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Original article

Effects of short-term PAP treatment on endurance exercise performance in obstructive sleep apnea patients

D. Edward Shifflett Jr[a], Eric W. Walker[a], John M. Gregg[b], Don Zedalis[c], William G. Herbert[d,*]

[a]*Laboratory for Health and; Exercise Sciences, 230 War Memorial Hall, Virginia Polytechnic Institute and State University, Blacksburg, VA 24061, USA*

[b]*Department of Biomedical Sciences and Pathobiology, Virginia-Maryland Regional College of Veterinary Medicine, Blacksburg, VA 24061, USA*

[c]*Sleep Disorders Network of Southwest Virginia, 2955 Market Street, Christiansburg, VA, USA 24073*

[d]*Laboratory for Health and; Exercise Sciences, 213 War Memorial Hall, Virginia Polytechnic Institute and State University, Blacksburg, VA 24061, USA*

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Abstract

Objective: To measure the effects of 4 weeks of nasal positive airway pressure therapy (PAP) on exercise performance in obstructive sleep apnea patients (OSA).

Background: Little published research is available which describes the effects of OSA on exercise tolerance or upon the potential of exercise testing to evaluate the outcomes of PAP therapy.

Methods: Exercise testing was performed on an electronic cycle ergometer with continuous ramping to allow collection of numerous data points for each subject, up to a vigorous terminal intensity. Linear regression established each subject's pre-treatment scores for the dependent variables at 60% of estimated peak power ($W_{60\%}$). Responses at the pre-treatment $W_{60\%}$ test were used to quantify and compare to responses at the same power output after treatment.

Results: OSA by nocturnal polysomnography was moderately severe in this group; the respiratory distress index was 48 ± 22 (mean ± SD; $n = 9$). Exercise heart rates after PAP therapy averaged 10.2 bt/min less at $W_{60\%}$ ($P < 0.05$). Other variables were lower but non-significantly so, further suggesting a lower cardiorespiratory exercise demand after treatment, i.e. oxygen consumption (↓7.6%), and Rating of Perceived Exertion (↓8.8%).

Conclusion: Brief treatment with PAP therapy improves objective markers of aerobic exercise performance.

Keywords: Obstructive sleep apnea, Nasal continuous positive pressure breathing treatment, Exercise tolerance, Oxygen consumption, Perceived exertion, Exercise heart rate, Exercise blood pressure

1. Introduction

Obstructive sleep apnea (OSA) is a serious health disorder of the upper airway that afflicts 1–4% of the population [1–2]. OSA is associated with increased risk for cardiovascular disease conditions, including

* Corresponding author. Tel.: +1-540-231-6565; fax: +1-540-231-8476.

E-mail address: wgherb@vt.edu (W.G. Herbert).

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myocardial ischemia [3–4] and myocardial infarction [5]. Continuous or variable nasal positive airway pressure (PAP) is a non-invasive first-line therapy used to treat this disorder. A few investigations have shown that PAP reduces resting blood pressure in the OSA patient [6–7].

Information concerning exercise tolerance of OSA patients is notably limited in the published literature, as is evidence of the potential for physical activity to enhance long-term medical management of OSA patients [8–14]. Furthermore, the quantification of exercise tolerance may add new and clinically meaningful data to the process of grading disease severity in OSA patients or in assessing treatment outcomes following alternative interventions. Once airway patency and the apnea–hypopnea index (AHI) have been improved with a trial of PAP therapy or surgical interventions, might the capacity for performing physically demanding exercise improve? Such an outcome, in response to short-term PAP therapy for example, would have direct implications for spontaneous resumption of vigorous physical activities in daily living and for consideration of exercise in the long-term management of those OSA patients who are able to adhere to PAP therapy. The study reported here is foundational to these issues. The objective was to determine the effects of short-term PAP treatment, for newly diagnosed patients with moderate-severe OSA, on the cardiorespiratory and perceptual costs of aerobic exercise.

