Prolonged Hypoxemia after 10 min Walking Exercise in Aged Patients with Chronic Obstructive Pulmonary Disease

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FUKUSHIMA, T., OHRUI, T., ITABASHI, S., SEKIZAWA, K., AIKAWA, T., YANAI, M., SASAKI, H. and TAKISHIMA, T. Prolonged Hypoxemia after 10 min Walking Exercise in Aged Patients with Chronic Obstructive Pulmonary Disease. Tohoku J. Exp. Med., 1990, 162 (4), 345-353 — Although the behavior and factors of exercise tolerance have been studied during exercise in patients with chronic obstructive pulmonary disease (COPD), little attention has been paid to the after-effects of such activity. Arterial oxygen saturation (SaO₂) was monitored during and after a 10 min walking exercise in aged patients with COPD. Neither baseline SaO₂ nor mean SaO₂ during exercise correlated to the 10 min walking distance. However, the recovery time of SaO₂ to the baseline value shows significant correlation to the 10 min walking distance. Careful attention should be paid to prolonged hypoxemia after exercise in severe cases of COPD.

arterial oxygen saturation ; 10 min walking exercise ; chronic obstructive pulmonary disease

Exercise tolerance in patients with chronic obstructive pulmonary disease (COPD) may be limited by the respiratory system for several reasons: (1) altered lung mechanics, (2) impaired gas exchange, (3) the development of pulmonary hypertension, and/or (4) respiratory muscle fatigue (Asmussen 1964). The fall in arterial oxygen pressure (PaO₂) during exercise has been widely studied but exercise tolerance could not be simply validated by the changes of PaO₂. Jones, in 1966, described the changes in arterial blood gases during exercise in patients with emphysema or chronic bronchitis (Jones 1966). He found that patients with severe emphysema had a significant fall in PaO₂ whereas patients with chronic bronchitis actually had an increase. The patients with severe emphysema had a lower diffusion capacity (D_{LCO}), suggesting more alveolar capillary destruction. The improvement in oxygenation in patients with chronic bronchitis was thought

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to be the result of improved ventilation in areas of the lung that had had low ventilation-perfusion ratios. In patients with chronic obstructive pulmonary disease (COPD), the exercise-induced arterial oxygen desaturation is much more variable and seems to depend on the severity of the airway obstruction as well as on the presence of resting hypoxemia and hypercapnia (Dantzker and D'Alonzo 1986).

In the recovery period after exercise in COPD, consistent result on the changes of PaO₂ has not been reported (Ries et al. 1983; Frye et al. 1988; Forkert et al. 1989). All of the previous reports measured changes of PaO₂. But for O₂ supply to the tissue, arterial oxygen saturation (SaO₂) is practically needed. In the present study, using SaO₂ measurement hypoxemia after exercise in COPD was monitored. Since increase of PaO₂ after exercise little affect to SaO₂, only oxygen debt of the whole body, thereby disturbing exercise tolerance, could be observed.

In aged patients with COPD, as an alternative to complicated laboratory exercise testing using an ergometer or treadmill, the walking distance covered over a 12 min could be safely measured. McGavin et al. (1976) reported that the distance covered in 12 min of walking is a reproducible measure of effort tolerance in patients with COPD. Preliminary study suggested that the 12 min walking exercise was a little too long to be tolerated by aged patients with COPD (Evans 1984) so we adopted a 10 min walking test in the present study. We monitored SaO₂ during and after the 10 min walking test in order to observe how prolonged hypoxemia correlated to exercise tolerance.

METHODS

Fifteen hospital in-patients with COPD who were more than 60 years old were studied. Their physical characteristics and pulmonary function results are shown in Table 1. (1) Forced expiratory volume at one second (FEV₁) was 41±13% (mean±S.D.) of predicted value but exceeded 600 ml and FEV₁/vital capacity (VC) was 44±13% (mean±S.E.): (2) They had never received inhaled or oral corticosteroids: (3) FEV₁ did not increase more than 200 ml 10 min after inhalation of 200 µg albuterol delivered by a metered-dose inhaler: (4) Peripheral blood eosinophil count was less than 400/mm³. Their regular medications were either ipratropium bromide, a β₂-agonist, from a metered-dose inhaler or oral aminophylline, or combinations of these drugs. One subject had not received any medication. Subjects were asked to stop oral bronchodilators 24 hr before the study and inhaled bronchodilators 12 hr before the study.

