

SCIENTIFIC INVESTIGATIONS

A Randomized Crossover Trial Comparing Autotitrating and Continuous Positive Airway Pressure in Subjects With Symptoms of Aerophagia: Effects on Compliance and Subjective Symptoms

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Study Objectives: To assess the benefit and tolerance of autotitrating positive airway pressure (APAP) versus continuous positive airway pressure (CPAP) in subjects who experience aerophagia.

Methods: This is the report of a prospective, two-week, double-blinded, randomized crossover trial set in an Australian clinical sleep laboratory in a tertiary hospital. Fifty-six subjects who reported symptoms of aerophagia that they attributed to CPAP were recruited. Full face masks were used by 39 of the 56 subjects recruited. Subjects were randomly and blindly allocated to either CPAP at their treatment recommended pressure or APAP 6–20 cm H₂O, in random order. Subjects spent two weeks on each therapy mode. Therapy usage hours, 95th centile pressure, maximum pressure, 95th centile leak, and residual apnea-hypopnea index (AHI) were reported at the end of each two-week treatment period. Functional Outcome of Sleepiness Questionnaire, Epworth Sleepiness Scale, and visual analog scale to measure symptoms of aerophagia were also completed at the end of each 2-week treatment arm.

Results: The median pressure ($P < .001$) and 95th centile pressure ($P < .001$) were reduced with APAP but no differences in compliance ($P = .120$) and residual AHI were observed. APAP reduced the symptoms of bloating ($P = .011$), worst episode of bloating ($P = .040$), flatulence ($P = .010$), and belching ($P = .001$) compared to CPAP. There were no differences in Epworth Sleepiness Scale or Functional Outcome of Sleepiness Questionnaire outcomes between CPAP and APAP.

Conclusions: APAP therapy reduces the symptoms of aerophagia while not affecting compliance when compared with CPAP therapy.

Clinical Trial Registration: Australian and New Zealand Clinical Trials Registry at <https://www.anzctr.org.au>, trial number ACTRN12611001250921.

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Keywords: aerophagia, autotitrating positive airway pressure (APAP), continuous positive airway pressure (CPAP), CPAP side effects, sleep apnea therapy,

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INTRODUCTION

Obstructive sleep apnea (OSA) is a prevalent disorder that is associated with daytime sleepiness,¹ reduced quality of life,² increased risk of motor vehicle accidents,³ and cardiovascular disease.⁴ The treatment of OSA is predominantly through continuous positive airway pressure (CPAP), which delivers pressurized air to splint the upper airway open and increase end-expiratory lung volume.⁵ CPAP has been demonstrated to reduce the apnea-hypopnea index (AHI), improve objective and subjective sleepiness, and improve quality of life.⁶

Despite the obvious efficacy of CPAP, uptake and compliance with this therapy is still an ongoing problem. Reports of long-term CPAP compliance vary between 40% to 80%,^{7,8} although some of this variation can be attributed to different definitions of compliance. This has led many clinicians to examine the side effects associated with CPAP as a contributor to poor compliance rates. Very early on, it was recognized that a significant proportion of patients experienced side effects with CPAP.⁹ These side effects experienced by patients include claustrophobia, nasal dryness, pressure intolerance, and interface leak (with sleep fragmentation arising from this

BRIEF SUMMARY

Current Knowledge/Study Rationale: Aerophagia is a known side effect of continuous positive airway pressure (CPAP) therapy for obstructive sleep apnea. Currently there is no evidence for the use of autotitrating positive airway pressure (APAP) in reducing the symptoms of aerophagia in affected patients.

Study Impact: This study showed that using APAP reduces the symptoms of aerophagia but does not increase compliance with therapy. APAP is a viable alternative to CPAP in patients experiencing aerophagia.

phenomenon).¹⁰ Another reported side effect of CPAP therapy is aerophagia or bloating.

