Ventilatory Responses in Patients with Essential Hypertension

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Abstract We investigated the ventilatory responses to hypoxia and hypercapnia in patients with essential hypertension (HT) as compared with healthy subjects (NV). Further, to evaluate the contribution of the peripheral chemoreceptors to ventilatory response, we used a withdrawal test. Hypoxic ventilatory drive (HVR) was measured as the parameter A denoting the shape of $\dot{V}_t$ (inspiratory minute ventilation)-$P_{ETO_2}$ (end-tidal $P_{O_2}$) curve which was calculated by the empirical equation: $\dot{V}_t = \dot{V}_0 + A/P_{ETO_2} (32)$. Hypercapnic ventilatory drive (HCVR) was measured as the parameter S denoting the shape of the $\dot{V}_t$-$P_{ETCO_2}$ (end-tidal $P_{CO_2}$) relation which was calculated by the empirical equation: $\dot{V}_t = S(P_{ETCO_2} - B)$. There were no significant differences in the parameters of HVR and HCVR between NV and HT. A positive correlation between $A/BSA$ and $S/BSA$ was found to be significant in NV ($r = 0.873, p < 0.05$). Conversely, there was no significant correlation between $A/BSA$ and $S/BSA$ ($r = 0.547$) in HT. On the other hand, the withdrawal responses ($\Delta \dot{V}_t/BSA$ and $\%\Delta \dot{V}_t; \Delta \dot{V}_t/\dot{V}_t \times 100\%$) were obtained from the magnitude of depression in ventilation caused by two breaths of $O_2$ in hypoxic hypercapnia. In the withdrawal responses, $\Delta \dot{V}_t/BSA$ and $\%\Delta \dot{V}_t$ in HT were significantly higher than those in NV. $A/BSA$ significantly correlated with $\Delta \dot{V}_t/BSA$ (NV, $r = 0.684, p < 0.05$; HT, $r = 0.648, p < 0.05$) in both NV and HT. However, $\Delta \dot{V}_t/BSA$ in HT tended to be higher than that in NV, under the same value of $A/BSA$. These results suggested that the peripheral chemoreceptor activity was augmented in HT.

Key words: hypertension, peripheral chemoreceptor, ventilatory response, withdrawal test.

Recently, it has been reported that the structures and the activities of the peripheral chemoreceptors were involved in the pathophysiological change in established hypertension (Przybylski, 1981; Trzebski et al., 1982). In an

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autopsy study of patients with essential hypertension, the carotid bodies were found
to be hyperplastic (PRZEMYSLAW, 1985). Further, other reports showed that the
size of the carotid bodies increased and that glomic cell hyperplasia has already
been reported in human hypertension (EDWARDS et al., 1971; SMITH et al., 1982).
Regarding the functional change in the carotid bodies, TAPILO and TRZEBSKI
(1981) found that the respiratory and the cardiovascular responses to isocapnic
hypoxia were altered already in early hypertensive stage. Furthermore, an alveolar
hyperventilation and a respiratory alkalosis were found in young spontaneously
hypertensive rats (SHR) (PRZBYLSKI, 1978; PRZBYLSKI et al., 1982), suggesting
that the arterial chemoreceptor reflex is hyperactive in early hypertension. This
suggestion is strongly supported by the result of FUKUDA et al. (1987). They found
a higher increase in the chemoreceptor discharge during hypoxia in SHR as
compared with normotensive rats. In old SHR with established hypertension,
the chemoreceptor pressor reflex and the ventilatory response to hypoxia are attenuat-
ed, whereas the ventilatory response to hypoxia is enhanced (PRZBYLSKI and
TRZEBSKI, 1980; PRZBYLSKI et al., 1982). This result is consistent with the
known depression of the chemoreceptor response after prolonged, excessive stim-
ulation by hypoxia. Hypertension appears to be accompanied by alterations of the
structures and the chemoreceptor reflex function in the carotid bodies.