FEV₁ and VC were measured in the seated position with a dry bellows spirometer (DISCOM-21, Chest, Tokyo). The P wave height of lead II of an electrocardiogram (ECG) without exercise was obtained according to the recommendations of the American Heart Association (1954), Padmavati and Raizada (1972) and mean P wave height from 5–10 beats was measured and used for analysis. The reference from which its voltage was measured was the isoelectric level of T-P interval. Patients were instructed to walk as far as possible within 10 min. However, when patients felt it impossible to continue walking during the test, they could slow down or stop walking. Each subject was accompanied by a doctor who acted as timekeeper and gave encouragement as necessary. The ECG was monitored continuously with a wireless remote control system during the study for monitoring heart
Table 1. Physical characteristics and results of 10 min walking exercise of subjects with COPD

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Age (year)</th>
<th>Sex</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>Spirogram</th>
<th>Arterial blood gas before exercise</th>
<th>10 min walking exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>VC (liter)</td>
<td>FEV₁ (liter)</td>
<td>FEV₁/VC (%)</td>
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<tr>
<td>1 H.T.</td>
<td>66</td>
<td>M</td>
<td>155</td>
<td>41</td>
<td>1.5</td>
<td>47</td>
<td>0.6</td>
</tr>
<tr>
<td>2 S.K.</td>
<td>80</td>
<td>M</td>
<td>169</td>
<td>41</td>
<td>1.8</td>
<td>57</td>
<td>0.8</td>
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<tr>
<td>3 M.M.</td>
<td>72</td>
<td>F</td>
<td>152</td>
<td>40</td>
<td>1.1</td>
<td>47</td>
<td>0.8</td>
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<tr>
<td>4 H.S.</td>
<td>63</td>
<td>M</td>
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<td>41</td>
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</tr>
<tr>
<td>5 Y.A.</td>
<td>66</td>
<td>M</td>
<td>160</td>
<td>53</td>
<td>3.7</td>
<td>114</td>
<td>1.2</td>
</tr>
<tr>
<td>6 T.T.</td>
<td>61</td>
<td>M</td>
<td>162</td>
<td>53</td>
<td>2.2</td>
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<td>7 S.Y.</td>
<td>70</td>
<td>M</td>
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<td>8 I.K.</td>
<td>66</td>
<td>M</td>
<td>167</td>
<td>48</td>
<td>2.6</td>
<td>77</td>
<td>1.0</td>
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<tr>
<td>9 K.S.</td>
<td>76</td>
<td>M</td>
<td>166</td>
<td>50</td>
<td>2.5</td>
<td>78</td>
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<td>10 S.I.</td>
<td>67</td>
<td>M</td>
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<td>58</td>
<td>1.5</td>
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<td>11 Y.S.</td>
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<td>12 U.T.</td>
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<td>F</td>
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<td>F</td>
<td>153</td>
<td>30</td>
<td>1.4</td>
<td>63</td>
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<tr>
<td>14 G.S.</td>
<td>85</td>
<td>M</td>
<td>157</td>
<td>59</td>
<td>2.8</td>
<td>99</td>
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<tr>
<td>15 A.O.</td>
<td>67</td>
<td>M</td>
<td>156</td>
<td>52</td>
<td>2.9</td>
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<tr>
<td>Mean</td>
<td>69</td>
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<td>± S.D.</td>
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<td>6</td>
<td>7</td>
<td>0.8</td>
<td>26</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Subjects are ordered by 10 min walking distance.
rate and ischemic changes. Blood pressure was measured by another doctor who accompanied the subject, using a sphygmomanometer with an arm manschette and the respiratory rate was counted by the chest wall movement at one min intervals. Arterial oxygen saturation (SaO₂) was measured with a finger oxymeter (Model 880241A; Hewlett-Packard, Waltham, MA, USA) and a portable oxymeter carried by the accompanying doctor. To stabilize the SaO₂ measurement, the position of the right third finger was fixed to the shoulder by an arm band. We measured SaO₂, blood pressure, ECG and respiratory rate before and during the walking test, and until 10 min after the walk. To study the reproducibility of the 10 min walking distance, all patients performed the test three times on different days. All exercise testing was done in the morning with intervals of at least 3 days apart but not more than 7. In preliminary studies, we found that SaO₂ did not change more than ± 1% during the 10 min walk with maximal effort in three normal subjects. SaO₂ could be measured linearly above 50% by the manufacturer's specification. For analysis of SaO₂ changes during exercise, the mean of all SaO₂ values taken at one min intervals (mean SaO₂ during exercise) and baseline SaO₂ value were calculated. We defined the recovery time as the time required for an 80% recovery of the decrease in SaO₂ following the cessation of exercise. If SaO₂ did not change or increase during or after exercise we calculated zero recovery time. When SaO₂ increase during exercise and decrease after exercise, recovery time to 80% initial SaO₂ was calculated.

