A randomized, controlled, single-blind study was performed on 20 patients with chronic obstructive pulmonary disease and exercise-induced hypoxaemia. Ten patients each were randomly assigned to one of two groups, one training with air and the other training with oxygen. There were no significant differences between the groups regarding values measured prior to the study. The patients trained 3 times per week for 30 minutes each time for a duration of 8 weeks. The training consisted of interval walking on a treadmill (intensity set according to Borg ratings) with either air or oxygen administered through a nasal cannula at a rate of 5 l/min. Training significantly improved the 6-minute walking distance by 20% and 14% in the air and oxygen group, respectively, when the patients were tested on air. In the same test the air group significantly decreased Borg ratings for perceived exertion. Borg ratings for dyspnoea and perceived exertion significantly decreased in the oxygen group when they were tested on oxygen. It was concluded that oxygen supplementation did not further improve the training effect, compared with training with air, in patients with chronic obstructive pulmonary disease and exercise-induced hypoxaemia.

Key words: chronic obstructive pulmonary disease, exercise training, hypoxaemia, oxygen, 6MWD, walking, Borg.
Hospital in Umeå, Sweden. The patients were asked to participate and were included if they accepted and fulfilled the following inclusion criteria: were under the age of 75, had stopped smoking at least 6 months before entering the study, presented hypoxaemia during exercise (SaO₂ < 92% in 6MWD (6-minute walking distance test) performed in corridor), had FEV₁ < 70% of predicted value, had PaO₂ < 8 kPa at rest, had no infection the last 3 weeks and had no change in medical treatment the last month before entering the study. There were 20 patients (10 men and 10 women). The differences between the groups at baseline were not statistically significant.

**Study design**

The study was designed as a controlled, randomized, single-blind trial. The included patients were randomly allocated (randomization by blocks, men and women were randomized separately) to train either with air (AG) or with oxygen (OG).

**Training procedures**

After randomization, the patients started the training programme with air or oxygen at a flow rate of 5 l/min through a dual-prong nasal cannula (19). The training programme consisted of walking on a treadmill for 30 minutes, 3 times per week for 8 weeks. The subjects were allowed to be absent for a maximum of three training sessions.

During the 30-minute training sessions, the patients exercised on a motorized treadmill (Rodby RL 1500 E, Enköping, Sweden). The programme was designed as interval training, comprised of 5 minutes warming up, 2–3 minutes higher speed alternated with 2–3 minutes lower speed, and ending with 2–5 minutes cooling down. Normally one session consisted of five intervals with higher speed. A physiotherapist adjusted the speed, and slowed down or stopped the treadmill on request from the patients. SaO₂ and heart rate were continuously monitored with a pulse oximeter using a finger probe or a forehead probe (Ommeda Biox 3700e, Louisville, USA or Nellcor N-20, Pleasanton, USA). The patients rated their perceived dyspnoea according to Borg CR10 (scale 0–10) and perceived exertion according to Borg RPE (scale 6–20) (25) every 5th minute and after every speed interval. The intensity of the sessions was individualised with respect to the patients’ saturation and their subjective ratings of dyspnoea and perceived exertion (26). Target dyspnoea was set to 7/10 and target perceived exertion was set to 17/20.

The treadmill was stopped if the patients rated 7/17 (respectively) or more on the Borg scales and/or if the patients’ SaO₂ fell below 90%. The treadmill was started again when SaO₂ rose above 90% and/or when the ratings lowered. When the walking speed of patients had to be increased above 6.0 km/hour, the treadmill was inclined instead of further increasing speed. In these cases some of the higher-speed-intervals included an inclined treadmill during weeks 2–7 (not the first and last training week). The inclination varied between 1.0 and 5.0 degrees. The distance walked was noted after every session.

**Measurements during the tests**

Oxygen saturation (SaO₂) and heart rate were continuously measured during the tests with a pulse oximeter (Ommeda Biox 3700e, Louisville, USA) using a finger probe. Transcutaneous Carbon dioxide (TcpCO₂) was continuously measured with a TcpCO₂-meter (“Tina TCM 3” Radiometer, Copenhagen, Denmark). The probe was connected to the 3rd rib or to the temple of the patient. The pulse oximeter and the TcpCO₂-meter were connected to a recorder (Yokogawa LR 4200, Tokyo, Japan) that continuously printed the levels. The time below 90% in SaO₂ was registered. Arterial blood gases were taken from arteria radialis at rest, and again directly after the test. The pCO₂-values from the arterial blood gas tests were used to calibrate the TcpCO₂-meter. Venous blood samples to determine the lactate levels were taken from a venous catheter on three occasions—at rest, directly after the test, and 3 minutes after the test. The samples were analysed in an arterial blood gas analyser (IRMA Blood analysis system, St Paul, USA or “ABL 520” Radiometer, Copenhagen, Denmark). The lactate levels were taken from a venous catheter on three occasions—at rest, directly after the test, and 3 minutes after the test. The samples were analysed in a YSI 1500 Sport L-Lactate Analyzer (Yellow Springs, USA). Subjective experience of dyspnoea and perceived exertion were scored by showing the Borg CR10 and Borg RPE (25) to the patients at rest, after 3 minutes walk, immediately following the test, and 2 minutes after test completion. Frequency of breathing was measured by counting the frequency for 15 seconds, at rest and immediately following the test. The reason for using a treadmill for the 6MWD was to simplify continuous registrations of TcpCO₂, SaO₂, and heart rate and to simplify the blood sampling from the patients. In our laboratory the test-retest variation for the non-motorized treadmill used during tests was 3.0%.