We investigated the ventilatory response to hypoxia and hypercapnia in
patients with essential hypertension. Further, to make clear the contribution of the
peripheral chemoreceptors to ventilatory response. We performed a withdrawal
test on these subjects. We considered that this method was the most appropriate for
evaluating the peripheral chemoreceptors activity independently. We defined the
change in minute ventilation during a period of 5–20s following the end of the first
O₂ inspiration as the withdrawal response, since the lung-to-the-CNS circulation
period was considered to be about 20s. Thus, the withdrawal test eliminates the
peripheral chemoreceptors activities with the humoral environment of the central
respiratory regulating system left unchanged, and therefore the withdrawal re-
response is caused by the peripheral chemoreceptors activity.

SUBJECTS AND METHODS

Twelve patients with hypertension (HT) (female, 4; male, 8) and eight
age-matched healthy volunteers (NV) (female 2; male, 6) were studied. We
explained the experiments to the subjects and obtained the informed consent from
the subjects. All subjects were given routine medical examination, and found to be
free of heart or lung diseases. Anthropometric data, pulmonary function and
systemic arterial blood pressure in these subjects are shown in Table 1. All patients
with hypertension were examined for secondary hypertension and diagnosis of
essential hypertension was confirmed. We measured each subject’s arterial blood
pressure every day during 1 week in the sitting position, and selected subjects whose
arterial blood pressure were over 160mmHg in systolic pressure and/or over 95

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Table 1. Anthropometry, pulmonary function, and systemic arterial blood pressure in the investigated subjects.

<table>
<thead>
<tr>
<th></th>
<th>NV</th>
<th>HT</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numbers</td>
<td>8 (F, 2; M, 6)</td>
<td>12 (F, 4; M, 8)</td>
<td>N.S.</td>
</tr>
<tr>
<td>Age (years)</td>
<td>54.5±11.1</td>
<td>54.6±13.0</td>
<td>N.S.</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>158.5±7.9</td>
<td>154.5±9.8</td>
<td>N.S.</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>59.3±10.8</td>
<td>59.0±12.4</td>
<td>N.S.</td>
</tr>
<tr>
<td>%VC (%)</td>
<td>97.5±18.3</td>
<td>89.9±15.8</td>
<td>N.S.</td>
</tr>
<tr>
<td>FEV_{1.06} (%)</td>
<td>77.4±10.1</td>
<td>80.9±8.7</td>
<td>N.S.</td>
</tr>
<tr>
<td>pH</td>
<td>7.39±0.02</td>
<td>7.40±0.02</td>
<td>N.S.</td>
</tr>
<tr>
<td>$P_{ACO_2}$ (mmHg)</td>
<td>40.5±1.8</td>
<td>40.9±2.1</td>
<td>N.S.</td>
</tr>
<tr>
<td>$P_{AO_2}$ (mmHg)</td>
<td>92.7±7.2</td>
<td>88.5±9.8</td>
<td>N.S.</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>128±15</td>
<td>153±17</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>76±6</td>
<td>92±10</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

WHO Stage 1 4
Stage 2 7
Stage 3 1

Mean±S.D. NV, normal volunteers; HT, patients with hypertension; F, female; M, male; SBP, systolic blood pressure; DBP, diastolic blood pressure. Statistics are used by Student’s t-test.

mmHg in diastolic pressure. The subjects had not received antihypertensive drugs for a week. Before the ventilatory tests, systemic arterial blood pressure was measured in the sitting position by a standard sphygmanometer. Systolic arterial blood pressure and diastolic arterial blood pressure in HT were significantly higher than those in NV.

The physiique of HT was matched with NV. The routine pulmonary function tests and blood gas analyses showed no significant difference between HT and NV. Both the responses to hypercapnia and hypoxia were measured in each subject on the same day before noon.

