Ventilatory responses to progressive hypercapnia were analyzed in the normocapnic and hypercapnic obstructive sleep apnea patients (OSA). The rebreathing hypercapnic and hypoxic tests were performed using the computerized equipment (Lungtest, MES), according to Read's method. The ventilatory response to hypoxia was impaired in all OSA patients. Concerning the hypercapnic ventilatory response, there were no differences between the OSA patients with normal end-tidal PCO$_2$ and controls. Nine moderately hypercapnic OSA patients showed a right shift with a normal slope of the regression curve describing the relationship between the end-tidal PCO$_2$ and minute ventilation. In contrast, three severely hypercapnic OSA patients showed a right shift with a decreased slope of this regression curve. We conclude that awake OSA patients who developed hypercapnic ventilatory insufficiency showed an impaired hypercapnic defense reaction.

**Key words:** hypoxic ventilatory response, hypercapnic ventilatory response, obstructive sleep apnea

**INTRODUCTION**

Our previous study showed an impaired ventilatory response to progressive hypoxia in obstructive sleep apnea patients (1, 2, 3). Chronic hypercapnia might change the peripheral and central sensitivity to physiological chemical stimuli (hypoxia and hypercapnia). An impairment of chemosensitivity probably contributes to respiratory failure, resulting in instability of the feedback control
mechanisms of the respiratory system. The aim of the present study was to investigate the hypoxic and hypercapnic ventilatory responses in normocapnic and hypercapnic obstructive sleep apnea patients (OSA).

MATERIAL AND METHODS

The study protocol was approved by the Ethics Committee of Bydgoszcz Medical University (permit No. KB/252/2002/2004). Twenty seven OSA patients and 25 age-matched healthy controls were involved in the study. Of the 27 patients, 15 were normocapnic (OSA I), 9 moderately hypercapnic (OSA II), and 3 severely hypercapnic (OSA III) (Table 1). In all patients studied OSA was diagnosed by polysomnography. All controls were screened for cardiovascular, hypertensive and respiratory disorders and all were physically active.

In order to activate the arterial chemoreceptors, a progressive hypoxia test (normo- and isocapnic) was used. Central chemosensitivity was evaluated by a progressive hypercapnia test (hyperoxic). Progressive hypoxia and progressive hypercapnia were induced by a rebreathing method by using computerized equipment (Lungtest; MES, Cracow). The ventilatory response to hypoxia was measured for each subject as a slope of the regression curve describing the relationship between the arterial blood hemoglobin saturation (SaO₂) and the minute ventilation (Vₑ). The ventilatory response to hypercapnia was measured as a slope of the regression curve describing the relationship between the end-tidal PCO₂ (PETCO₂) and Vₑ.

RESULTS AND DISCUSSION

The ventilatory response to progressive hypoxia was impaired in all groups of OSA patients, as compared with controls. That included also the three severely hypercapnic patients (OSA III) in whom there was no increase in ventilation in response to hypoxia. The value of the slope of the regression curve for the hypoxic ventilatory response was 0.83 ±0.12 in OSA I and OSA II patients vs. 1.62 ±0.19 L/min/%SaO₂ in the control subjects.

Concerning the ventilatory response to progressive hypercapnia, there were no differences between the OSA patients with normal PETCO₂ (OSA I) and controls (Fig. 1, Fig. 2). The nine moderately hypercapnic patients (OSA II) showed a right shift with the normal slope of the regression curve for the hypercapnic ventilatory response (Fig. 2). The three severely hypercapnic patients (OSA III), in whom no ventilatory response to hypoxia was found, showed a right shift with the decreased slope of the regression curve (Fig. 2).

<table>
<thead>
<tr>
<th>Groups of subjects</th>
<th>n</th>
<th>Age (years)</th>
<th>PETCO₂ (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OSA I</td>
<td>15</td>
<td>45 ±1.1</td>
<td>41 ±2</td>
</tr>
<tr>
<td>OSA II</td>
<td>9</td>
<td>47 ±1.3</td>
<td>49 ±1</td>
</tr>
<tr>
<td>OSA III</td>
<td>3</td>
<td>51 ±1.1</td>
<td>58 ±1</td>
</tr>
<tr>
<td>Controls</td>
<td>25</td>
<td>46 ±1.8</td>
<td>39 ±2</td>
</tr>
</tbody>
</table>
Abnormalities of ventilatory control have been associated with sleep apnea. The study of patients with sleep apnea and hypercapnic respiratory failure suggested that a characteristic abnormality is low or absent hypoxic responsiveness (4, 5). Although the hypercapnic response is in the low range, there is usually a clear response (6) without an interaction between arterial carbon dioxide and hypoxia. The second important fact is that "the daytime respiratory failure usually resolves after the upper airway obstruction is controlled" (6). It seems that sleep apnea itself leads to a reversible depression of central respiratory drive (7).

Our results showed the dynamics of the adaptation process of the hypercapnic ventilatory response: from no change in normocapnic patients, to a right shift in the moderately hypercapnic patients, and to a right shift with a decrease in the slope in the three patients with severe hypoventilation. It is possible that a key abnormality lies in the control of the peripheral chemoreceptor system (6). Carotid bodies are the "front-line" system detecting changes in oxygen level in

Fig. 1. Regression curves of individual control subjects, describing the relationship between the $P_A CO_2$ and minute ventilation ($V_e$).

Fig. 2. Regression curves of individual OSA patients, describing the relationship between the $P_A CO_2$ and minute ventilation ($V_e$).
the arterial blood. Reduction of function of this system allows more hypoxia and hypercapnia. The first step of the adaptation process to hypercapnia is a shift to the right of the response curve (changes in cerebrospinal fluid); the next step is, additionally, a decrease of the slope of the response curve - the decrease of reactivity.

The mechanisms of depressed sensitivity to hypoxia are not known. An important contributor to the depressed chemoreceptor drive - a long period of alcohol consumption - might be considered. A direct effect of alcohol itself, interaction of alcohol and hypoxia, might cause depression of responsiveness to hypoxia (6, 8). A combination of several factors, like alcohol consumption, obesity, heavy snoring, heavy smoking, and airflow limitation may depress chemoreceptor function, including both reversible and irreversible elements.

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