Continuous positive airway pressure (CPAP) is an effective treatment for obstructive sleep apnea. It is known, that there are beneficial effects on cardiac function, which might be explained by suppression of apnea and specific hemodynamic effects of CPAP. Therefore, CPAP might act as an adjunct therapy in heart failure, even in the absence of sleep apnea. In the present study, 11 patients with congestive heart failure (EF = 23.1 ±6.9%) without sleep apnea (AHI 3.0 ±1.2/h) were treated with nocturnal CPAP. Cardiopulmonary exercise testing was performed at baseline and after 8.6 ±1.3 months. All patients underwent heart catheterization and myocardial biopsy to exclude myocarditis at baseline. Five (46%) of the 11 patients did not complete the study because of poor compliance and irregular use of the CPAP device. Six (54%) of the patients used CPAP regularly (>6 h/night) and completed the study. Cardiopulmonary exercise testing showed an improvement of work load (96 ±36 Watt vs. 112 ±34 Watt; P=0.025) and VO2 peak (1227 ±443 ml vs. 1525 ±470 ml; P=0.01). Oxygen-pulse was increased, although that did not reach significance (11.2 ±4.8 ml/beat vs. 12.6 ±3.9 ml/beat). In conclusion, CPAP might have beneficial effects on exercise capacity in patients with congestive heart failure even in the absence of sleep apnea. Nevertheless, poor compliance seems to be a limiting factor.

Key words: CPAP, heart failure, hemodynamics

INTRODUCTION

Congestive heart failure is a common disorder marked by ventricular dilation, increased end-diastolic pressure, diminished left ventricular ejection fraction and neurohumoral activation. Despite major advantages in medical treatment (e.g.,
angiotensin converting enzyme inhibitors, beta blocking agents) and modern therapeutic concepts like intracoronary stem cell transplantation (1), congestive heart failure is still associated with a high morbidity and mortality.

Several studies found beneficial effects of continuous positive airway pressure (CPAP) on ventricular function in patients with obstructive (2-6) and central (7-9) sleep apnea. Nevertheless, there is evidence that CPAP *per se* has some favorable short-term and long-term hemodynamic and neurohumoral effects, even in the absence of sleep apnea (10). These effects might be explained by decreases of myocardial work and oxygen consumption (11). Furthermore, respiration depends on intrathoracic pressure swings. As a consequence of this, spontaneous respiration is associated with an increase of transmural left ventricular pressure. In other words, respiration causes an increase of afterload (12). Therefore attenuation of intrathoracic pressure swings, which is a result of CPAP therapy, might result in a decrease in afterload (13).

Concerning these pathophysiologic mechanisms, we hypothesized that nocturnal application of continuous positive airway pressure will be beneficial in patients with congestive heart failure. Since limitation of exercise capacity is one of the most symptoms of these patients, we perform cardiopulmonary exercise testing in patients with congestive heart failure who were treated with long term CPAP therapy.

**PATIENTS AND METHODS**

Eleven patients referred to the department of Cardiology, Pneumology, and Angiology of the Heinrich Heine University in Düsseldorf, Germany were recruited to the study using the following inclusion criteria: congestive heart failure with a left ventricular ejection fraction <40% as measured by left ventricular angiography, New York Heart Association (NYHA) functional class II to III, while on optimal cardiac medication for >1 month. Origin and severity of left ventricular dysfunction were determined by heart catheterization. Myocarditis was excluded by myocardial biopsy at baseline. All patients were on sinus rhythm. We excluded patients who had the following conditions: percutaneous coronary intervention or cardiac surgery within 3 months before the study, obstructive or central sleep apnea, and those with contraindications for CPAP therapy. The study was approved by the Heinrich Heine University of Düsseldorf Ethics Committee. Informed consent was obtained from all subjects.

**Sleep studies, CPAP therapy**

The following parameters were recorded: respiratory flow, electrocardiogram, effort (thoracic and abdominal induction plethysmography), snoring signals, and oxygen saturation (Schwarzer, Germany (14)) between 10.00 pm and 6.00 am. The AHI was calculated as the number of respiratory events per hour, whereas an AHI >5 episodes was considered as sleep apnea syndrome. Minimal nocturnal oxygen saturation was defined as the lowest saturation reached during sleep after manual exclusion of clear artifacts. Patients with an AHI >5/h (central or obstructive apnea/hypopnea) were excluded from the study. Patients with an AHI <5/h were adapted on continuous positive airway pressure (Weinmann; Somnotron IV, Germany). All patients were
educated in the mechanisms and technique of CPAP treatment, and were advised to use CPAP all night and every night. They underwent an overnight CPAP titration study to establish the maximal pressure tolerated. CPAP was applied using a comfortably fitting nose mask (Weinmann, Hamburg, Germany, Size S-M).