We designed an apparatus to evaluate the ventilatory response to hypercapnia and hypoxia. The subjects breathed through a low resistive valve (Hans Rudolph, model 2700: dead space 95 ml) and wore a rubber mouthpiece, nose clips, and headphones, which supplied music devoid of strong rhythmic content. Inspiratory airflow was monitored by a Fleish-type pneumotachograph (Nihon Kohden, MFP-1T-S) connected to the inspiratory site of the valve. Inspiratory tidal volume was derived by integration of the flow signal. During each test, minute ventilation, tidal volume, and breathing frequency were measured. On the inspiratory valve, an electromagnetic shutter was inserted to measure the occlusion pressure, which is the mouth pressure generated at 0.1 s by the inspiratory muscles at functional residual capacity. The measurement of the occlusion pressure ($P_{0.1}$) was performed randomly every 5 to 10 breaths during the hypercapnia and hypoxia tests. Two rubber bags of 50 l capacity were connected to each tube of a three-way stopcock. N₂ and
O$_2$ flowed through the rubber bag on one side, and the other bag was filled with pure oxygen prepared for the withdrawal tests. Respiratory gas was continuously sampled from the mouthpiece for the measurement of breath-by-breath end-tidal $P_{CO_2}$ ($PET_{CO_2}$) and end-tidal $P_{O_2}$ ($PET_{O_2}$) by a mass spectrograph (CHEMETRON, Med Spect II). The heart rate was obtained from electrocardiogram (Fukuda Denshi, MIC 680) and thus incidental arrhythmias due to hypoxia were monitored. Oxygen saturation was measured by an oximeter (Minolta, Pulsox 7). Monitored variables were recorded on a multichannel recorder.

1. Hypoxic ventilatory response and hypercapnic response. Hypoxic ventilatory response (HVR) was measured as previously described (Weil et al., 1968). In brief, $PET_{O_2}$ was lowered from 120 to 45 mmHg over 7 min by the addition of nitrogen. Carbon dioxide was added in sufficient amounts to maintain isocapnia. The curve relating $PET_{O_2}$ and minute ventilation is hyperbolic and described by $\dot{V}_1 = \dot{V}_0 + A/(PET_{O_2} - 32)$, where $\dot{V}_1$ are minute ventilation in l/min (BTPS), and $PET_{O_2}$ in mmHg, respectively. $\dot{V}_0$ is the asymptote for ventilation obtained by extrapolation, and $A$ determines the shape of the curve.

Hypercapnic ventilatory response (HCVR) was measured by using the Read's rebreathing method (Read and Leigh, 1967). Briefly, a 6 l bag filled with a gas of 5% CO$_2$, 50% O$_2$, and N$_2$ balance was connected to the breathing valve and the subject rebreathed into the bag until $PET_{CO_2}$ reached 70 mmHg, at which point he was returned to room air breathing. $PET_{CO_2}$ was increased from resting levels to 75 mmHg over 7 min and $PET_{O_2}$ was maintained at a level greater than 100 mmHg.

2. Withdrawal test. To evaluate the contribution of the peripheral chemoreceptor to the ventilatory response, we used the withdrawal test advocated by Miller et al. (1974). The detailed procedures were as follows: first, the subject breathed through a rubber bag filled with room air, and the level of $PET_{CO_2}$ observed in this period was defined as a level for the control. Then $PET_{O_2}$ was gradually lowered to 60 mmHg, and at the same time $PET_{CO_2}$ was elevated by 5 mmHg above the control level.

When a steady ventilation was attained, oxygen was given from the rubber bag during two breaths by opening the three-way stopcock during expiration. Since this maneuver was performed as surreptitiously as possible, the subject was not aware of it.

Ventilation after two oxygen breaths was observed for about 1 min. Minute ventilation before changing inspired gas was taken as $\dot{V}_1$, and minute ventilation between 5 and 20 s after changing the inspiratory gas was taken as $\dot{V}_1'$. The differences between $\dot{V}_1$ and $\dot{V}_1'$ were defined as the withdrawal response ($\Delta \dot{V}_1$/BSA), and we used the %$\Delta \dot{V}_1$ ($\Delta \dot{V}_1/\dot{V}_1 \times 100$) as the index of the peripheral chemoreceptors activity. This withdrawal test was performed three times at intervals of 10 min.
RESULTS

