 75% of maximum mandibular advancement. Most of the participants were contacted every 2 weeks by phone during the acclimatization period to assess self-reported adherence and perceived changes in their sleep. Specifically, participants were asked: "Are you wearing the device every night? If no, how long per night and how many times per week?" and "Did you notice any differences in your sleep?" Following acclimatization, participants were reassessed by the dentist immediately prior to their treatment efficacy sleep study where any necessary device adjustments were made to ensure comfort and maximum tolerable advancement.

Awake nasal resistance assessments

Awake nasal resistance was objectively quantified (discussed in the next paragraphs) in the evening prior to the sleep study. At least 5 minutes of quiet nasal breathing in three body positions (supine, seated upright, and left lateral recumbent) with and without mandibular advancement were assessed. Both

Figure 1—An image of the novel oral appliance used in this study.

The oral appliance is a two-piece titratable device with a hollow core in the maxillary arch to allow oral breathing directly to the oropharynx without mouth opening and mandibular retraction.

body positions and order of mandibular advancement were randomized. The built-in oral airway of the oral appliance device was blocked to ensure nasal breathing during the nasal resistance protocol.

Overnight polysomnography

Standard in-laboratory split-night polysomnography was conducted to assess oral appliance treatment outcome. The study allocation order (oral appliance versus no oral appliance) was randomized to either oral appliance followed by no oral appliance or no oral appliance followed by oral appliance (**Figure 2**). Where possible, at least one period of REM sleep was obtained during the first intervention period before switching to the other intervention arm (either oral appliance or no oral appliance).

Participant setup and equipment

Nasal resistance setup

Nasal resistance was measured using gold standard methodology.[33] Briefly, participants were instrumented with a modified nonvented nasal mask (ComfortGel, Philips Respironics, Murrysville, Pennsylvania, USA) with a pneumotachograph (Series 3700A, Hans-Rudolph, Shawnee, Kansas, USA) connected to a differential pressure transducer (DP-45, Validyne, Northridge, California, USA) to measure flow, in addition to another pressure transducer (DP-45, Validyne) for mask pressure. Choanal pressure was measured using a pressure transducer tipped catheter (MPR-500, Millar, Houston, Texas, USA) inserted via the most patent nostril to the level of the choanae. Data acquisition was performed using a 16-bit analog to digital converter (Power 1401, Cambridge Electronic Design, Cambridge, UK) and data acquisition software (Spike 2, version 7.2, Cambridge Electronic Design, Cambridge, UK).

Overnight polysomnography

Electroencephalograms (F3, F4, C3, C4, O1, O2, referenced to A1-A2), electrooculograms, surface submental and leg electromyograms, pulse oximetry, body position, nasal pressure flow, oronasal thermistor flow, thoracic and abdominal respiratory bands, and snore sound were measured. Data acquisition was conducted using a Level 1 diagnostic sleep system (Alice 6 LDxN, Philips Respironics) and data acquisition software (Sleepware G3, version 3.7.4, Philips Respironics).

Data analysis

Nasal resistance measurements were analyzed on a breath-by-breath basis using in-house semiautomated software.[34] Quantification of nasal resistance commenced 2 minutes after each change in body position. Nasal resistance was calculated as the difference between choanal pressure and mask pressure at a flow rate of 0.2 L/s.[33] In cases where the participant did not achieve a nasal airflow of 0.2 L/s or higher, nasal resistance was calculated at either 0.1 L/s or 0.05 L/s as necessary. Values for nasal resistance of > 3 cm H_2O/L/s were deemed high, as defined previously.[35]

Polysomnography data were scored for sleep and respiratory events according to American Academy of Sleep Medicine criteria.[36] Scoring was performed by a single board-registered sleep technologist who was blinded to the order of treatment. Responders to oral appliance therapy were defined according to several commonly used definitions: (1) treatment AHI < 5 events/h, (2) treatment AHI < 10 events/h, (3) ≥ 50% reduction in baseline AHI, and (4) proportion of participants who had a reduction in OSA severity category (eg, from severe to moderate or moderate to mild; where mild > 5 and < 15 events/h, moderate ≥ 15 and < 30 events/h and severe ≥ 30 events/h).

