Effects of Hemodialysis on Cerebral Circulation Evaluated by Transcranial Doppler Ultrasonography

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Background and Purpose  The effects of hemodialysis on the cerebral circulation of humans and the correlation between changes in blood flow velocity in the basal cerebral arteries and those of several physiological variables influenced by hemodialysis have been inadequately studied.

Methods  Blood flow velocities were obtained from the middle cerebral artery and the basilar artery by transcranial Doppler ultrasonography in 27 patients receiving chronic maintenance hemodialysis immediately before and after the procedure. Changes in body weight, hematocrit, blood pressure, and arterial blood gases were recorded simultaneously.

Results  There was a significant reduction in mean flow velocity in the middle cerebral artery \( (P<0.01) \) and the basilar artery \( (P<0.01) \) after hemodialysis. We observed a significant negative correlation between the relative change in mean flow velocity and the loss of weight after hemodialysis, the amount of fluid removed, and the increase in hematocrit in the middle cerebral artery and the basilar artery.

Conclusions  Hemodialysis and the associated physiological changes can significantly affect the cerebral circulation. Blood flow velocities in the middle cerebral artery and the basilar artery decrease significantly with hemodialysis. The loss of body weight, the amount of fluid removed, and the change in hematocrit significantly correlate with the change in mean flow velocity. The transcranial Doppler method can effectively monitor rapid changes in the cerebral circulation during potentially harmful procedures. (Stroke. 1994;25:408-412.)

Key Words  • blood flow velocity • cerebral circulation • Doppler • hemodialysis

Both the age of patients at the start of hemodialysis and the number with concomitant systemic disorders such as ischemic heart disease and cerebrovascular accidents have risen. According to the Japanese Society for Dialysis Therapy,1 the average age of patients who entered hemodialysis between 1980 and 1987 was 7.6 years, from 48.3 to 55.9 years. Moreover, 32.7% of the deaths were caused by cardiac events, with an additional 14.2% caused by cerebrovascular accidents. Major vascular events, even if not fatal, usually led the patients or their families to discontinue dialysis. Although it is important to understand the effects of hemodialysis on the cerebral circulation, few such studies have been conducted. Holzer et al2 demonstrated that the cerebral blood flow (CBF), as measured by the \(^{133}\)Xe intravenous injection method, was significantly correlated with the hemoglobin level and was decreased after hemodialysis. Gottlieb et al3 also demonstrated that the CBF, as measured by the \(^{133}\)Xe inhalation method, was significantly decreased after hemodialysis. Although the measurement of CBF with radioisotopes is noninvasive, it is not convenient for bedside use and requires sophisticated equipment. There has been no noninvasive, convenient method for detecting rapid changes in the cerebral circulation, so that little is known about such changes related to hemodialysis. Recent advances in ultrasonic technology now allow the detection of Doppler signals through the cranium. By using the transcranial Doppler (TCD) sonographic method established by Aaslid and colleagues,4 a real-time evaluation of blood flow velocity in major intracranial arteries can be done at bedside, even during hemodialysis. Recently Postiglione et al5 applied TCD to demonstrating a significant decrease in the blood flow velocity of the middle cerebral artery in anemic patients who were administered hemodialysis.

We attempted to confirm the results of those authors by monitoring changes in blood flow velocity in the middle cerebral artery as well as in the basilar artery in patients during hemodialysis. We also evaluated the factors that affected the cerebral circulation by performing correlation analyses evaluating the relation between changes in blood flow velocity and alterations in physiological parameters related to hemodialysis.

Subjects and Methods  
We investigated 27 patients (13 men and 14 women) who ranged in age from 28 to 72 years (mean±SD, 52.4±11.3 years) and were receiving chronic maintenance hemodialysis. All patients had end-stage renal disease, which was due to various etiologies (Table 1). They had no evidence of cardiac, peripheral, or cerebrovascular disorders, including transient ischemic attacks or minor stroke. Hemodialysis had been administered for periods of 0.1 to 14.5 years (mean±SD, 3.6±3.8 years). All patients were receiving hemodialysis with a bicarbonate buffer solution, three times each week for 4 to 5 hours each time. The type of antihypertensive medication taken by patients, including angiotensin-converting enzyme...
Variables were analyzed using the Pearson’s correlation model. We also checked for changes in body weight, blood pressure, volume of saline infused during hemodialysis. Simultaneously, we used paired and unpaired tests. Correlations between other variables measured are summarized in Table 3.

