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Improvement of Exercise Performance with Short-Term Nasal Continuous Positive Airway Pressure in Patients with Obstructive Sleep Apnea

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Taguchi, O., Hida, W., Okabe, S., Ebihara, S., Ogawa, H., Kikuchi, Y. and Shirato, K. *Improvement of Exercise Performance with Short-Term Nasal Continuous Positive Airway Pressure in Patients with Obstructive Sleep Apnea.* Tohoku J. Exp. Med., 1997, **183** (1), 45-53 —— We examined the effects of nasal continuous positive airway pressure (CPAP) on exercise performance in patients with obstructive sleep apnea (OSA). Six patients were treated with nasal CPAP on seven successive days and underwent overnight sleep studies and multiple sleep latency test (MSLT) at the beginning and after the last day of the treatment. The subjects also performed incremental exercise testing using a bicycle ergometer followed by 0-w, 25-w, 50-w, — (3 minutes each) until maximum level. Arterial oxygen pressure, arterial carbon dioxide pressure at rest while awake, apnea/hypopnea index, longest apnea duration, the lowest percutaneous oxygen saturation measured by a pulse oximeter and the value of MSLT were significantly improved after nasal CPAP. Moreover, maximal oxygen consumption was significantly increased from 1841 ml/min$\pm$350 to 2125 ml/min$\pm$351 ($p<0.05$); however, other cardiorespiratory parameters did not change significantly. The improvement of exercise performance by short-term nasal CPAP treatment in OSA patients may correlate with the improvement of sleepiness. ———— oxygen consumption; sensation of dyspnea; bicycle ergometer; sleep deprivation

Hypoxemia by repetitive apneas, sleep depriviation (SD) by frequent microarousal, excessive daytime sleepiness, moods change and psychological dysfunction frequently occur in obstructive sleep apnea (OSA) syndrome (Yesavage et al. 1985; McNamara et al. 1993). On the other hand, a treatment by nasal continuous possitive airway pressure (CPAP) for OSA patients eliminates obstructive apneas and hypopneas, and improves overall sleep symptomatology (Sullivan et

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al. 1981; Sullivan and Grunstein 1989). To our knowledge, however, there have been few studies about effects of nasal CPAP on exercise performance in OSA patients. The effects of SD on exercise performance and psychiatric changes have been well investigated. Most studies indicated that SD has deleterious effects on psychiatric states including mood, cognitive performance and perceived exertion (Martin 1981; Martin and Gaddis 1981; Martin and Chen 1984; Martin et al. 1986; Plyley et al. 1987; Orton and Gruzelier 1989; VanHelder and Randomski 1989). Furthermore, some papers reported that SD decreased maximal oxygen consumption ($\dot{V}O_2max$) (Bond et al. 1986; Martin et al. 1986; Plyley et al. 1987; Chen 1991).

If nasal CPAP improves SD and daily activity in OSA patients, nasal CPAP may also improve exercise performance. In the present study, we investigated the effects of nasal CPAP on exercise performance using a bicycle ergometer in patients with OSA.

Subjects and Methods

Subjects

Six men (age 44.7 ± 13.7 years; body mass index [BMI] 29.9 ± 2.3 kg/m^2; mean $\pm$ S.D.) with OSA previously diagnosed by polysomnography were recruited for this study. All had been engaged in sedentary physical activities and were habitual snorers and complained of excessive daytime sleepiness. All were clinically stable and free from cardiorespiratory diseases. Each subject gave informed consent to the protocol.

Pulmonary function testing

Vital capacity (VC) and forced expiratory volume in one second (FEV_1) were measured with a 13.5 liter spirometer (Tatebe Seishudo Co., Tokyo). The predicted normal values of Cotes (1993) were used. A 2 ml arterial blood sample was drawn anaerobically before the exercise to measure arterial blood gas tensions and pH with a pH/blood gas analyzer (Model 213; Instrumentation Laboratories, Lexington, MA, USA).

Sleep study

The overnight sleep study was performed in a quiet, darkened room in our hospital using standard polysomnographic techniques (Rechtschaffen and Kales 1968), in the similar manner as in the previous study (Hida et al. 1994). Briefly, an electroencephalogram(C4/A1 and C3/A2), electrooculogram, electromyogram, airflow at the nose and mouth were recorded with two thermistors, respiratory movement with inductive plethysmography (Respitrace; Ambulatory Monitoring, Ardsley, NY, USA) and percutaneous arterial oxygen saturation (SpO_2) with a pulse oximeter (Biox 3700; Ohmeda, Boulder, CO, USA) were simultaneously measured. All variables were continuously recorded on a multichannel thermal

polygraph (Recti-horiz-8K;NEC San-ei, Tokyo) and a data recorder (A-109; Sony, Tokyo).

