High Ventilatory Response to Hypoxia Observed in Obese Judo Athletes

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Abstract Fifty-two active Judo athletes were examined using an isocapnic progressive hypoxia test. The results were analyzed by the hyperbola ventilation equation $\dot{V} = \dot{V}_0 + A/(P_{ET_{O_2}} - C)$, where $\dot{V}$ is observed ventilation, $\dot{V}_0$ the horizontal asymptote in ventilation for infinite end-tidal P_{O_2} ($P_{ET_{O_2}}$), A the slope constant indicating magnitude of hypoxic sensitivity, and C the vertical asymptote in $P_{ET_{O_2}}$ for infinite ventilation.

Hypoxic sensitivity, A , was positively correlated with body weight (BW). Such correlation in the light and middleweight groups ($BW < 95$ kg) and the heavyweight group ($BW > 95$ kg) with Röhler's index being less than 200 became insignificant when the A value was recalculated after normalization of ventilation for 70 kg body mass. However, the heavyweight group with a Röhler index of higher than 200 still exhibited a significantly higher A value than the light and middleweight groups after normalization of ventilation. These results indicated that body weight plus obesity were determining factors in the increase of hypoxic sensitivity in our subjects.

Key Words: progressive hypoxia, ventilation, Judo athlete, obesity.

Obesity is known to often be accompanied by hypoventilation, somnolence, hypoxemia, and/or hypercapnia, symptoms collectively called "Pickwickian syndrome" (BURWELL *et al.*, 1956). Decreased ventilatory or respiratory motor responses to hypoxia and CO_2 have also been verified in patients suffering from this syndrome (CULLEN and FORMEL, 1962; LOURENÇO, 1969; ZWILLICH *et al.*, 1975a; KRONENBERG *et al.*, 1977; GARAY *et al.*, 1981). However, in 1975 Kronenberg *et al.* demonstrated that impairments in these respiratory functions are not invariably associated with obesity. In the present study, we found an increased instead of a decreased ventilatory response to hypoxia in obese Judo athletes who were in excellent health with severe training conducted daily.

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MATERIALS AND METHODS

Subjects. Fifty-two male subjects ranging from 17 to 23 years of age were studied. They were all physically active and participating in at least 3 hr training every day except Sunday. Informed consent was obtained from all the subjects upon explanation of the experimental design. Subjects weighing less than and over 95 kg were designated as being of light and middleweight class and heavy-weight classes, respectively. The latter was further divided on the basis of Röhrrer's index (RI) expressing degree of obesity: Groups A and B were up to and above RI 200, respectively. Mean values of the physical characteristics and the pulmonary functions of the above three groups are shown in Table 1. In general, all the subjects were above normal as regards physical characteristics of the Japanese, and were in excellent health. They had been trained for about 8–10 yrs. In all three groups, both per cent vital capacity (%VC) and per cent forced expiratory volume in one second (FEV_1 %) were well in the range of normal values,

Table 1. Physical characteristics, pulmonary functions and ventilatory responses to hypoxia of the subjects.

	Group I Light and middleweight class (BW < 95 kg)	Group II Heavyweight class (BW > 95 kg)	
		A (RI < 200)	B (RI > 200)
<i>N</i>	35	11	6
Physical characteristics:			
Height (cm)	172 ± 6	180 ± 3	175 ± 5
Weight (kg)	76 ± 9	105 ± 7	116 ± 10
Röhrrer's index	149 ± 13	181 ± 13	215 ± 9
Age	20 ± 1	20 ± 1	21 ± 1
Training period (yrs)	8 ± 1	8 ± 1	10 ± 1
Pulmonary functions:			
%VC	109 ± 11	10.8 ± 13	110 ± 16
FEV_1 %	85 ± 7	85 ± 7	87 ± 6
Ventilatory responses to hypoxia:			
<i>A</i> (liters · min ⁻¹ · mmHg)	295 ± 264	458 ± 323*	1,155 ± 1,027***
<i>A_N</i> (liters · min ⁻¹ · mmHg)	271 ± 220	333 ± 224	770 ± 657**
<i>C</i> (mmHg)	30 ± 6	29 ± 10	24 ± 14
<i>A_a</i> (liters · min ⁻¹ · mmHg)	278 ± 249	431 ± 304*	1,087 ± 966***
<i>A_{Na}</i> (liters · min ⁻¹ · mmHg)	255 ± 207	313 ± 210	725 ± 618**
<i>Ca</i> (mmHg)	24 ± 6	23 ± 10	18 ± 13

Values are mean ± S.D. BW: body weight. RI: Röhrrer's index. %VC: per cent vital capacity. FEV_1 %: per cent forced vital capacity in one second. *A*: slope index of hypoxic ventilatory response curve in the hyperbola equation. *A_N*: normalized *A* for 70 kg body mass. *C*: asymptote for end-tidal P_{O_2} in the hyperbola equation. Suffix *a* for *A*, *A_N* and *C* indicates that analysis for hypoxic response is conducted in terms of arterial P_{O_2} .