Cardiopulmonary exercise testing

In all patients a symptom limited cardiopulmonary exercise test was performed using the same incremental protocol at baseline and after 8-9 months of CPAP therapy. Patients performed bicycle exercise in a 45° semi-supine position. After adaptation on mouth piece and resting conditions, exercise work load was increased by 25 Watt every two minutes (ramp protocol). A 12 lead ECG was monitored and the heart rate derived from it. Blood pressure was measured using a sphygmomanometer before starting the test, two minutes into each stage, at peak exercise and after the test. Oxygen consumption (VO$_2$) was measured using a breath-by-breath method (Jaeger, Würzburg, Germany). Oxygen pulse was calculated as VO$_{2peak}$/maximal heart rate. Peak circulatory power was calculated as the product of VO$_{2peak}$ and the maximal systolic arterial pressure as described elsewhere (15). Indications to stop the test were ST-Segment depression or new onset angina pectoris, or systolic blood pressure >230 mmHg.

Statistics

All variables are given as means ±SD. VO$_2$, workload and oxygen pulse were compared by using the Wilcoxon matched pair signed rank test. A significant difference was assumed at the level of error <5%. Tests between 5% and 10% were considered as statistical trends. The data were analyzed using the Statistical Package for Social Sciences (SPSS 11.0 for Windows, Munich Germany).

RESULTS

Baseline hemodynamic profiles of the patients are shown in Table 1. All patients reported dyspnea and muscular weakness as the limited symptom at the end of exercise. Five patients (46%) did not complete the study, because of poor compliance and irregular use of the CPAP device. There was no difference in regard to left ventricular function, nocturnal oxygen desaturation, or NYHA class between patients who use CPAP and those who did not finish the study. There were no serious side effects of CPAP therapy. Six patients (54%) used CPAP regularly (>6 h/night, pressure 7.6 ±1.3) and completed the study. Cardiopulmonary exercise testing was done at baseline and after 8.6 ±1.3 months of CPAP therapy. According to the inclusion criteria, sleep apnea was not diagnosed in any of the patients (AHI 3.2 ±1.2/h), minimal nocturnal oxygen desaturation was 88.2 ±2.1%.

CPAP therapy resulted in a significant increase of exercise duration (443 ±145 s vs. 360 ±165 s; P=0.042). Cardiopulmonary exercise testing showed an improvement of workload (96 ±36 Watt vs. 112 ±34 Watt; P=0.025, Fig. 1) and peak oxygen consumption (VO$_2$ peak 1227 ±443 ml vs. 1525 ±470 ml; P=0.001, Fig. 2). Oxygen-pulse was increased after CPAP therapy, although that did not reach significance (11.3 ±4.79 ml/beat vs. 12.6 ±3.9 ml/beat; P=0.4, Fig. 3). There was a
Table 1. Data of 6 patients who finished the study (baseline).

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>60 ±12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (M/F)</td>
<td>6/0</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>93 ±26</td>
</tr>
<tr>
<td>Height (m)</td>
<td>179 ±7</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29 ±8</td>
</tr>
<tr>
<td>Diagnosis (DCM/ICM)</td>
<td>4/2</td>
</tr>
<tr>
<td>NYHA Grade (II/III)</td>
<td>2/4</td>
</tr>
<tr>
<td>LV- EF (%)</td>
<td>23</td>
</tr>
<tr>
<td>LV-ESV (ml)</td>
<td>229 ±63</td>
</tr>
<tr>
<td>LV-EDV (min)</td>
<td>297 ±78</td>
</tr>
</tbody>
</table>

Table 2. Cardiopulmonary exercise test at baseline and after 8.6 ±1.3 months of CPAP treatment.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>After CPAP</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Workload (Watts)</td>
<td>96 ±36</td>
<td>112 ±34</td>
<td>0.025</td>
</tr>
<tr>
<td>Duration of exercise (s)</td>
<td>360 ±165</td>
<td>443 ±145</td>
<td>0.042</td>
</tr>
<tr>
<td>VO₂/AT (ml/min)</td>
<td>898 ±250</td>
<td>1154 ±463</td>
<td>0.185</td>
</tr>
<tr>
<td>Max. HF (beats/min)</td>
<td>118 ±17</td>
<td>122 ±16</td>
<td>0.656</td>
</tr>
<tr>
<td>RRmax max (mmHg)</td>
<td>157 ±25</td>
<td>158 ±22</td>
<td>0.819</td>
</tr>
<tr>
<td>VO₂peak (ml/min)</td>
<td>1227 ±443</td>
<td>1525 ±470</td>
<td>0.001</td>
</tr>
<tr>
<td>VO₂peak/kgKG (ml/min/kgKG)</td>
<td>12.9 ±3.8</td>
<td>16.3 ±1.8</td>
<td>0.001</td>
</tr>
<tr>
<td>Max. Oxygen pulse (l/min/beat)</td>
<td>11.2 ±4.9</td>
<td>12.6 ±3.8</td>
<td>0.402</td>
</tr>
<tr>
<td>Circulatory power (mmHg ml/min)</td>
<td>216494 ±72162</td>
<td>262580 ±76424</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**Fig. 1.** Maximal workload at baseline and after CPAP treatment.