**Statistical analysis**

The data were analysed using SPSS (version 7.5). Non-parametric
Both groups significantly increased their 6MWD after training when tested on air (Test A, Table II). When tested on oxygen (Test B, Table II), the AG showed a significant increase in distance walked, but the OG did not change the distance walked. No significance was found when comparing the two groups regarding change in walking distance in either of the tests.

The short-term effect of exercising with oxygen was evaluated by comparing 6MWD with air (A) and with oxygen (B) before training. The patients (not separated in groups) improved the distance walked with 30 meters (−30–60) when walking with oxygen (B) compared with walking with air (A) ($p < 0.01$). When evaluating the short-term effect of oxygen after the training period it was found that the patients (not separated in groups) walked 25 meters (−90–60) longer when tested with oxygen (B) compared with the test with air (A) ($p < 0.05$). There were no significant differences regarding these short-term effects before and after training, within or between the groups.

The sum of distance walked during the first training week and the last week (a total of 90 minutes walking each week) is shown in Fig. 1. The AG increased the total distance walked, between the first and the last training week by 1952 meters (843–3003) (50%), and the OG increased the distance by 2173 meters (1405–2895) (43%). The increase for each group was statistically significant ($p < 0.01$). No difference was found between groups.

The perceived exertion (Borg RPE) was significantly lower after training compared to before training for the AG during Test A (with air). The OG showed no significant changes and the difference between the groups was not significant (Table III). The results were opposite in Test B (with oxygen) with the OG reporting a significantly lower dyspnoea and perceived exertion after training (Table III). In Test B there was a significant difference between the AG and OG regarding change in dyspnoea ratings (Borg CR10) before and after training ($p < 0.05$).

The OG showed a significantly larger increase in lactate levels during exercise (difference between pre- and post-test) in the test with air (Test A) after compared with before training. The increase was 1.51 mMol/l (0.77–4.89) after the training period compared with an increase of 0.98 mMol/l (0.30–2.37) before training ($p < 0.01$) (Fig. 2). No significant changes were found for the AG in any of the tests or for the OG in test with oxygen (Test B) (Fig. 2).

There was no statistically significant change in pCO$_2$ in any of the tests.

The total time during which the patients desaturated below 90% was significantly longer after training in the OG when tested on air (Test A). The time below 90% in SaO$_2$ was 174 seconds (0–291) before training and 251 seconds (0–288) after training ($p < 0.05$). In the AG there was no significant change. Regarding heart rate (Table II), the lowest level of SaO$_2$ and breathing frequency, no significant changes were found between the tests before and after training either within or between groups.

**DISCUSSION**

Although a number of studies have investigated the short-term effects of oxygen on exercise performance (12–20), only a few studies exists, the present study included, that have investigated the long-term effect of oxygen used during longer training periods.

In our study both groups increased the distance walked after training in the test with air, which indicates a positive training effect. In addition, the AG rated lower perceived exertion (Borg RPE) and displayed an unchanged increase in lactate during exercise after training. The OG increased the distance walked in this test but did not decrease their Borg ratings. They also
displayed a higher increase in lactate during exercise after training. Also, an increase in time during which the patients were below 90% in SaO\textsubscript{2} during the test was found for the OG group. One possible explanation why the patients in the OG did not have the same positive training effect as those in the AG, could be that they were too well oxygenated during training. Training with a slight hypoxemia gives physiologic stress, which is required for improvements in physical capacity. During training sessions the OG performed better than the AG but when tested on air the OG did not show the same improvements as the AG. These results imply that training of patients with COPD and exercise-induced hypoxemia can be conducted without supplemental oxygen.

In the test with oxygen only the AG increased the distance walked. However, this group showed no decrease in subjective ratings, while the OG did. These findings suggest that the patients preferred to walk with the supplementation that they had trained with. Other studies have also shown that general exercise training leads to improved ratings regarding dyspnoea (5, 9, 27). Oxygen supplementation during training has also been shown to lower the ratings of dyspnoea during exercise (15, 22).

Previous studies show contrasting results regarding long-term effects after training with oxygen. Zack & Palange (23) found that training with oxygen supplementation increased work performance. However, they did not have a control group training with air. No differences between training with oxygen and air have been shown in previous studies using various designs. McDonald et al. (21) assessed the effects of supplemental air and oxygen on exercise performance during activities that normally caused dyspnoea. They found no difference in exercise tests (6MWD or steps achieved) when comparing oxygen and air. In the study by Rooyackers et al. (22), no difference in training effects when training with air or oxygen was found, although the patients in the study were not blinded as to which treatment they received. Patessio et al. (28) found similar results in a single-blind controlled study, but their COPD patients did not desaturate during exercise.

