Acute Effect of Cigarette Smoking on Serum Angiotensin-Converting Enzyme Activity in Normal Man

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The acute effect of cigarette smoking on serum angiotensin-converting enzyme activity was evaluated in 6 healthy subjects consisting of 4 non-smokers and 2 habitual smokers. Cigarette smoking resulted in rapid increases in serum converting enzyme activity in 5 of 6 subjects within 5 min, and the converting enzyme activity remained above the control value at 30 min. The increase in the enzyme activity of non-smokers was higher than that of habitual smokers at any time when the enzyme activity was determined. It is therefore suggested that cigarette smoke (or smoking) can cause the secretion of angiotensin-converting enzyme from the pulmonary endothelial cell, in which the enzyme may be produced, to the systemic circulation. It is also speculated that the increase in the enzyme activity may contribute to the initiation of cardiovascular changes associated with cigarette smoking.

Angiotensin-converting enzyme (E.C. 1.4.15.1.), a peptidyl-dipeptide hydrolase, liberates the C terminal histidyl-leucine from angiotensin I, transforming it into the active octapeptide, angiotensin II. This enzyme has been extensively studied in peripheral tissues because of the importance of angiotensin II in hypertension (Cushman and Cheung 1971). Although plasma source of the enzyme is not clear, there is increasing evidence that the enzyme is localized on the luminal surface of vascular endothelial cells of the lung, leading the concept that the enzyme is mainly produced in the lung (Erdoes 1975). On the other hand, it has been demonstrated that exposure to cigarette smoke increased the conversion of angiotensin I into angiotensin II in the rat isolated lung (Bakhlo et al. 1979). In humans, however, the direct effect of cigarette smoke on angiotensin-converting enzyme has not been described. The present study aims to clarify this point.

Six healthy males consisting of 4 non-smokers and 2 habitual smokers, aged 24–31 years, were kept fasted and recumbent overnight. After drawing −15 and 0 min blood samples, the subjects smoked 2 commercial cigarettes containing 2.1 mg nicotine and 25 mg tar, as quoted by the manufacturer, within a period of 3 min. Blood was drawn at 1, 3, 5, 15, and 30 min after the smoking. Serum angiotensin-converting enzyme activity for each sample was determined by the spectrophotometric assay using hippryl-l-histidyl-l-leucine (Protein Research Foundation, Osaka) as substrate (Mizuno et al. 1981). One unit of the

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enzyme activity was defined in terms of one nmole hippuric acid formed/ml/min at 37°C. The assay was performed in duplicate. Values were given as mean ± s.E. Statistical analysis was performed with Student’s t-test.

Table 1 depicts our principal data on the effect of cigarette smoking on serum angiotensin-converting enzyme activity. The enzyme activity rose from 16.0±2.2 to 34.1±9.7 units at 5 min after the smoking, and it remained above the control value at 30 min. The increase in the enzyme activity of non-smokers was higher than that of habitual smokers at any time, and the difference was significant at 5 min (p<0.01) and 30 min (p<0.01).

Table 1. Effect of cigarette smoking on serum angiotensin-converting enzyme activity in normal male subjects

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>15</th>
<th>0</th>
<th>1</th>
<th>3</th>
<th>5</th>
<th>15</th>
<th>30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total subjects (n=6)</td>
<td>17.5±2.0</td>
<td>16.0±2.2</td>
<td>26.9±6.3</td>
<td>31.9±8.4</td>
<td>34.1±9.7</td>
<td>30.5±8.3</td>
<td>23.9±4.8</td>
</tr>
<tr>
<td>Habitual smokers (n=2)</td>
<td>13.3±2.0</td>
<td>12.5±2.6</td>
<td>22.1±12.7</td>
<td>21.9±11.4</td>
<td>14.6±1.0</td>
<td>16.9±7.9</td>
<td>12.1±3.1</td>
</tr>
<tr>
<td>Non-smokers (n=4)</td>
<td>16.4±3.1</td>
<td>17.8±2.9</td>
<td>29.4±8.4</td>
<td>36.9±11.4</td>
<td>43.8±11.9*</td>
<td>37.3±10.7</td>
<td>30.1±4.8*</td>
</tr>
</tbody>
</table>

Significance of differences: * p<0.01 as compared with the habitual smokers.

In the present study, it was demonstrated that cigarette smoke increased serum angiotensin-converting enzyme activity in man. Although the mechanism by which the enzyme rose immediately after cigarette smoking remains obscure, the increase may show that the event occurs at the pulmonary endothelial cell membrane as an effect of cigarette smoke in the airways. Since serum angiotensin-converting enzyme is an indispensable component for the conversion of angiotensin I to an active octapeptide, angiotensin II, the increase may produce changes in blood pressure (Bakhle et al. 1979). Thus, the present data may suggest a mechanism for the initiation of cardiovascular changes associated with cigarette smoking. It is not clear at present why the elevation of converting enzyme activity in non-smokers was higher than that in habitual smokers.

References