Evaluation of Cerebral Oxygenation in Patients Undergoing Long-Term Hemodialysis

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Key Words
Blood volume · Cerebral oxygenation · Hemodialysis · Regional saturation of oxygen

Abstract
Background/Aims: Patients undergoing hemodialysis (HD) have higher occurrence rates of cerebral diseases, including uremic encephalopathy, cognitive impairment, dementia, and cerebrovascular disease, than the general population. During HD, ultrafiltration is performed to maintain an adequate fluid condition and is associated with subsequent blood volume (BV) reduction. We aimed to (1) monitor changes in cerebral oxygenation and BV reduction during HD, and (2) clarify the mechanism that influences cerebral oxygenation in HD patients.

Methods: Eighteen HD patients and 12 healthy controls were recruited. Regional saturation of oxygen (rSO2) was continuously monitored in the frontal cortex using INVOS 5100C before, during, and after HD, and in healthy controls. Relative change in BV (%ΔBV) was simultaneously monitored during HD using a BV monitor.

Results: Before HD, patients had significantly lower rSO2 values than controls (56.1 ± 1.4 vs. 70.4 ± 2.5%, p < 0.001). Although %ΔBV significantly decreased from 20 min to the end of HD (20 min: –3.3 ± 0.3%, p < 0.05; end of HD: –12.0 ± 1.0%, p < 0.01), changes in rSO2 values during HD were not significant. No relationship existed between rSO2 values and blood pressure levels, hemoglobin levels, oxygen pressure, HCO3, oxygen saturation, and arterial O2 content before and after HD. Furthermore, changes in rSO2 were not correlated with changes in these parameters.

Conclusion: rSO2 values before HD were significantly lower in HD patients than in healthy controls. rSO2 values were maintained during HD and were not influenced by BV reduction.

Introduction
The development of conditions involving central nervous system (CNS) dysfunction, such as uremic encephalopathy, cognitive impairment, dementia, and cerebrovascular disease, is common in patients undergoing hemodialysis (HD) [1]. In particular, stroke occurs approximately 4–6 times more frequently in HD patients than in the general population [2]. Moreover, the risk of subclinical cerebrovascular disease increases due to microvascular disease and chronic hypoperfusion in the...
brain [2–4]. This silent cerebral ischemia might be related to the severity of cognitive impairment in HD patients [5]. HD is performed to remove accumulated substances, improve electrolyte disturbances, and control body-fluid disturbances. However, whether HD provides a beneficial effect on cerebral tissue remains unclear, and changes in cerebral blood flow during HD also remain controversial [6–9]. Few reports have examined the relationship between cerebral oxygenation and blood volume (BV) reduction induced by ultrafiltration during HD.

This study aimed to (1) monitor changes in cerebral oxygenation and BV reduction during HD and examine their interrelationship, and (2) clarify the mechanism influencing the value of cerebral oxygenation in HD patients.

Methods

Patients

In this study, we included HD patients who met the following criteria: (1) been on HD >6 months and (2) no symptoms such as intradialytic hypotension and muscle cramping during HD. The exclusion criteria were: (1) occurrence of one or more intradialytic hypotension episode in the previous month, (2) absence of BV reduction during HD, and (3) coexisting major disease including congestive heart failure and apparent neurological disorders, and history of cerebrovascular disease.

Eighteen anuric HD patients were recruited (13 men and 5 women; mean age: 69.9 ± 2.5 years, HD duration: 7.0 ± 2.5 years). The causes of chronic renal failure were chronic glomerulonephritis (8 patients), non-insulin-dependent diabetes mellitus (8 patients), and other (2 patients). Each patient received HD 2 or 3 times a week, and the duration of each HD session was 4 h. The patients’ general characteristics are summarized in Table 1. Informed consent was obtained from each patient. This study was approved by the institutional review board of Nishikawa Town Hospital, Japan, and conforms to the provisions of the Declaration of Helsinki (as revised in Tokyo in 2004). Furthermore, 12 healthy volunteers (8 men and 4 women; mean age: 50.1 ± 5.4 years) were recruited as the control group.

