Differences in regional cerebral blood flow in two types of leuko-araiosis

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Abstract

Cerebral blood flow and cerebrovascular acetazolamide reactivity were investigated in patients with periventricular hyperintensity and in patients with leuko-araiosis in centrum semiovale. Fifteen patients with periventricular hyperintensity, 15 patients with leuko-araiosis in centrum semiovale and 15 age-matched controls without leuko-araiosis were studied. The regional cerebral blood flow was measured using the stable xenon CT method before and 20 min after intravenous injection of 17mg/kg acetazolamide. The blood flow and the cerebrovascular acetazolamide reactivity in the area of leuko-araiosis were significantly lower in the periventricular hyperintensity group and the leuko-araiosis in centrum semiovale group than the control group. The blood flow in the cerebral cortex was significantly lower in the leuko-araiosis in centrum semiovale group than in the periventricular hyperintensity group and the control group. The cerebrovascular acetazolamide reactivity in the cerebral cortex did not show any significant difference among the three groups. The blood flow in the cerebral cortex was decreased in patients with leuko-araiosis in centrum semiovale but the cerebrovascular acetazolamide reactivity in the cerebral cortex was normal in patients with leuko-araiosis.

Keywords: Leuko-araiosis; Periventricular hyperintensity; Cerebral blood flow; Acetazolamide

1. Introduction

Leuko-araiosis [1] is a radiological finding and its pathophysiology is not uniform [2]. Leuko-araiosis may be divided into two types; periventricular hyperintensity and leuko-araiosis in centrum semiovale [2–5]. The disturbance in cerebrospinal fluid circulation may be related to periventricular hyperintensity and hypertension may be related to leuko-araiosis in centrum semiovale [6]. The two types may have some difference in cerebral circulation. In order to find out the difference, we investigated cerebral blood flows and cerebrovascular acetazolamide reactivity in the two types of leuko-araiosis.

2. Patients and methods

Fifteen cases of periventricular hyperintensity (A), 15 cases of leuko-araiosis in centrum semiovale (B) and 15 age-matched controls without leuko-araiosis (C) were studied with their informed consent. The patients with leuko-araiosis were admitted to our hospital and head computed tomography (CT), head magnetic resonance imaging (MRI), echocardiography and blood viscosity were studied on the patients. A is defined as hyperintensity areas in head MRI which are contiguous to the ventricles (Fig. 1) and B is defined as hyperintensity areas in head MRI which are located at a distance from the ventricles (Fig. 2). The patients who have both A and B, the patients who have signs or symptoms of cerebral infarction, and the patients with hydrocephalus and leukodystrophy were excluded from this study. Medications which influence cerebral blood flow were discontinued 2 weeks prior to the cerebral blood flow examination. Fifteen cases in each group were selected by the order of admission date. Table 1 shows the subjects’ characteristics in the three groups. The total volume of leuko-araiosis on MRI was determined according to the method of Waldemar et al. [7].

The regional cerebral blood flow was measured using the stable xenon CT method [8–11]. The basal ganglia
section and the lateral ventricle section parallel to the orbito-meatal line were studied. The subjects inhaled room air followed by a mixture of 30% xenon and 50% oxygen for 3 min. Serial scanning was performed once before xenon inhalation, three times in the wash-in process and five times in the washout process of 5 min. The serial scanning program consisted of a total of 18 scans consisting of nine serial scans on each section. The xenon concentration in the end-tidal expired gas was continuously recorded by the thermoconductivity method. We used the xenon delivery and analysis system (AZ-7000 model, Anzai Sogyo, Tokyo, Japan) and the CT equipment (PreSage, Yokogawa Medical Systems, Tokyo, Japan). Regional cerebral blood flows were measured in the leuko-araiosis area, and in the cerebral cortex and cerebral white matter where the influence of the leuko-araiosis was considered to be little. Round region of interest (ROI) with a diameter of 7 mm was used and the ROI was placed in the center of each leuko-araiosis area in bilateral anterior and posterior regions. The leuko-araiosis area blood flow was calculated as the average of the blood flows in the four leuko-araiosis areas. In bilateral frontal lobes, parietal lobes, temporal lobes and occipital lobes, the ROI was placed in the area where leuko-araiosis was not adjacent.

The cerebral cortex blood flow and cerebral white matter blood flow were calculated as the average of the blood flows in the eight areas.

The regional cerebral blood flow was measured before and 20 min after intravenous injection of 17mg/kg acetazolamide. Mini-mental state examination [12] was performed and underlying diseases were examined.

Statistical analysis was performed using Mann–Whitney’s U-tests for comparison of the cerebral blood flows and using Fisher’s exact probability tests for comparison of underlying diseases among the three groups.

3. Results

Fig. 3 shows the actual records of xenon CT in A, B, and C before and after injection of acetazolamide. Before injection of acetazolamide, the blood flow in the leuko-araiosis area is lower than that in the cerebral white matter. The blood flow in the cerebral cortex is lower in B than in A and C. After injection of acetazolamide, the blood flow is increased. The increase rate in blood flows by acetazola-
mide is lower in the leuko-araiois area than in the cerebral white matter.

Table 2 shows the mean and standard deviation of the blood flows in the cerebral cortex, cerebral white matter and leuko-araiois area. The blood flow in the leuko-araiois area was significantly lower than that in the cerebral white matter. The blood flow in the cerebral cortex was significantly lower in B than in A and C. The increase rate in blood flows by acetazolamide was significantly lower in the leuko-araiois area than in the cerebral white matter.