The parameters of HVR and HCVR in HT and NV are shown in Table 2. In the parameters of HVR, $A/BSA$ ($l/(min \cdot (mmHg/m^2))$, $A(P_{a1})/BSA$ (cmH$_2$O.mmHg/m$^2$), and $A\dot{V}i/SaO_2/BSA$ ($l/(min \cdot % \cdot m^2)$), there were no significant differences between NV and HT. Furthermore, there were no significant differences in $S/BSA$ ($l/(min \cdot mmHg \cdot m^2)$), $S(P_{a1})/BSA$ (cmH$_2$O/(mmHg.m$^2$)) of HCVR between NV and HT. Figure 1 presents the relationship between HVR and HCVR in NV and HT. A significant positive correlation between $A/BSA$ and $S/BSA$ was found in NV ($r = 0.873$, $p < 0.05$). Conversely, there was no significant correlation between $A/BSA$ and $S/BSA$ ($r = 0.547$, not significant) in HT.

Results of the withdrawal tests in NV and HT are shown in Table 3a and b. There were not significant differences in steady-state ventilation in hypoxic and

| Table 2. Parameter of HVR and HCVR in the investigated subjects. |
|-------------------------|----------------|----------------|
|                         | NV (n = 8)     | HT (n = 12)    | p    |
| $A(\dot{V}i)/BSA$ ($l/(min \cdot (mmHg/m^2)$) | 124.3±53.7     | 184.5±118.1    | N.S. |
| $A(P_{a1})/BSA$ (cmH$_2$O.mmHg/m$^2$)        | 36.7±25.3      | 49.5±20.3      | N.S. |
| $A\dot{V}i/A_{So2}/BSA$ ($l/(min \cdot % \cdot m^2)$) | 0.39±0.19     | 0.47±0.57      | N.S. |
| $S(\dot{V}i)/BSA$ ($l/(min \cdot mmHg \cdot m^2)$) | 0.67±0.26      | 0.62±0.21      | N.S. |
| $A(P_{a1})/P_{ETCO2}/BSA$ (cmH$_2$O/(mmHg.m$^2$)) | 0.35±0.22      | 0.49±0.98      | N.S. |

Mean±S.D. Statistics by Student’s t-test.

![Graph](image)

Fig. 1. Correlation of the ventilatory response to hypoxia ($A/BSA$) and to hypercapnia ($S/BSA$).
Table 3a. Results of withdrawal responses in normal volunteers.

<table>
<thead>
<tr>
<th>No.</th>
<th>( P_{ET\text{CO}_2} ) (mmHg)</th>
<th>( \dot{V}_i/\text{BSA} ) (l/min)</th>
<th>( \dot{V}_T/\text{BSA} ) (l/min)</th>
<th>( f ) (l/min)</th>
<th>Withdrawal response</th>
<th>%Δ( \dot{V}_i )</th>
<th>%Δ( \dot{V}_T )</th>
<th>%Δf</th>
</tr>
</thead>
<tbody>
<tr>
<td>NV 1</td>
<td>43.1</td>
<td>7.11</td>
<td>0.43</td>
<td>20.7</td>
<td>1.41</td>
<td>19.44</td>
<td>25.23</td>
<td>-2.24</td>
</tr>
<tr>
<td>2</td>
<td>46.7</td>
<td>6.75</td>
<td>1.03</td>
<td>10.7</td>
<td>1.28</td>
<td>18.58</td>
<td>19.06</td>
<td>-1.10</td>
</tr>
<tr>
<td>3</td>
<td>44.4</td>
<td>9.32</td>
<td>0.71</td>
<td>23.0</td>
<td>1.04</td>
<td>11.59</td>
<td>8.42</td>
<td>3.17</td>
</tr>
<tr>
<td>4</td>
<td>48.4</td>
<td>13.48</td>
<td>1.03</td>
<td>21.1</td>
<td>2.68</td>
<td>18.85</td>
<td>13.64</td>
<td>6.15</td>
</tr>
<tr>
<td>5</td>
<td>46.8</td>
<td>14.28</td>
<td>1.00</td>
<td>20.2</td>
<td>2.78</td>
<td>18.85</td>
<td>14.49</td>
<td>5.56</td>
</tr>
<tr>
<td>6</td>
<td>46.1</td>
<td>14.83</td>
<td>1.07</td>
<td>21.5</td>
<td>0.97</td>
<td>6.60</td>
<td>1.12</td>
<td>5.49</td>
</tr>
<tr>
<td>7</td>
<td>42.9</td>
<td>11.50</td>
<td>0.59</td>
<td>29.0</td>
<td>1.51</td>
<td>13.00</td>
<td>8.75</td>
<td>4.69</td>
</tr>
<tr>
<td>8</td>
<td>45.6</td>
<td>7.56</td>
<td>0.74</td>
<td>16.7</td>
<td>0.98</td>
<td>12.05</td>
<td>17.85</td>
<td>-6.97</td>
</tr>
</tbody>
</table>