Aerophagia appears to occur when some of the pressurized air is swallowed and collects in the gastrointestinal system. This air causes abdominal discomfort and reports of excessive belching and/or flatulence. In some cases, the aerophagia can be severe enough for the patient to discontinue CPAP therapy. Aerophagia in CPAP patients has a prevalence of 16%,⁹ and has been reported in infants as well as adults.¹¹ It may also be associated with gastroesophageal reflux disease.¹² Current clinical

management of aerophagia in CPAP therapy is largely anecdotal and includes empiric reductions in therapeutic pressure or the use of autotitrating positive airway pressure (APAP) therapy. Even if reduction of therapeutic pressure is successful in relieving the symptoms of aerophagia in some patients, these pressure reductions can also leave the patient undertreated with recurrence of OSA symptoms. Clinicians have therefore utilized APAP in order to effectively treat the OSA while lowering the mean pressure across the night.¹³ There is, however, no published evidence to demonstrate that APAP is effective in adequately treating the OSA while reducing the symptoms of aerophagia.

In this study, we examine the effectiveness of APAP in CPAP patients who report aerophagia symptoms. Measures to determine the effectiveness of APAP in this cohort included objective therapy compliance, aerophagia symptoms, and sleep-related quality of life.

METHODS

Study Design and Sample Size Determination

This was a double-blind, randomized, crossover study of APAP versus CPAP (Autoset Spirit S8, ResMed Ltd., Sydney, Australia) with no washout period. The study took place at the Sleep Disorders Centre, an Australian accredited clinical sleep laboratory in a tertiary hospital. Data collection occurred at baseline, and after two weeks of each trial arm. Our primary outcome measure in this study was compliance with positive airway pressure (PAP) therapy. We determined that a 30-minute difference in average nightly therapy was clinically significant. Based on average CPAP compliance recorded within the previous 12 months, *a priori* power calculations indicated that a sample size of 56 subjects was required to detect a 30-minute difference in nightly objective usage with a power of 0.8 ($\alpha = 0.05$). Secondary outcomes measures were residual AHI, device pressure and leak, Epworth Sleepiness Scale (ESS), Functional Outcomes of Sleep Questionnaire (FOSQ), and an in-house visual analog scale (VAS) of aerophagia symptoms questionnaire. The aerophagia symptoms questionnaire was developed with input from the Princess Alexandra Hospital Gastroenterology Department and is available from the corresponding author.

Subject Selection

Subjects were recruited between 2009 and 2013. Subjects who reported symptoms of aerophagia attributed to CPAP use (during medical review) were invited to participate. Aerophagia was confirmed by responding positively to the following question: Do you experience any bloating, excessive flatulence, excessive belching or abdominal pain or discomfort, due to CPAP use? Subjects were excluded if they were younger than 18 years, had an intellectual impairment, had comorbid central sleep apnea (central apnea index ≥ 5 events/h), regularly used sedatives or narcotics, had preexisting lung or psychiatric disease, or were unable to attend the protocol appointments. The study protocol was approved by the Institutional Human Research Ethics Committee (HREC/09/QPAH/088) and written consent

was obtained from all subjects. The study is registered in the Australian and New Zealand Clinical Trials Registry at <https://www.anzctr.org.au>, trial number ACTRN12611001250921.

Study Protocol

All outcomes were assessed on three occasions, at baseline prior to randomization and then at the end of each of the two-week treatment arms. Subjects were randomized by a clinical staff member not involved in data collection for this study (KH) using the technique of shuffled sealed envelopes containing equal numbers of each treatment arm. An Autoset Spirit S8 was then programmed for subject use and used for both treatment arms. The APAP device was programmed by clinical staff not involved in the patient recruitment and data collection (KH, BD). The device display screen was then covered to discourage discovery of therapeutic mode. The clinical staff member (TS) who collected study data was also blinded to the therapeutic mode.