Statistical analysis

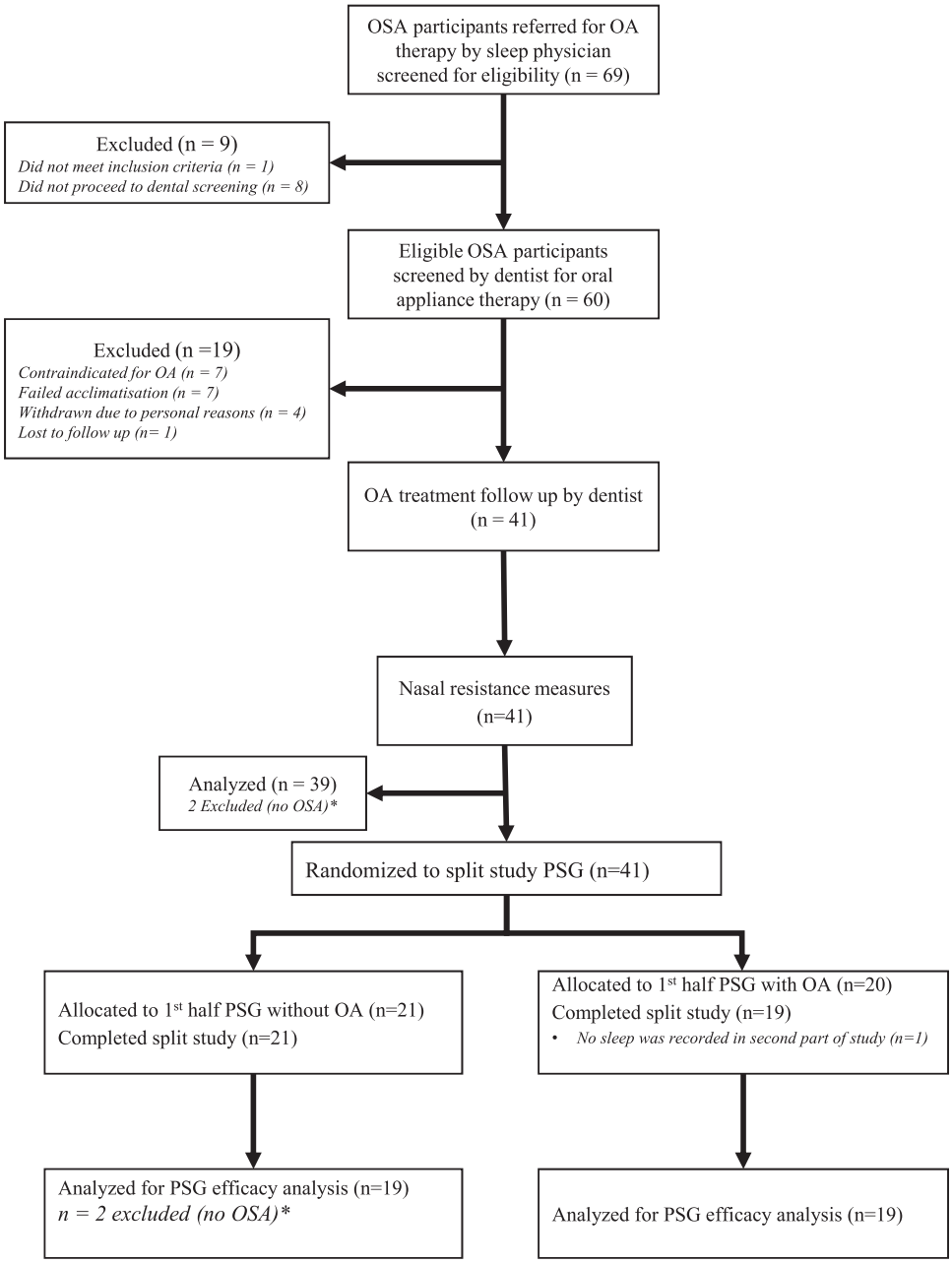
A mixed-model analysis was used to determine the effects of body position (seated, supine, and lateral recumbent) and the effect of mandibular advancement (with and without oral appliance therapy) on nasal resistance (SPSS version 24, IBM Corp, Armonk, New York, USA). In the absence of an interaction, Friedman repeated-measures analysis of variance on ranks (SigmaPlot version 12.5, IBM) were performed to examine the effects of body position on nasal resistance (with and without oral appliance). Pairwise comparisons were performed according to the Student-Newman-Keuls method (SigmaPlot version 12.5, IBM). Sleep and breathing parameters were compared between conditions (no oral appliance vs. oral appliance) using two-tailed, paired *t* tests for normally distributed data or Wilcoxon signed-rank tests (SigmaPlot version 12.5, IBM) for nonnormally distributed data (Shapiro-Wilk). Data are reported as mean ± standard deviation or median (interquartile range [IQR]) for nonnormally distributed variables.