2. Methods

Subjects were nine non-consecutive volunteer patients referred for evaluation to the Sleep Disorders Network of Southwest Virginia, Christiansburg, VA, between November 1997 and February 1998. The Virginia Tech Institutional Review Board approved the study protocol and each subject gave informed consent before participation. The mean values for age in years and for BMI in kg/m^2 were 52 and 30.3, respectively. Medical records were reviewed to exclude candidates with the following physician-diagnosed conditions: coronary artery disease; uncontrolled hypertension or diabetes mellitus; chronic obstructive pulmonary disease; carotid vascular disease; orthopedic or musculoskeletal disabilities that precluded exercise; and a recent history of regular participation in moderately vigorous physical activity. At baseline, each patient completed an overnight polysomnography study (PSG) from which a diagnosis of OSA was made. Immediately upon arising in the morning following the PSG study, subjects completed a ramping cycle ergometer test. The exercise test was completed again at 4 weeks after PAP therapy.

2.1. Polysomnography and administration of PAP treatment

A trained technician performed the PSG studies, all of which were performed at our clinical facilities. A full-night PSG study was performed with each patient. Conventional techniques were utilized when performing the PSG studies and were similar to those previously published [15,16].

Patients with resulting AHI scores >5 and identified as candidates for positive airway pressure therapy (either constant or variable PAP) were asked to return to the Sleep Center on a second night to undergo a repeat PSG for the purpose of PAP titration. Continuous or variable PAP flow generators were accepted by these patients (Sullivan® V Elite or VPAP® II; ResMed, San Diego, CA) and were equipped with electronic means for monitoring hours of daily usage. Upon accepting PAP treatment, each patient was requested to use the devices on a nightly basis and then return to the Center 4 weeks later to complete the exercise test again.

2.2. Cycle ergometry test procedures

Each subject performed a total of three submaximal cycle ergometer tests in our clinical facilities and all tests were completed in the early morning. The first was administered just after the patient completed their overnight PSG study. The second exercise test was completed within 7 days of the first, immediately after the patient's PAP titration PSG study at our facility. The final exercise test was completed 4 weeks after the start of PAP therapy, with the patients coming to our facility soon after arising from a night of sleep with PAP therapy in their homes. The following measures were obtained in each exercise test: height; weight; blood pressure and heart rate at rest in a sitting posture; and BMI. The exercise tests were performed on a Medgraphics® electronically-braked

stationary cycle ergometer (Cardio2, St. Paul, MN). The loading rate for the ramping of the exercise test was pre-determined on the basis of each subject's body weight and their self-rating of exercise tolerance. This permitted matching of the ramp rate to individual capabilities, so that each subject would reach an intensity of 75% $\dot{V}O_2$pk within 17 ± 2 min, i.e. △ 6, 9, or 12 W/min at 50 rev/min. Exercise was monitored by trained technicians and provision was made to terminate exercise upon appearance of adverse responses, or when 75% of the age-adjusted predicted heart rate reserve and a perceived exertion of 16 (Hard$^+$ exercise) [17] were attained. Ratings of perceived exertion and arterial blood pressure via auscultation were taken at 3-min intervals. The blood pressure measurements were averaged from simultaneous values taken by two technicians who used a teaching stethoscope. Heart rhythm and rate were assessed from continuous ECG monitoring throughout exercise. Respiratory gas exchange measurements including oxygen consumption ($\dot{V}O_2$) were made throughout exercise using a computer controlled breath-by-breath gas exchange system (Sensormedics Vmax® 22, Yorba Linda, CA).