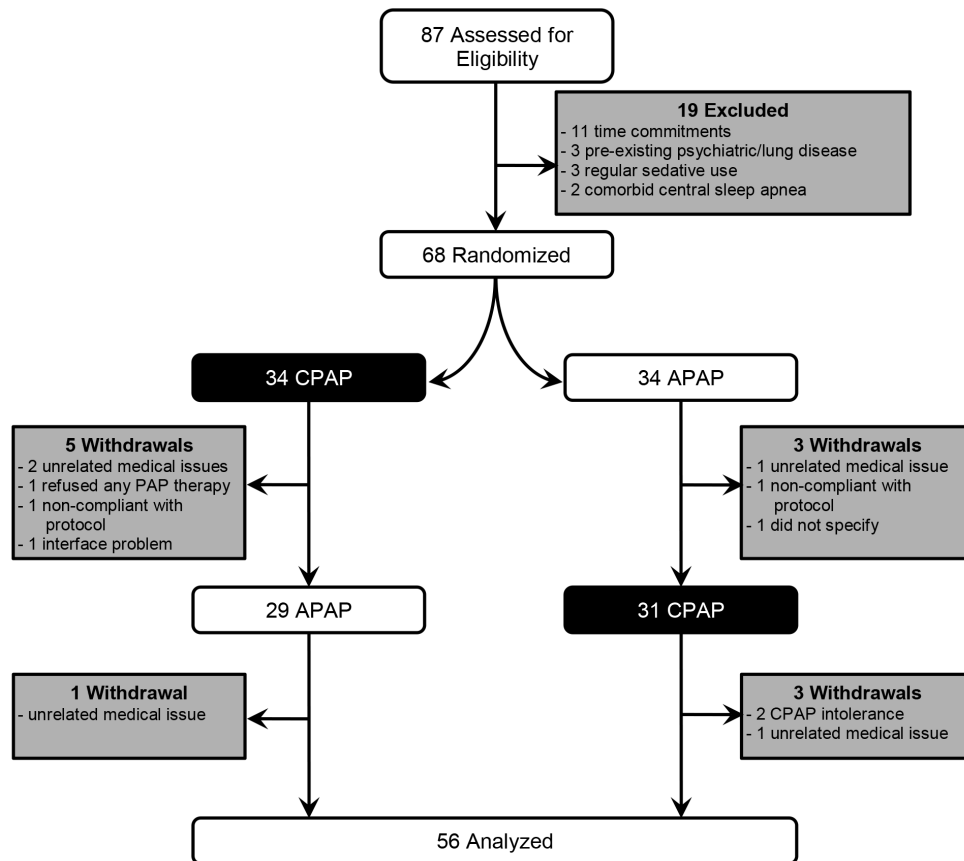
APAP therapy was delivered using a minimum pressure of 6 cm H₂O and a maximum pressure of 20 cm H₂O according to our standard laboratory protocol. CPAP therapy was delivered according to their sleep physician-recommended setting that was determined during a Type 1 CPAP titration study. Subjects were asked to use the same interface throughout the study, and remain either on or off humidification use for the duration of the study. Subjects were provided with a diary and asked to make a daily record of the incidence of belching and flatulence as well as consumption of aerated drinks, the time between eating and retiring to bed and time of sleep onset. The subjects were also asked to measure their abdominal girth upon waking and to rate their abdominal discomfort on waking between 0 (none) and 10 (severe). Education about completing the diary was provided both verbally and in written form.

After the first two weeks of either fixed pressure CPAP at their recommended setting or autotitrating PAP with a window of 6 to 20 cm H₂O, subjects were reassessed in clinic. At this visit, PAP usage (hours per night used for all nights in the trial arm, % of nights used and % of nights used > 4 hours), aerophagia symptoms (using VAS), weight, ESS, FOSQ and clinical global index of change were recorded and the 2-week diary was retrieved. The APAP device data was downloaded using ResScan software (version 4.3, ResMed Ltd., Sydney, Australia) and then the device was reprogrammed to the alternate therapy. Another diary was provided. Subjects continued on the alternate therapy for two weeks and were then reassessed in clinic. PAP usage (hours per night used for all nights in the trial arm, % of nights used and % of nights used > 4 hours), aerophagia symptoms (using VAS), weight, ESS, FOSQ, and clinical global index of change were again recorded and the two-week diary was retrieved. At this final visit, subjects were asked which therapy they preferred, and the main reason for this. Subjects were then given the opportunity to have the order of therapy type revealed and to discuss their ongoing management with a nonblinded researcher (KH, BD).

Statistical Analysis

All statistical analyses were undertaken on an intention-to-treat basis. Subgroup analysis was also conducted to examine

Figure 1—Trial flow chart.