RESULTS

Participant characteristics

Forty-one participants fitted with an oral appliance for the study returned for an overnight polysomnography to assess treatment response. Data for three participants were excluded from analysis (two individuals were found not to have OSA without the oral appliance and one had insufficient sleep). Thus, data from 39 participants with OSA were analyzed for awake nasal

Figure 2—CONSORT diagram detailing participant recruitment and flow through the study procedures.



A total of 69 participants recommended for oral appliance therapy were screened for eligibility. A total of 60 eligible participants were screened by a qualified sleep dentist for oral appliance therapy. Following 8 to 12 weeks of acclimatization to oral appliance therapy, n = 41 participants were studied for awake nasal resistance measurements and oral appliance efficacy (split-night in-laboratory PSG). Two participants were excluded from analysis because they were found not to have OSA during the split-night PSG. One participant was excluded from analysis because there was no sleep recorded in the second portion of the sleep study. Data from a total of n = 39 participants were analyzed for awake nasal resistance and n = 38 for the efficacy split-night PSG. The asterisk indicates the same participants without OSA were excluded from analysis. OA = oral appliance, OSA = obstructive sleep apnea, PSG = polysomnography.

resistance measurements and 38 for oral appliance efficacy (**Figure 2** shows the CONSORT diagram). Participant characteristics are detailed in **Table 1**.

Effect of posture and mandibular advancement on awake nasal resistance

Awake nasal resistance increased from seated, to supine, to lateral posture with and without mandibular advancement ($P < .001$, **Figure 3**). However, mandibular advancement had no overall effect on nasal resistance ($P = .338$, **Figure 3**) and there was no interaction effect with posture ($P = .12$). When separated according to responders (n = 18) versus nonresponders (n = 21), defined as > 50% reduction in AHI with oral appliance therapy, nonresponders had an increase in nasal resistance with mandibular advancement when seated (1.8 [1.3, 2.4] versus 2.4 [1.2, 3.3] cm H_2O/L/s, $P = .007$). This increase in

Table 1—Participant characteristics (n = 39).

Sex (female, male)	7, 32
Age (years)	49 ± 11
Body mass index (kg/m^2)	29 ± 4
Maximum mandibular advancement (%)	80 ± 14
Epworth Sleepiness Scale	8 ± 4

Epworth Sleepiness Scale scores were obtained during oral appliance therapy. Data are mean ± standard deviation unless otherwise stated.

nasal resistance with mandibular advancement did not occur in responders (2.0 [1.5, 3.2] versus 2.3 [1.5, 4.2] cm H_2O/L/s, P = .347). There was no difference in nasal resistance with mandibular advancement in responders or nonresponders compared to no advancement in the supine or lateral postures (data not shown).

Effect of mandibular advancement on OSA severity and sleep parameters

Oral appliance therapy significantly reduced OSA severity, as measured by the total AHI, by 47 [−6.1, 70]% (**Figure 4A**). **Table 2** summarizes the effects of oral appliance therapy on other key polysomnographic variables. Similar to the total AHI, supine AHI (48 [2.2, 69.0] %), and NREM supine AHI (58 [6.0, 88.8] %) were significantly reduced with oral appliance therapy. However, oral appliance therapy did not change the total REM AHI in those who had REM sleep during both conditions (31 ± 22 versus 24 ± 17 events/h, P = .113, n = 28) but did reduce the supine REM AHI (**Table 2**). When present, hypopneas were of shorter duration during oral appliance therapy.