Mean ±S.E. | 45.60 ±0.62 | 10.60 ±1.18 | 0.82 ±0.09 | 18.27 ±3.07 | 1.58 ±0.26 | 14.87 ±1.67 | 13.57 ±2.64 | 1.84 ±1.68 |

Abbreviations: \( \dot{V}_i/\text{BSA} \) and \( \dot{V}_T/\text{BSA} \), minute ventilation and tidal volume before \( O_2 \) breathing; \( \Delta \dot{V}_i/\text{BSA} \), difference between \( \dot{V}_i/\text{BSA} \) and minute ventilation after \( O_2 \) breathing; %Δ\( \dot{V}_i \), %Δ\( \dot{V}_T \), and %Δf, expressed as the ratio of values following \( O_2 \) breathing to values before \( O_2 \) breathing in %.

Table 3b. Results of withdrawal responses in patients with hypertension.

<table>
<thead>
<tr>
<th>No.</th>
<th>( P_{ET\text{CO}_2} ) (mmHg)</th>
<th>( \dot{V}_i/\text{BSA} ) (l/min)</th>
<th>( \dot{V}_T/\text{BSA} ) (l/min)</th>
<th>( f ) (l/min)</th>
<th>Withdrawal response</th>
<th>%Δ( \dot{V}_i )</th>
<th>%Δ( \dot{V}_T )</th>
<th>%Δf</th>
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<tbody>
<tr>
<td>HT 1</td>
<td>43.2</td>
<td>10.34</td>
<td>0.45</td>
<td>25.6</td>
<td>3.27</td>
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<td>2</td>
<td>45.4</td>
<td>6.89</td>
<td>0.34</td>
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<td>18.6</td>
<td>2.11</td>
<td>27.77</td>
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<tr>
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<td>25.57</td>
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<tr>
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<td>1.55</td>
<td>23.22</td>
<td>6.76</td>
<td>17.87</td>
</tr>
</tbody>
</table>

Mean ±S.E. | 45.98 ±0.58 | 11.22 ±1.23 | 0.81 ±0.09 | 21.22 ±1.35 | 3.69* ±0.76 | 31.70** ±3.45 | 30.84** ±4.83 | 3.44 ±5.12 |

Abbreviations are the same as in Table 3a. *\( p<0.05 \), **\( p<0.01 \) indicate a statistically significant difference as compared to the values of NV (Table 3a).
Fig. 2a. Correlation of the ventilatory response to hypoxia ($A_{\text{f}_{1}/\text{BSA}}$) and the withdrawal response ($\Delta V_{\text{f}}/\text{BSA}$).

Fig. 2b. Correlation of the ventilatory response to hypercapnia ($S/\text{BSA}$) and the withdrawal response ($\Delta V_{\text{f}}/\text{BSA}$).

hypercapnic condition between NV and HT. The withdrawal responses in patients with HT exhibited a markedly greater fall in ventilation by changing the gas from hypoxic to hyperoxic. $\Delta V_{\text{f}}/\text{BSA}$, $\% \Delta V_{\text{f}}$, and $\% \Delta V_{\text{f}}$ in HT were significantly higher than those of NV. However, there was no significant difference in $\Delta f$ (frequency) between NV and HT. Reduced ventilation depended on reduced tidal volume, but not breathing frequency.