APAP = autotitrating positive airway pressure, CPAP = continuous positive airway pressure, PAP = positive airway pressure.

the effects of subjects using a full face mask compared to subjects using a nasal mask. Statistical analyses were performed using GraphPad Prism 7.01 (GraphPad Software, La Jolla, California, United States). Tests of period and carryover effects were calculated according to Senn.¹⁴ The normality of group data collected was determined by the D'Agostino-Pearson omnibus K2 test.¹⁵ Data are presented as mean \pm standard deviation or median (interquartile range) where appropriate. Differences between baseline, CPAP, and APAP arms were compared using the Friedman test with Dunn posttest (nonparametric). Differences between the CPAP and APAP arms were compared using the Wilcoxon matched-pairs signed-rank test (nonparametric). The effect size of changes between the two arms was calculated according to Nakagawa and Cuthill (nonparametric).¹⁶ Pearson r was selected to determine effect size with the cutoffs of $r = 0.10$ small effect, $r = 0.30$ medium and $r = 0.50$ large effect.¹⁷ A value of $P < .05$ was considered statistically significant.

RESULTS

Subject Flow

A total of 87 subjects were assessed for eligibility. The study flow chart is shown in **Figure 1**. Sixty-eight subjects who volunteered aerophagia symptoms were randomized for the trial.

Thirty-four subjects were randomly selected to receive CPAP and the other 34 to receive APAP during the first arm of the trial. Five subjects withdrew from CPAP in the first arm for the reasons of: hospitalization for unrelated medical issues (two subjects), did not wish to continue with any PAP therapy (one subject), did not wish to complete any questionnaires or diary (one subject), and could not replace broken mask interface (one subject). Three subjects withdrew from APAP in the first arm for the reasons of: cracked ribs after a fall (one patient), did not wish to attend clinic (one patient), and did not wish to specify (one subject). This left 29 subjects to continue on to APAP in the second arm of their trial and 31 subjects to continue on to CPAP in the second arm of their trial. One subject withdrew from the APAP arm for the reason of hospitalization for an unrelated medical issue. Three subjects withdrew from the CPAP arm for the reasons of: intolerance of CPAP (two subjects) and on the advice of their general physician due to worsening cardiac history (one subject).

Subject Characteristics

The baseline demographic and clinical characteristics of the group are shown in **Table 1**. The recruited subjects were of older age, obese, and predominantly male. Comorbidities such as hypertension, depression, gastroesophageal reflux disease, and hyperlipidemia were common in this group. Subjects were diagnosed with severe OSA. Obstructive respiratory events

Table 1—Patient characteristics of the study cohort.

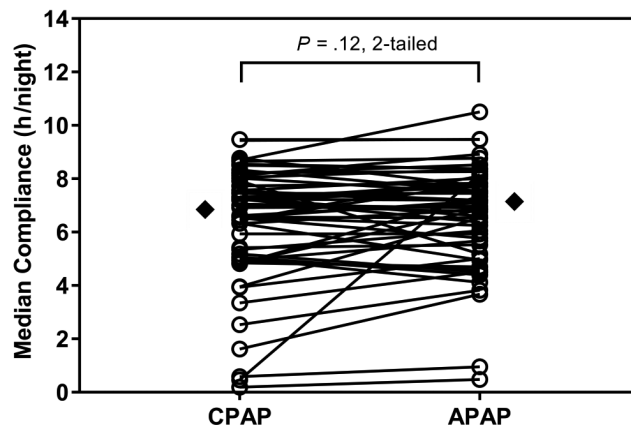
Parameter	Recruited	Withdrawn
Number	56	12
Age, y	65 ± 13	68 ± 12
BMI, kg/m ²	34.2 ± 6.2	39.0 ± 7.5
Neck circumference, cm	44 ± 4	44 ± 8
Sex, male : female	39 : 17	5 : 7
Cigarette smoker, %	14	17
Comorbidities, n (%)		
Hypertension	30 (54)	5 (9)
Depression	11 (20)	2 (4)
GERD	10 (18)	0 (0)
Dyslipidemia	10 (18)	1 (2)
Ischemic heart disease	8 (14)	2 (4)
Type 2 diabetes	7 (13)	5 (9)
Diagnostic TST, min	289 (241, 347)	330 (250, 359)
Diagnostic Ari, events/h	35.1 (19.6, 55.5)	27.0 (12.9, 33.9)
Diagnostic AHI, events/h		
Total	45.0 ± 29.5	37.1 ± 23.5
NREM sleep	46.1 ± 33.0	44.9 ± 24.3
REM sleep	44.6 ± 28.1	39.1 ± 20.2
Supine	56.3 ± 33.0	57.5 ± 40.1
Nonsupine	22.7 (5.9, 44.7)	35.4 (9.2, 67.3)
Titrated pressure, cm H ₂ O	14.6 ± 4.1	15.1 ± 3.2
Mask interface, full : nasal	39 : 17	9 : 3
Time on CPAP therapy, y	0.9 (0.3, 3.7)	0.4 (0.2, 5.9)

