Changes in Middle Cerebral Artery Blood Velocity in Uremic Patients After Hemodialysis

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Background and Purpose: Strokes are a frequent complication in uremic patients on dialysis. We wanted to evaluate the effect of this treatment on cerebral hemodynamic parameters, particularly those of patients with carotid stenosis, who are at higher risk for atherothrombotic ischemic events.

Methods: We used transcranial Doppler ultrasonography to evaluate blood velocity of the middle cerebral artery in 18 uremic patients before and after hemodialysis. Carotid stenosis was evaluated by echo-Doppler investigation. Six patients were also studied before and after recombinant human erythropoietin treatment.

Results: Dialysis treatment decreased mean blood velocity in all patients (p<0.001). Eight of 18 patients (44%) with mild (16–50%), moderate (51–80%), or severe (>80%) carotid stenosis had lower velocity than patients with normal carotid arteries (p<0.01), and they experienced a further decrease to even lower levels after hemodialysis (p<0.05). In patients treated with recombinant human erythropoietin, hematocrit increased from 28±8% to 37±5% (p<0.001), and blood velocity had a further decrease by 11%. All changes were associated with modifications toward normality of pH, PaCO₂, and hematocrit.

Conclusions: Transcranial Doppler ultrasonography represents a useful method for monitoring cerebral circulation of uremic patients, especially of those at possible risk for ischemia. (Stroke 1991;22:1508–1511)

Strokes are a frequent complication in uremic patients on dialysis and are commonly due to hypertensive encephalopathy or ischemic events secondary to diffuse arteriosclerosis. However, few studies have evaluated the cerebral circulation of and the effects of hemodialysis on these patients. Gottlieb et al. in 1985 showed that cerebral blood flow (CBF), as measured by the xenon-133 inhalation method, did not differ significantly before dialysis from that measured in age-matched normal controls. However, a significant decrease in CBF was observed after hemodialysis, which was attributed to changes in blood viscosity and biochemical parameters induced by treatment. In uremic patients, even small CBF differences can be dangerous, especially if the patient has a carotid stenosis. A decrease in tissue perfusion might be deleterious because these patients have a very low hematocrit and other risk factors that could worsen their hemodynamic conditions.

We evaluated changes in mean blood velocity of the middle cerebral artery (MCA) by transcranial Doppler ultrasonography (TCD) in uremic patients on chronic hemodialysis. Our study could prove useful in evaluating hemodynamic changes, particularly in patients with carotid stenosis, who are at risk for atherothrombotic ischemic events.

Subjects and Methods

We evaluated 18 uremic patients (11 men and 7 women, aged 22–68 [mean 50] years) on hemodialysis three times a week. Underlying diagnosis was chronic glomerulonephritis in 14 patients, diabetes mellitus in two, hypertensive nephropathy in one, and systemic lupus erythematosus in one other. None of the patients had symptoms or signs of cerebrovascular disease, such as transient ischemic attack or stroke, and all had discontinued any drug therapy on the morning of the dialysis.
Hemodialysis treatment was performed for 4 hours in each patient using a capillary filter with an effective surface area of 1 m² and a wall thickness of 8 µm. The dialysate flow was 500 ml/min, and blood flow was 280 ml/min. The dialytic equipment automatically prepared the following dialysate (meq/l): Na⁺ 139, K⁺ 2, Ca²⁺ 3.5, Mg²⁺ 1.5, Cl⁻ 108, acetate⁻ 38, and glucose 1 g/l. If hypotension occurred during the dialysis, it was treated by saline infusion, but never by hypertensive drugs.

We evaluated extracranial and intracranial arteries by echo-Doppler and TCD, respectively. Echo-Doppler examination of the carotid arteries was performed with a duplex scanner (ATL, USA) and included common carotid artery, bulb, and internal carotid artery. The diagnosis was based on the spectral analysis of the pulsed Doppler signal. With the subject in a supine position, we performed TCD before and within 60 minutes after the hemodialysis in a quiet room under constant environmental conditions at 22°C, using a 2-MHz pulsed-wave Doppler instrument (model SD100, Vingmed, Norway) with on-line spectrum analysis. The probe was placed over a temporal bone "window" to insonate MCA. Arterial tension of carbon dioxide (Paco₂) and pH were measured simultaneously of the degree of the stenosis. Before hemodialysis, P| in patients with both 16—50% and >50% carotid stenosis, in whom changes were similar independently of the degree of the stenosis. Before hemodialysis, P| in patients with both 16—50% and >50% carotid stenosis was lower than the MCA velocity below normal carotid arteries (44 versus 61 cm/sec, p<0.01). Mean MCA blood velocity decreased after hemodialysis in all patients (p<0.001). Mean MCA velocity reached the lowest values in patients with both 16—50% and >50% carotid stenosis, in whom changes were similar independently of the degree of the stenosis. Before hemodialysis, P| was significantly higher in the MCA below mild and moderate-to-severe carotid stenosis than below normal carotid artery. After hemodialysis, P| did not change in the MCA below patent carotid artery and