The relationship between $\Delta V_{\text{f}}/\text{BSA}$ and $A/\text{BSA}$, $S/\text{BSA}$ is shown in Fig. 2. A/
BSA in both NV and HT, correlated with $\dot{V}_1/BSA$ (NV, \( r = 0.684, p < 0.05 \); HT, \( r = 0.648, p < 0.05 \)) significantly. However, $\dot{V}_1/BSA$ in HT tended to be higher than that in NV, under the same value of $A/BSA$. Furthermore, the relationship between $\dot{V}_1/BSA$ and $S/BSA$ was not significant in both NV and HT (Fig. 2b).

DISCUSSION

So far, alveolar hyperventilation has been found in both hypertensive humans and spontaneously hypertensive rats of the Okamoto strain (SHR), and striking hemodynamic and breathing responses due to exposure to either hypoxia or hyperoxia have been observed (Przybylski, 1978; Tafil and Trzebski, 1981; Przybylski et al., 1982). These results suggest that the reactivity of the arterial chemoreceptors appears to be altered by the influences of hypertension. Furthermore, in postmortem studies an enlargement of the carotid bodies in both hypertensive subjects (Lange, 1962; Heath et al., 1970; Edwards et al., 1971; Przemyslaw, 1985) and SHR has been described (Habecck et al., 1981, 1984; Pfeiffer et al., 1984; Smith et al., 1984).

However, the previous studies did not provide information on the mechanism whether peripheral or central chemoreceptor played a role in the enhancement of the chemoreceptor reflex drive in hypertensive subjects. Thus, we investigated the ventilatory response to hypoxia and hypercapnia. Moreover, we used the withdrawal test to make clear the contribution of the peripheral chemoreceptors to the ventilatory response.

In general, the ventilatory response to isocapnic progressive hypoxia reflects the activity of the peripheral chemoreceptor. In contrast, the ventilatory response to hyperoxic hypercapnia is the index of the central chemosensitivity. However, it was known that these parameters of HVR and HCVR were highly variable and had a large range standard deviation for the normal range in normal subjects. Further, $A/BSA$ values express the magnitude of ventilation resulting from the peripheral chemoreceptor activity plus the hypoxic ventilatory depression in the central nervous system. The existence of hypoxic ventilatory depression resulted in an underestimation of the ventilatory response on steady-state ventilation. The higher rate of hypoxic ventilatory depression was $1/3$ in the report by Miller et al. (1974) and $1/12$ by Honda et al. (1981). Thus, we considered that the withdrawal test was the most appropriate for evaluating the activity of the peripheral chemoreceptor independently.

In this study, no significant differences in ventilatory responses to hypoxia and hypercapnia between HT and NV were observed. These results were not similar to the previous studies. Trzebski et al. (1982) indicated a significant difference in $A/BSA$ as an index of the ventilatory response to hypoxia between HT and NV.

Regarding the relationship between HVR and HCVR, Trzebski et al. (1982) reported that the correlation between the two responses was significantly high in normotensive subjects, but no correlation was found between them in hypertensive
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subjects. Some dissociation of the peripheral and the central chemosensitivity might occur due to the augmentation of the peripheral chemoreceptors activity in early hypertension. In our study, the relationship between $A/BSA$ and $S/BSA$ was correlative in NV, but not in HT. At this point, our result was similar to that of Trzebski et al. (1982). Furthermore, although there was no significant difference in $S$ value as an index of the central chemosensitivity between NV and HT, $A$ values in four patients with HT were much greater than 200 ($l/(min \cdot mmHg)$), the highest value in NV. These results suggest that the activity of the peripheral chemoreceptors in some patients with HT is augmented.

