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Dr. Doghramji is a consultant for Pfizer, Teva, Jazz, Xenoport, Merck. He is also part of research study for Inspire therapy for OSA. He is also a stockholder for Merck. The article submitted is not related to these relationships.

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Abstract

Study Objective:

Prior studies have demonstrated reduced inflammation after chronic use of CPAP therapy. This may lead to reduced pressures over time as the upper airway becomes more compliant. We sought to determine if there was a reduction in 90th percentile pressure requirements in patients on Auto PAP for OSA.

Methods:

A retrospective chart review of 988 patients who underwent a sleep study at our sleep center was performed. Those with moderate to severe sleep apnea who were prescribed and compliant with Respironics Auto PAP were included, yielding a total of 46 patients for analysis. All statistical analysis analyses were performed using in SAS version 9.3.

Results:

Mean age of patients was 57.20 years and majority was male. Mean baseline AHI was 43.10. Mean follow up interval was 9.99 months. There was a trend towards decrease in pressure requirements over time, with a mean change of 0.46 cmH20 which was not significant. Patients with a baseline AHI ≥ 50 had a greater decrease in pressure requirements upon follow-up compared to those with an AHI<50. Patients who lost weight over the study period experienced a greater decrease in pressure requirements upon follow-up compared to those who gained weight.

Conclusions:

Our study demonstrated that 90th percentile pressure decreased over time with continuous use of Auto CPAP in patients with severe OSA (AHI >50) and in patients who lost weight.

BRIEF SUMMARY:

Study Rationale: Few previous studies have shown that chronic CPAP use may be lead to reduced upper airway inflammation and edema. We hypothesized that this may lead to reduced pressure requirements over time as the upper airway becomes more compliant. However, there have been no studies that have studied change in pressure requirements with Auto PAP treatment in patients not undergoing bariatric surgery.

STUDY IMPACT:

There was no significant change in pressure requirements for patients with moderate to severe OSA treated with Auto PAP, after a mean follow up interval of 10 months. On subgroup analysis, patients with a baseline AHI ≥ 50 (severe OSA) had a greater decrease in pressure compared to those with an AHI<50 (non-severe OSA), potentially because they tend to lose weight on Auto CPAP while those with AHI<50 gained weight. This suggests that AutoPAP may be more suitable for those with severe OSA.

Introduction:

Repeated closure and opening of the upper airway in obstructive sleep apnea (OSA) can lead to edema, inflammation and reduce upper airway compliance[1]. Studies have reported reduced inflammation after chronic use of continuous positive airway pressure (CPAP)[1] therapy. We hypothesized that this may lead to reduced pressure requirements over time as the upper airway becomes more compliant. Auto CPAP has gained greater acceptance in the last few years due to the high costs associated with in-lab titration and studies demonstrating similar efficacy when compared to fixed CPAP[2]. Hence, we examined the 90th percentile pressures in patients with moderate to severe OSA to determine if there was a reduction in the 90th percentile pressure requirements over time while on treatment with Auto CPAP.

Methods:

A retrospective chart review was performed of 988 patients who underwent a sleep study (from January 2011 to January 2014) after being assessed by sleep specialists at a university-based sleep disorders center. Sleep studies were a combination of home sleep study Type III, in-laboratory polysomnography and split-night studies.

Inclusion criteria included the following:

1. Moderate to severe obstructive sleep apnea (AHI > or =15)
2. Compliant with treatment as defined by Medicare criteria (minimum 4 hours of use for at least 70% of days in a 30 day period)[3]
3. Patients who received treatment with one manufacturer only, the Respironics Auto CPAP were included to diminish variability between different systems

Exclusion criteria:

1. Patients being considered for bariatric surgery
2. Lack of data at 6 months following institution of treatment

Based on these criteria, 46 patients were included in the analysis. Demographic information and 90th percentile pressure information were collected from the data storage card one month, after starting treatment. Subsequent data collection was performed between 6 months (1st measurement) and 1 year (2nd measurement) following institution of treatment.

Statistical Analysis

Descriptive statistics for baseline characteristics and measurements were performed. Mean changes in 90th percentile pressure requirements for each subgroup were compared using t-tests. All statistical analyses were performed in SAS 9.3.