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before Hemodialysis</th>
<th>After Hemodialysis</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAM (mm Hg)</td>
<td>119±13</td>
<td>107±19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>pH</td>
<td>7.301±0.08</td>
<td>7.369±0.08</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PCO₂ (mm Hg)</td>
<td>36±1±3</td>
<td>32±2±3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>10.3±2</td>
<td>5.0±1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Urea (mg/dl)</td>
<td>177±38</td>
<td>65±19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>26±5</td>
<td>30±6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>64±9</td>
<td>61±9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum protein (g/dl)</td>
<td>6.7±0.5</td>
<td>7.8±0.7</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are mean±SD.
decreased below stenoses. Similar changes were also observed for $R_f$. Moreover, in four patients in whom one carotid artery was normal or had mild stenosis and the other a stenosis $>50\%$, mean blood velocity reduction in the MCA was $27\%$ on the nonstenotic side and $13\%$ on the stenotic side. In six patients investigated after human recombinant erythropoietin treatment, hematocrit levels increased after dialysis from $28\pm8\%$ (mean$\pm$SD) to $37\pm5\%$ ($p<0.001$). Middle cerebral artery blood velocity decreased (11%) after treatment to even lower levels both before and after hemodialysis (Table 3). Similar decreases measured for $P_f$ and $R_f$ were not statistically significant.

**Discussion**

In our study, we measured blood flow velocity by TCD within the MCA of uremic patients before and after hemodialysis and evaluated the changes according to carotid patency or stenosis.

The MCA blood velocity was normal, but was lower beyond the carotid stenosis. Hemodialysis caused a decrease in blood velocity in MCA in all patients and reached very low values in those with carotid stenosis. Blood velocity was very similar and presented comparable changes after dialysis in the MCA below mild (16–50%) and moderate-to-severe flow-reducing stenosis (>50%). Because changes in MCA velocity are correlated to changes in CBF, a decrease of CBF in all patients under investigation was highly conceivable. The increase in both $P_f$ and $R_f$ in the group of patients with carotid stenosis could have reflected a higher peripheral vascular resistance in the MCA territory or a decreased vascular compliance as the result of an increased prevalence of arteriolar atherosclerotic changes.

In uremic patients, brain oxygen delivery could be very similar to that in ischemic patients. Because they have severe anemia, the oxygen extraction rate probably could not be augmented, and hypotension occurring after hemodialysis could precipitate a low blood flow–induced transient ischemic attack, especially in those suffering from carotid stenosis. However, this might not be the case because, despite the probable decrease in MCA blood velocity and CBF after dialysis, sufficient brain oxygen delivery could be maintained by the hematocrit increase. In fact, high hematocrit leads to blood flow decrease but does not reduce tissue oxygen tension, as shown in the skeletal muscle even after human recombinant erythropoietin treatment. In our six patients treated with human recombinant erythropoietin as well, further hematocrit increase was associated with small reductions in MCA blood velocity. Human recombinant erythropoietin treatment of uremic patients increases not only hematocrit, but also blood pressure and peripheral resistance. These factors might increase the risk of atherothrombotic stroke in uremic patients, especially in those with diffuse atherosclerosis.

Changes in MCA velocity were lower on the stenotic side (13%) of the four patients with monolateral flow-reducing stenosis, whereas blood flow decreased by 27% on the side with non-flow-reducing carotid stenosis. These observations are in agreement with other studies, which show a lower CO$_2$ vasomotor reactivity on the stenotic side than on the contralateral normal side. Of course, the vasomotor reactivity reserve of these patients before and after hemodialysis should be tested by adequate investigation of factors such as CO$_2$ reactivity and hyperventilation.

Reduction in MCA blood flow velocity and, most likely, in CBF could be secondary to the metabolic changes that occur after hemodialysis, such as reduction in Pco$_2$, and increase in hematocrit concentrations. Changes in blood pressure could not be correlated to changes in blood velocity and do not seem to interfere with CBF reduction because cerebral autoregulation is normally maintained even with very low hematocrit levels and, in general, increases with Pco$_2$ reduction.

In conclusion, uremic patients on chronic hemodialysis have a high prevalence of carotid arteriosclerosis. Dialysis decreased MCA blood velocity in all patients, especially in those with carotid stenosis. Human recombinant erythropoietin treatment increased hematocrit levels, but slightly decreased MCA velocity. Transcranial Doppler ultrasonography represents a reliable and suitable method for monitoring the hemodynamic features of uremic patients under dialysis, especially those at risk for cerebral events induced by low blood flow. The results of TCD examination might indicate that some uremic patients need more intensive efforts, including drug therapy, to prevent acute cerebral ischemia.

**References**


KEY WORDS: cerebral ischemia • hemodialysis • ultrasonics • uremia