*** and ** differences between Group I and II B are significant at 0.1 and 1% levels, respectively.

* difference between Group II A and B is significant at 5% level.

and no significant differences were seen between the respective groups.

Experimental procedure. The experiment was conducted at least 3 hr after the final meal and a 30-min rest was taken before the test. Figure 1 illustrates the experimental setup used in the study. The subject holding a mouthpiece in place sat comfortably on a chair. He breathed room air first, and end-tidal P_{O_2} and P_{CO_2} ($P_{ET_{O_2}}$ and $P_{ET_{CO_2}}$, respectively) were continuously monitored by rapid response O_2 and CO_2 analyzer (San-ei Expired Gas Monitor 1H21). Then, the subject started rebreathing by turning a three-way stopcock to the bag filled by approximately 10 liters room air. By adjusting the amount of O_2 inflow from a cylinder and of CO_2 absorbed by a CO_2 absorber in the by-pass circuit, $P_{ET_{O_2}}$ and $P_{ET_{CO_2}}$ were set at 100 mmHg and 5 mmHg higher than the control values during room-air breathing, respectively. These $P_{ET_{O_2}}$ and $P_{ET_{CO_2}}$ values were maintained for at least 3 min to obtain steady state ventilatory conditions. Then, while maintaining the $P_{ET_{CO_2}}$ level unchanged, $P_{ET_{O_2}}$ was progressively lowered by turning off the supply of O_2 from the O_2 cylinder. The rate of $P_{ET_{O_2}}$ fall was approximately 10 mmHg/min. When a vigorous ventilatory response appeared in severe

Fig. 1. Experimental setup for the progressive hypoxia test. The subject first breathes room air by turning three-way stopcocks shown at right. End-tidal P_{O_2} ($P_{ET_{O_2}}$) and P_{CO_2} ($P_{ET_{CO_2}}$) are continuously monitored and recorded. From a hot-wire flow anemometer inserted between mouthpiece and respiratory valve, respiratory flow, integrated tidal volume, inspiratory (T_i), and expiratory time (T_e) are continuously recorded. After closing the three-way stopcocks to the rebreathing circuits, $P_{ET_{CO_2}}$ is maintained 5 mmHg higher than the $P_{ET_{CO_2}}$ at room-air breathing by adjusting the three-way stopcock to the CO_2 absorber, and $P_{ET_{O_2}}$ is progressively lowered at a rate of about 10 mmHg/min by cutting off the O_2 supply or adding N_2 from cylinders. About 10 liters of room air are introduced into an 18 liters rubber bag before rebreathing.

hypoxia, the addition of N_2 into the rebreathing bag was sometimes necessary to keep a continuous $P_{ET_{O_2}}$ fall. The rebreathing was terminated when $P_{ET_{O_2}}$ decreased to 40 mmHg.

A respiratory flowmeter hot-wire probe (Minato Medical Science Co., Ltd.) inserted between the rebreathing bag and the mouthpiece was used to detect breath-by-breath respiratory flow, integrated tidal volume (V_T) and inspiratory (T_i) and expiratory time (T_e). On a 6-channel pen-recorder (San-ei Recti-Horiz-8K), $P_{ET_{O_2}}$, $P_{ET_{CO_2}}$, respiratory flow, V_T , T_e , and T_i were simultaneously recorded.

Data analysis. The ventilatory response to hypoxia was evaluated using a modified hyperbola equation originally advocated by LLOYD and CUNNINGHAM (1963).

$$\dot{V} = \dot{V}_0 + A / (P_{ET_{O_2}} - C),$$

where $\dot{V}$ is minute ventilation, $\dot{V}_0$ the horizontal asymptote in ventilation for infinite $P_{ET_{O_2}}$, A the slope constant of the hyperbola expressing the degree of hypoxic sensitivity of the subject, and C the vertical asymptote in $P_{ET_{O_2}}$ for infinite $\dot{V}$. To obtain the above three parameters in the equation, C was first determined by a curve-fitting procedure using a microcomputer (Apple II), i.e., seeking the C value which gave the best correlation coefficient between $\dot{V}$ and $1/(P_{ET_{O_2}} - C)$. Then, from the linear regression between $\dot{V}$ and $1/(P_{ET_{O_2}} - C)$, $\dot{V}_0$ and A were determined as the intercept at the ordinate and the slope of the regression line, respectively.