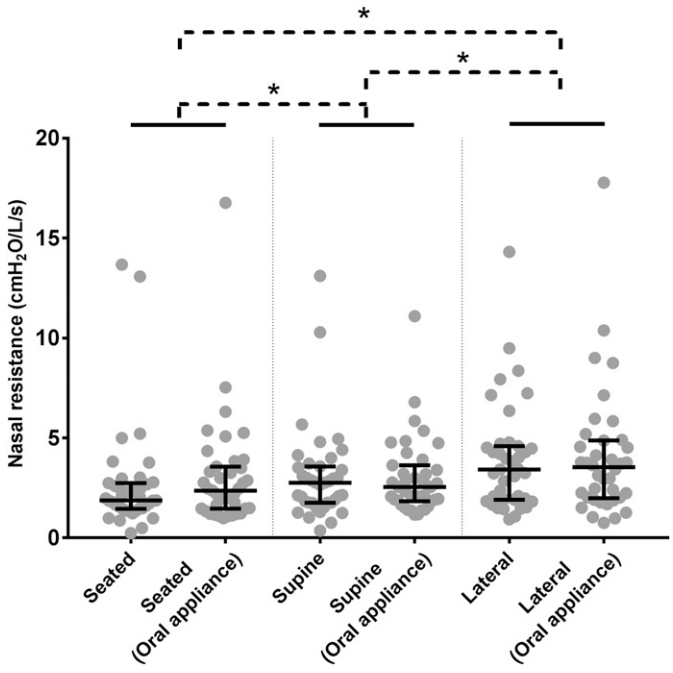
Fourteen participants were classified to have high nasal resistance in the supine position. Oral appliance therapy reduced OSA severity (total AHI) in these individuals by 61% [−8, 82 %]. There was no difference between the percentage reduction in OSA severity between participants with high versus low nasal resistance (**Figure 4B**).

The proportion of treatment responders on oral appliance therapy according to commonly used definitions is summarized in **Table 3**. Oral appliance therapy reduced the total AHI by 50% or more in half of the participants. Approximately 50% of participants had a reduction in OSA severity on oral appliance therapy. **Table 4** further illustrates treatment response rates of participants categorized according to the presence of high versus low nasal resistance.

Total sleep time was similar between conditions. Sleep efficiency was high in both arms during these split-night studies. Sleep quality improved on oral appliance therapy as reflected by reduced wake after sleep onset (WASO) events, less stage N1 sleep, and a reduction in the arousal index. There was no statistical significance between stage N2, N3, and REM sleep duration with oral appliance therapy. This is despite significantly more time spent supine on oral appliance therapy.

The oxygen desaturation index was lower and the amount of sleep time spent below an O_2 saturation of 90% was less with oral appliance therapy. However, nadir O_2 saturation was similar between the split night conditions.

Figure 3—Diagram showing awake nasal resistance scatter plots at different postures with and without an oral appliance (n = 39).



Each data point denotes an individual participant. Lines and error bars indicate the median and interquartile ranges. Asterisk indicates a significant difference (P < .05) in nasal resistance between each posture.