Values presented as mean ± standard error of the mean or median (interquartile range) where appropriate. AHI = apnea-hypopnea index, Ari = arousal index, BMI = body mass index, GERD = gastroesophageal reflux disease, NREM = non-rapid eye movement, REM = rapid eye movement, TST = total sleep time.

were spread evenly throughout non-rapid eye movement and rapid eye movement sleep. There was a supine predominance in the occurrence of these obstructive respiratory events. During their CPAP titration study, subjects were manually titrated to a little over 14 cm H₂O. Subjects were predominantly using a full face mask and had been on therapy for almost one year. None of the included patients had a history of previous uvulopalatopharyngoplasty.

Therapy Outcomes

Statistical analysis of our primary outcome data (average compliance between each trial arm) demonstrated no period effect ($P = .62$), carryover effect $P = .63$ or interaction between treatment and period ($P = .57$). Objective compliance during the CPAP and APAP trial arms are shown in **Figure 2** and **Table 2**. Both the CPAP and APAP arms demonstrated increased objective compliance compared to baseline CPAP therapy ($P = .010$ and $P < .001$ for CPAP and APAP therapy arms, respectively). There was no statistically significant difference between CPAP arm and APAP arm compliance ($P = .12$) during the trial. The device-calculated AHI was within clinically acceptable limits for both trial arms. The median pressure and the 95th centile pressure were reduced in the APAP trial arm

Figure 2—Compliance with CPAP and APAP in all subjects after two weeks of treatment.

The diamonds mark the median value for each treatment arm. APAP = autotitrating positive airway pressure, CPAP = continuous positive airway pressure.

($P < .001$ for both median pressure and 95th centile pressures). Similarly, the median pressure and the 95th centile leak were also reduced in the APAP trial arm ($P < .001$ for both median leak and 95th centile leak). At the end of the trial 35 subjects preferred APAP, 11 subjects preferred CPAP, and 10 subjects had no specific preference between the therapy modes.

Symptoms of Aerophagia

The effect of CPAP and APAP therapy on aerophagia symptoms in this group is shown in **Table 3**. Both CPAP and APAP arms described less total aerophagia symptoms compared to baseline ($P = .021$ and $P < .001$ for CPAP and APAP, respectively). APAP therapy was associated with a moderate reduction in total aerophagia symptoms compared with CPAP therapy ($P = .003$; $r = 0.308$). The individual symptoms of bloating ($P = .010$), worst episode of bloating ($P = .006$), and flatulence ($P < .001$) were significantly less with CPAP therapy compared with baseline symptoms. The individual symptoms of abdominal pain ($P = .010$), worst episode of abdominal pain ($P = .003$), and belching ($P < .001$) were also significantly less with APAP therapy in addition to the individual symptoms of bloating ($P < .001$), worst episode of bloating ($P < .001$), and flatulence ($P < .001$) when compared with baseline symptoms. APAP therapy was associated with moderate reductions in bloating ($P = .011$; $r = 0.291$), worst episode of bloating ($P = .040$; $r = 0.275$), flatulence ($P = .010$; $r = 0.221$), and belching ($P = .001$; $r = 0.319$) compared with CPAP therapy. There were no differences in morning abdominal girth (CPAP: 117 ± 14 cm versus APAP: 116 ± 14 cm, $P = .780$), subject-reported average daily consumption of aerated drinks ($P = .914$), and interval between consumption of last meal and bedtime ($P = .439$) between each arm.

Sleep-Related Outcomes

The effect of CPAP and APAP therapy on subjective sleepiness and sleep-related quality of life is shown in **Table 4**. At

Table 2—Comparison of CPAP and APAP outcome measures.