Relationship between $P_{ET_{O_2}}$ and $P_{a_{O_2}}$. In three normal healthy males, blood samples from a catheter inserted in the radial artery were withdrawn six times from each subject during the course of progressive hypoxia. Figure 2 shows that differences between end-tidal and arterial oxygen pressure, $D(ET-a)P_{O_2}$, are

Fig. 2. End-tidal to arterial P_{O_2} difference, $D(ET-a)P_{O_2}$, plotted against end-tidal P_{O_2} , $P_{ET_{O_2}}$. Six blood samples from the radial artery were obtained for each subject during progressive hypoxia. Different symbols indicate different subjects. A regression line is drawn for the pooled samples.

well within reasonable values and linearly correlated with $P_{ET_{O_2}}$. To estimate $P_{a_{O_2}}$, the linear relationship with $P_{ET_{O_2}}$ was ascertained by high correlation coefficient ($r=0.99$) as follows:

$$P_{a_{O_2}} = 0.941(P_{ET_{O_2}} - 4.65) .$$

RESULTS

Figure 3 illustrates examples of progressive hypoxia response in light (I) and

Fig. 3. An example of the experimental record. Upper half: data from lightweight subject I. Lower half: data from heavyweight subject II with a Röhler index of 206. The subject first has $P_{ET_{O_2}}$ made 100 mmHg and $P_{ET_{CO_2}}$ 5 mmHg higher than in the control; at the arrow indicated at left, progressive hypoxia started. The two arrows shown for subject II at right, indicated that the gain of the recorder for respiratory flow and tidal volume (V_T) was reduced by 50% because the recordings would otherwise have exceeded the pen limit. On the other hand, the lowest arrow for subject II indicated that the magnitude of T_e and T_i was doubled because of increasing respiratory frequency. Vigorous hypoxic ventilatory response was seen in subject II.

heavyweight athletes (II). A vigorous ventilatory response with increasing hypoxia is clearly shown in subject II. As seen in Table 1, the parameter A 's indicating the slope of the hyperbola response were 295 ± 264 , 458 ± 323 , and $1,155 \pm 1,027$ liters $\cdot$ min $^{-1} \cdot$ mmHg (mean $\pm$ S.D.) in the light and middleweight class (Group I), and A and B of the heavyweight class (Group II A and B), respectively. The differences between Groups II B and I and II B and A were significant ($P < 0.001$ and $P < 0.05$, respectively).

Such augmentation of hypoxic sensitivity with increasing body weight and Röhler's index was still seen even after A was recalculated as A_N by using normalized ventilation for 70 kg body mass using the allometric coefficient $BW^{0.75}$ (BW: body weight). In Table 1, the difference in A_N between Groups I and II B

Fig. 4. An index of hypoxic sensitivity, A , is plotted against body weight. A_N : recalculated A value after ventilation was normalized for 70 kg body mass using allometric coefficient. High A_N is still seen in the heavyweight subjects.

Fig. 5. Vertical asymptote for end-tidal P_{O_2} , C , plotted against hypoxic sensitivity index, A . Significant inverse correlation is seen.

is significant ($P < 0.01$), indicating increased hypoxic sensitivity in obesity. A_N and A plotted against body weight are shown in Fig. 4.

Hyperbola analysis for hypoxic ventilatory response was also conducted in terms of the Pa_{O_2} value which was estimated from the linear relation existing between Pa_{O_2} and PET_{O_2} described in the MATERIALS AND METHODS section. The results are indicated as Aa , A_{Na} , and Ca in Table 1. Although the numerical figures were different, the same conclusions as derived from using PET_{O_2} values were obtained.

The relationship between A and hyperbolic asymptote for infinite ventilation, C , is illustrated in Fig. 5. A significant inverse relationship was seen.