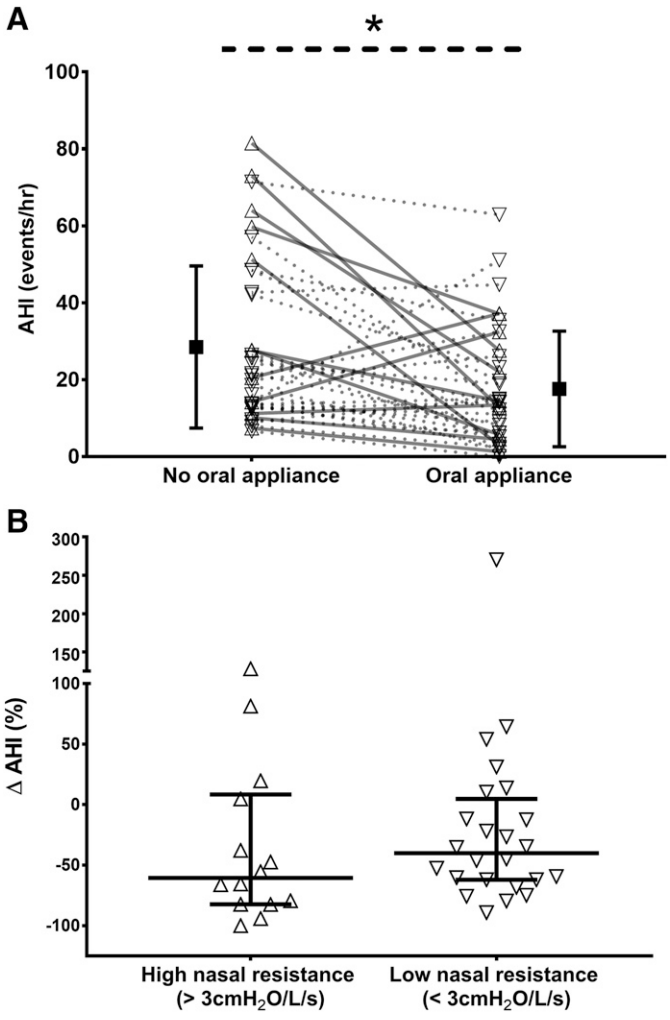
Self-reported adherence and perceived changes in sleep with oral appliance therapy

Data on self-reported adherence and perceived changes in sleep were collected in 34 participants during the acclimatization period. Just prior to the efficacy study, participants reported using the oral appliance device for an average of 6.7 h/night (range 3–7 h/night) for 6.4 nights/wk (range: 3–7 nights/wk). Thirty of these 34 participants (88%) were deemed adherent with therapy based on the definition of at least 4 h/night for at least 5 days/wk.[37] Of these 34 participants, 11 did not notice any difference in their sleep with oral appliance therapy, 1 reported waking up feeling tired whereas 22 participants reported improvements in their sleep and/or reduced snoring or apneas.

DISCUSSION

The main finding of this study is that nasal resistance increased from seated to supine, with even higher values in the lateral position. Mandibular advancement however, did not alter nasal resistance within each corresponding posture. The exception was nonresponders to oral appliance therapy in whom nasal resistance increased with mandibular advancement while seated. The novel oral appliance was efficacious in reducing OSA severity by approximately 50% in people with and without high nasal resistance. Other key sleep parameters also

Figure 4—Diagram showing effect of the novel oral appliance on obstructive sleep apnea severity.



(A) Effect of oral appliance therapy on obstructive sleep apnea severity (total apnea-hypopnea index [AHI]). Black squares with error bars = group mean ± standard deviation. **(B)** Percentage reduction in total AHI with oral appliance therapy between people with high and low nasal resistance. Each data point denotes an individual participant. Horizontal lines indicate the medians and interquartile ranges. Triangles indicate people with high nasal resistance, inverted triangles indicate individuals with low nasal resistance. Asterisk indicates a significant difference ($P < .05$) between no oral appliance and oral appliance conditions.

improved with oral appliance therapy including WASO and the arousal index.

Postural effects on awake nasal resistance

Similar to the current findings, previous studies in healthy individuals have demonstrated increases in nasal resistance from the seated to supine posture.[26,38,39] Another study in healthy individuals also detected higher total nasal resistance in the lateral position compared to supine.[40] Our OSA cohort had an increase in nasal resistance of approximately 10% from seated to supine and approximately 20% from supine to lateral. In comparison, the data in healthy individuals from previous nasal resistance studies tend to show greater positional changes of up to 50% from seated to supine[26,39] and, similarly, almost 50% from supine to lateral.[40] Smaller postural changes in nasal resistance in the current study may be due to several factors including differences in methodology. First, quantification of nasal resistance in previous studies was measured using anterior rhinomanometry[26,39,40] rather than the gold standard posterior nasal resistance methodology used in the current study. In addition, two of the previous studies quantified nasal resistance unilaterally and estimated total nasal resistance as the mean values of each nostril measured.[39,40] This approach is highly dependent on the patency of each nostril and anterior measurements may not necessarily mirror posterior nasal resistance values.[38]

