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Initial Cardiopulmonary Response to Exercise in Chronic Obstructive Pulmonary Diseases (COPD)

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The present study was undertaken to assess the cardiopulmonary response during the initial period of exercise at a low workload in 8 patients with COPD and 10 normal subjects. In the patients with COPD $\dot{V}O_2/VE$ and $\dot{V}CO_2/VE$ were significantly lower than in the normal controls, and more markedly so during the initial period of exercise. SaO_2 and SvO_2 decreased dramatically in the initial period of exercise in the COPD compared with the normal subjects. In contrast to the normal subjects, pulmonary artery mean pressure (PAMP) increased substantially during the initial period of exercise in the patients with COPD. These findings imply that blood gas changes on exercise can be explained by the differences in the relative increase of $\dot{V}O_2$, $\dot{V}CO_2$, VE and cardiac output. Our study also suggests that the measurement of $\dot{V}O_2/VE$, $\dot{V}CO_2/VE$ and SvO_2 and PAMP on exercise at a low workload, especially during the initial period, may be useful for evaluating the cardiopulmonary response to COPD patients.

Introduction

Cardiopulmonary exercise testing can help to determine where lies the factor limiting the exercise in the lungs, the heart, or in both organs. Although the basic physiologic response to exercise has been studied extensively, there are still several controversies regarding the cardiopulmonary response to exercise in patients with chronic pulmonary disease including COPD. The present study was undertaken to assess the cardiopulmonary response to exercise at a low work load in patients with COPD and normal individuals. We concentrated on the response in the initial period of exercise to investigate whether or not it could be used to distinguish COPD patients from normal subjects.

Method

Eight patients with COPD and 10 normal individuals were studied. The clinical characteristics of both groups are presented in Table 1. All 8 patients with pulmonary disease had a clinical course consistent with COPD and none of them had clinical or radiographic evidence of cardiac disease.

An arterial catheter was inserted into the radial artery and balloon-tipped thermal dilution cardiac output catheter was inserted into a subclavicular vein and advanced to the pulmonary under fluoroscopic visualization and pressure recording. Cardiac output (CO) was measured at rest as well as after 3 min. and 15 min. of exercise. Arterial and mixed venous blood gases were measured at rest and during exercise using an ABL3 automated blood gas machine. The O_2 saturation in arterial and mixed venous blood was measured continuously by pulse oximetry (Edwards Critical Care Explorer Mode (EXP-N)). The values of $A\dot{a}DO_2$, VD/VT, O_2 Extra, O_2-transport (O_2T) and overall $\dot{V}A/\dot{Q}$ were calculated using standard formulas. Expired gas was analyzed with an expired gas analyzer (Medical Gas Analyzer MG-360). Using this gas analyzer, a printout was produced at 15-sec intervals of the following parameters ; ventilation /min.($\dot{V}E$), oxygen uptake ($\dot{V}O_2$), carbon dioxide production ($\dot{V}CO_2$), the respiratory gas exchange ratio(R)s and other calculated parameters such as $\dot{V}O_2/VE$ and $\dot{V}CO_2/VE$. Exercise testing was performed on a electrically braked bicycle ergometer at a constant load of 35 W for 15 min.

Data are expressed as the mean and standard deviation. The unpaired t-test was used to compare variables between groups, and the paired t-test was used to compare variables within the same group. Differences were accepted as significant at $p < 0.05$.