2.3. Data analysis

Results from the pre-PAP and 4 week post-PAP exercise tests were evaluated on the basis of exercise test scores derived from linear regressions of individual subject test results. These regressions were established for several responses, in each case using data for work rate (W) heart rate (HR); oxygen consumption ($\dot{V}O_2$); systolic blood pressure (SBP); and perceived exertion (RPE). Utilizing the slopes and intercepts for each subject's regression for the pre-PAP condition, the power output at the estimated functional capacity was predicted ($W_{100\%}$). The intercepts on the HR, $\dot{V}O_2$, SBP, and RPE regression lines that coincided with each subject's age-adjusted predicted maximal heart rate were accepted as their maximums ($W_{100\%}$). The subject's pre-PAP score for each dependent measure then was selected as the HR, $\dot{V}O_2$, SBP, or RPE that corresponded to a demand level of $W_{60\%}$. Scores for the post-PAP test were derived in the same way so that direct comparisons could be made for each measure at the same pre-PAP load of $W_{60\%}$. Changes between the pre and post-PAP conditions were analyzed by dependent t-tests.

3. Results

Descriptive and PSG data for the subjects who participated in this study are presented in Table 1. Application of multiple exclusion criteria utilized in this study limited the size of the sample that could be recruited. Eight of the nine subjects were males and the age range was 37–74 years. All of the patients in this group met BMI standards for Grade 1 or 2 obesity. This group had moderate-severe OSA, as suggested by a mean AHI of 47.5 (range = 24–90). The cardiopulmonary and perceived exertion results for the exercise tests at the pre-PAP and post-PAP trials are presented in Table 2. After treatment with PAP, heart rates at $W_{60\%}$ were significantly lower by an average of 10.2 bt/min (T-ratio = 2.41; $P = 0.043$). Yet, neither heart rate nor systolic blood pressure responses at rest were different after PAP therapy (not shown in Table 2 ; mean changes in these variables at rest were <2 bt/min and 4 mmHg after PAP treatment, respectively). Thus, resting status for these two variables did not affect the corresponding exercise responses. Upon analysis of the regression of

Table 1
Subject characteristics and polysomnographic test results at baseline (N =9)

Physical measures	Mean	SD	Range
Age (years)	51.6	12.9	37–74
Weight (kg)	91.9	6.9	79–102
BMI (kg/m^2)	30.3	3.1	26–33
Heart rate (bt/min)	84.6	4.2	79–91
Blood pressure (mmHg)			
Systolic	129.1	16.2	102–144
Diastolic	83.6	12.6	70–98
PSG test measures			
AHI	48.0	21.6	24–90
Time in bed (min)	361.1	40.5	263–402
Total sleep time (min)	291.6	40.5	236–336
Awake (min)	76.6	40.6	22–126
Stage 1 (min)	53.7	47.7	7–144
Stage 2 (min)	150.5	71.3	51–253
Slow wave sleep (min)	19.9	10.8	3–35
REM (min)	28.5	24.1	0–79
Baseline SaO_2	94.4	1.7	92–97
Lowest SaO_2	80.1	9.7	67–94

Table 2
Cardiopulmonary and perceptual responses to cycle ergometer exercise at $W_{60\%}$ intensity for osa patients before and after 4-week PAP treatment[a]

Variable	Pre-PAP	Post-PAP
Heart rate (bt/min)	135.1	126.9[b]
	7.4	12.2
Systolic blood pressure (mmHg)	182.4	180.7
	22.2	16.1
$\dot{V}_E$STPD (L/min)	54.4	50.3
	12.9	12.1
$\dot{V}O_2$ (L/min)	1.85	1.71
	0.44	0.33
Rating of perceived exertion (6–20)	16.0	14.6
	2.6	2.2

[a] Values are means and standard deviations ($N = 9$).
[b] Changes in heart rate were significant at $P < 0.05$.

