The Influence of Body Size on the Ventilatory Response to Hypercapnia

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Summary The slope of ventilatory response to hypercapnia at rest was determined in 77 healthy male students by means of the CO₂-rebreathing method. It was found that the hypercapnic ventilatory response slope (*S*) was significantly lower in the lean group with BMI (body mass index) below 19 than that in the normal group, while there were no significant correlation between *S* and body weight or height. These results indicate that sensitivity of hypercapnia in the lean subjects differed from that of normal and overweight subjects.

Key words: hypercapnia, ventilatory response, body size.

Although there are considerable variations in the slope of ventilatory response to hypercapnia, the reasons for this scatter are not fully understood. They may be related to various factors such as age, sex, temperature, training, measurement intervals, and body size. Concerning the last factor, contradictory results have been reported by other investigators. PATRICK and HOWARD (1972) reported that the slope of ventilatory response to CO₂ was not significantly related to body size. By contrast, HIRSHMAN *et al.* (1975) found significant correlation between hypercapnic ventilatory response slope (*S*) and height or weight, implying that some of the variation in *S* is attributable to body size. It should be emphasized here, however, that the experiments were conducted in a small number of subjects in the case of Patrick and Howard, and in forty males and four females between 21 and 51 years of age in the case of Hirshman *et al.*, respectively.

Since females have a lower hypercapnic ventilatory drive than males (IRSIGLER, 1976; WHITE *et al.*, 1983) and older males have significantly lower *S* than younger men (KRONENBERG and DRAGE, 1973; BRISCHETTO *et al.*, 1984), we intended to further investigate whether the slope of ventilatory response line to

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hypercapnia is independent of body size.

Seventy-seven healthy students, age 18–26 years, participated in this study. All had not participated in any regular physical training. All subjects gave their consent after the nature of the experiments had been explained.

The subjects came to the laboratory twice. On the first day, each subject was familiarized only with the apparatus and testing procedure. The actual experiment was conducted on a separate day at least one week after from first day.

Ventilatory response to hypercapnia was determined by the rebreathing method after the subject rested in a sitting position for about 30 min; the subject rebreathed a gas mixture (about 7% CO₂ in O₂) of 5–6 l for 4 min as described by READ (1967). Value for minute ventilation ($\dot{V}_E$) was calculated for successive 30 sec intervals from spirometric recording. A continuous record of alveolar P_{CO_2} (P_{ACO_2}) in the expired gas was obtained by drawing gas from the mouth piece through an infrared CO₂ analyzer. The relationship between P_{ACO_2} and $\dot{V}_E$ is represented as follows: $\dot{V}_E = S(P_{ACO_2} - B)$. The parameter S of the CO₂ response line is the slope representing the sensitivity to CO₂ in the absence of hypoxia, and the intercept B represents the CO₂ threshold. S was recalculated as S_N by using normalized ventilation for 70 kg body weight (BW), using the allometric coefficient $BW^{0.75}$.

The ventilation corresponding to P_{ACO_2} of 60 mmHg ($\dot{V}_{E(60)}$) was calculated from the response line to compare the magnitude of ventilation in actually measured P_{ACO_2} range among the subjects, since the ventilatory response lines obtained here were located around a P_{ACO_2} of about 50 to 70 mmHg (MIYAMURA *et al.*, 1980). Moreover, the breathing pattern was analyzed in terms of the slope and intercept (M and K) of the linear regression of ventilation to tidal volume as proposed by HEY *et al.* (1966): $\dot{V}_E = M(V_T - K)$.

As described previously, PATRICK and HOWARD (1972) have reported that there are no significant correlations between body size and the slope of ventilatory response to hypercapnia, but the number of subjects was not provided. Despite the same rebreathing method, however, HIRSHMAN *et al.* (1975) observed a significant correlation between S and height or weight. In this study, the ventilatory response curve to hypercapnia for each subject was also measured by means of Read's rebreathing method, and the response slope is plotted against body weight and height in Fig. 1. No significant relationship between slope and body weight ($r=0.221$, $p>0.05$) or height ($r=0.032$, $p>0.05$) were seen. Moreover, there are no significant correlations between slope (S) and body surface area ($r=0.214$, $p>0.05$). These results basically agree with data reported by Patrick and Howard. The discrepancy of results between the present and Hirshman *et al.*'s studies may be due to the difference in the subjects; *i.e.*, among their subjects are included a few women and older men.

To clarify the relation between body size and the slope of ventilatory response to hypercapnia, the body mass index (BMI, sometimes called the Quetelet index), weight in kilograms divided by the square of height in meters (W/H^2), was cal-

Fig. 1. Slope of ventilatory response to hypercapnia is plotted against body weight and height in 77 normal students.

Table 1. Physical characteristics and ventilatory response to hypercapnia in the four groups.

