Effects of chest wall vibration on breathlessness during hypercapnic ventilatory response

HIDENORI EDO, HIROSHI KIMURA, MAFUMI NIJJIMA, HIDEO SAKABE, MASATO SHIBUYA, ARATA KANAMARU, IKUO HOMMA, and TAKAYUKI KURIYAMA. Effects of chest wall vibration on breathlessness during hypercapnic ventilatory response. J. Appl. Physiol. 84(5): 1487–1491, 1998.—Vibratory stimulation applied to the chest wall during inspiration reduces the intensity of breathlessness, whereas the same stimulation during expiration has no effect or may increase breathlessness. The purpose of the present study was to determine whether vibration reduced the intensity of breathlessness during progressive hypercapnia with and without the addition of an external resistive load. A second objective was to see whether the mouth occlusion pressure at 0.2 s (P0.2) was reduced by the vibratory stimulation. Hypercapnic ventilatory response was conducted in 10 healthy male volunteers with simultaneous measurement of visual analog scale, P0.2, and minute ventilation. Hypercapnic ventilatory response was performed and randomly combined with or without vibratory stimulation (100 Hz) as well as with or without inspiratory load. With inspiratory load, in-phase vibration did not cause any significant changes in the slopes of P0.2 and minute ventilation to CO2, whereas the slope of visual analog scale to CO2 significantly decreased from 0.47 ± 0.15 to 0.34 ± 0.11 (SE) cmH2O/Torr (P < 0.05). We conclude that in-phase vibration could decrease the slope of breathlessness elicited by inspiratory load combined with hypercapnia without changing motor output.

BREATHLESSNESS HAS AN ABSOLUTE MAGNITUDE and consists of a complex body of information of efferent and afferent signals arising from various kinds of peripheral receptors (2, 5, 17, 18). Mechanoreceptors are also recognized as playing important roles in producing or modifying breathlessness (11). For instance, muscle spindles, which are located in the intercostal muscles, can easily respond to vibratory stimulation. So far, some useful techniques such as in-phase vibration (IPV) and out-of-phase vibration have been established by the use of a vibrator (11, 14, 16). IPV reduced breathlessness at rest in patients with chronic obstructive pulmonary disease, whereas out-of-phase vibration, differing from IPV only in timing, increased breathlessness. Because the main pathophysiology of chronic obstructive pulmonary disease includes hypercapnea and airway obstruction, in the present study, the effect of IPV on the intensity of breathlessness during progressive hypercapnia with and without the addition of an external resistive load was investigated in normal subjects. To compare several variables at a certain chemical drive, the rebreathing method of Read (15) was used. Also, a linear relationship between breathlessness and central respiratory motor command (2, 12) has been suggested. Thus it is possible that IPV decreases breathlessness by decreasing the central respiratory motor command. Hence, a second objective was to see whether the mouth occlusion pressure at 0.2 s (P0.2), which may reflect central motor command, is affected by IPV.

METHODS

Subjects. Ten healthy male volunteers, aged 24.9 ± 1.3 (SE) yr (range 19–32 yr), were studied in this experiment. All subjects were nonsmokers and free of any signs of pulmonary and cardiac disease. All subjects were naive to chest wall vibration and were not informed beforehand of the purpose of this study. Informed consent was obtained before the experiment.

Hypercapnic respiratory response. Hypercapnic respiratory response was performed by using Read's method (15), with subjects in a sitting position. The subjects rebreathed ~6 liters of 7–8% CO2 in O2 mixture through a closed-circuit system containing a low-resistance one-way valve. The existence of an alveolar plateau on the recording of end-tidal PCO2 (PETCO2) was confirmed within 20–30 s from the beginning of rebreathing in each experiment (13). Rebreathing was terminated within 4 min. Respiratory flow was measured by a hot-wire flowmeter (RM-300, Minato Medical Products) attached to a mouthpiece. Minute ventilation (Vi) and tidal volume (Vt) were electrically computed from the flow signal. Respiratory gases were continuously measured by a gas analyzer (MG-360, Minato Medical Products) with rapid response. P0.2 was monitored with a pressure transducer (Toyo Baldwin LPU-0.1). During the course of CO2 rebreathing, the inspiratory line was shut with a magnetic valve 6–10 times from the beginning of inspiration. The subjects were not aware of when the occlusion would occur. Occlusion pressure was read at 0.2 s from the onset of inspiration and defined as P0.2, which was found to be less variable than the conventional occlusion pressure read at 0.1 s (19).