However, the results of the ventilatory response to hypoxia did not accurately reflect the augmented peripheral chemoreceptor activity, because the ventilatory response included the influence of the central nervous system. Their integrated responses resulted in no significant difference between HT and NV in the ventilatory response to hypoxia. Both the previous studies and our data about the ventilatory responses to hypoxia and hypercapnia did not provide further information on the mechanism of the augmented peripheral chemoreceptor activity. However, the withdrawal responses showed a markedly greater fall in ventilation by changing the gas from hypoxic to hyperoxic in HT than those in NV. Since the differences in the withdrawal responses between NV and HT was clearly recognized, we conclude that the peripheral chemoreceptors activity is augmented in patients with hypertension.

Tafil-Klawe et al. (1989) indicated that the augmented ventilatory response to hypoxia was found in 20- to 40-year-old patients, whereas the older patients (41–60 years) were not different from the age-matched normotensive. In our study, since we investigated the subjects in the range of 35 to 67 years old who had early hypertension and long-illness hypertension, we could not obtain any significant difference from the aged-matched normotensive subjects.

Further, Tafil-Klawe et al. (1989) reported 15 healthy normotensive young subjects with a family background of hypertension, who had markedly augmented hypoxic ventilatory response. They also suggested that the augmented ventilatory response to hypoxia leads to attenuation of ventilatory response to hypoxia in hypertensive subjects with aging, similar to normotensive subjects. These findings supported that some genetic factor may play a role in the augmented peripheral chemoreceptor activity. We do not have any data in contradicting this assumption. However, in other previous studies, it was confirmed that the alterations of both carotid body structure and reflex effects in hypertensive humans and animals are the result of the high systemic arterial blood pressure (Daly, 1983).

The interrelation between arterial baroreceptor and chemoreceptor has been debated. The question arises as to whether the interrelation may exist between arterial chemoreceptor activity and the level of the systemic arterial blood pressure or not. There is no doubt that acute hypoxic in most mammals is accompanied by a reflex constriction of the systemic arterioles and an increase in the systemic arterial pressure. Thus, it has been supposed that a pathologic hyperactivity of the
arterial chemoreceptors might lead to hypertension. If so, then alterations of chemoreceptor morphology and reflex effects should be demonstrable before the onset of hypertension. Moreover, assuming that a high activity of the arterial chemoreceptor may play a role in a “trigger mechanism” leading to hypertension, we would have to expect that the incidence of hypertension is enhanced at high altitude where the peripheral chemoreceptor is always stimulated. However, all epidemiologic studies showed that the frequency of hypertension is considerably low in highlanders (Frisancho, 1975; Makela et al., 1978; Voors and Johnson, 1979). Chronic stimulation of the peripheral chemoreceptors seems to be more effective in inhibiting the development of systemic hypertension than in facilitating it. We have no evidence for the peripheral chemoreceptor hyperactivity as a leading factor to hypertension. Further, we could not recognize the relationship between the degree of hypertension and the withdrawal responses.

Some mechanisms which make the peripheral chemoreceptors alter have been speculated. If the arterial disease processes such as those that occur in hypertension also involve the blood vessels of the carotid bodies, the respiratory and the cardiovascular control by these chemoreceptors may be affected. The mechanism of the increased chemoreceptor discharge in SHR may be due to a greater decrease in blood flow through narrowed vessels in the carotid bodies by arteriosclerosis. A reduction in the arterial supply to the carotid bodies, unnecessarily exciting the chemoreceptors, may occur in patients with hypertension. In SHR as experimental hypertension model, Fukuda et al. (1987) speculated that the actual degree of hypoxic stimulus may be higher in SHR than in NTR even at the same oxygen tension level. Further, a membrane abnormality expressed as an increased passive permeability to sodium in essential hypertension (Garay et al., 1980) may also be considered as a possible cause of the hypersensitivity in the carotid bodies.

Our result indicates that the peripheral chemoreceptor activity is augmented in hypertension compared with normotensive subjects. It will be necessary to investigate further the relationship of hypertension with the activity of the peripheral chemoreceptor.

REFERENCES


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