Table 1 Clinical profile of the normal subjects and the COPD patients

	Normal subjects (n = 10)	COPD (n = 8)
Age (yrs)	63.7±7.7	65.0±4.6
%VC (%)	99.5±26.5	95.1±22.6
$FEV_{1.0}\%$ (%)	73.2±14.2	45.1±11.6
%DLco (%)	81.8±24.6	46.6±17.4
PaO_2 (Torr)	89.7±10.9	71.6±14.9
$PaCO_2$ (Torr)	32.6±3.6	36.2±5.4
pHa	7.384±0.034	7.377±0.016
PAMP (mmHg)	13.1±2.1	19.9±6.6
CO (L/min)	5.27±1.79	4.42±0.88

Results

Table 2 summarizes the mean values at the gas exchange variables at rest and on exercise. There were no significant differences in $\dot{V}O_2$ and $\dot{V}CO_2$ between the 2 groups at rest or during exercise. $\dot{V}E$ was higher at rest and the difference became more marked during early exercise in the patients with COPD compared with the normal subjects. However, $\dot{V}O_2/\dot{V}E$ and $\dot{V}CO_2/\dot{V}E$ were higher in the normal subjects than in the COPD patients, and the difference was prominent after 1 min and 2 min of exercise ($p = 0.0146$ and $p = 0.0175$, respectively) (Figs.1 and 2). R values were higher in the COPD patients both at rest and during exercise.

Table 3 summarizes the mean values of the arterial and mixed venous blood gas data. The patients with COPD showed mild hypoxemia ($PaO_2 = 71.6 \pm 14.9$ mmHg) at rest and a further decrease in PaO_2 (65.9 ± 15.5 mmHg) during exercise. In normal individuals, PaO_2 increased slightly from 89.7 ± 10.9 mmHg at rest to 95.4 ± 12.6 mmHg after exercise. In the patients with COPD, $PaCO_2$ showed a tendency to increase from 36.2 ± 5.4 mmHg at rest to 39.0 ± 9.7 mmHg after exercise. In contrast, the normal subjects showed no changes in $PaCO_2$ between rest and exercise. Normal subjects had a significantly higher PvO_2 than the COPD patients both at rest and after exercise ($p = 0.0249$ and $p = 0.0040$, respectively), while $PvCO_2$ tended to be higher in the COPD patients both at rest and after exercise. In addition, $AaDO_2$ was higher in the

