

Does either obesity or OSA severity influence the response of autotitrating CPAP machines in very obese subjects?

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Abstract

Purpose

The pressures delivered by autotitrating CPAP devices not only treat OSA effectively, they also give potentially interesting physiological information about the forces impinging on the pharynx. In earlier work from this unit, we used correlations between autoCPAP pressure and both OSA severity and obesity, to construct an algorithm to estimate the fixed CPAP pressure a patient required for subsequent clinical use. We wished to discover if these relationships could be reliably extended to a much more obese group.

Methods

We performed a prospective cohort study in an obese population. Measurements of obesity were made, OSA severity was recorded, and the 95th centile autoCPAP pressure was recorded during one week of autoCPAP. Spearman's rank correlation was performed between measurements of obesity and autoCPAP pressure, and between OSA severity and autoCPAP pressure.

Results

Fifty-four obese individuals (median BMI 43.0kg/m²), 52% of whom had OSA (AHI \geq 15), had a median 95th centile autoCPAP pressure of 11.8 cmsH₂O. We found no significant correlation between autoCPAP pressure and neck circumference, waist circumference or BMI. There was a moderate correlation between autoCPAP pressure and OSA severity (AHI; $r=0.34$, $p=0.02$. ODI; $r=0.48$, $p<0.001$).

Conclusions

In this population neither BMI, nor neck circumference, nor waist circumference are predictive of autoCPAP pressure. Therefore the previously derived algorithm does not adequately predict the fixed CPAP pressure for subsequent clinical use in these obese individuals. In addition, some subjects without OSA generated high autoCPAP pressures, and thus the correlation between OSA severity and autoCPAP pressure was only moderate.

ClinicalTrials.gov, NCT01380418

Key Words

Obstructive sleep apnoea; obesity; autotitrating CPAP; respiratory physiology

Introduction

Obstructive sleep apnoea (OSA) is a common problem affecting up to 4% of the adult population [1]. OSA is associated with significant comorbidity in the form of increased arterial hypertension [2] cardiovascular events [3] and an increased accident rate [4]. Obesity is the major risk factor for developing OSA [1] and, with rising obesity rates, understanding the physiology of OSA in a subset of very obese patients is of importance.

Continuous positive airways pressure (CPAP) is the gold standard treatment for OSA. For subsequent long-term use, it can be set at a fixed pressure following either a one-night attended titration, a period on an autotitrating machine (autoCPAP), or by using an algorithm (based on obesity indices and OSA severity) to determine an appropriate pressure [5-7]. AutoCPAP machines utilise an inbuilt algorithm, which varies between manufacturers, to calculate the delivered CPAP pressure in real time. AutoCPAP can also be used for diagnosis, trouble-shooting and long-term therapy in OSA [8-9].

In addition to its clinical utility, the pressure derived from autoCPAP machines provides an interesting physiological measure. Upper airways collapsibility is commonly measured using P_{crit} , which is the calculated intra-pharyngeal pressure at which the pharynx would completely collapse, and block airflow. The calculation of P_{crit} requires specialised equipment (measuring flows and supra-glottic pressures) while intermittently dropping applied CPAP pressure, and thus involves attended in-hospital polysomnography. AutoCPAP in contrast can collect information over many nights in the patient's home. AutoCPAP pressure is essentially the pressure required to enlarge the pharynx and reduce flow limitation to a pre-set level. Most autoCPAP machines increase pressure in response to some or all of: apnoeas, hypopnoeas, snoring, inspiratory flow limitation and, in some, the calculation of upper airway resistance from a forced oscillation technique [10-11]. Thus the pressure delivered is that which is required to offset the collapsing forces, and thus hold the pharynx fully open. This is in contrast to P_{crit} , which is the pressure that fully collapses it. Thus the 95th centile autoCPAP pressure, maintaining the pharynx almost fully open, is at the opposite end of the pressure/flow (or volume) relationship of the pharynx to the P_{crit} , when the pharynx is completely closed.

Our previous work validated an algorithm to predict the required fixed CPAP pressure in a normal sleep clinic population. Based on neck circumference and the oxygen desaturation index (ODI, >4% SaO₂ dips) the algorithm predicts the 95th centile autoCPAP pressure [7,12]. In patients who are very obese, in addition to the contribution of upper airways adipose deposition measured by neck circumference [13-15], it is thought that waist circumference also contributes to upper airways collapsibility. Increasing abdominal obesity reduces the end expiratory lung volume and pharyngeal traction, thus increasing pharyngeal compliance and raising P_{crit} [16].

We have looked at a morbidly obese population to assess 1) the correlation between waist circumference, neck circumference and autoCPAP pressure in order to assess whether one or both are important in the determination of upper airways collapsibility and 2) whether our previous algorithm to determine the fixed pressure required for long-term use, (which was derived from the relationship between autoCPAP pressure and both neck circumference and ODI), could be safely extrapolated into this considerably more obese group.