A significant increase of circulatory power (216494 ±72162 vs. 262580 ±76424 mmHg mlO₂/min). Table 2 summarizes the data of the cardiopulmonary exercise tests.
DISCUSSION

Our study demonstrates that long-term CPAP treatment was possible in patients with congestive heart failure without sleep apnea. Long term treatment was associated with an improvement of cardiopulmonary exercise capacity. Therefore, CPAP might be used as an adjunct therapy in those patients. Nevertheless, poor compliance seems to be a limiting factor.

To our knowledge, there is only one study using CPAP in heart failure patients without sleep apnea. Sin et al (9) examined the effects of CPAP therapy on Cheyne Stokes breathing and central sleep apnea in heart failure patients. In this study, a group of 17 patients without sleep apnea was randomized to a CPAP treatment for 3 month. Nevertheless, there was no benefit of CPAP concerning the primary end point which was defined as transplant free survival. There are few studies focusing on the short-term effects of CPAP on ventricular stroke volume with different...
protocols and conflicting results. Bradley et al (16) applied CPAP at a level of 5 cmH2O pressure in 22 stable patients with congestive heart failure. In that study a high left ventricular filling pressure was predictive for an improvement of cardiac index in consequence of CPAP. These results were approved in a further study (17). Moreover, the authors found a dose related positive effect using different pressures (5 and 10 cmH2O, respectively). In this regard, it can be summarized that a decompensated left heart with a high preload will response to CPAP with a rise in stroke volume (2). Consequently, a higher stroke volume might be associated with an increase in exercise tolerance in these patients.

The most important aspect of cardiac dysfunction in heart failure is not the depressed cardiac performance noted at basal resting states, but rather the loss of cardiac reserve. The loss of cardiac reserve is a common feature of congestive heart failure leading to inability to cope with exercise. Therefore, cardiopulmonary exercise testing is a standard non-invasive procedure to determine cardiopulmonary capacity in heart failure patients. Furthermore, it has been shown that this method gives excellent information on prognosis and might help to select patients for heart transplantation. The measurement of oxygen consumption (VO2) in patients with heart failure was first described by Weber et al (18) as a non-invasive method for characterizing cardiac reserve and prognosis. This was affirmed by several studies, e.g., the Veterans Administration Heart Failure Trial (VHeFT) (19). In our study, initial VO2peak was 12.9 ±2.8 ml/kg. Therefore, the patients were identified as heart transplantation candidates at baseline (20). After CPAP therapy, there was an increase not only of exercise duration but also of prognostic relevant parameters, such as VO2peak or circulatory power.

There are several pathophysiologic approaches to explain the effects of CPAP on left ventricular function and exercise capacity. Since the patients who use CPAP regularly seem to be highly motivated, training effects and changes of lifestyle might be one reason for the increase in exercise capacity. Nevertheless, oxygen consumption at anaerobic threshold, which is modulated by training, was not significantly different after CPAP therapy. CPAP per se might have beneficial effects on left ventricular geometry and function. Kaye et al (11) measured myocardial oxygen consumption by arterial and coronary sinus blood sampling. It has been shown that application of CPAP resulted in a significant decrease of left ventricular stroke work and myocardial oxygen consumption. Additionally, this effect might be explained by an inhibition of cardiac sympathetic nervous activity, documented by a reduction of cardiac noradrenaline spillover (21) and a reduction of left ventricular preload and afterload due to CPAP. In a recent study, we found that particularly enlarged left ventricles and a high filling pressure respond to CPAP with an increase of stroke volume (unpublished observation). Therefore, it can be assumed that the patients reported in our study (LVEDV 297 ±78 ml) responded to CPAP with an increase of stroke volume. Stroke volume can be estimated non-invasive using the oxygen pulse. Nevertheless, there was only a marginal rise in oxygen pulse after CPAP in the small study group.
There are several limitations of this study. Firstly, we did not carry out overnight polysomnography, which is still the gold standard in the diagnosis of nocturnal breathing disorders. Another limitation refers to the study design, which did not allow to verify causal relationships.

In summary, we found an increased exercise capacity in heart failure patients after long term treatment with continuous positive airway pressure. Since none of the patients suffered from sleep apnea, this might be explained by specific cardiac effects of CPAP. Nevertheless, poor compliance is still a problem to be resolved.

REFERENCES


Author’s address: Stephan Steiner, Department of Medicine, Division of Cardiology, Pneumology and Angiology, University Hospital Düsseldorf, Moorenstr. 5, 40225 Düsseldorf; phone: +49 211 8118800, fax: +49 211 8118858, e-mail: Steinest@uni-duesseldorf.de