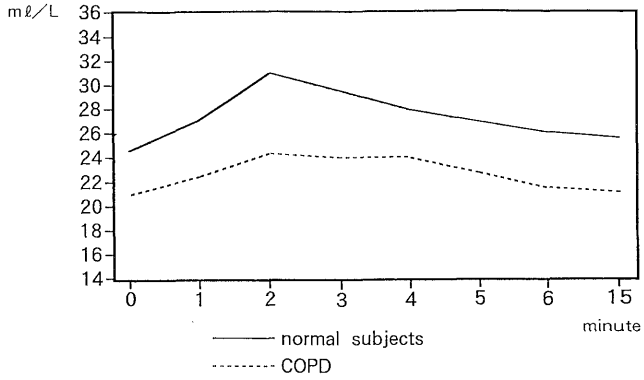

Fig. 1 Changes of $\dot{V}O_2/\dot{V}E$ during exercise

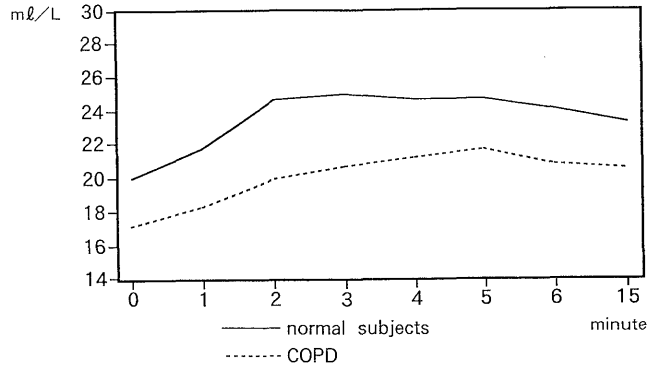

Fig. 2 Changes of $\dot{V}CO_2/\dot{V}E$ during exercise

Table 2 Changes of gas exchange parameters during exercise

	rest	1min	2min	3min	4min	5min	6min	15min
$\dot{V}O_2$ NR	211.3±40.3	301.9±73.4	442.5±80.4	476.2±68.6	468.2±89.7	497.5±84.5	476.4±76.9	500.8±90.4
mℓ/min COPD	213.0±27.7	327.9±62.7	401.4±76.8	455.1±107.1	469.1±102.4	472.6±106.1	459.4±127.5	522.2±134.1
$\dot{V}CO_2$ NR	170.7±36.1	242.4±48.8	354.0±78.6	404.4±68.2	415.7±64.2	455.8±97.4	441.6±83.5	459.0±100.1
mℓ/min COPD	173.0±20.4	277.9±99.9	331.9±48.8	392.1±86.6	418.9±85.3	444.6±84.0	436.3±115.8	496.8±136.7
R NR	0.81±0.08	0.81±0.10	0.80±0.08	0.85±0.10	0.90±0.10	0.91±0.12	0.93±0.09	0.91±0.10
COPD	0.82±0.07	0.83±0.13	0.84±0.12	0.87±0.09	0.90±0.07	0.95±0.09	0.96±0.05	0.95±0.05
$\dot{V}E$ NR	8.65±1.67	11.12±2.60	14.59±3.87	16.14±2.64	16.84±3.44	18.27±3.85	17.99±2.98	19.12±3.58
L/min COPD	10.11±1.56	15.22±4.91	16.76±4.00	19.19±5.79	19.94±5.97	21.00±6.41	21.07±7.26	23.99±7.09
$\dot{V}O_2/\dot{V}E$ NR	24.8±2.9	27.5±3.6	31.4±5.4	30.0±5.3	28.3±4.9	27.7±3.7	26.8±4.4	26.4±3.2
mℓ/L COPD	21.2±3.9	22.7±3.6	24.5±5.1	24.4±5.8	24.4±5.1	23.4±6.7	22.4±5.4	22.1±5.2
$\dot{V}O_2/\dot{V}E$ NR	20.0±2.5	22.0±2.9	24.7±2.8	25.3±3.3	25.0±2.9	25.0±3.1	24.7±3.9	24.1±3.2
mℓ/L COPD	17.1±2.0	18.4±1.7	20.2±3.1	21.0±3.5	21.7±3.4	22.2±5.6	21.4±4.3	21.3±5.2

Table 3 Mean arterial and mixed venous blood gases in normal subjects and COPD patients

	Normal subject (n = 10)		COPD (n = 9)	
	Rest	Exercise	Rest	Exercise
pHv	7.384±0.034	7.329±0.019	7.377±0.016	7.306±0.037
$PvCO_2$ (Torr)	37.3±5.3	42.4±4.6	41.1±6.2	47.5±8.7
PvO_2 (Torr)	40.7±5.0	33.6±2.9	35.9±2.6	28.7±3.1
pHa	7.402±0.024	7.372±0.015	7.399±0.024	7.364±0.047
$PaCO_2$ (Torr)	32.6±3.6	33.2±1.9	36.2±5.4	39.0±9.7
PaO_2 (Torr)	89.7±10.9	95.4±12.6	71.6±14.9	65.9±15.5
$AaDO_2$ (Torr)	18.2±12.0	16.8±10.8	33.8±14.1	40.2±13.1
$\dot{V}_D/\dot{V}_T$	0.42±0.09	0.35±0.09	0.54±0.03	0.48±0.07
$\dot{V}A/\dot{Q}$	0.72±0.48	1.30±0.27	0.70±0.21	1.36±0.51
O_2Extra	0.2239±0.0992	0.3840±0.0609	0.2566±0.0359	0.4694±0.0525
	48.7±17.2	63.0±20.6	40.4±5.1	59.7±8.9