Methods

In this current study we have utilised unreported autoCPAP data from a previously published obesity trial. Full methodology has been published previously [17]. This was a prospective observational study conducted in a single tertiary care hospital. The study was registered prospectively with a global trials registry site (ClinicalTrials.gov, NCT01380418). The study was approved by the Oxford research ethics committee (Oxfordshire REC B 11/H0605/9).

Subjects

Patients were enrolled following referral to the sleep and ventilation clinic at our tertiary centre, or during assessment for possible bariatric surgery. Referrals were all comers and were not biased by the presence or absence of sleep symptoms. Detailed baseline clinical assessment included body mass index (BMI), waist and neck circumference measurements.

Polysomnography

Patients underwent baseline one-night, level 3, in-hospital cardiorespiratory polysomnography (Win-Visi monitoring system; Stowood Scientific Instruments, Oxford, UK) at the Oxford Sleep Unit, Oxford Centre for Respiratory Medicine. This included nasal pressure via nasal cannula, oximetry, pulse rate, and respiratory effort via thoracic and abdominal bands. Body movements (derived automatically from the video signal), heart rate and pulse transit time changes were also routinely recorded as markers of arousal from sleep. Apnoea was defined as ≥ 10 seconds with $<10\%$ airflow, and hypopnoea as ≥ 10 seconds with 50% reduction in nasal airflow (or summed thoraco-abdominal movement in the absence of a nasal flow signal) with $>4\%$ oxygen desaturation. The apnoea hypopnoea index (AHI), **apnoea index (AI) and hypopnoea index (HI) were defined as the number of events per hour of sleep. To measure the contribution of apnoeas to all events the apnoea to hypopnoea ratio was calculated.** ODI was calculated as the number of oxygen desaturations $> 4\%$ per hour of sleep.

AutoCPAP pressure

Regardless of AHI, all patients were trialled on autoCPAP (S9 Elite, ResMed, Abingdon, UK). This device has a pneumotachograph measuring airflow, leak and snoring. It was set to starting pressure of 4cmH₂O with a maximum of 20cmH₂O. The pressure increases in response to apnoeas, flow limitation (derived by the shape of inspiratory flow profile), and snoring. In the absence of apnoea, flow limitation or snoring, the pressure gradually decreases to 4cmH₂O. AutoCPAP pressure was measured and averaged over at least 7 nights of analysis, and the 95th centile pressure over these nights was recorded for those individuals using autoCPAP for greater than four hours per night.

Statistical analysis

Statistical analysis was performed using SPSSTM (version 20, IBM Corporation Ltd, USA). Normality was assessed using Shapiro-Wilk's test. Data is expressed as mean (standard deviation or SD) where normally distributed, or median (interquartile range or IQR) where non-normally distributed. Categorical variables are expressed as number (%). Differences in the 95th centile autoCPAP pressure in those with and without OSA (defined as an AHI ≥ 15) were compared. The correlation between measures of obesity (BMI, neck and waist circumference) and measures of sleep severity (AHI, ODI, **AI, HI and apnoea: hypopnoea ratio**) were each compared with the 95th centile autoCPAP pressure. Mann-Witney U tests and Spearman's rank correlation were used as autoCPAP pressure and **sleep parameters** were not normally distributed.

Results

77 patients were recruited. It was not possible to calculate autoCPAP pressures in 23 patients as they did not use autoCPAP for sufficient time (>4 hours per night), leaving a study cohort of 54 patients. 50 of these patients also had inpatient overnight cardiorespiratory sleep studies, with four other patients not attending, thus AHI and ODI could be calculated in a total of 50 patients. Baseline characteristics are displayed in Table 1.

26 patients (52%) had an AHI ≥ 15 events/hour and 19 patients (38%) had an AHI > 30 events/hour.

The median of the 7 night 95th centile autoCPAP pressure was 11.8cm H₂O (IQR 10.7 to 13.7 and 100% range 5 to 19.8).

Patients with OSA had a median (IQR) autoCPAP pressure of 12.8 cmH₂O (11.3, 14.5). Those with an AHI < 15 events/hour had a median pressure of 11.5 cmH₂O (10.1, 12.9). The difference between these two groups was statistically significant ($p=0.02$).

There were statistically significant correlations between autoCPAP pressure and both the AHI and ODI ($r=0.34$, $p=0.02$ and $r=0.48$, $p<0.001$ respectively). Figure 1 shows the relationship between both AHI and ODI, and autoCPAP pressure. **There were also statistically significant correlations between autoCPAP pressure and the AI ($r=0.30$, $p=0.03$), the HI ($r=0.34$, $p=0.02$), and the apnoea to hypopnoea ratio ($r=0.31$, $p=0.03$).**

There were no statistically significant correlations between the autoCPAP pressure and neck circumference ($r=0.17$, $p=0.21$), waist circumference ($r=0.04$, $p=0.78$), nor BMI ($r=-0.09$, $p=0.54$).

