【短 報】

RELATIONSHIP BETWEEN EXERCISE HYPERPNEA AND EXERCISE
TOLERANCE IN PATIENTS ON CHRONIC HEMODIALYSIS

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Introduction

It is known that exercise hyperpnea (EH) occurs during physical exertion in patients on chronic hemodialysis (HD). It is believed that EH prevents maximal physical activity and is a critical factor in limiting the quality of life. However, until now no objective evaluation of EH in patients on HD has been published. In the present study, we used the slope of minute ventilation to carbon dioxide production during incremental exercise ($\dot{V}E/\dot{V}CO_2$ slope)^{1~4)} to evaluate EH in these patients. In addition, we investigated the relationship between EH and exercise tolerance in patients on HD.

Subjects and Methods

Two groups of subjects were included in the study. The first group, consisting of 63 patients with a mean age of 38.1 ± 11.8 years, had undergone regular hemodialysis for a mean duration of 29.3 ± 29.5 months. The underlying disease pro-

cesses were chronic glomerulonephritis ($n=61$), vesicoureteral reflux ($n=1$), and chronic pyelonephritis ($n=1$). Exclusion criteria included heart disease, diabetes mellitus, and liver dysfunction. No patient was receiving therapy with beta blockers, antiarrhythmics, or digitalis. The second group, consisted of 59 healthy age-matched controls (mean age, 37.5 ± 11.3 years).

Patients were placed on a treadmill according to the modified Bruce protocol (Sheffield) on a non-dialysis day. The 12-lead electrocardiograph and heart rate were monitored throughout the test. Cuff blood pressure was measured every minute with a manual sphygmomanometer. Subjects were encouraged to continue the exercise until they perceived exhaustion in themselves. $\dot{V}E$ and $\dot{V}CO_2$ were measured continuously using a system-5 respiratory gas analyzer (AIC, Tokyo, Japan). The slope of $\dot{V}E$ and $\dot{V}CO_2$ was calculated by linear regression analysis with $\dot{V}E$ and $\dot{V}CO_2$ values obtained during exercise before the point of respiratory compensation. The maximum oxygen up-

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take ($\dot{V}O_2$ max) was corrected with functional aerobic impairment (FAI) to exclude the effect of age and gender⁵⁾. FAI was calculated as follows :

$$FAI = (\text{predicted } \dot{V}O_{2\text{max}} - \text{observed } \dot{V}O_{2\text{max}}) / \text{predicted } \dot{V}O_{2\text{max}} \times 100$$

The results are expressed as the mean value $\pm$ SD. The significant differences in ventilatory parameters were determined by the unpaired t-test. The relationship between FAI and the slope of the $\dot{V}E/\dot{V}CO_2$ was assessed by linear regression analysis. $p < 0.05$ was considered significant.

Results and Discussion

No significant difference was seen between the

healthy controls and patients on HD in ventilatory parameters at rest (Table 1). This suggests that the hyperventilation does not occur at rest, assuming HD is performed correctly and effectively. However, the slope of $\dot{V}E/\dot{V}CO_2$ in patients on HD (36.9 ± 4.7) was significantly steeper than that of healthy controls (27.9 ± 3.6). The values obtained in this study for healthy controls were similar to those reported by Metra¹⁾ and Reindl²⁾ in healthy individuals (28.0 ± 4 and 27.4 ± 3.5 , respectively), while values for patients on HD were similar to those reported by Clark et al.³⁾ and Levra et al.⁴⁾ for patients with severe chronic heart failure (the measured values were 37.8 ± 9.0 and 36.7 ± 13.1

Table 1. Comparison of ventilatory parameters between patients with HD and healthy controls at rest and during exercise.