patients with COPD than the normal subjects both at rest ($p = 0.0256$) and after exercise ($p = 0.0011$). In the COPD patients, $AaDO_2$ tended to increase on exercise to 4 0.22 ± 13.09 mmHg from 33.83 ± 14.11 mmHg. However, the normal subjects showed a decrease of $AaDO_2$ after exercise compared with at rest (16.81 ± 10.79 mmHg vs.18.16 ± 11.97 mmHg). VD/VT was significantly higher in the COPD patients than the normal subjects both at rest ($p = 0.0036$) and after exercise ($p = 0.0046$), but VD/VT tended to decrease after exercise in both groups. Overall $\dot{V}A/\dot{Q}$ increased significantly in both the COPD patients and the normal subjects from rest to exercise, and there was no difference between the 2 groups. In the COPD patients, O_2 Extra was higher at rest and significantly so after exercise ($p = 0.0078$) when compared with the normal subjects.

The SaO_2 and SvO_2 values measured by pulse oximetry are shown in Fig.3. In normal subjects, SaO_2 showed almost no changes, but it decreased in the COPD patients during exercise and showed the most rapid decline during the first 2 min. SaO_2 decreased from $95.6 \pm 3.3\%$ at rest to $91.8 \pm 8.8\%$ after 2 min of exercise. SvO_2 was much higher in the normal subjects than the COPD patients both at rest ($77.10 \pm 4.25\%$ vs $70.50 \pm 3.63\%$, $p = 0.0031$) and after exercise ($59.38 \pm 7.85\%$ vs $50.50 \pm 6.80\%$, $p = 0.00336$). Sv O_2 decreased significantly in both the COPD patients and the normal subjects from rest to exercise and the largest decline occurred in the initial period of exercise. However, in normal subjects there was no further decrease of SvO_2 after 1 min of exercise while it continued to fall until 3 min in the COPD patients.

Figures 4 and 5 show the changes of hemodynamic variables during exercise. CO tended to be lower in the patients with COPD (4.4 ± 0.9 L/min.) than in the normal subjects (5.3 ± 1.8 L/min.) at rest. It increased significantly in both groups during exercise. However, the normal subjects had a higher CO after 3 min at the end of exercise, while the patients with COPD had a higher CO at the end of exercise (Fig.4). Thus, CO increased more slowly in