Measurement of breathlessness. The sensations of breathlessness had been evaluated during rebreathing every 30 s with a 100-mm visual analog scale (VAS).

Chest wall vibration. Two vibrators were attached bilaterally at the second or third intercostal spaces with a rubber band, and two other vibrators were similarly attached at the seventh to ninth intercostal spaces. The frequency of vibration applied was 100 Hz, as previously reported (11, 16). IPV represents the condition of the upper vibrators being triggered to run during inspiration, whereas the lower vibrators were triggered to run during expiration. Two pairs of vibrators were synchronized in accordance with respiratory phases by using the signal from the flowmeter, and vibration was reversed automatically.

Inspiratory flow-resistive loading. Flow-resistive loading was applied by interposing a pored disk with a resistance of 10 cmH2O·l−1·s in the inspiratory line. A preliminary test
was conducted to determine an appropriate concentration of CO$_2$ gas mixture for the rebreathing run. The protocol is summarized in Fig. 1. Hypercapnic ventilatory responses (HCVR) were performed in association with or without vibratory stimulation and the inspiratory resistive load. Each subject was examined for four kinds of HCVR in random order. At the beginning, for the subjects doing the vibratory rebreathing run, CO$_2$ rebreathing was not started until the air had been breathed for 5 min with vibratory stimulation to confirm that ventilatory parameters had become steady. All variables measured were fed into a signal processor (NEC-Sanei 7T17) and were simultaneously recorded on a multichannel pen recorder (NEC-Sanei, Recti-Horiz). CO$_2$ response was evaluated by the slope of linear-regression analysis between V˙I and PETCO$_2$ as well as between P$_{0.2}$ and PETCO$_2$. The linear-regression line between breathlessness and PETCO$_2$ was calculated similarly. The differences in the slopes of these responses between with and without IPV were examined by paired t-test, and a P value < 0.05 was considered significant.

RESULTS

Typical data from one subject are shown in Fig. 2. Each measurement point of VAS during hypercapnic ventilatory responses was plotted with and without resistive load, and the linear-regression line between breathlessness and PETCO$_2$ was drawn. IPV little affected the regression line in the unloaded condition, whereas it reduced the VAS slope of the regression line with load. Similarly, the slopes of VAS, V˙I, and P$_{0.2}$ to CO$_2$ were calculated in all subjects.

Figure 3 illustrates a comparison of the mean response lines of VAS, P$_{0.2}$, and V˙I during CO$_2$-rebreathing test performed both with and without the application of inspiratory resistive load. Without the inspiratory resistive load, the mean slopes of V˙I and P$_{0.2}$ to CO$_2$ were not changed by IPV. In addition, no difference was elicited in terms of magnitudes of ventilation and occlusion pressure. Furthermore, the effects of IPV on the slope of breathlessness were not consistent, i.e., there were considerable increases in 4 and decreases in 5 of the 10 subjects, with the remaining 1 subject showing a magnitude of change within 15%. Finally, however, the mean response line of VAS was not significantly affected by IPV in either slope or magnitude. On the other hand, IPV prominently affected breathlessness with the application of resistive load. With the application of load, breathlessness decreased in seven and increased in one subject, whereas the other two subjects showed little change in response to IPV. The mean response lines with resistive load are demonstrated in Fig. 3B. IPV significantly decreased the sensation of breathlessness in terms of slope from 0.47 ± 0.15 to 0.34 ± 0.11 cm/Torr. Moreover, there was a significant decrease in the magnitude of breathlessness.
ness at a given level, such as, for example, at PETCO2 of 70 Torr from 5.97 ± 1.41 to 4.50 ± 1.10 cm by IPV. However, no significant changes in slopes of P0.2 and V˙I to CO2 were observed.