Mechanically, positional changes in nasal resistance have been attributed to hydrostatic effects in response to changes in venous blood flow through the nasal mucosa[26] and positional reflex responses under autonomic sympathetic control.[41] Reduced positional changes in nasal resistance between healthy individuals and people with OSA suggest attenuated positional reflex responses in OSA. Consistent with attenuated postural changes in nasal resistance in OSA but in contrast to our findings, Hellgren and colleagues found no change in nasal patency from seated to supine in people with OSA.[28] This may be due, at least in part, to increased OSA severity (AHI: 46 versus 29 events/h) and the treatment status of the participants. For example, in the previous study all patients were treatment naïve whereas participants in the current study were all on oral appliance therapy for 2 to 3 months prior to testing. Intermittent hypoxia and reoxygenation in OSA contributes to elevated levels of proinflammatory cytokines.[42] Proinflammatory cytokines can contribute to nasal obstruction and, thus, may mask any positional effects.[43] Impaired neurovascular control in OSA may also diminish positional changes in nasal resistance,[28] an effect that may be more pronounced in severe OSA. The current findings of reduced positional changes in nasal resistance compared to healthy control patients, but not an absence of an effect similar to the earlier findings in people with untreated OSA, suggests that impaired neurovascular control may be reversible, at least in part, after OSA therapy. These possibilities require further investigation.

Effects of mandibular advancement on nasal resistance

Consistent with our findings, a previous study[17] in patients with OSA showed no overall effect of mandibular advancement on nasal resistance while seated. Additionally, similar to the current findings during the seated position, nasal resistance increased with an oral appliance in the supine posture in nonresponders but not in responders.[17] The patient characteristics in our study were similar to the previous report with the exception of higher baseline (seated) nasal resistance in the earlier study.[17] In addition, measurement techniques and the oral appliance used were different, both of which could have influenced the findings. Nonetheless, both studies showed increased nasal resistance with mandibular advancement in nonresponders to therapy albeit during different postures. The mechanisms mediating increased nasal resistance with mandibular advancement

Table 2—Polysomnography data on versus off oral appliance therapy.

	No Therapy	Oral Appliance	*P*
Sleep efficiency (%)	88 (78, 91)	89 (81, 94)	.567
Total sleep time (minutes)	181 ± 56	190 ± 53	.545
Stage N1 sleep (%TST)	11(7, 17)	7 (4, 11)	< .001
Stage N2 sleep (%TST)	57 ± 10	53 ± 12	.062
Stage N3 sleep (%TST)	11 ± 13	17 ± 12	.092
REM sleep (%TST)	18 (11, 29)	23 (13, 30)	.31
Wake after sleep onset (minutes)	20 (11, 35)	12 (8, 25)	.026
Arousal index (events/h)	21 (16, 30)	14 (10, 20)	< .001
Percent supine (%TST)	67 ± 31	78 ± 27	.01
NREM supine AHI (events/h)	33 ± 25	17 ± 18	< .001
REM supine AHI (events/h)	41 ± 21	26 ± 17	.003
Total supine AHI (events/h)	36 ± 2	21 ± 18	< .001
Hypopnea event duration (seconds)	23 ± 4	21 ± 7	.049
Nadir SpO_2 (%)	87 (81, 91)	89 (83, 90)	.51
Total ODI (3%)	14 (8, 34)	8 (3, 23)	.004
T90 (minutes)	0.6 (0.1, 4.8)	0.25 (0, 4.1)	.01
T90 (%TST)	0.3 (.01, 2.8)	0.1 (0, 2)	.023

Data are mean ± standard deviation or median (interquartile range). Supine REM AHI data during both conditions were available in 21 participants. All other values n = 38. AHI = apnea-hypopnea index, NREM = non-rapid eye movement sleep, ODI = oxygen desaturation index, REM = rapid eye movement, SpO_2 = estimated blood oxygen saturation via pulse oximetry, T90 = time spent with a blood oxygen saturation level below 90%, TST = total sleep time.