In agreement with previous exercise studies (12–20) we found that supplemental oxygen led to an immediate increase in 6MWD compared with walking with air during the tests. The patients in the OG walked longer distance during the training sessions than the AG group, and this difference persisted during the whole period (Fig. 1). It appears then that the acute positive effect of oxygen prevails during and after training. According to this it is important to differ between the positive acute effects and the actual training effects of supplemental oxygen.

### Table III. Borg ratings during Test A (with air) and Test B (with oxygen) before and after training. Values are presented as median (min–max). Borg CR10 and Borg RPE measure dyspnoea and perceived exertion, respectively

<table>
<thead>
<tr>
<th>Training groups</th>
<th>Pre-training at rest</th>
<th>Pre-training after test</th>
<th>Post-training at rest</th>
<th>Post-training after test</th>
<th>% change</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Test A (air)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Borg CR10 (0–10)</td>
<td>AG 1.5 (0–3)</td>
<td>6.5 (4–9)</td>
<td>1 (0–3)</td>
<td>6 (1–7)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>OG 0 (0–3)</td>
<td>6.5 (3–10)</td>
<td>0 (0–2)</td>
<td>4.5 (3–9)</td>
<td>−5.0</td>
</tr>
<tr>
<td>Borg RPE (6–20)</td>
<td>AG 7.5 (6–11)</td>
<td>16.5 (13–19)</td>
<td>9 (6–11)</td>
<td>15 (12–17)</td>
<td>−15.5*</td>
</tr>
<tr>
<td></td>
<td>OG 6 (6–13)</td>
<td>15 (9–19)</td>
<td>6 (6–11)</td>
<td>15 (10–17)</td>
<td>5.5</td>
</tr>
<tr>
<td><strong>Test B (oxygen)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Borg CR10 (0–10)</td>
<td>AG 0.5 (0–3)</td>
<td>4.5 (3–7)</td>
<td>1 (0–2)</td>
<td>5 (3–6)</td>
<td>12.5</td>
</tr>
<tr>
<td></td>
<td>OG 0 (0–3)</td>
<td>6.5 (3–8)</td>
<td>0 (0–3)</td>
<td>3.5 (2–7)</td>
<td>−34.0***†</td>
</tr>
<tr>
<td>Borg RPE (6–20)</td>
<td>AG 7.5 (6–11)</td>
<td>15 (11–17)</td>
<td>8 (6–10)</td>
<td>15 (12–17)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>OG 6 (6–13)</td>
<td>15.5 (11–17)</td>
<td>6 (6–12)</td>
<td>13.5 (9–17)</td>
<td>−17.5*</td>
</tr>
</tbody>
</table>

* p < 0.05 and **p < 0.01 when comparing pre- and post-training tests.
† Significant difference in relative change pre- and post-training between training groups at p ≤ 0.05.

AG—patients training with air, OG—patients training with oxygen. % change is the change in difference between the rest rating and the rating after test post-training compared with pre-training.
and after training. Our patients worked at a greater intensity in tests after training. We used lactate measurement as a complement to provide a more objective assessment of the stress of the patient during the test. Unchanged lactate levels in combination with increased walking distance indicated that the aerobic physical capacity had increased.

In patients with COPD there are difficulties in deciding the exercise intensity because of the limited possibility in using heart rate as a target. Since the respiration, and not the cardiovascular system, is often the limiting factor, we chose to use the subjective ratings of dyspnoea and perceived exertion in addition to the saturation as targets during training. In the OG the saturation could not be used because for this group the value never reached low enough, although according to the subjective ratings the two groups trained at the same intensity level. In a recent study on COPD patients (26), dyspnoea ratings were found to be reliable as a target to produce an expected exercise intensity. When comparing the heart rate and breathing frequency during the tests before and after training in this study there was no difference in any of the groups, which agrees with most previous studies (7, 10, 17, 18).

When patients with COPD and hypoxaemia are treated with oxygen there is always a risk of retention of CO₂. We therefore examined the pCO₂-levels when the patients were walking with supplemental oxygen during tests. The pCO₂-level tended to be higher than when walking with air but there was no significant increase during or after the test with oxygen. Additionally, when the patients were lying down after the test while still breathing oxygen, the pCO₂-level did not differ from when tested with air. Thus, it does not seem to be a risk of CO₂-retention during walking with oxygen in patients with COPD and exercise-induced hypoxaemia despite the relatively high oxygen flow.

Fig. 2. Blood lactate levels during Test A, with air. Open bars, sample taken at rest; grey bars, sample taken directly after test. Both groups before and after training. Values presented as median. ** Significant difference in lactate increase between pre- and post-training tests at p ≤ 0.01.

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