Results:

Baseline characteristics of the study sample appear in Table 1. Notably, as seen in this table, our sample mean AHI was in the severe range (43.1), yet 93.5% reached goal AHI of <10 at first follow up visit (i.e. 4-6 weeks after starting Auto CPAP). Females had significantly higher BMI than males (BMI 39.47 vs 33.01 p=0.045). BMI did not change significantly for the entire group (34.98 vs 34.50 p=0.204). BMI at baseline showed a strong positive correlation with the AHI at baseline (R=0.41, p=0.005). There was no significant change in pressure (-0.46 cmH20, p= 0.118) for the entire group. On subgroup analysis, patients with a baseline AHI ≥ 50 had a greater decrease in pressure compared to those with an AHI<50 (-1.24 vs. -0.05, p=0.05), as did patients who lost weight, 21/46 (45.6%) compared to those who gained weight (-1.14 vs. 0.34, p<0.01).

Discussion

Our study showed that the 90th percentile pressure requirements did not change significantly in patients with moderate to severe OSA treated with Auto CPAP over a mean treatment duration of 10 months. This may be secondary to certain unmodifiable factors leading to apnea such as neck size, structural issues such as retrognathia or tongue size, as well as the presence and location of weight loss. Other factors which potentially can explain lack in pressure change with Auto CPAP use over time, include airway structure of the individual, along with the distribution of excess tissue. At present, it is unknown whether long-term exposure to repeated apneic events can result in permanent changes to the airway and/or central nervous system structures responsible for mediating breathing during sleep[4] which would unmodifiable by Auto CPAP use.

In comparison, previous studies have shown that the upper airway caliber increases following chronic CPAP therapy. This may potentially lead to reduced pressure requirements. In the study by Mortimore et al chronic CPAP therapy was defined as duration of 3 months on CPAP. They also suggested that the magnitude of increase in upper airway caliber is proportional to CPAP compliance (defined in this study as regular use of CPAP for more than 4 hours/night) [1]. Ryan and colleagues studied the upper airway anatomy with MRI in five patients with moderate to severe OSA before and after 4-6 weeks of CPAP therapy and noted that pharyngeal volume and pharyngeal cross sectional area increased, and tongue volume decreased. Oropharyngeal mucosal water content also decreased. These changes were felt to be related to resolution of upper airway edema[5]. Similarly, Schwab et al studied the effect of incremental levels of CPAP (pressure range of 0-15 cm H20) on the upper airway and surrounding soft tissue structures in 10 normal subjects. Progressive increases in CPAP pressure resulted in parallel increase in airway volume and airway area within the retropalatal and retroglossal regions. An inverse relationship was demonstrated between CPAP level and pharyngeal wall thickness[6].

Baetz reported a case where utilization of CPAP for a year completely resolved moderately severe OSA[7]. Series and colleagues noted that nasal CPAP pressures in forty-five patients with OSA decreased from 9.6 cm H20 to 7.7 cm H20 during the first eight months of treatment. The decrease in CPAP pressure plateaued after 8 months and was greater when the initial CPAP pressures were higher. The authors postulated that an improvement in upper airway morphology, correction of sleep fragmentation and changes in ventilatory control were the main mechanisms were accountable for these changes[8]. Jokic et al noted that CPAP pressure requirements in patients with severe OSA fell within 2 weeks of starting CPAP treatment[9].

Reduced pressure requirements could potentially have several benefits for our patients. It could lead to improved tolerance to CPAP, although this possibility has never been previously demonstrated. Reduction in pressure requirements may result in reduced changes in intrathoracic pressure, potentially with an increase in venous return and cardiac output. This may be especially true for patients with congestive heart failure as their hemodynamics are very sensitive to changes in preload and afterload. Other CPAP complaints which may be pressure related include nasal or sinus pressure, flatulence, chest discomfort which could potentially improve with exposure to lower CPAP pressure[10,11]. Difficulty with mask fitting and air leaks are also more common with higher CPAP pressure [12].