Table 3—Oral appliance response rates according to different treatment outcome definitions.

	Responders, % (n)		
	Total AHI	NREM Supine AHI[a]	Supine AHI[a]
Treatment AHI < 5 events/h	18 (7)	38 (14)	16 (6)
Treatment AHI < 10 events/h	38 (14)[b]	51 (19)[b]	35 (13)[b]
≥ 50% reduction in baseline AHI	47 (18)	59 (22)	46 (17)
Reduction in OSA severity category	54 (20)	59 (22)	46 (17)

Number of participants in each category are listed in parentheses. [a]Data calculated from n = 37 participants with OSA, 1 participant did not have any NREM sleep in the supine position. [b]Count includes participants with AHI < 5 events/h. AHI = apnea-hypopnea index, NREM = non-rapid eye movement, OSA = obstructive sleep apnea, reduction in OSA severity category = proportion of participants who had a reduction in OSA severity category (eg, from severe to moderate or moderate to mild etc. where mild = AHI 5 to < 15, moderate = AHI 15 to < 30 and severe = AHI ≥ 30 events/h).

in nonresponders are unclear. Regardless, these findings highlight the complex interactions that can occur when one section of the upper airway is altered resulting in changes in adjacent structures. This may be especially true in those with highly crowded upper airways given the confines of the upper airway.

In contrast, two studies in healthy individuals have shown reductions rather than increases in nasal resistance with mandibular advancement in both the seated[29,30] and supine[30] positions. The increase in nasal patency with mandibular protrusion was postulated to occur due to passive displacement of the soft palate and changes that affect the nasal valve.[29] Absence of a similar effect in OSA may be explained by an impaired functional response within the nasopharynx due to airway crowding. Mandibular advancement is known to change structural dimensions in the upper airway including within the velopharynx.[12] This is further supported by findings in which the soft palate stretches following anterior tongue movement via the palatoglossal arch.[44] The pattern of anterior tongue motion from mandibular advancement in severe OSA is variable and smaller compared to that in healthy individuals.[13] Thus, this may explain, at least in part, the lack of overall change in nasal resistance with mandibular advancement in the current study.

Efficacy of the novel oral appliance including in people with high nasal resistance

Previous data show that on average, oral appliance therapy reduces OSA severity by approximately 55%.[45] A recent study in which an earlier version of the current novel oral appliance was used reported a similar overall reduction in the AHI of about 60%,[31] which is comparable to our findings of approximately 50%. The self-reported adherence rate was also similar (88% versus 83%).[31]

Table 4—Treatment response rates with oral appliance therapy separated according to high versus low nasal resistance.

	Responders, % (n)	
	High Nasal Resistance (n = 14)	Low Nasal Resistance (n = 24)
Treatment AHI < 5 events/h	29 (4)	13 (3)
Treatment AHI < 10 events/h	36 (5)[a]	38 (9)[a]
≥ 50% reduction in baseline AHI	57 (8)	42 (10)
Reduction in OSA severity category	57 (8)	50 (12)

Treatment response rates based on total AHI in participants with high and low nasal resistance. Number of participants in each category are listed in parentheses. [a]Count includes participants with AHI < 5 events/h. AHI = apnea-hypopnea index, OSA = obstructive sleep apnea, reduction in OSA severity category = proportion of participants who had a reduction in OSA severity category (eg, from severe to moderate or moderate to mild etc. where mild = AHI 5 to < 15, moderate = AHI 15 to < 30 and severe = AHI ≥ 30 events/h).

However, the overall treatment success rate was on the lower range compared to the reported literature.[45] This may be due to the fact that our participants spent more time supine on the oral appliance therapy arm of the study, which tends to worsen OSA severity and oral appliance efficacy.[19] Despite this, there were major improvements in several polysomnographic indices with oral appliance therapy including reduced stage N1 sleep, WASO, arousal frequency and overnight oxygenation. Most participants also reported they thought their sleep improved and/or their snoring or apneas decreased.