Monitoring of Cerebral Oxygenation and Relative BV Change

Cerebral oxygenation was monitored at the forehead using an INVOS 5100C saturation monitor (Covidien Somanetics, Essex, UK), based on near-infrared spectroscopy technology. This instrument uses a light-emitting diode transmitting near-infrared light in 2 wavelengths (735 and 810 nm) and 2 silicon photodiodes as light detectors to provide a single numerical value that represents the regional cerebral oxygen saturation (rSO2) [10, 11]. All data gained by this instrument were immediately and automatically stored sequentially. Interobserver variance for this instrument, i.e. reproducibility of rSO2 measurement, is quite acceptable as reported previously; thus, rSO2 values are reliable for estimating the actual cerebral oxygenation value [12].

Ultrafiltration-induced BV reduction during HD, measured using a BV monitor mounted on Nikkiso DCS-27 dialysis equipment (Tokyo, Japan), was evaluated as the relative BV change (%ΔBV) in each patient. The principles and accuracy of %ΔBV measurements have been previously reported [13].

Before HD, each patient rested in the supine position for at least 15 min to reduce the influence of posture-induced BV change [14]. Next, an rSO2 measurement sensor was attached to the patient’s forehead for measurement during HD. The %ΔBV was also observed during the HD session. While observing rSO2 and %ΔBV, each patient was instructed to lie quietly in bed and refrain from eating.

Blood samples were obtained from each patient before and after HD. Arterial O2 content (CaO2) was calculated using the following equation [15]:

\[
\text{CaO}_2 (\text{ml/dl}) = 1.34 \times \text{Hb} \times \text{SpO}_2 /100 + (0.0031 \times \text{pO}_2),
\]

where Hb represents the hemoglobin concentration (g/dl), SpO2 represents the oxygen saturation (%), and pO2 represents the oxygen pressure (mm Hg).

In healthy controls, rSO2 was measured for at least 10 min in the supine position to obtain the mean value.

Statistics

Data are expressed as means ± standard error (SE). Student’s t test for paired or nonpaired values was used for comparing 2 groups. Correlations between 2 groups were evaluated by Pearson’s correlation coefficient and linear regression analysis. Changes in rSO2 and %ΔBV values were evaluated by repeated-measured ANOVA using general linear models and Scheffe’s test, respectively. A difference of p < 0.05 was considered significant.

Results

rSO2 values before HD were compared with those in healthy controls (fig. 1). The rSO2 values before HD were significantly lower than those in healthy controls (56.1 ± 1.4 and 70.4 ± 2.5%, respectively, p < 0.001). During HD,

<table>
<thead>
<tr>
<th>Table 1. General characteristics of patients undergoing HD in this study</th>
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<tbody>
<tr>
<td>Patients</td>
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<tr>
<td>Women/men</td>
</tr>
<tr>
<td>Age, years</td>
</tr>
<tr>
<td>Cause of chronic renal failure</td>
</tr>
<tr>
<td>Chronic glomerulonephritis</td>
</tr>
<tr>
<td>Non-insulin-dependent diabetes mellitus</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>HD duration, years</td>
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<tr>
<td>Dry weight, kg</td>
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<td>Ultrafiltration during HD, liters</td>
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<tr>
<td>Kt/V</td>
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<tr>
<td>BUN before HD, mg/dl</td>
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<tr>
<td>BUN after HD, mg/dl</td>
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<td>Values represent means ± SE or n.</td>
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a gradual change in %ΔBV was observed, and a significant decrease was observed at 20 min from the initiation of HD (−3.3 ± 2.5%, p < 0.01). %ΔBV reduced constantly, finally reaching −12.0 ± 1.0% at the end of HD (fig. 2a). However, rSO₂ values during HD showed little changes during HD. ● = p < 0.01 vs. at the start of ultrafiltration.

Evaluation of CNS dysfunction is very important in various diseases and clinical conditions. However, monitoring of CNS condition is technically difficult, some-
Table 2. Changes in \(rSO_2\) values and clinical parameters before and after HD

<table>
<thead>
<tr>
<th></th>
<th>Before HD</th>
<th>After HD</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>(rSO_2), %</td>
<td>56.1±1.4</td>
<td>55.8±1.1</td>
<td>NS</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>138±5</td>
<td>143±4</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>72±3</td>
<td>75±2</td>
<td>NS</td>
</tr>
<tr>
<td>Hb, g/dl</td>
<td>10.4±0.2</td>
<td>11.2±0.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>32.0±6.0</td>
<td>34.2±7.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>pH</td>
<td>7.37±0.01</td>
<td>7.42±0.01</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(pO_2), mm Hg</td>
<td>82.6±2.5</td>
<td>89.3±2.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HCO(_3), mEq/l</td>
<td>20.7±0.5</td>
<td>24.6±0.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SpO(_2), %</td>
<td>96.0±0.3</td>
<td>97.0±0.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Arterial O(_2) content, ml/dl</td>
<td>13.7±0.3</td>
<td>14.8±0.3</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values represent means ± SE.