Results are reported as mean ± s.D. Statistical analysis was performed with one-way analysis of variance and Duncan's multiple range test. Significance was accepted at p < 0.05.

RESULTS

The 10 min walking distances (ranging from 60 m to 700 m) covered on the three days were 410 ± 161 m on the first day, 402 ± 183 m on the second day, and 405 ± 179 m on the third day. FEV₁ on the three days were 0.9 ± 0.2, 0.9 ± 0.2 and 0.9 ± 0.3 liters, respectively. Individual values of FEV₁ varied within ± 0.1 liters among the three days. The 10 min walking distance of each patient varied within ± 15% among the three days. Furthermore, there were no significant average differences in either the 10 min walking distance or FEV₁ among the three test days. There were also no different systematic results in each subject's data noted on the second or the third day when compared to the first day. Therefore, we analysed the data obtained on the first test day.

Fig. 1 shows the time course of SaO₂ in 15 patients during and after exercise. The 15 patients were divided into three groups, 5 subjects in each group in order to describe all time course in Fig. 1.: Group I, 5 patients with a 10 min walking distance of less than 370 m; Group II, 5 patients with a 10 min walking distance of less than 470 m; Group III, 5 patients with a 10 min walking distance of more than 475 m. In some of the patients of group I, SaO₂ decreased after exercise rather than at the end of exercise. Neither baseline SaO₂ nor mean SaO₂ during exercise differed among the three groups. However, differences in the recovery time of SaO₂ after exercise were noted between the groups. Fig. 2 shows a significant correlation between the recovery time of SaO₂ and the 10 min walking distances of all patients (p < 0.01). But there is no correlation between baseline SaO₂ or mean SaO₂ during exercise and 10 min walking distance. There is a
significant correlation between $\%$VC and 10 min walking distance ($p < 0.05$) but not with FEV$_1$ predicted. DLCO does not correlate to 10 min walking distance. The height of the P wave in lead II measured at rest shows significant inverse correlation to the 10 min walking distance (Fig. 3, $p < 0.05$), but height of the P wave in lead II does not correlate to FEV$_1$ predicted or $\%$VC. Blood pressure (systolic/diastolic) increased from 122/76 ± 14/12 to 147/85 ± 26/13 mmHg and respiratory rate from 22 ± 5 to 30 ± 5 breath/min. Heart rate increased from 93 ± 15 to 123 ± 16 beat/min. There was no systematic extrasystole or ST depression on the ECG during exercise.

**DISCUSSION**

It has been documented that the 12 min walking test correlates well to the maximum oxygen uptake and ventilation achieved during a progressive exercise...
Fig. 2. Baseline (a) and mean arterial oxygen saturation ($\text{SaO}_2$) (b) plotted against 10 min walking distance. There is no significant correlation. Recovery time of oxygen saturation plotted against 10 min walking distance (c). There is a significant inversely correlation.