RPE across the full range of exercise intensities between $W_{10\%–70\%}$ for the entire group, the mean slope of RPE was found to be significantly lower ($P = 0.04$) in the *P*ost-PAP test. A secondary analysis revealed a 36% shared variance between severity of OSA (AHI score) before treatment and the individual changes observed in RPE at the *W*60% exercise load after PAP treatment (Fig. 1). Thus, patients with the worst scores on their initial PSG study tended to have a greater reduction in reported effort needed to perform exercise at a moderately demanding load after treatment. Similar analyses between initial AHI scores and other exercise variables, however, did not disclose statistically significant relationships.

4. Discussion

This study demonstrates that a trial of PAP as brief as 4 weeks for patients with moderate-severe OSA is accompanied by enhanced aerobic exercise tolerance. Our cycle ergometer exercise scores reflected pre-treatment aerobic performance at a load of 100 W. This approximates 63% of the aerobic capacity for these patients, corresponding to an oxygen consumption of 20 ml/kg/min. This level of metabolic demand characterizes the upper limit of daily physical activities that might be sustained, at least for several min, in fairly demanding occupational and recreational tasks. Examples include scrubbing floors, vigorous walk/running activities with children, hiking on clear trails, and downhill skiing [18]. After PAP treatment, the same workload required only 51% of the apparent aerobic capacity of these subjects, i.e. 12% less of their peak power. These estimates of improved fitness are based on the assumption that the PAP treatment did not alter either the resting or maximal heart rate. We were able to document that resting heart rate did not change after PAP treatment. Although we did not assess change in maximal exercise heart rate, such a change would not be expected and in any case unlikely to affect our estimate of fitness improvement

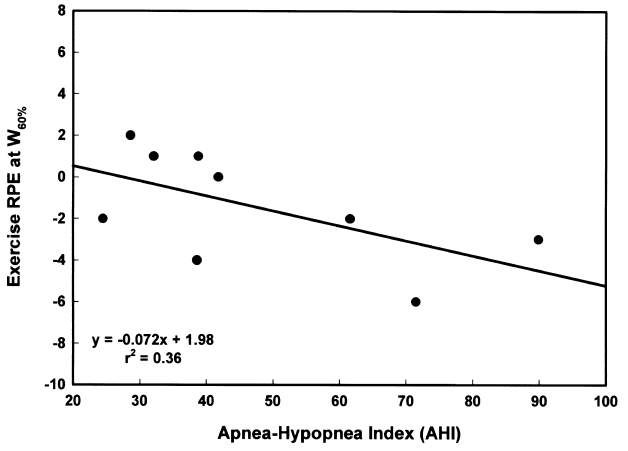

Fig. 1. Relationship between severity of obstructive sleep apnea by the apnea/hypopnea index (AHI) and change in perceived exertion (RPE) during cycle ergometry exercise at the reference workload, $W_{60\%}$, after 4 weeks of PAP treatment.

associated with PAP. Heart rate at high intensities of aerobic exercise is modulated largely by sympathetic activity, with minimal effects exerted by the parasympathetic system [19]. Nevertheless, at the moderate exercise intensity that we tested our subjects increased parasympathetic tone likely contributed to the reduced heart rate response observed after PAP treatment. It is well established that OSA is associated with high levels of sympathetic nervous activity during sleep and wakefullness [19–22] and that these sympathetic effects are ameliorated by PAP treatment [19,23].

In our study, respiratory gas exchange variables during exercise, such as $\dot{V}O_2$ at the $W_{60\%}$ workload, did not change after PAP treatment. Because their OSA patients had blood lactate responses during exercise that were lower than controls, Vanuxem's group [13] concluded that OSA patients might have impaired glycolytic and oxidative muscle metabolism. This question deserves further investigation; particularly the possibility that impaired skeletal muscle metabolism is mediated by high levels of sympathetic activity in OSA patients and whether this may be reversed by PAP therapy.