Within seconds to maintain a constant rCBF within the autoregulatory range (mean arterial pressure between 60 and 160 mm Hg) [20]. A previously detailed examination showed that the regional cerebral oxygen metabolism measured by positron emission tomography (PET) is depressed in HD patients compared to healthy controls [21].

The low levels of \(rSO_2\) values before HD in this study could have occurred for the following reasons. The first is the existence of renal anemia. The mean Hb level before HD was 10.4 ± 0.2 g/dl, which is nearly within the target range recommended for renal anemia management [22]. However, from the viewpoint of oxygen supply into the brain tissue, renal anemia would decrease the oxygen carrying capacity, and indeed the \(CaO_2\) level before HD was rather low (13.7 ± 0.3 ml/dl). Second, changes in the pH of red blood cells influence the affinity between Hb and oxygen, which is known as the Bohr effect. Acidemia with arterial blood metabolic acidosis usually occurs in HD patients, which induces a rightward shift in the HbO\(_2\) curve [23] that decreases affinity between Hb and oxygen, causing reduced microcirculatory oxygen saturation. In this study, the arterial blood pH values indicated slight acidemia, which might have influenced the \(rSO_2\) values before HD via the decreased affinity between Hb and O\(_2\).

The %ΔBV during HD reduced gradually and significantly, whereas \(rSO_2\) was well maintained or not increased during HD (fig. 2; table 2). In a previous study, \(rSO_2\) during HD increased slightly (mean slope: 0.004 ± 0.12%/min) in patients who did not undergo ultrafiltration [1]. Our results are not consistent with those of this report. In general, BV reduction by ultrafiltration during HD reflects the increase in blood Hb concentration. In this study, the Hb levels after HD were significantly higher than those before HD, and \(CaO_2\), an oxygen supply indicator, was also significantly increased after HD. Furthermore, blood acidemia before HD changed to alkalemia after HD due to HCO\(_3\) loading; therefore, the affinity between Hb and oxygen could improve after HD. Thus, the increase of \(rSO_2\) could strongly be expected, but there was no significant change in \(rSO_2\) during HD. The association between increased Hb levels and changes in rCBF investigated by PET in HD patients was reported by Metry et al. [24]. In this report, rCBF significantly decreased and the oxygen metabolism remained disturbed after normalization of hematocrit, which was due to decreased erythrocyte velocity in the cerebral capillaries owing to the decreased blood deformability and increased plasma viscosity. In this study, ultrafiltration increased the total protein concentration from...
6.3 ± 0.1 to 7.0 ± 0.1 g/dl and increased the Hb concentration, which in turn increased whole blood and plasma viscosity. Furthermore, in HD patients, CaO₂ was reported to be the most important determinant of interindividual middle cerebral artery blood flow velocity variance and intradividual middle cerebral artery blood flow velocity variation. Also, the increase in CaO₂ by ultrafiltration during HD would induce the decrease of middle cerebral artery blood flow velocity via vasoconstriction in small intracerebral vessels to maintain oxygen delivery to the brain [8, 25]. Therefore, it would be unlikely that brain circulation and oxygen metabolism including rSO₂ values could be improved in these conditions. To clarify the mechanism influencing the cerebral oxygenation values in HD patients, we also compared the rSO₂ values and clinical parameters before and after HD (table 2), but could not confirm any relationship between the rSO₂ values and clinical parameters. However, since the sample size of the present study was small, further study will be required to clarify the relationships between rSO₂ and various clinical parameters.

In conclusion, rSO₂ values before HD were significantly lower in HD patients than in healthy controls. rSO₂ values were maintained during HD and were not influenced by BV reduction.

**Disclosure Statement**

The authors have no conflicts of interest to declare.

**References**