	Group I (Lean)	Group II (Normal)	Group III (Overweight)	Group IV (Obese)
<i>n</i>	19	43	5	10
Age (yr)	19.5±1.1	19.1±1.0	19.2±1.3	20.8±2.4
Weight (kg)	52.3±4.0**	63.2±6.6	73.7±5.8**	98.8±12.1**
Height (cm)	170.6±5.0	169.8±6.3	172.9±6.5	171.5±4.7
BSA (m ²)	1.61±0.07	1.73±0.11	1.87±0.09	2.11±0.16
BMI	17.6±1.0**	22.1±1.6	26.8±0.8**	33.9±2.8**
<i>S</i> (l·min ⁻¹ ·mmHg ⁻¹)	1.15±0.50**	1.79±0.86	1.76±0.59	1.73±0.86
<i>S_N</i> (l·min ⁻¹ ·mmHg ⁻¹)	1.44±0.63*	1.95±0.95	1.68±0.50	1.31±0.57*
<i>S</i> /BSA (l·min ⁻¹ ·mmHg ⁻¹)	0.71±0.30**	1.05±0.53	0.93±0.27	0.80±0.35
<i>B</i> (mmHg)	40.2±6.7*	44.3±4.8	46.0±5.4	42.0±10.8
$\dot{V}_{E(80)}$ (l·min ⁻¹)	21.4±8.2	26.3±12.3	23.2±11.9	25.1±9.8
<i>M</i> (min ⁻¹)	23.3±7.3	24.7±10.1	24.7±11.9	23.3±7.5
<i>K</i> (l)	0.22±0.32	0.28±0.30	0.34±0.32	0.29±0.38

Values are mean±S.D. BSA: Body surface area, BMI: Body mass index, *S*: Slope of ventilatory response to hypercapnia estimated from regression equation ($\dot{V}_E = S(P_{A_{CO_2}} - B)$), *S_N*: normalized *S* for 70 kg body weight, *S*/BSA: *S* divided by body surface area, *B*: intercept on the $P_{A_{CO_2}}$ axis, *M*: Slope in Hey *et al.*'s equation ($\dot{V}_E = M(V_T - K)$), *K*: intercept on the V_T axis. Significant level of difference from Group II (normal) represented by stars.

* $p < 0.05$, ** $p < 0.01$

culated for each subject (KEYS *et al.*, 1972). The subjects were divided into four groups based on body mass index. Group 1: 19 lean males with BMI below 19; Group 2: 43 normal males with BMI between 20–25; Group 3: 5 overweight males with BMI 26–29; Group 4: 10 obese males with BMI over 30.

Table 1 summarizes average value and standard deviations for *S*, *S_N*, *S*/BSA, *B*, $\dot{V}_{E(80)}$, *M*, and *K* in the four groups. Average values and standard deviations of the slope (*S*) of ventilatory response to hypercapnia were 1.15 ± 0.50 for the lean group, 1.79 ± 0.86 for the normal group, 1.76 ± 0.59 for the overweight group, and 1.73 ± 0.86 l/min/mmHg for the obese group, respectively. The normal, overweight, and obese groups had about the same *S*. Since hypercapnic ventilatory response is known to diminish in the subjects with obese-hypoventilation syndrome or Pickwickian syndrome, but not in those with simple obesity (LOURENCO, 1969; ORENSTEIN *et al.*, 1980), our obese subjects were not considered to be patients with hypoventilation syndrome.

Although significant correlation ($r=0.67$, $p<0.001$) was found between parameter of Hey-plot (*M*) and the CO₂ response line (*S*), and the lean group exhibited lower *S* value than the normal group, average values of *M* obtained here were almost the same in the four groups (Table 1). These results indicate that *M* is not influenced by body size and may be a fundamental parameter of each individual's respiratory mechanism as described by HEY *et al.* (1966).

On the other hand, if the slope of ventilatory response to hypercapnia at rest is related to body size, the slope obtained with a different body weight should be same when the S value was recalculated after normalization of ventilation for 70 kg body weight (S_N) or after division by body surface area (S/BSA). However, the lean group with a BMI of lower than 19 still exhibited significantly lower S_N and S/BSA values than the normal group. At present, we cannot explain the reason for lower S in the lean group based on definite physiological grounds. It has been reported that catecholamine concentration increased and body temperature decreased with CO_2 inhalation (BULLARD, 1964), and that raising body temperature and catecholamine cause a significant augmentation in hypercapnic ventilatory response (CUNNINGHAM *et al.*, 1958; NATALINO *et al.*, 1977). Although lack of measurement of body temperature and catecholamine concentration in the present study made it difficult to draw valid inferences, such factors may be related to the present results. Therefore, the degree of decrement in body temperature and/or increment in catecholamine concentration during CO_2 rebreathing might differ between lean and normal subjects. However, these possibilities must be confirmed by further investigation.

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