DISCUSSION

Ventilatory responses to hypoxia as measured by the slope index, A , obtained from hyperbola equation were higher with increasing body weight in the Judo athletes. The positive relationships between A and body weight or height have also been observed by WEIL *et al.* (1971b). However, they admitted that such relationships disappeared when ventilation was normalized by body size (HIRSHMAN and WEIL, 1976). In our subjects, the difference in A between Group I (light and middleweight class) and Group II A (heavyweight class with Röhler's index less than 200) became insignificant when ventilation was normalized for 70 kg body mass. However, a significant difference in A still existed between Group I and Group II B (heavyweight class with Röhler's index higher than 200) after such normalization of ventilation. Moreover, the positive correlation seen between A and body height disappeared when A was recalculated on the basis of normalized ventilation in our subjects. These results indicated that body weight plus obesity may have contributed to the increase of hypoxic sensitivity, A .

In addition to the obesity factor described above, numerous other factors

have been reported to affect hypoxic sensitivity: altitude exposure (MILLEDGE and LAHIRI, 1967; WEIL *et al.*, 1971a), athleticism (BYRNE-QUINN *et al.*, 1971; MARTIN *et al.*, 1978), hyperthermia (NATALINO, 1977), mixed venous P_{CO_2} level (REBUCK and WOODLEY, 1975), malnutrition (DAEKEL, 1976), aging (KRONENBERG and DRAGE, 1973), familial or genetic factor (COLLINS *et al.*, 1978; SCOGGIN, 1978; KAWAKAMI *et al.*, 1981a; KAWAKAMI *et al.*, 1981b), congenital cyanotic heart disease (SØRENSEN and SEVERINGHAUS, 1968; BLESÁ *et al.*, 1977), various drugs, anesthesia or sedation (HIRSHMAN *et al.*, 1975a; HIRSHMAN *et al.*, 1975b; YACOB *et al.*, 1976; HIRSHMAN *et al.*, 1977; KNILL and GELB, 1978; KNILL *et al.*, 1978; LAKSHMINARAYAN *et al.*, 1978; SANDERS *et al.*, 1980), and alveolar hypoventilation syndromes (SHANNON and KELLY, 1977; BRADLEY *et al.*, 1979; SCHIFFMAN *et al.*, 1980; BERMAN *et al.*, 1981; HUNT *et al.*, 1981). None of the above factors, however, seems to satisfactorily explain the results obtained in the present study.

One of the possible reasons why our obese Judo athletes exhibited higher ventilatory activity in hypoxia is inferred to be their strong physical activity with high metabolism in everyday training. ZWILLICH *et al.* (1975b) observed that thyroid hormone replacement therapy augmented the A value significantly in myxedema and hypothyroidism. On the other hand, STOCKLEY and BISHOP (1977) detected augmented peripheral chemosensitivity using oxygen breath testing in 7 thyrotoxicosis patients. LEVINE and HUCKABEE (1975) also demonstrated in dogs that drug-induced hypermetabolism caused hyperventilation which seemed to arise in the peripheral tissues other than the peripheral or central chemoreceptors. In all probability, the metabolic activity of our subjects may be higher than in sedentary obese patients who exhibit hypoventilation and decreased hypoxic and/or hypercapnic sensitivity. Whether or not the degree of metabolic activity definitely explains our results needs further clarification.

It must be mentioned here why we examined hypoxic response with the P_{ETCO_2} 5 mmHg higher than the control level. Generally, hypoxic stimulation is very weak until P_{ETCO_2} decreases to about 60 mmHg. Therefore, if ventilatory response is obtained at the resting P_{ETCO_2} level, its magnitude is easily changeable up to about P_{ETCO_2} 60 mmHg. However, when P_{ETCO_2} is increased by several mmHg as in the present experiment, stable ventilatory volume can be assessed even in light and moderate hypoxia, and thus consistent hypoxic response curves are assured. REBUCK *et al.* (1973) also conducted a progressive hypoxia test with P_{ETCO_2} kept at a mixed venous P_{CO_2} level which was probably about the same as the P_{ETCO_2} value used in this study.

Finally, the magnitude of C , the vertical asymptote for P_{ETCO_2} in the hyperbola equation, must be considered. WEIL *et al.* (1971b) have been conducting an extensive study using the hyperbola equation, and they put a constant C value of 32 mmHg into this equation. The reason why they used a fixed C is not clear to us. In fact, as shown in Table 1 and Fig. 5, there was some scatter in this value. Such a variation in the C level has been reported by MILLEDGE and LAHIRI (1967)

on comparing hypoxic response between lowlanders and sherpa highlanders. Even in Fig. 6 of the original paper of WEIL *et al.* (1971b), there seems to be an increasing C level with an increasing isocapnic level in the hypoxia test. As shown in Fig. 5, we found a positive inverse relationship between C and A values. This result indicated that the hypoxic threshold level for infinite ventilation decreased with increasing A .

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