The rate of association of hypertension was significantly higher in B than in A and C (Table 1). There was no significant correlation between hypertension and cerebral blood flow in the three groups. There was no significant difference in total volume of leuko-araiois on MRI (Table 1).

4. Discussion

Leuko-araiois has many causes [2] but the common causes are considered to be arteriolosclerosis [13–15] and normal aging [16–18]. Cerebral blood flow has been reported to be decreased in leuko-araiois [19–22]. Leuko-araiois may be divided into two types: A and B [2–5]. The mechanism of the two types is considered to be different [4,5]. There was no report on the difference in cerebral blood flow between the two types. The blood flow in the cerebral cortex was significantly lower in B than in A and C. Because the total volume of leuko-araiois on MRI did not show any significant difference between the two groups, the difference in blood flow in the cerebral cortex between the two groups is considered to be not due to the amount of leuko-araiois but due to the location of leuko-araiois.

Xenon CT with the wash-in/washout protocol has been reported to show considerable reliability in measuring blood flow in the cerebral white matter [9] and has been used in patients with pathological conditions [10,23,24]. Using the same instrument and the same method of xenon CT as ours, Haku et al. [25] reported a significant correlation ($r=0.68$, $P<0.001$) between regional cerebral blood flow values (10–30 ml/100 g/min) of the white matter area obtained by xenon CT and those of $^{133}$Xe single-photon emission CT, which has been accepted as a standard method for the measurement of regional cerebral blood flow.

Acetazolamide is considered to dilate the cerebral arterioles by inhibiting the carbonic anhydrase in the red

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Table 1
Subjects’ characteristics in three groups

<table>
<thead>
<tr>
<th></th>
<th>(A) Periventricular hyperintensity group</th>
<th>(B) Leuko-araiois in centrum semiovale group</th>
<th>(C) Age-matched control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>15</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Age (years)*</td>
<td>66.8±8.4</td>
<td>63.2±8.3</td>
<td>65.1±8.5</td>
</tr>
<tr>
<td>Male:female</td>
<td>8:7</td>
<td>7:8</td>
<td>7:8</td>
</tr>
<tr>
<td>Hypertension</td>
<td>6/15</td>
<td>12/15*</td>
<td>4/15</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>7/15</td>
<td>8/15</td>
<td>3/15</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>5/15</td>
<td>6/15</td>
<td>3/15</td>
</tr>
<tr>
<td>Mini-mental state examination score*</td>
<td>26±3</td>
<td>18±4</td>
<td>30±0</td>
</tr>
<tr>
<td>Total volume of leuko-araiois on MRI (cm$^3$)*</td>
<td>7.1±4.3</td>
<td>6.5±4.2</td>
<td>–</td>
</tr>
</tbody>
</table>

* Mean±standard deviation.  
* $P<0.05$ versus B, $P<0.01$ versus C.

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Table 2
Blood flow (ml/100g/min) before the intravenous injection of acetazolamide and increase rate (%) in blood flow by the intravenous injection of acetazolamide (mean±standard deviation)

<table>
<thead>
<tr>
<th></th>
<th>(A) Periventricular hyperintensity group</th>
<th>(B) Leuko-araiois in centrum semiovale group</th>
<th>(C) Age-matched control group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Before the intravenous injection of acetazolamide</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebral cortex blood flow</td>
<td>50.1±7.2</td>
<td>41.9±7.1*</td>
<td>57.9±7.5</td>
</tr>
<tr>
<td>Cerebral white matter blood flow</td>
<td>25.6±4.3</td>
<td>25.2±4.2</td>
<td>28.4±4.4</td>
</tr>
<tr>
<td>Leuko-araiois area blood flow</td>
<td>16.9±2.8**</td>
<td>17.1±2.9**</td>
<td>–</td>
</tr>
<tr>
<td><strong>After the intravenous injection of acetazolamide</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increase rate in cerebral cortex blood flow</td>
<td>52.1±7.5</td>
<td>58.2±8.2</td>
<td>56.2±8.0</td>
</tr>
<tr>
<td>Increase rate in cerebral white matter blood flow</td>
<td>45.9±6.8</td>
<td>45.9±7.2</td>
<td>47.1±7.5</td>
</tr>
<tr>
<td>Increase rate in leuko-araiois area blood flow</td>
<td>31.6±7.4**</td>
<td>29.7±6.8**</td>
<td>–</td>
</tr>
</tbody>
</table>

* $P<0.01$ compared with the other two groups.  
** $P<0.01$ compared with the cerebral white matter.
blood cells and increasing CO₂ in the arterioles [26,27]. Acetazolamide has been used for examining cerebrovascular dilatory reserve capacity [28].

In the present study, cerebrovascular acetazolamide reactivity was decreased in the leuko-araiosis area. This suggests that cerebrovascular dilatory reserve capacity is decreased in the leuko-araiosis area. The cerebrovascular acetazolamide reactivity in the cerebral cortex did not show any significant difference among the three groups. This suggests that cerebrovascular dilatory reserve capacity is preserved in the cerebral cortex and that decreased cerebral cortex blood flow may be due to overlying cortex diaschisis in cases of B.

The present study showed that the blood flow in the cerebral cortex was lower and the rate of hypertension was higher in B than in A. This suggests that hypertension and
arteriolosclerosis are related more to B than A and that the pathogenesis of the two types is different. Because the sample size is small in the present study, we hope that a study in a large sample size will be performed.

References