Variables	Controls	HD patients
Rest		
$\dot{V}E$ (ml/kg/min)	140.9 ± 28.7	134.9 ± 21.6
$\dot{V}O_2$ (ml/kg/min)	3.57 ± 0.40	3.55 ± 0.44
$\dot{V}CO_2$ (ml/kg/min)	2.98 ± 0.44	2.82 ± 0.46
$\dot{V}E/\dot{V}CO_2$	47.2 ± 6.0	48.1 ± 4.7
$\dot{V}E/\dot{V}O_2$	39.7 ± 7.7	38.2 ± 5.8
$\dot{V}CO_2/\dot{V}O_2$	0.84 ± 0.09	0.80 ± 0.12
RR (time/min)	14.1 ± 4.0	14.7 ± 3.8
VT (ml/kg/min)	10.8 ± 4.0	9.6 ± 2.5
Submaximum		
$\dot{V}E/\dot{V}CO_2$ slope	27.9 ± 3.6	$36.9 \pm 4.7^*$
AT (ml/kg/min)	24.5 ± 5.0	$17.6 \pm 3.6^*$
OUES	2307.9 ± 645.4	$1490.5 \pm 366.8^*$
Maximum		
$\dot{V}E$ (ml/kg/min)	1295.0 ± 318.5	$1037.0 \pm 262.1^*$
$\dot{V}O_2$ (ml/kg/min)	37.43 ± 7.5	$25.5 \pm 5.0^*$
$\dot{V}CO_2$ (ml/kg/min)	40.8 ± 8.2	$25.7 \pm 6.4^*$
$\dot{V}E/\dot{V}CO_2$	31.8 ± 4.0	$40.6 \pm 4.9^*$
$\dot{V}E/\dot{V}O_2$	34.7 ± 5.0	$42.0 \pm 6.2^*$
$\dot{V}CO_2/\dot{V}O_2$	1.10 ± 0.09	1.04 ± 0.08
RR (time/min)	41.3 ± 7.1	39.1 ± 7.5
VT (ml/kg/min)	31.4 ± 5.5	$27.0 \pm 6.1^*$
FAI (%)	4.5 ± 16.2	$30.7 \pm 13.0^*$

$\dot{V}E$: minute ventilation ; $\dot{V}O_2$: oxygen uptake ; $\dot{V}CO_2$: carbon dioxide production ; RR : respiration rate ; VT : tidal volume ; FAI : functional aerobic impairment ; AT : anaerobic ventilatory threshold ; OUES : oxygen uptake efficiency slope.

* : $p < 0.001$ cf. controls

Fig. 1. Relationship between functional aerobic impairment (FAI) and the slope of ventilation to carbon dioxide production in patients on chronic hemodialysis (open circle) and healthy controls (open cross).

for patients with left ventricular ejection fraction of $25.9 \pm 3.4\%$ and $25.8 \pm 14.8\%$, respectively). These findings suggest that EH in patients on HD is substantially greater than in healthy individuals, occurring on the same order as in patients with severe chronic heart failure.

Adequate investigations have not yet been conducted on the mechanism of EH in HD patients; and the present study has not clarified the matter. However, it appears that an important contribution is made by pathologic factors such as an increase of the physiologic dead space ventilation⁶⁾ caused by a decrease in pulmonary perfusion⁷⁾ and a decrease in pulmonary diffusion capacity due to calcification⁸⁾, occurrence of metabolic acidosis early in exercise⁹⁾, and anemia associated with renal failure.

No correlation between the slope of $\dot{V}E/\dot{V}CO_2$ and either age or gender was found in any group, indicating that this slope can be used to evaluate EH without concern over the affect of these factors.

In patients on HD, a positive correlation was seen between the $\dot{V}E/\dot{V}CO_2$ slope and FAI, while no such correlation was found in normal controls

(Fig. 1). Although the association between slope of $\dot{V}E/\dot{V}CO_2$ and exercise tolerance in healthy individuals was not established in a previous report¹⁾, this study supports the conclusion that exercise tolerance and EH are not related. On the contrary, a positive correlation was seen between the slope of $\dot{V}E/\dot{V}CO_2$ and exercise tolerance in patients on HD, suggesting that the pathology associated with EH may be related to exercise tolerance.

In conclusion, these findings suggest that the slope of $\dot{V}E/\dot{V}CO_2$ is useful for correlating EH with exercise tolerance in patients on HD.

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