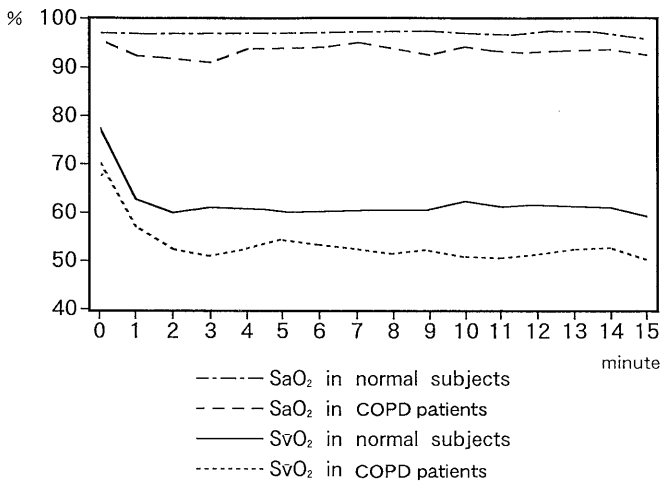

Fig. 3 Changes of SaO_2 and SvO_2 during exercise

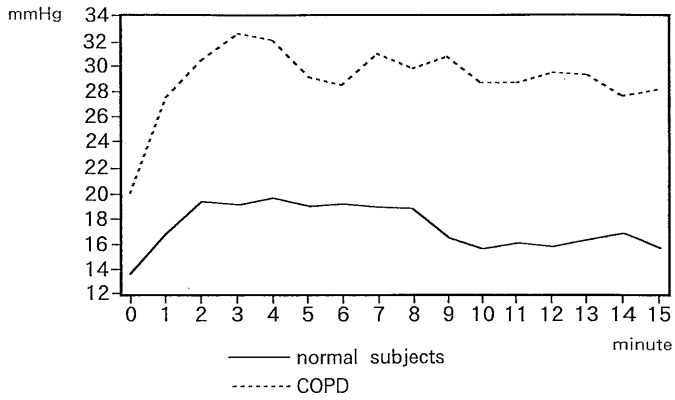

Fig. 4 Changes of CO during exercise

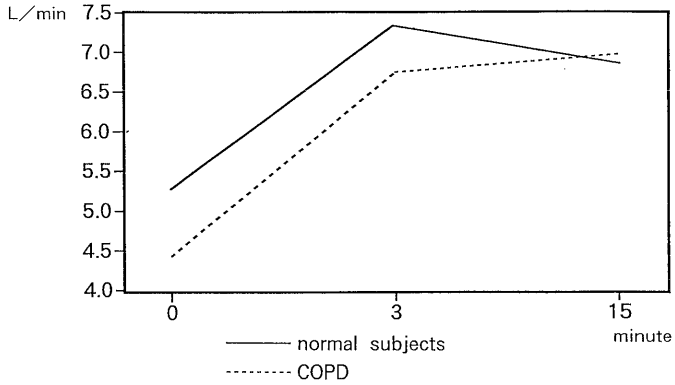

Fig. 5 Changes of PAMP during exercise

COPD. PAMP in patients with COPD showed a higher value both at rest and during exercise than that of normal subjects. In the COPD patients, PAMP increased rapidly during the first 3 min of exercise from 19.9 ± 6.6 mmHg to 32.6 ± 14.0 mmHg ($p = 0.0116$). In contrast, the normal subjects showed no significant change of PAMP with exercise (Fig.5).

Discussion

This study showed that there were no significant differences in $\dot{V}O_2$ and $\dot{V}CO_2$ between the COPD patients and the normal control subjects both at rest and during exercise. However $\dot{V}O_2/\dot{V}E$ and $\dot{V}CO_2/\dot{V}E$ were significantly higher in the normal subjects than in the COPD and the difference was greatest at the initial period of exercise. Thus, COPD patients had a higher $\dot{V}E$ than the normal subjects. It has been shown that COPD patients exhibit a high ventilatory response at any level of oxygen uptake during exercise (1), which implies that alveolar ventilation does not show as great a relative increase as $\dot{V}O_2$ and $\dot{V}CO_2$ when compared with normal subjects. Although $\dot{V}E$ is higher (hyperventilation) in COPD patients than normal subjects because of poor gas exchange, $\dot{V}E$ cannot counterbalance the

increment of $\dot{V}O_2$ and $\dot{V}CO_2$ on exercise, and this seems to be more of a problem in the initial period of exercise. Accordingly, the values of $\dot{V}O_2/\dot{V}E$ and $\dot{V}CO_2/\dot{V}E$ were lower in COPD patients than in normal subjects. Inefficient gas exchange is reflected by the pulmonary function data at rest, as well as by $AaDO_2$ and VD/VT at rest and on exercise. Since alveolar ventilation cannot increase relatively as much as $\dot{V}O_2$ and $\dot{V}co_2$ during exercise in COPD, both PaO_2 and SaO_2 must fall and $PaCO_2$ tends to rise. However, the overall $\dot{V}A/\dot{Q}$ relationship seems to be improved after exercise in patients with COPD and showed no significant difference from that in the normal subjects. Similar findings have been previously reported by others (2)(3). Gledhill and coworkers (3) pointed out the importance of an increase in mean $\dot{V}A/\dot{Q}$ (caused by a greater increase of ventilation than cardiac output during exercise) for preserving a normal PaO_2 despite the increased $\dot{V}A/\dot{Q}$ inbalance and decreased PvO_2. Because the PvO_2 influences the end-capillary PO_2 of every lung unit (4), one might expect that exercise would lead to a fall in PaO_2. However, as $\dot{V}A/\dot{Q}$ increases above 1.0, the impact of a falling PvO_2 on end-capillary PO_2 diminishes (5) and significant arterial desaturation is prevented. In the patients with COPD, $AaDO_2$ and VD/VT were significantly higher than in the normal subjects both at rest and after exercise suggesting that pulmonary O_2 transfer may be partially limited by diffusion in COPD. In addition, R tended to increase and PvO_2 to decrease during exercise, which could be another causes of an increase in $AaDO_2$ in COPD.(6). Further studies are needed to confirm these observations.