Fig. 3. Voltage of P wave on II derivative from ECG taken at rest versus 10 min walking distance. There is a significant inversely correlation.
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Exercise on a bicycle ergometer or treadmill is useful for performing fixed exercise tasks and for monitoring cardiopulmonary parameters during exercise performance. On the other hand, the 10 min walking distance is a realistic measure of quality of life and could be performed relatively easily by the aged subjects in the present COPD group. The patient can choose and adjust his own pace throughout the test, pausing for rest if necessary. The use of a standard time rather than a standard distance provides a more uniform test of endurance. A 12-min walking test was originally described by Cooper as a guide to physical fitness (Cooper 1968). He found a close relation in healthy young men between the distance covered in 12 min running and the maximum oxygen uptake measured on a treadmill, and subsequently published tables relating to oxygen consumption, fitness, and 12-min distance in both sexes over a range of ages (Cooper 1970). The decrease in SaO2 during exercise in COPD subjects has been reported previously (Degaute et al. 1981). We observed a similar decrease in SaO2 during the 10 min walking distance test. However, these changes in SaO2 did not correlate to the 10 min walking distance. We found that the recovery time after cessation of exercise significantly correlated to the 10 min walking distance.

The limited work tolerance in patients with COPD is largely the result of pulmonary-mechanical limitation, rather than metabolic or cardiovascular limitations as is the case in normal subjects (Casey and Weber 1986). In patients with COPD bronchial hyperreactivity has been reported (Boushey et al. 1980). Bronchoconstriction has been observed after exercise not only in subjects with bronchial asthma (Suzuki et al. 1984) but also in normal subjects (O'Cain et al. 1980). Pulmonary artery wedge pressure during mild exercise increases markedly in patients with COPD even though they have no overt left heart disease and no increase in the esophageal pressure as a reflection of mean intrathoracic pressure (Butler et al. 1988). Vascular congestion is reported as one of the factors that causes bronchoconstriction and ventilation-perfusion unevenness (Kikuchi et al. 1984). Physical signs are those of chronic obstructive airflow disease with widespread airway adventitial sounds such as rhonchi or wheeze, the severity of the latter depending upon whether the precipitating deterioration is predominantly asthmatic or not. Those factors may limit work tolerance in patients with COPD.

We observed a significant correlation between the VC predicted and 10 min walking distance. Jones et al. (1971) reported on the maximal work load and the severity of the subject's airway obstruction, as assessed by FEV1, VC and Dl,co. On the other hand, a striking lack of correlation between FEV1 and 12 min walking distance has been reported, emphasizing the range of performances found in patients with established airway obstruction (McGavin et al. 1976). Although the FEV1 in COPD correlated to maximum performance (Jones et al. 1971), it does not predict effort intolerance in tests requiring more prolonged submaximal
effort (McGavin et al. 1978). We do not understand the discrepancy between the two results but it may largely depend on the patients studied. Electrocardiographic observation at rest suggests that pulmonary vascular impairment exists in patients with severe obstructive impairment. Dantzker and D'Alonzo reported no significant change in the degree of ventilation-perfusion mismatch, and a decreased mixed venous oxygen saturation may play a role in hypoxemia during exercise in patients suffering from COPD with pulmonary hypertension (Dantzker and D'Alonzo 1986). In the present results, pulmonary vascular impairment may be partly contributed to the reduction of and prolonged decrease in SaO2.

Some studies reported increased PaO2 after exercise (Ries et al. 1983; Forkert et al. 1989). In the present study, some patients with COPD showed little decrease of SaO2 during and after exercise, which suggests well tolerated exercise performance. In patients with COPD, prolonged hypoxemia has to be carefully investigated, because general fatigue is usually prolonged in those patients who have undergone serious rehabilitation. Baseline SaO2 did not correlate to the 10 min walking distance. However, we do not know the reason for the discrepancy in exercise tolerance between patients with baseline hypoxemia and patients with prolonged hypoxemia after exercise. Subjects with different baseline states may accommodate to hypoxia differently.

Oxygen supply may also reduce prolonged hypoxemia as well as pulmonary vascular resistance (Degaute et al. 1981) and hypoxic bronchoconstriction (Sekizawa et al. 1985), resulting in increased walking distance (Calverley et al. 1981). Oxygen supply also improved hypoxemia during exercise. Present results suggest that oxygen supply is important after exercise as well as during exercise. Therefore, it may be more meaningful to observe the characteristics of SaO2 during recovery time of the 10 min walking exercise, than before and during exercise in aged patients with COPD.

References

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