Parameter	Baseline	CPAP	APAP	Effect size
Compliance, h/night	5.5 (4.0, 7.5)	6.8 (5.0, 7.9)*	7.0 (5.6, 7.8)*	0.149
% of nights used		100 (93, 100)	100 (100, 100)	-0.152
% of nights used > 4 h		92 (74, 100)	100 (83, 100)	-0.092
Median AHI, events/h		4.3 (2.9, 7.5)	5.0 (3.7, 7.5)	0.141
Median pressure, cm H ₂ O		14.0 (11.3, 17.2)	9.8 (8.6, 11.2)§	-0.562
95th centile pressure, cm H ₂ O		14.0 (12.0, 17.9)	12.0 (11.0, 13.2)§	-0.355
Median leak, L/min		3.6 (0, 12.9)	2.4 (0, 6) §	-0.311
95th centile leak, L/min		20.1 (8.0, 43.2)	10.8 (4.8, 24.9)§	-0.413

Values presented as median (interquartile range). AHI = apnea-hypopnea index, APAP = autotitrating positive airway pressure, CPAP = continuous positive airway pressure, 95th pressure = pressure value exceeded 5% of the time. * = $P < .05$ versus baseline. § = $P < .05$ versus CPAP.

Table 3—Comparison of aerophagia-related symptoms during two weeks of CPAP and APAP treatment.

Parameter	Baseline	CPAP	APAP	Effect size
Total score	34.1 (27.4, 39.8)	24.3 (13.9, 36.7)*	13.2 (3.4, 23.8)*§	0.308
Abdominal pain	3.3 (0.4, 5.4)	2.6 (0.4, 4.5)	1.0 (0.2, 2.5)*	0.251
WE abdominal pain	5.4 (2.1, 8.0)	4.3 (0.6, 6.5)	1.3 (0.3, 4.6)*	0.282
Bloating	6.7 (4.4, 8.1)	3.8 (1.4, 7.4)*	1.5 (0.2, 4.6)*§	0.291
WE bloating	8.0 (5.5, 9.1)	5.2 (3.2, 8.1)*	2.3 (0.2, 6.3)*§	0.275
Flatulence	7.6 (4.8, 8.7)	5.1 (2.2, 7.4)*	3.3 (0.4, 5.9)*§	0.221
Belching	3.2 (1.2, 6.0)	2.7 (0.6, 5.5)	1.1 (0.2, 2.7)*§	0.319

Values presented as median (interquartile range). Effects sizes were calculated for comparisons between CPAP therapy and APAP therapy trial arms that were significantly different. APAP = autotitrating positive airway pressure, CPAP = continuous positive airway pressure, WE = worst episode. * = $P < .05$ versus baseline. § = $P < .05$ versus CPAP.

Table 4—Comparison of subjective sleep and sleep-related outcomes scores during two weeks of CPAP and APAP treatment.

Parameter	Baseline	CPAP	APAP	Effect size
ESS	7 (4, 12)	7 (4, 10)	7 (4, 11)	-0.026
FOSQ Total	15.6 (11.4, 17.5)	15.9 (12.9, 17.6)	15.8 (12.5, 17.9)	0.069
Activity	3.0 (2.0, 3.0)	3.0 (2.8, 3.0)	3.0 (2.0, 3.1)	-0.033
Vigilance	3.1 (2.3, 3.7)	3.1 (2.7, 3.6)	3.2 (2.6, 3.7)	0.039
General productivity	3.5 (2.8, 3.9)	3.6 (3.0, 3.9)	3.7 (3.1, 3.9)	0.053
Social outcomes	4.0 (3.0, 4.0)	4.0 (2.7, 4)	3.5 (3.0, 4.0)	0.056
Sexual function	1.5 (0, 3.0)	1.3 (0.0, 3.0)	1.0 (0.0, 3.0)	0.027

Values presented as median (interquartile range). APAP = autotitrating positive airway pressure, CPAP = continuous positive airway pressure, ESS = Epworth Sleepiness Scale, FOSQ = Functional Outcomes of Sleep Questionnaire. All between-group comparisons were not significant.

baseline, subjects ESS was within the normal range (< 10) and remained the same after the CPAP and APAP trial arms ($P < .066$). Subjects also described their quality of life as not being affected by their disorder or side effects. Both subjective sleepiness and their quality of life remained the same after the CPAP and APAP trial arms.