OSA severity worsens and oral appliance therapy efficacy tends to reduce during REM sleep.[19] Indeed, in one study oral appliance therapy resolved REM-predominant OSA in just 12% of patients,[19] which is comparable to 11% in the current study. Oral appliance therapy decreases upper airway collapsibility[46,47] without systematically altering upper airway muscle function.[47] The upper airway is also more collapsible and dilator muscle activity is lower during REM sleep.[48] Thus, decreased oral appliance efficacy during REM sleep may be explained by REM-related decrements in airway collapsibility, which cannot always be overcome with an anatomic intervention that yields variable absolute and relative levels of improvement in airway collapsibility between individuals.[47] Additionally, physiologic variability increases during REM sleep and there is relatively less time available in which to obtain an accurate estimate of REM AHI, particularly during a split-study design and in people with severe OSA in whom REM duration may be limited. This may have also contributed to a lack of a significant difference in the overall REM AHI with oral appliance therapy in the current study. However, when a major source of variability in AHI was controlled (ie, body position), the supine REM AHI was significantly reduced with therapy albeit to a lesser absolute extent compared to NREM.

In addition, high nasal resistance is associated with increased OSA severity[21] and oral appliance treatment failure.[17] Consistent with our findings, Lavery and colleagues found comparable treatment response rates between those with self-reported high and low nasal resistance with a similar oral appliance.[31] Thus, unlike traditional mandibular advancement devices, these findings suggest that the addition of an oral breathing route within the oral appliance device provides an alternate route of breathing without requiring mouth opening, which may cause mandibular retraction for those with nasal obstruction resulting in efficacy rates similar to those without nasal obstruction.

Methodologic considerations

A major strength of this study was that nasal resistance was objectively measured using gold standard methodology whereby total nasal resistance is measured at the choanae. This is likely to be more relevant for upper airway collapsibility and OSA compared to anterior rhinomanometry. The sleep physician referral pathway with clinical follow-up, titration, and acclimatization with a qualified dentist prior to the treatment efficacy study also reflects best standards of care.

Despite its strengths, this study is not without limitations. Efficacy studies were conducted via a split-night polysomnography. This limits the amount of sleep available in each portion of the night. Additionally, REM sleep duration is longer as the night progresses.[49] OSA is also more severe during REM sleep.[50] This may result in the AHI being higher in the second portion of the split night. However, to minimize the effects of these potential confounders, we attempted to obtain at least one period of REM sleep in each portion of the polysomnography and the order of intervention was randomized. Interruptions to sleep due to the changeover of interventions was also minimal and was carried out during lighter stages of sleep where possible.

OSA severity is known to be dependent on body position, with more apneic episodes occurring in the supine position.[51] Body position was not controlled in this study. As highlighted, participants slept predominantly in the supine position in both portions of the night. However, there was less supine sleep during the baseline portion of the night. Hence, OSA severity may have been underestimated in some cases and treatment effect may have been underestimated. To address this potential limitation, we analyzed our data during NREM and REM supine sleep to minimize the variability from positional and sleep stage effects.

Finally, because we did not have a traditional mandibular advancement device arm in the current protocol, we cannot be certain that people with high nasal resistance would have been poor responders with a traditional device. Rather, these statements rely on historical data in which high nasal resistance was a

predictor of mandibular advancement treatment failure.[17] Thus, to address this question definitively, an appropriately designed prospective crossover study is required to directly compare the current novel oral appliance with a traditional mandibular advancement in those with high nasal resistance.

Summary

We found that nasal resistance is dependent on body posture in people with OSA following approximately 3 months of oral appliance therapy. Mandibular advancement did not alter awake nasal resistance except in the seated posture where nasal resistance increased in nonresponders to therapy. The novel oral appliance with a built-in oral airway had similar efficacy in reducing the total AHI in people with objectively quantified high versus low nasal resistance. These findings suggest that this novel oral appliance may be a treatment alternative for people with high nasal resistance in whom traditional mandibular advancement devices may be less efficacious.

ABBREVIATIONS

AHI, apnea-hypopnea index
BMI, body mass index
CPAP, continuous positive airway pressure
REM, rapid eye movement
NREM, non-rapid eye movement
WASO, wake after sleep onset

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