Slopes and magnitudes in ventilatory variables and VAS during CO2 rebreathing are compared with and without IPV in Tables 1 and 2. The results suggest that the sense of breathlessness was attenuated by in-phase vibratory stimulation, although respiratory motor output was kept constant with resistive load. The relationship between breathlessness and respiratory motor output is demonstrated in Fig. 4, as illustrated by the replotted values of P0.2 and VAS, with or without resistive load, combined with the presence or absence of IPV. In the unloaded condition, relationships between

Table 1. Magnitude of ventilatory variables and VAS during CO2 rebreathing

<table>
<thead>
<tr>
<th></th>
<th>At PCO2 = 60 Torr</th>
<th>At PCO2 = 70 Torr</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No vibration</td>
<td>IPV</td>
</tr>
<tr>
<td>P0.2, cmH2O</td>
<td>7.3 ± 1.1</td>
<td>6.8 ± 0.4</td>
</tr>
<tr>
<td>VAS, cm</td>
<td>0.8 ± 0.4</td>
<td>0.5 ± 0.3</td>
</tr>
<tr>
<td>Vl, l/min</td>
<td>20.8 ± 2.41</td>
<td>23.7 ± 2.7</td>
</tr>
<tr>
<td>VT, liters</td>
<td>1.15 ± 0.30</td>
<td>1.16 ± 0.29</td>
</tr>
</tbody>
</table>

With resistive load

|                | No vibration     | IPV              |
| P0.2, cmH2O   | 6.7 ± 1.0        | 8.1 ± 0.7        |
| VAS, cm        | 1.4 ± 0.4        | 1.2 ± 0.3        |
| Vl, l/min      | 18.9 ± 1.95      | 21.7 ± 2.65      |
| VT, liters     | 1.15 ± 0.25      | 1.17 ± 0.32      |

Values are means ± SE. IPV, in-phase vibration; P0.2, occlusion pressure at 0.2 s; VAS, visual analog scale; Vl, minute ventilation; VT, tidal volume. *Significant difference of P < 0.05 between no vibration and IPV.

Table 2. Slope of ventilatory variables and VAS during CO2 rebreathing

|                | Unloaded        | IPV              |
| P0.2/CO2, cmH2O/Torr | 0.68 ± 0.22 | 0.58 ± 0.18 |
| VAS/CO2, cm/Torr      | 0.31 ± 0.10 | 0.24 ± 0.08 |
| Vl/CO2, l·min⁻¹·Torr⁻¹ | 1.57 ± 0.50 | 1.70 ± 0.54 |
| VT/CO2, ml/Torr       | 75.3 ± 9.79 | 72.7 ± 9.71 |

With resistive load

| P0.2/CO2, cmH2O/Torr | 0.99 ± 0.15 | 0.96 ± 0.18 |
| VAS/CO2, cm/Torr      | 0.47 ± 0.15* | 0.34 ± 0.11* |
| Vl/CO2, l·min⁻¹·Torr⁻¹ | 1.66 ± 0.53 | 1.39 ± 0.44 |
| VT/CO2, ml/Torr       | 90.1 ± 13.3 | 74.8 ± 7.9 |

Values are means ± SE. *Significant difference of P < 0.05 between no vibration and IPV.
P0.2 and VAS were almost the same with and without IPV, i.e., there was no significant difference at the same level of P0.2 of 10 cmH2O. With the presence of resistive load, however, with the use of IPV, the magnitude of VAS significantly declined from 3.0 ± 0.4 to 1.8 ± 0.3 cm at the same level of P0.2 of 10 cmH2O. Thus IPV reduced the breathlessness derived from the combined condition of hypercapnia with resistive load without changing P0.2. It was suggested that parallel relationships between breathlessness and respiratory motor output, which were relatively retained even if resistive load was applied, were dissociated by IPV.