On subset analysis in our study, patients with a baseline AHI ≥ 50 (severe OSA) had a greater decrease in pressure requirements compared to those with an AHI<50 (non severe OSA) as did patients who lost weight, 21/46 (45.6%) compared to those who gained weight (Table 2). One plausible explanation for this finding is that patients with severe OSA had a tendency to lose more weight when compared to those with non-severe OSA. A greater proportion of patients with severe OSA lost weight (69%) compared to those with non-severe OSA (33%). This may indicate that weight loss is a significant factor in determining decreases in average pressure requirements. Interestingly, patients with AHI <50 had a tendency to gain weight as opposed to lose weight on Auto CPAP. Previous studies have shown conflicting results on the effect of CPAP in OSA on weight change[13,14]. Our study shows that those with AHI>50 tend to lose weight on Auto CPAP while those with AHI<50 gained weight. The weight loss certainly can explain the reduced pressure requirements in this group based on reduced upper airway collapsibility as described in previous studies[15]. Other studies have also implicated obesity via inflammation, insulin resistance, visceral adiposity, and central neural mechanisms, e.g. hypofunctioning hypothalamic CRH to play a major role in the pathogenesis of sleep apnea, sleepiness, and the associated cardiovascular co-morbidities[16]. To our knowledge this is the first study that describes association of weight loss with reduced pressure requirements in severe OSA patients not undergoing bariatric surgery.

Another possible reason for lack of significant pressure change over time in our study group, when compared to previous literature, is use of an Auto titrating PAP device. Previous studies studied pressure changes with fixed CPAP device, whereas this study utilized an Auto titrating PAP device to look at pressure changes over time (in a non-bariatric surgery population). Certainly the fluctuation in pressure requirements based on day to day variability and intranight variability in severity of sleep apnea could lead to potential lack of change in pressure requirements over time in this group.

Limitations of the study include small sample size, different types of sleep studies were obtained at the time of diagnosis which may preclude detection of accurate AHI. We did not review average hours of use of CPAP for patients, other than documenting compliance by Medicare guidelines, which may be insufficient usage to improve upper airway compliance. It has been suggested that patients with more severe OSA maybe more motivated to use their CPAP because of potentially greater relief of symptoms and greater disease related sequelae[17]. This may potentially explain the reduced pressure requirements in this subset. If conducted on a prospective basis with a greater sample size, it would also provide a clearer picture of the relationship of weight loss to CPAP pressure changes especially in patients with severe OSA.

In conclusion, our study demonstrated that 90th percentile pressure decreased over time with continuous use of Auto CPAP in patients with severe OSA (AHI >50) and in patients who lost weight.

Variable	Mean	SD	Maximum	Minimum
Age (yrs)	57.2	11.4	78.0	30.0
Change in 90th percentile Average Pressure (AVP) Requirements (cm H_2O)	-0.5	2.0	4.9	-6.7
Time between follow-up (months)	10.0	4.4	24.3	4.7
Apnea Hypopnea Index (AHI, baseline)	43.1	24.1	105.7	15.0
AHI 1st measurement	4.1	3.5	16.1	0.2
AHI 2nd measurement	3.7	4.1	22.7	0.3
BMI 1st measurement (kg/m^2)	35.0	8.1	59.3	23.3
BMI 2nd measurement (kg/m^2)	34.5	7.5	54.0	23.4
Change in BMI (kg/m^2)	-0.5	2.5	4.6	-9.7

Table 1: Baseline Characteristics (N=46)

Subgroups	N (patients)	Mean (± SD)	P-value
Baseline AHI			0.048
AHI < 50	30	-0.05 ± 1.93	
AHI ≥ 50	16	-1.24 ± 1.81	
Age			0.053
≥ 65 years	14	0.38 ± 1.47	
< 65 years	32	-0.83 ± 2.05	
Gender			0.840
Males	32	-0.50 ± 1.99	
Females	14	-0.37 ± 1.95	
Obesity			0.694
Obese (BMI ≥30)	34	-0.53 ± 2.00	
Non-obese (BMI < 30)	12	-0.27 ± 1.92	
Weight Change			0.002
> 0 kg	25	0.34 ± 1.46	
≤ 0 kg	21	-1.41 ± 2.08	

Table 2: Demographic sub group analysis

Table 3

Statistics by Weight Difference

Variable: Weight change (lbs)

Weight_cat	N	Mean	Std Dev	Std Err	Minimum	Maximum
Lost weight (1)	21	-6.3852	7.4671	1.6295	-29.4500	0
Gained weight (2)	25	3.4144	2.7901	0.5580	0.4500	13.1800
Diff (1-2)		-9.7996	5.4397	1.6102		

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