In a sensitivity analysis including only patients with obstructive sleep apnoea (AHI ≥ 15 , $n=26$) there remained no significant correlations between autoCPAP pressure and neck circumference ($r=0.29$, $p=0.15$), waist circumference ($r=0.05$, $p=0.82$) or BMI ($r=0.35$, $p=0.08$).

Discussion

This study in very obese patients has shown that autoCPAP pressures are not correlated with measures of obesity (BMI, waist and neck circumferences). However, there was a moderate relationship between autoCPAP pressures and measures of sleep apnoea severity. Increasing weight does not necessarily mean increasing collapsibility of the pharynx during sleep, and thus in this population our previous algorithm would fail to predict the CPAP pressure delivered by an autoCPAP machine.

There are probably several reasons why we only found moderate correlations here, and why our previously derived algorithm [7] would not predict the autoCPAP pressure in this population; the probable reasons are discussed below.

1. Cohort differences

There are several important differences between these individuals and our original cohort of patients [7]. The median BMI in the current study was 43.0 kg/m² compared with a mean of 36.5 kg/m² in our original study. It is possible that the increase in observed autoCPAP pressure plateaued in these very obese individuals, as their median autoCPAP pressure was 11.8 cmH₂O compared to a mean of 9.8cmH₂O in our previous study, which is only slightly higher. In this current study only 52% of patients had an AHI ≥ 15 whereas all our previous study had diagnosed OSA. Patients recruited on the basis of obesity, rather than obstructive sleep apnoea, may tend to have different upper airway anatomy and/or function. However, when only including patients with AHI ≥ 15 in a sensitivity analysis, we found no significant relationships between autoCPAP pressure and measures of obesity. **This sensitivity analysis included only 26 patients and therefore did not have the power to identify statistically significant modest relationships (BMI and autoCPAP $r=0.35$ $p=0.08$, neck $r=0.29$ $p=0.15$) but did exclude stronger correlations ($r \geq 0.39$).**

2. AutoCPAP as a passive rather than active measure of upper airways collapsibility

We observed a moderate relationship between OSA severity and autoCPAP pressure, with significant outliers for whom this relationship did not apply. This is in contrast to the relationship between AHI and P_{crit} found by others [18]. A recent study by Sands *et al.* found less upper airways collapsibility in obese non-apnoeic individuals, as compared to obese apnoeic patients [19]. Obese non-apnoeic individuals showed a three-fold increase in upper airways muscle responsiveness, compared to both obese apnoeics and normal weight controls. This suggests that obese non-apnoeic patients have less collapsible airways, perhaps due to well maintained upper airways muscle responsiveness to collapsing forces. This ability to adequately increase dilator muscle action, in the face of increasing weight-related passive collapsing forces, may be protecting this group from developing OSA. However, because the dilator muscles become inactive during adequate CPAP pressure [20-21], autoCPAP pressure is a passive measure of the collapsing pharyngeal pressures, unlike P_{crit} . AutoCPAP here is therefore measuring anatomic susceptibility, but does not incorporate protective dilator muscle activity, which would clearly explain why some of our patients had high autoCPAP pressures, despite no evidence of OSA.

3. Airflow without pathological consequence

It has been shown that people, with apparently normal sleep studies, can have a degree of inspiratory flow limitation with no consequences [22], to which autotitrating CPAP machines will respond by raising the pressure until the flow limitation is abolished. This work from the Edinburgh group showed no significant difference in the number of resistive (reduced nasal airflow in association with increasingly negative intrathoracic pressure swings) and flow limited events (flattening of nasal inspiratory flow tracing) between patients with upper airways resistance syndrome (UARS) and healthy controls. Patients however, had significantly more arousals and significantly larger pleural pressure swings associated with such resistive events. Healthy controls demonstrated a degree of flow limitation with a median of 12 resistive and 16 flow limited

events/hour, these will trigger an autoCPAP response. Thus if an autoCPAP machine reacts during sleep and delivers pressures above its minimum setting (usually 4cmH₂O), this does not mean that this pressure is required to prevent significant pharyngeal collapse, and is thus not necessarily indicative of the presence of OSA or the need for therapy. **This is supported by our finding that neither apnoeas nor hypopnoeas were strongly correlated with autoCPAP pressure and another factor, such as flow limitation, is likely to be more important in determining autoCPAP pressure.**

Limitations

One of the limitations of this study is that we have not been able to elucidate the cause of the break down in the relationship between autoCPAP pressure and measures of obesity or OSA severity (measured by AHI or ODI). First, it is possible that over a certain threshold of obesity there is simply no longer a relationship between measures of obesity or OSA severity and the CPAP pressure required to treat this OSA. Second, the relationship between measures of obesity, OSA severity and the CPAP pressure needed to truly treat OSA may continue to be valid, but autoCPAP pressure is no longer a correlate of this. Instead, in some individuals, autoCPAP pressure is raised to trivial airflow limitation alone. Finally, it may be that the AHI and ODI are not capturing the pathology, and that responding to this flow limitation is indeed therapeutically useful. Anecdotally, some of the non-apnoeic patients felt better on CPAP but this requires further work.