DISCUSSION

The effect of IPV on breathlessness, P0.2, and ventilation during CO2 rebreathing was examined with and without inspiratory resistive loading. The results show that, with resistive loads, IPV significantly decreased breathlessness, whereas P0.2 and ventilation remained unchanged at a given CO2 level. Analysis indicated that IPV decreased breathlessness for any given P0.2.

The decrease in breathlessness for the CO2 level tested with resistive loads could be due to one or more of the following: 1) decrease in central motor command, 2) decrease in sensitivity in the sensory system, and 3) modification in breathlessness-related afferent activity from the periphery.

Chest wall vibration has been reported to elicit a spinal tonic vibration reflex (TVR) in the intercostal muscles, resulting in an increase in Vr (10). Although Vr did not increase in the present study, IPV could have elicited spinal TVR and could have been an additional factor for the occlusion pressure. Because P0.2 is an index of motor output, P0.2 during IPV would be the sum of central motor command and spinal TVR. IPV did not cause any change in occlusion pressure. Therefore, it is possible that during IPV application central motor command was decreased. The respiratory motor command is considered to be a crucial factor for determining the sensation of breathlessness (1–3, 7, 8, 12). Thus the possible IPV-elicited decrease of the central motor command might have been a factor in decreasing breathlessness during IPV application.

Another explanation for the decrease in breathlessness for a given P0.2 level by IPV would be a decrease in the sensitivity of the central sensory system. This may, indeed, be a possibility, as distraction from the vibration could decrease breathlessness. In fact, this might have happened had the primary cause of IPV during the loaded trials been distraction. However, this is unlikely to be the chief factor for decrease in breathlessness, since during unloaded trials, IPV did not affect either the CO2-VAS relationship or the P0.2-VAS relationship.

The effect of IPV might also have been to modify breathlessness-related afferent activity from the respiratory sensory receptors. Possible factors may be mechanoreceptors in the airway, lungs, and respiratory skeletal systems. It has been reported that the afferent information arising from muscle spindles in the intercostal muscle may play a role in modifying dyspneic sensation (11, 16). One possible explanation for the present results is that IPV might cause afferents from muscle spindles to the central sensory system and might influence the central nervous system.

IPV reduced breathlessness at PCO2 of 70 Torr and with resistive load added, but not in any other condition. This could be because breathlessness was at its most extreme in this condition. In previous IPV studies on breathlessness at rest, patients with strong breathlessness at rest had it reduced with IPV, but not patients with moderate breathlessness at rest (14, 16). Also, in an IPV study on exercise breathlessness, strong breathlessness toward the end of a constant-load ergometer-exercise session was reduced with IPV, but the light breathlessness at the beginning of the session did not decrease. Thus IPV seems capable of reducing stronger, rather than milder, states of breathlessness.

Another speculation in the present results is that IPV might be more effective in reducing breathlessness induced by resistive load. The addition of resistive load causes activation of muscle spindle afferents via the spinal or supraspinal reflexes, which is called “the load-compensation reflex” (6, 13). Chest wall vibration also stimulates muscle spindles, and this probably contributes to the response with resistive load as well.

In conclusion, the present data indicate that IPV diminishes breathlessness elicited by inspiratory resistive load combined with CO2. This could be due to decreased central motor command and/or modification...
in breathlessness-related afferent activity from the respiratory system.

The authors thank Drs. K. Tatsumi, S. Masuyama, T. Uruma, H. Igari, and A. Mizoo for their helpful cooperation.

This study was partly supported by Research Grants for Intractable Diseases from the Ministry of Health and Welfare, Japan.

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Received 26 March 1997; accepted in final form 17 January 1998.

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