We calculated the relative change in mean flow velocity (%MFV) using the following equation: %MFV = 100 x MFV_after / MFV_before, where MFV_before was the mean flow velocity of each basilar arterial cerebral artery and MFV_after was the mean flow velocity of each corresponding artery before hemodialysis. The mean arterial blood pressure (MABP) was calculated from the following simple equation: MABP = (BP_systolic - BP_diastolic) / 3 + BP_diastolic, where BP_systolic and BP_diastolic were the systolic arterial blood pressure and diastolic arterial blood pressure, respectively. The amount of fluid removed by hemodialysis was calculated from the following simple equation: (total volume removed by hemodialysis) - (total volume infused during hemodialysis) = (MABP x heart rate x arterial blood flow rate x sampling from the insonated middle cerebral artery and mean flow velocity of each artery before and after hemodialysis). Adequate Doppler signals were obtained from the basilar artery in all 27 patients. In 8 of the 27 subjects the ratio of signal to noise was either too low or no signal could be obtained. Adequate Doppler signals were obtained from the basilar artery in all 27 patients. Average MFVs from the middle cerebral artery before hemodialysis are shown in Table 2. Except for the hematocrit, values remained within the physiological range. The hematocrit, pH, and body weight each exhibited a significant change during hemodialysis.

Results

The physiological variables evaluated before and after hemodialysis are shown in Table 2. Except for the hematocrit, values remained within the physiological range. The hematocrit, pH, and body weight each exhibited a significant change during hemodialysis.

The correlations observed between %MFV and the other variables measured are summarized in Table 3.

Table 1. Primary Etiology of End-Stage Renal Disease

<table>
<thead>
<tr>
<th>Etiology</th>
<th>No. (n=27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic glomerulonephritis</td>
<td>18</td>
</tr>
<tr>
<td>Diabetic nephropathy</td>
<td>4</td>
</tr>
<tr>
<td>Chronic pyelonephritis</td>
<td>2</td>
</tr>
<tr>
<td>Polycystic kidney disease</td>
<td>2</td>
</tr>
<tr>
<td>Obstructive uropathy</td>
<td>1</td>
</tr>
</tbody>
</table>

Values were expressed as mean±SD. Statistical comparisons were made by paired Student’s t test. BW indicates body weight; MABP, mean arterial blood pressure; PR, pulse rate; bpm, beats per minute; and Ht, hematocrit.

Results

The physiological variables evaluated before and after hemodialysis are shown in Table 2. Except for the hematocrit, values remained within the physiological range. The hematocrit, pH, and body weight each exhibited a significant change during hemodialysis.

Average MFVs from the middle cerebral artery before and after hemodialysis were 57.2±19.2 and 33.5±13.0 cm/s, respectively. Average MFVs from the basilar artery before and after hemodialysis were 41.8±16.1 and 33.5±13.0 cm/s, respectively. The mean depths of sampling from the insonated middle cerebral artery and basilar artery were 51.8±6.3 mm and 83.1±7.7 mm, respectively. MFVs from the middle cerebral artery and the basilar artery were significantly reduced after hemodialysis (%P<.01) (Fig 1); the %MFV in the middle cerebral artery and the basilar artery was 78.5±13.1 and 81.0±11.9%, respectively.

The correlations observed between %MFV and the other variables measured are summarized in Table 3.

Figure 1. Plots show changes in mean blood flow velocity (MFV) before and after hemodialysis (HD) in middle cerebral artery (MCA) (left panel) of 19 patients (38 hemispheres) and in basilar artery (BA) (right panel) of 27 patients.
The %MFV in the middle cerebral artery was inversely correlated with the amount of fluid removed by hemodialysis \((r=-.61, P<.01)\) and the loss of weight after hemodialysis \((r=-.64, P<.01)\) (Fig 2). The %MFV in the basilar artery was also inversely correlated with the amount of fluid removed by hemodialysis \((r=-.56, P<.01)\) and the weight loss produced by hemodialysis \((r=-.62, P<.01)\) (Fig 2). There were significant negative correlations between the change in hematocrit by hemodialysis and the %MFV in both the middle cerebral artery \((r=-.43, P<.01)\) and the basilar artery \((r=-.48, P<.02)\) (Fig 2).

**Discussion**

Our results demonstrated that MFV in the middle cerebral artery was significantly reduced after hemodialysis, a finding consistent with the previous report by Postiglione et al.\(^3\) We also demonstrated that MFV in the basilar artery was significantly reduced after hemodialysis and that the %MFV in the basal cerebral arteries was significantly correlated with the weight loss and the increase in hematocrit produced by hemodialysis.

One possible mechanism to explain the observed decrease in MFV after hemodialysis is the reduction in CBF produced by hemodialysis. Although TCD measures blood flow velocity, not CBF, the flow velocity is proportional to CBF when the vessel diameter is constant. Hemodilution does not significantly dilate the basilar artery of cats.\(^9\) In humans the diameter of a large cerebral artery with an internal diameter greater than 2.5 mm does not change significantly during alterations in blood osmolality and \(\text{PaCO}_2\).\(^10\) We investigated the blood flow velocity from the main trunks of the middle cerebral artery and the basilar artery in our patients. Therefore, we assumed that the diameter of the middle cerebral artery and the basilar artery would not change significantly during hemodialysis. In fact, the carbon dioxide reactivity of the blood flow in the basal cerebral arteries reportedly can be determined from the change in flow velocity measured by TCD.\(^7,8,11\) Another possible mechanism is the passive alteration in vessel diameter after the reduction in circulating intravascular volume produced by hemodialysis, which could lead to a decrease in MFV but not in CBF. However, if the CBF does not decrease, the MFV may increase after hemodialysis because the diameter of the vessel may be reduced by the decrease in the distensible force of the blood column. We therefore believe it is more likely that the reduction in CBF by hemodialysis decreased the MFV in the basal cerebral arteries.