Apnea was defined as a cessation of airflow at the nose and mouth lasting longer than 10 seconds (McNamara et al. 1993). Hypopnea was defined as more than 50% reduction in thoracoabdominal amplitude (Respitrace sum signals) associated with a reduction in SpO_2 of more than 4% from the preceeding values (Gould et al. 1988).

Multiple sleep latency test

A multiple sleep latency test (MSLT) was performed to assess sleepiness according to the recommendation of the American Sleep Disorders Association (Carskadon et al. 1986). The subjects were placed in a dark room for 20 minutes four times a day (10 : 00 a.m., 12 : 00 p.m., 2 : 00 p.m., and 4 : 00 p.m.). All the subjects maintained a sleep diary from one week prior to the experiment to confirm that they had not deviated from their usual routine. Polysomnographic recordings were obtained during the measurement. Sleep latency was measured when the first epoch of any stage of sleep appeared. Each sleep latency time was measured and then the mean value of four sleep latency times was calculated.

Exercise testing

Exercise was performed on a seated bicycle ergometer (Model 18070; Godart, Utrecht, the Netherland). The temperature of the room was monitored at 26± 2°C to avoid the effect of changes in temperature on metabolism. To eliminate learning or habitual effects, all the subjects were requested to perform one or two familiarization trials prior to the beginning of the study. The test consisted of 3 minutes at rest (quietly sitting) followed by 3 minutes at each of 0-, 25-, 50-, 75-w — work loads. Subjects were asked to fix their pedal rate at around 60 rpm at all work loads. Since motivation might affect the results of the experiment, each exercise was performed with vocal encouragement. Expiratory airflow was measured at the expiratory line through a directional low resistance mask (Model 7900-M; Hans Rudolph, Kansas City, MO, USA) by the pressure drop across a heated (37°C) pneumotachograph with a differential pressure transducer (MP 45± 5 cm H_2O; Validyne Corp., Northridge, CA, USA) and electrically integrated to obtain minute ventilation (VE). Respiratory rate (RR) was obtained from the expired flow signal. Samples of mixed expired gas were analyzed on a breath-by-breath basis to calculate oxygen consumption ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$) using an Aerometer AE-280S (Minato, Tokyo)(Midorikawa et al. 1997). $\dot{V}O_2$max was determined by a plateau of $\dot{V}O_2$, as defined by established criteria (Mitchell et al. 1958).

Heart rate (HR) was monitored with an electrocardiographic signal measured with Kartizer 5500 (NEC, Tokyo). Blood pressure was measured with a photoelectric plethysmography (Finapress, Ohmeda, Englewood, CO, USA) dur-

ing the last 30 seconds of each work load. The subjects were asked to rate the sensation of difficulty in breathing (dyspnea) using a modified Borg category scale (zero to 10) (Borg 1970) during the last 30 seconds of each work load. The term "difficulty in breathing" was not defined any further for the subjects, and they were instructed not to assess nonrespiratory sensations such as headache or irritation of the pharynx.

No subjects were allowed to take any medication including sedatives, nor caffenated drinks or any other beverages other than water. Cigarette smoking was prohibited during the experimental session (Only one subject was a current smoker and the rest had never smoked). Ordinary meals served at the hospital were permitted.

Protocol

Six subjects underwent pulmonary function testing during the day and overnight polysomnography beginning at 9 : 00 p.m. on day 0. On day 1, an MSLT was begun at 10 : 00 a.m. and ended at 4 : 00 p.m. followed by exercise testing beginning at 4 : 30 p.m. Before the exercise testing, arterial blood samples were collected to analyze blood gas tensions and hemoglobin concentrations. On the night of day 1 application of nasal CPAP was initiated in each subject and both thoracoabdominal movements and SpO_2 were monitored. The magnitude of pressure applied to the mask was adjusted to abolish snoring and apnea, and to maintain SpO_2 at more than 90% during the whole night. From days 2 through 7, nasal CPAP was applied with the same pressure as on day 1 and its effectiveness was ascertained by the absence of a drop in SpO_2 below 90%. On day 7, the overnight polysomnographic study was performed under nasal CPAP treatment. On day 8, MSLT and exercise testing including analysis of arterial blood gas tensions and hemoglobin concentrations were performed in the same manner as on day 1. All measurements and nasal CPAP therapy for subjects were performed during admission to our hospital.