Nasal Mask Versus Full Face Mask Subjects

The subjects using a nasal mask were similar to subjects using a full face mask in nearly all aspects. No statistical differences were observed at baseline in body mass index (34 kg/m² versus 33 kg/m² for nasal mask vs full face mask, respectively, $P = .121$), diagnostic AHI (40.9 events/h versus 31.3 events/h for nasal mask versus full face mask, respectively, $P = .400$) or

titrated pressure (12.0 cm H₂O versus 14.5 cm H₂O for nasal mask versus full face mask, respectively, $P = .126$). Compliance with therapy between the two mask types was also similar throughout the study (baseline: 6.0 h/night versus 5.5 h/night, $P = .369$; CPAP arm: 7.2 h/night versus 6.6 h/night, $P = .989$; APAP arm: 7.2 h/night versus 6.9 h/night, $P = .836$). During the APAP trial arm there were no differences in median pressure (9.8 cm H₂O versus 9.8 cm H₂O for nasal mask versus full face mask, respectively, $P = .581$), 95th centile pressure (11.8 cm H₂O versus 12.1 cm H₂O for nasal mask versus full face mask, respectively, $P = .968$), or 95th centile leak (13.2 L/min versus 8.4 L/min for nasal mask versus full face mask, respectively, $P = .059$). The 95th centile leak was also similar during the CPAP trial arm (25.2 L/min versus 17.4 L/min for

nasal mask versus full face mask, respectively, $P = .126$). No differences were observed in residual AHI for both the CPAP (4.6 events/h versus 3.6 events/h for nasal mask versus full face mask, respectively, $P = .516$) and APAP (5.0 events/h versus 5.0 events/h for nasal mask versus full face mask, respectively, $P = .563$) trial arms. Symptoms of aerophagia were similar at baseline (29.4 versus 35.6 events/h for nasal mask versus full face mask, respectively, $P = .091$), and after the APAP trial arm (18.1 versus 13.0 for nasal mask versus full face mask, respectively, $P = .328$). However, the symptoms of aerophagia were reduced with nasal mask use during the CPAP trial arm (19.1 versus 28.8 for nasal mask versus full face mask, respectively, $P = .019$, effect size $r = 0.311$).

DISCUSSION

In this study, we investigated the ability of APAP to alleviate the effects of aerophagia in OSA patients who complain of this side effect in comparison with CPAP. Aerophagia is a side effect of CPAP therapy whereby the pressurized air is swallowed and results in abdominal pain, bloating, belching, and flatulence. Our results demonstrate that, in patients who experience symptoms of aerophagia, APAP reduces these aerophagia symptoms while still effectively treating their OSA. The use of APAP reduces the median and 95th centile therapeutic pressures and reduces the leak compared to CPAP therapy. This reduction in aerophagia symptoms does not, however, result in any improvement in therapy compliance or sleep-related outcome measures.

This is the first study that we are aware of that tries to formally address this side effect of CPAP therapy. The use of APAP, in addition to reductions in therapeutic pressure, has been a common intervention for aerophagia in the clinical sleep laboratory. These interventions are initiated on the belief that they will improve therapy acceptance and thus lead to improved compliance with therapy. Furthermore, anecdotal evidence in our laboratory suggested that APAP therapy was associated with increased compliance. It was therefore somewhat surprising that APAP did not improve therapy compliance compared with CPAP for patients with aerophagia; patients often cite this complication as a reason for discontinuing CPAP. There may be a couple of factors that could explain the lack of difference in compliance between CPAP and APAP. First, a recent meta-analysis comparing CPAP with APAP for the treatment of OSA¹⁸ demonstrated a slight increase in compliance for APAP compared to CPAP. This increase in compliance with APAP therapy was in the magnitude of approximately 10 minutes. Because our study was powered on the basis of a 30-minute difference in compliance, considered by our sleep physicians to be clinically significant, it is unlikely to find any difference. Furthermore, according to the same meta-analysis, groups with an AHI of greater than 20 events/h did not display any difference in compliance overall. The patient group recruited for this trial had mostly moderate to severe OSA and would appear to complement this subgroup analysis. Second, CPAP compliance has been demonstrated to be unaffected by side effects experienced by users.⁷ There has yet to be any studies that demonstrate that the incidence and severity of side-effects reliably account for variances in therapeutic compliance.

Last, our baseline compliance at 5.5 h/night could be considered quite good in comparison with various CPAP trials in the literature. An argument could be made that this relatively high CPAP compliance at commencement of the study could make it less likely to demonstrate an appreciable change in compliance between the two therapy modes.