While seven of nine subjects in our study showed improved exercise tolerance based on heart rate results, there was considerable individual variability reflected in all exercise variables following PAP treatment. Several mediating factors could potentially account for this variability in the exercise outcome, including day-to-day adherence to PAP therapy, severity of OSA, physical fitness, changes in body weight or alcohol consumption, or changes in physical activity levels after beginning PAP treatment. Changes in exercise tolerance may occur from habituation, when subjects perform exercise tests on repeated days, even without a treatment interposed. This limitation may be addressed by a randomized design and contrasting exercise test results for a PAP treatment group with a group performing repeat exercise tests at the same intervals, but without OSA intervention. Though we did not conduct a randomized study with a control group, the habituation effect was not likely a factor in our patients' responses at the 4 week post-treatment evaluation. We exercise tested all of the study patients twice before PAP therapy was started and found no changes between these two tests for any of exercise variables reported here. PAP use is well known to be problematic for selected patients and poor adherence has been documented to preclude physiological benefits that otherwise are associated with this treatment, such as reduction in blood pressure [20]. In our sample, the improvement in the rating of perceived exertion during exercise tended to be greater in those with higher AHI scores (Fig. 1). The correlation between these two variables was only moderate at $r = -0.60$ ($P < 0.10$), but does suggest that severity of OSA had a moderate influence on how much better these patients felt after PAP therapy when they performed exercise at the $W_{60\%}$ exercise intensity. Paradoxically, correlations between AHI and exercise results after PAP treatment for heart rate, systolic blood pressure, and VO_2 showed no meaningful interdependence. Utilization data from the PAP flow generators were available for eight of the nine study patients at the 4-week follow-up. This data suggested that apparent adherence was not uniform among these patients for the 4-week treatment period. Total use averaged 23.5 days with a range of 8–28, while average time of use/day was 6.0 h/day of recorded use with a range of 2.6–8.1. None of these PAP adherence variables showed a positive correlation with improved responses to the $W_{60\%}$ load after PAP treatment with these patients. Over the 4-week period of PAP treatment, there were no body weight changes in our patients. Only one study patient was receiving any cardioactive medication at the outset of the study, i.e. a beta-blocker and, when queried, this patient indicated no change in medications after PAP treatment. Thus, despite examination of several potential confounding factors, we are left without a clear explanation of the individual variability in patient responses to exercise after short-term PAP treatment.

In general, the published research indicates that PAP treatment is associated with improved exercise capacity [8–10]. Taguci et al. [9] showed that OSA patients improved their maximal oxygen uptakes by 15.4% after only 7 days of PAP therapy. Konnermann et al. [8] utilizing a 'cardiovascular efficiency' index for exercise, found that OSA patients' work rate at maximal effort increased by 27.5% after 6 months of PAP treatment. Additionally, they noted a 15–20% greater efficiency in their patients exercise heart rate and blood pressure ratios.

Our study extends the research information avail-

able on the range and quantitative beneficial outcomes of PAP treatment. We documented an improvement in the cardiovascular response to moderately vigorous aerobic exercise after 4 weeks of PAP treatment, at a submaximal level representing the upper limit of common daily occupational and recreational physical activities. Our findings are consistent with those of the Konnerman group [8] in Europe and our findings extended those of Konnerman et al. [8] by providing evidence that the exercise heart rate improvements after PAP are not due to a reduction on oxygen demand of exercise. Specifically, our data showed reductions in heart rate without corresponding changes in exercise VO_2 and V_E after PAP treatment at the same workload. In contrast to the Taguchi group[9], we did find that OSA patients improved their heart rate responses to submaximal exercise after a period of PAP treatment. Our exercise test methodology was based upon objective physiologic indicators derived from responses collected across a wide range of demand levels ($W_{0\%} - W_{75\%}$).

We conclude that PAP therapy administered over 4 week results in significant increases in aerobic physical fitness, which is accompanied by patient perceptions of better sleep, improved health-related quality of life, and ratings of physical vitality. These results suggest that OSA patients, once effectively initiated on PAP therapy, have an improved capacity to participate comfortably in aerobic exercise.

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