Statistical analysis

The results are given as means $\pm$ S.D. Comparisons between the results were made by two-tailed paired t-test. Statistical significance was assumed at a p-value <0.05.

Results

In all cases spirometry was within normal limits (VC $=4.00\pm0.46$ liter, % VC $=107.0\pm15.7\%$, $FEV_1=3.32\pm0.50$ liter, $FEV_1\%=83.0\pm3.9\%$). Table 1 shows the effects of nasal CPAP on basal pulmonary functions and other parameters. Body weight did not change significantly at the second measurement. $PaCO_2$ before nasal CPAP was hypercapnic, and decreased significantly after nasal CPAP, and PaO_2 was significantly increased after the treatment. However,

TABLE 1. *Body weight, cardiorespiratory variables at rest, apneic episodes and MSLT before and after seven-days nasal CPAP treatment*

	Before	After
Body weight (kg)	83.2±6.6	82.0±6.9
Blood gas analysis		
pH	7.365±0.024	7.377±0.016
$PaCO_2$ (torr)	47.1±3.4	43.6±2.6**
PaO_2 (torr)	77.3±2.7	82.2±6.3*
Hemoglobin (g/100 ml)	16.8±1.1	16.5±0.9
Respiratory parameters		
$\dot{V}E$ (liter/min)	10.0±2.1	9.6±1.9
RR (min^{-1})	16.4±4.4	17.0±3.1
$\dot{V}O_2$ (ml/min)	279±45	268±21
$\dot{V}CO_2$ (ml/min)	243±40	235±22
Borg score	0.4±0.8	0.4±0.8
Circulation parameters		
HR (min^{-1})	87.3±12.8	73.5±9.1
SBP (mmHg)	124±20	114±5
DPB (mmHg)	90±18	73±4
Sleep study		
AHI (hr^{-1})	62.5±8.6	1.3±2.3**
Longest apnea (s)	71.5±19.4	5.3±8.6**
Lowest SpO_2 (%)	43.2±4.0	93.2±1.3**
MSLT (min)	4.1±2.7	7.4±2.4*

$\dot{V}E$, minute ventilation; RR, respiratory rate; $\dot{V}O_2$, oxygen consumption; $\dot{V}CO_2$, carbon dioxide production; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; AHI, apnea hypopnea index; SpO_2, percutaneous arterial oxygen saturation; MSLT, multiple sleep latency test.

Values are mean±S.D.

*$p<0.05$; **$p<0.01$

the hemoglobin concentration did not differ significantly between before and after the intervention. Minute ventilation ($\dot{V}E$), RR, $\dot{V}O_2$, $\dot{V}CO_2$, Borg score, HR, systolic blood pressure (SBP) and diastolic blood pressure (DBP) did not change significantly. Apnea/hypopnea index (AHI) and longest episodes of apnea were significantly reduced after nasal CPAP treatment with a significant improvement in the lowest SpO_2. Pressure applied to the subjects ranged from 8–10 cm H_2O except in one case which was 15 cm H_2O. The mean value of MSLT was significantly improved after the intervention.

Table 2 and Fig. 1 show the effects of seven days of nasal CPAP on exercise performance. $\dot{V}O_2$max was significantly improved from 1841±350 ml/min

TABLE 2. *Cardiopulmonary variables at maximum exercise level and anaerobic threshold before and after seven-days nasal CPAP treatment*

	Before	After
Respiratory parameters		
$\dot{V}E$ (liter/min)	68.3±16.7	73.8±19.9
RR (min^{-1})	35.1±10.0	34.8±6.4
$\dot{V}O_2$ (ml/min)	1841±350	2125±351*
$\dot{V}CO_2$ (ml/min)	2162±359	2413±549
Borg score	7.5±1.9	7.1±1.1
Circulation parameters		
HR (min^{-1})	134.0±28.1	131.0±30.2
SBP (mmHg)	186±35	196±31
DPB (mmHg)	109±32	105±14
TET[a] (min)	19.5±4.1	20.0±4.1
Anaerobic threshold		
AT (ml/min)	985±161	1050±139