Despite the lack of improvement in therapy compliance, we did see improvements in the subjective symptoms associated with aerophagia. These improvements were statistically significant for bloating, flatulence, belching, and overall symptoms of aerophagia. Although they were statistically significant, most of these were small in effect. APAP was only able to reduce the total symptom score and belching with a moderate effect. It is interesting to note that even with two weeks of CPAP, subjective symptoms of aerophagia decreased from baseline. Correspondingly, there was also an increase in compliance during the CPAP arm when compared to baseline. We believe that these differences in symptoms and compliance between baseline and the CPAP trial arm could be explained by a combination of recall bias of symptoms, the motivations of the patient, and the extra attention given to the patients. Evidence has shown that active coping can explain some of the variance associated with CPAP compliance.¹⁹ The motivation to enroll and actively participate in the study could be viewed as an active coping mechanism and lead to improved compliance overall and a reduction in the perception of symptoms.

A feature of this study that deserves comment is the high proportion of full face-mask interfaces used by subjects in this trial. In retrospective and experimental studies, full face masks decrease the retroglottal or retropalatal area^{20,21} leading to higher CPAP requirements^{22,23} although this has not been demonstrated by prospective studies conducted with small sample sizes.^{24,25} Still, the possibility that full face masks could predispose to aerophagia in CPAP patients cannot be discounted. With that in mind, we conducted *post hoc* subgroup analysis to assess this possibility. Our study could not demonstrate any difference in APAP pressure requirements (median and 95th centile pressures), leak, residual AHI, or compliance between subjects using a full face mask and subjects using a nasal mask. The use of a full face mask was, however, associated with greater aerophagia symptoms in comparison with a nasal mask during the CPAP trial arm but not the APAP trial arm. These results suggest that a full face mask could predispose to aerophagia but this is more likely due to the route of air delivery rather than elevated therapeutic pressure requirements in these subjects. Nonetheless, APAP therapy has shown to be beneficial in reducing the symptoms of aerophagia with both mask types.

There are a number of limitations to the study. Firstly, we have no objective measures of aerophagia in these enrolled subjects; therefore, it could not be confirmed that the symptoms were directly due to CPAP and the study could not be controlled for the severity of the aerophagia. It has been reported that other concerns such as pressure intolerance, mask interface problems, and even gastric cancer can mimic the subjective symptoms of aerophagia.²⁶ However, this limitation is somewhat mitigated by the fact that, in a usual clinical situation, a physician will take these patient symptoms at face value and instigate interventions to alleviate these symptoms immediately. Thus, our recruitment

could be considered a strength due to its generalizability. There was an attempt to blind patients to the therapy mode; however, a limitation of the study is the potential for patients to break their blinding and determine the mode by removing the concealment of the device display. We are not aware of any patient in this study attempting to break the blinding, but it should not be discounted as a possibility. Patients were not provided with any information on how to interrogate the study device. A possible limitation could be the lack of a formal washout period in the study design. The rationale was that aerophagia is likely a direct mechanical effect of the PAP and these effects are not likely to carry over from one mode to the next. Therefore, the lack of a washout period should not influence average treatment compliance over a two-week period. Our data proved our rationale to be correct with no discernible carryover or order effect observed. Another limitation of this study is that it is probably underpowered to detect any difference in therapy compliance. Recent meta-analysis has shown compliance to increase by approximately 10 minutes with APAP compared to CPAP. However, we determined 30 minutes to be the minimum clinical difference and powered the study accordingly. Again, we believe that this aspect enhances the applicability to your usual sleep clinic.

CONCLUSIONS

This study has demonstrated that APAP therapy is effective for the relief of aerophagia symptoms in OSA patients. Furthermore, APAP was able to reduce the effect of aerophagia without compromising effective treatment of OSA. More patients believed that APAP was more effective in relieving these symptoms and hence described their preference for this therapy.

ABBREVIATIONS

AHI, apnea-hypopnea index
 APAP, autotitrating positive airway pressure
 ArI, arousal index
 BMI, body mass index
 CPAP, continuous positive airway pressure
 ESS, Epworth Sleepiness Scale
 FOSQ, Functional Outcomes of Sleep Questionnaire
 GERD, gastroesophageal reflux disease
 NREM, non-rapid eye movement
 OSA, obstructive sleep apnea
 PAP, positive airway pressure
 REM, rapid eye movement
 TST, total sleep time
 VAS, visual analogue scale
 WE, worst episode

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