Our results showed that both PvO_2 and SvO_2 fell dramatically in the COPD patients and more obviously in the initial 3 min of exercise. As is well known, two mechanisms furnish oxygen to working muscles during exercise, with one being an increase in muscle blood flow and the other being an increase in tissue oxygen extraction. Even in normal subjects, PvO_2 and SvO_2 fall with exercise, because the ralative increase in $\dot{V}O_2$ exceeds that of the cardiac output (6). Our results showed that PvO_2 and SvO_2 fell while O_2 Extra increased during exercise in both the COPD patients and the normal subjects. However, the patients with COPD showed more substantial decreases of SvO_2, Pv O_2 and a greater increase of O_2 Extra than that of normal subjects, even with modest exercise. This suggests that the patients with COPD have pulmonary hypertension due to hypoxic vasoconstriction compounded by structural abnormalities. Thus, the cardiac output response to exercise may be subnormal or abnormal, so that SvO_2 along with PvO_2 is lower than in normal subjects. As our results showed, patient with COPD tended to have a lower CO than the normal subjects and this difference was more obvious in the initial period of exercise (up to 3 min). The COPD patients also showed a significant increase of PAMP that was marked during early exercise and appeared to be consistent with the changes of CO. Pulmonary hypertension limits the degree to which CO can be increased as a method of increasing tissue oxygen delivery (7).

In conclusion, our data indicate that $\dot{V}O_2/\dot{V}E$ and $\dot{V}CO_2/\dot{V}E$ are significantly lower in COPD than in normal controls and are more significantly so at the initial period of exercise. In the patients with COPD, SaO_2 and SvO_2 were significantly lower than in the normal subjects, and more substantially so in the initial period of exercise. In COPD patients, PAMP was also significantly increased during early exercise when compared with normal subjects. These findings imply that the blood gas changes on exercise can be explained by differences in the relative increase of $\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}E$, and cardiac output. Our results suggest that the measurement of $\dot{V}O_2/\dot{V}E$. $\dot{V}CO_2/\dot{V}E$, SvO_2, and PAMP on exercise, especially in the initial period at a relatively low workload, may be useful for evaluating the cardiopulmonary response to exercise in patients with COPD.

References

1) Joan A. Barbera, et al: Gas exchange during exercise in mild chronic obstructive pulmonary disease. Am. Rev. Respir. Dis. 144: 520, 1991.
2) Agusti AGN, Barbera JA, et al:Hypoxic pulmonary vasoconstriction and gas exchange during exercise in chronic obstructive pulmonary disease. Chest 97: 268, 1990.
3) Dantzker DR, Dalonzo GE:The effect of exercise on pulmonary gas exchange in patients with severe chronic obstructive pulmonary disease. Am. Rev. Respir. Dis. 134: 1135, 1986.
4) Mithoefer JC, Ramirez C, Cook W:The effect of mixed venous oxygenation on arterial blood in chronic obstructive pulmonary disease. Am. Rev. Respir. Dis. 117: 259, 1978.
5) West JB:Ventilation-perfusion relationships. Am. Rev. Respir. Dis. 116: 919, 1977.
6) Wagner PD:Ventilation-perfusion matching during exercise. Chest 101: 192 s, 1992.
7) Dantzker DR, et al:Pulmonary gas exchange during exercise in patients with chronic obstructive pulmonary hypertension. Am. Rev. Respir. Dis. 130: 412, 1984.