[a] TET, total exercise time.
Values are means±S.D.
*$p<0.05$

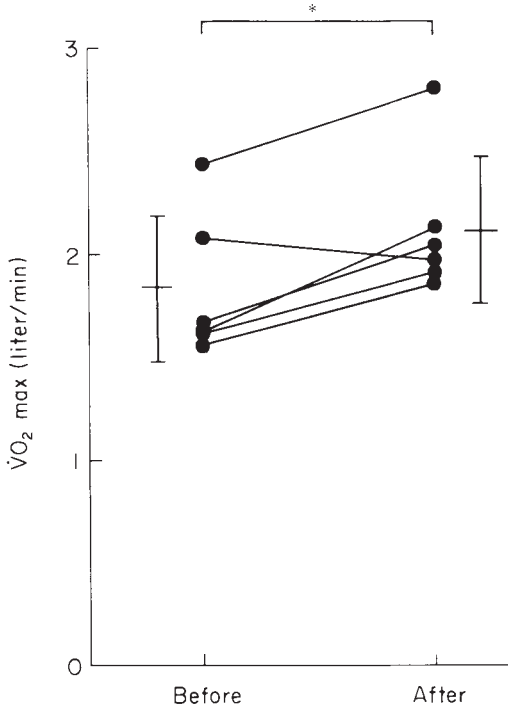

Fig. 1. Maximum oxygen consumption ($\dot{V}O_2$max) before and after the treatment by nasal continuous positive airway pressure. ●—●, individual data. Means±S.D.
*$p<0.05$

before to 2125 ± 350 ml/min after ($p < 0.05$). However, $\dot{V}E$, $\dot{V}CO_2$, RR, HR, blood pressures, Borg score and total exercise time did not change significantly. The ratings of sensation of dyspnea and anaerobic threshold (AT) obtained by the V-slope method (Sue et al. 1988; Midorikawa et al. 1997) also did not change significantly after the intervention.

Discussion

Six patients with OSA underwent overnight sleep study, MSLT and exercise testing before and after short-term nasal CPAP treatment. We found significant improvement of blood gas analysis at rest, apneic episodes, daytime sleepiness and $\dot{V}O_2$max after the treatment.

There are several critiques of this study. First, because of its nature, this type of study cannot be performed in a blind fashion. Therefore, since the experimental order might affect the results of the study, we did not tell the subjects about the purpose and nature of the study and we always had them perform exercise with vocal encouragement to keep this effect as small as possible. Second, basal metabolism affects oxygen consumption (Zwillich et al. 1975; Baier and Sonani 1984). We did not rigorously regulate food or water intake in this experiment; however, we asked the subjects during the session to take meals only at our hospital and not to take caffeinated drinks, tobacco or sedatives that might affect the results. Furthermore we asked them to perform the exercise at almost the same time of day and had controlled the room temperature as much as possible. Thus we believe that these biases were minimized.

There are several plausible mechanisms that may explain the increase in maximum oxygen consumption after the treatment with nasal CPAP. First, cardiovascular responses such as heart rate, stroke volume and blood pressure may have changed following the short-term nasal CPAP therapy. However, in the present study, there were no significant differences in heart rate and blood pressure responses before and after the intervention. Therefore, the observed improvement of exercise performance after nasal CPAP cannot be explained by the cardiovascular response.

Second, sleep deprivation hampers the ventilatory response to hypoxia and carbon dioxide (Cooper and Phillips 1982; White et al. 1983), and may reduce exercise performance. In the present study, we observed the improvement of PaO_2 and $PaCO_2$ at rest after the intervention. Therefore, although we did not check ventilatory response to chemical stimuli, we can speculate that the ventilatory response to chemical stimuli may have been improved by nasal CPAP, resulting in the increase in exercise performance.

Third, there may have been an improvement of cellular metabolism of exercise muscles after intervention. Vondra et al. (1981) stated that sleep is needed for the restoration of cellular functions which would expalin the decreased activity of aerobic enzyme activity after 130 hours of SD. As nasal CPAP

improves overall sleep symptomatology (Sullivan et al. 1981; Sullivan and Grunstein 1989), nasal CPAP may recover cellular functions of the vigilance system of the brain or exercise muscles, resulting in a increase in $\dot{V}O_2$max. We found the significant improvement of apneic episodes during sleep and daytime sleepiness after the intervention. These results would not deny a possibility of recovery of the aerobic enzyme activity of muscles.

Finally the improvement of sleepiness after treatment may have increased the performance capacity or motivation, resulting in an increase in $\dot{V}O_2$max. This possibility is most plausible.

In summary, we have observed that short-term nasal CPAP therapy improved PaO_2 and $PaCO_2$ at rest, apneic episodes, sleepiness assessed by MSLT and exercise performance in OSA patients. This improvement of exercise performance may correlate with the improvement of sleepiness.

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