Conclusions

We found that algorithms for CPAP pressure, based on neck circumference and ODI alone, cannot predict the autoCPAP pressure, and will not reliably determine the fixed pressure required to prevent OSA in morbidly obese populations. Furthermore many obese individuals generated a high autoCPAP pressure without significant OSA. Therefore morbid obesity alone is not enough to develop sleep apnoea and there may be other anatomic or non-anatomic predispositions that either protect, or lead to, the development of OSA.

Authors' contributions

All authors agree to be accountable for all aspects of the work. They have approved this final version. They have been involved in drafting the work and revising it for important intellectual content. AM and JS made substantial contributions to the conception, and design of the study. AM was responsible for data acquisition; AM, CT and JS are responsible for the analysis and interpretation.

Ethical approval

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments. The article does not contain any studies with animals performed by any of the authors.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Conflicts of interest

JS has done consulting work for ResMed UK. AM and CT declare that they have no conflicts of interest.

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Characteristic	Number of patients (n)	Mean (SD), median (IQR) or number (%)	100% Range
Age (years)	54	52.3 (9.0)	26 to 74
Number male (%)	54	27 (50%)	-
BMI (kg/m ²)	54	43.0 (38.6, 52.2)	33.4 to 70.0
Epworth sleepiness score	45	12.8 (5.5)	2 to 22
Neck circumference (cm)	54	46 (4.6)	38 to 57
Waist circumference (cm)	52	131 (122, 143)	99 to 180
AHI (events/ hour)	50	16.6 (6.4, 57.1)	0.1 to 91.6
ODI 4% (events/ hour)	50	45.9 (15.5, 71.2)	6.0 to 156
AI (events/ hour)	50	3.9 (1.1, 29.4)	0 to 82.0
HI (events/ hour)	50	8.6 (3.6, 15.7)	0 to 28.6
Apnoea: hypopnea ratio	49	0.56	0 to 8.5

Table 1: Baseline characteristics of 54 patients having valid autotitrating CPAP results

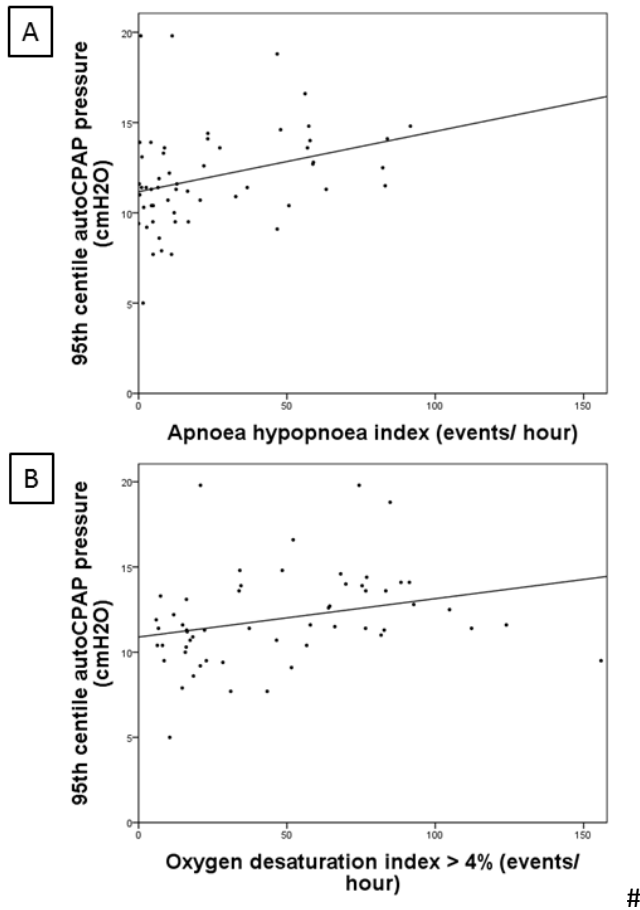


Figure 1: (a) Correlation between the apnoea hypopnea index (events/ hour) and the 95th centile autoCPAP pressure (cmH₂O). (b) Correlation between the oxygen desaturation index >4% (events/ hour) and the mean 95th centile autoCPAP pressure (cmH₂O).

Figure created using SPSS version 20.0 (IBM).