Under normal physiological conditions the CBF is not affected by a moderate change in MABP, ie, between 50 and 130 mm Hg.\(^12,13\) This phenomenon has been called the autoregulation of CBF. In our study both the MABP and pulse rate before and after hemodialysis remained within the normal range (Table 2). Therefore, reductions in MFV during hemodialysis should not have been induced by a breakdown in autoregulation of CBF. We also checked other physiological variables that might influence the CBF and performed correlation analyses to evaluate the relation between changes in blood flow velocity and alterations in these variables.

Although the \(\text{PaCO}_2\) and \(\text{PaO}_2\) can profoundly influence the CBF,\(^14,15\) these variables did not change significantly during hemodialysis. Furthermore, there were no significant correlations between %MFV and changes in \(\text{PaCO}_2\) and \(\text{PaO}_2\). It therefore seems unlikely that the alteration in \(\text{PaCO}_2\) or \(\text{PaO}_2\) during hemodialysis lowered the MFV. The pH of blood rose significantly after hemodialysis because of the infusion of NaHCO\(_3\) given to ameliorate the metabolic acidosis caused by end-stage renal disease. The blood-brain barrier is impermeable to H\(^+\) and HCO\(_3^-\), and the pH of the cerebrospinal fluid is little affected by the increase in pH of the blood in patients receiving hemodialysis.\(^14\) Furthermore, CBF is unchanged during the alterations in blood pH induced by the infusion of either NaHCO\(_3\) or lactic acid when the \(\text{PaCO}_2\) is kept constant.\(^15\) We therefore speculate that a significant rise in pH of blood during hemodialysis would not affect the MFV.

Numerous investigators describe an inverse association between the hematocrit and CBF.\(^16-18\) Changes in hematocrit may cause two mechanisms: an alteration in blood viscosity, leading to changes in vascular resistance, and alteration in oxygen transport capacity, leading to metabolically mediated vasodilation or constriction so as to maintain oxygen delivery to the brain. Blood viscosity can greatly influence the CBF when the perfusion pressure and vessel caliber are constant.\(^19\) However, this variable may have little influence on CBF, in vivo, presumably owing to autoregulatory adaptations in the diameter of the microvessels.\(^20\) On the other hand, the oxygen transport capacity greatly influences the CBF under normal physiological conditions.\(^21,22\) The oxygen transport capacity increases as the hematocrit rises to approximately 30% to 40%,\(^23,24\) All patients in this study were examined before treatment with erythropoietin and were suffering from chronic renal failure. For these reasons, they were all anemic patients. The mean hematocrit before and after hemodialysis was below 30%; the value rose significantly after hemodialysis. We observed a significant inverse correlation between the change in blood hematocrit produced by hemodialysis and the %MFV. It therefore seems likely that as the hematocrit was increased by hemodialysis, the MFV fell because the oxygen transport capacity rose, so that less CBF was required for oxygen delivery. Recently a negative correlation was...
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(A) (B)

(C) (D)

(E) (F)

Demonstrated between hematocrit and velocity of blood flow in the middle cerebral artery. A negative correlation was also demonstrated between hematocrit and CBF in hemodialysis patients. Furthermore, Macko et al demonstrated that arterial oxygen content was inversely related to MFV in the middle cerebral artery. Although other possible mechanisms such as the reduction in metabolic level of the brain tissue cannot be excluded, these reports are in good agreement with ours.

In conclusion, we demonstrated a significant decrease in MFV from the basal cerebral arteries after hemodialysis and an inverse correlation between the %MFV and both the weight loss and the increase in hematocrit produced by hemodialysis. One of the most likely explanations is that, as the circulating intravascular volume is reduced by hemodialysis, the hematocrit and the relative oxygen transport capacity increase, leading to a decrease in MFV. The present results suggest that hemodialysis, which should be accompanied by a reduction in CBF, would be a potentially harmful procedure because of a high prevalence of vascular disorders (ie, ischemic heart disease and cerebrovascular accidents) in patients receiving maintenance hemodialysis.

Transcranial Doppler ultrasonography provides a rapid, noninvasive, and real-time method for assessing cerebral hemodynamics. Its reproducibility for repeated measurements in clinical studies of blood flow velocity from both the middle cerebral artery and the basilar artery is acceptable. We also demonstrated the practical utility of the TCD method for monitoring rapid changes in the cerebral circulation during procedures such as hemodialysis that may adversely influence cerebral hemodynamics in humans.

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References


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