Cerebral haemodynamics in patients with chronic renal failure: effects of haemodialysis†

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Background. We measured middle cerebral artery (MCA) flow velocity (FV), dynamic pressure autoregulation, and carbon dioxide reactivity (CRCO2) in patients with chronic renal failure before and after haemodialysis using transcranial Doppler ultrasonography.

Methods. Twelve patients on long-term haemodialysis were recruited. MCA FV was measured continuously. The transient hyperaemic response test was used to assess cerebral autoregulation, and per cent change in FV per kPa change in end-tidal carbon dioxide was calculated to assess CRCO2. All measurements were recorded before and after haemodialysis.

Results. MCA FV (mean [SD]) decreased from 57 (10) cm s⁻¹ before to 46 (13) cm s⁻¹ after haemodialysis (P<0.01). The transient hyperaemic response ratio (THRR) was (mean [SD]) 1.29 (0.13) before haemodialysis and did not change significantly following haemodialysis (1.36 [0.10]). CRCO2 was 21.7 (8.3)% kPa⁻¹ before haemodialysis and remained unchanged afterwards (20.9 [3.8]% kPa⁻¹). Values in normal subjects for MCA FV, THRR and CRCO2 are 56 (12) cm s⁻¹, 1.26 (0.13) and 22 (6)% kPa⁻¹, respectively.

Conclusions. MCA FV decreases significantly after haemodialysis. Dynamic pressure autoregulation and CRCO2 remain normal in patients with chronic renal failure, and are not altered significantly by haemodialysis.


Keywords: brain, cerebral autoregulation; blood, cerebral blood flow; blood, haemodialysis; complications, chronic renal failure; carbon dioxide, reactivity; monitoring, transient hyperaemic response

Accepted for publication: September 21, 2004

Complications of chronic renal failure include autonomic neuropathy,1 and impaired sympathetic response to volume removal.2 The effects of chronic renal failure and/or haemodialysis on cerebral haemodynamics are not well documented in the literature. Some studies have shown that haemodialysis decreases cerebral blood flow.3 4 However, it is not clear whether the mechanisms involved in regulating cerebral blood flow (such as dynamic pressure autoregulation and carbon dioxide reactivity [CRCO2]) are also affected. This information is relevant when patients with renal failure undergo anaesthesia or when they are admitted to high-dependency/intensive care units. We aimed to investigate dynamic cerebral pressure autoregulation and CRCO2 in patients with chronic renal failure and to determine whether these variables were affected by haemodialysis.

Methods
Following Hospital Research Ethics Committee approval and written informed consent, 12 patients between 18 and 60 yr with chronic renal failure were recruited. These patients had been receiving maintenance haemodialysis for 6 months or more. Patients with cerebral disease or diabetes mellitus, which may cause autonomic neuropathy, were excluded. All patients had carotid artery sonography screening. Patients with carotid atheromatous disease were excluded from tests that involve pressure on the carotid arteries. Antihypertensive drug treatment was continued during the study and included alpha- and beta-adrenergic blockers, calcium antagonists and angiotensin converter enzyme inhibitors. Measurements were made with patients lying supine. Blood pressure was measured non-invasively with a cuff on the arm contralateral to the arteriovenous fistula.

The middle cerebral artery (MCA) was insonated via the temporal window using a 2-MHz transcranial Doppler...
ultrasound probe and previously described criteria.\textsuperscript{5} We secured the probe in place with a specially constructed head-band to maintain a constant angle of insonation throughout the study. The flow velocity (FV) trace was recorded continuously. The time-averaged mean of the outer envelope of the FV trace was taken for analysis.

The transient hyperaemic response (THR) test was used to assess dynamic cerebral pressure autoregulation.\textsuperscript{6,7} This test consists of compressing the common carotid artery ipsilateral to the insonated MCA for 10 s and then releasing it suddenly. If dynamic pressure autoregulation is intact, a hyperaemic response is typically seen at the release of common carotid artery compression. The test was accepted only if the following criteria were met:\textsuperscript{5} (i) a sudden and maximal decrease in FV at the onset of common carotid artery compression; (ii) stable heart rate for the period of the common carotid artery compression; (iii) steady Doppler signal during the duration of common carotid artery compression and; (iv) absence of flow transients following release of common carotid artery compression. The THR ratio (THR) was calculated as the ratio between the time-averaged mean of the FV waveform immediately after and the FV waveform before common carotid artery compression.

CRCO\textsubscript{2} was assessed by measuring the MCA FV while re-breathing expired carbon dioxide from a Water’s circuit, and during hyperventilation to achieve an \( F'\text{CO}_{2} \) of approximately 1 kPa above and 1 kPa below baseline, respectively. \( F'\text{CO}_{2} \) was measured with a capnograph as expired gas sampled from a mouthpiece. Each \( F'\text{CO}_{2} \) steady state was maintained for 10 s before recording FV. CRCO\textsubscript{2} was defined as the percentage change in FV per kPa change in end-tidal carbon dioxide.\textsuperscript{8} Immediately following the initial set of measurements, patients received their usual haemodialysis with bicarbonate buffer solution. Measurements were repeated on completion of dialysis. Arterial blood gases, urea and haemoglobin concentration were analysed with each set of measurements.

Paired t-tests were used to compare variables before and after dialysis (Minitab version 13). \( P<0.05 \) was considered significant. Power analysis indicated that 10 subjects would be required to detect a difference of 0.2 in the THR with a power of >0.85 and a \( P \)-value of <0.05: this was based on previous studies,\textsuperscript{7} and by taking a change of 1.5 in the SD to be significant. This change would also be similar to that induced by a 1 kPa change in carbon dioxide,\textsuperscript{7} which we thought would be clinically significant.

### Results

The underlying diseases in the patients studied were: glomerulonephritis in three patients; hypertension in three patients; systemic lupus erythematosus in two patients; haemolytic uraemic syndrome in one patient; renal vascular disease in one patient; and unknown in two patients. Patients had received haemodialysis for an average 76 (range 6–223) months. A satisfactory ultrasonographic record of MCA FV could not be established in one female patient. Because of the presence of carotid atheroma, two patients were excluded from THR tests. Thus, the results on changes in MCA FV and CRCO\textsubscript{2} were available on 11 patients (six males and five females), and that for THR on nine patients.

Patients had a mean (SD) age of 44 (10) (range 25–58) yr. Mean body weight was 71 (10) kg and 2.3 (1.3) litre of fluid were removed on haemodialysis. MCA FV was normal before haemodialysis; there was a significant decrease in MCA FV following haemodialysis but it remained within the normal range (Table I). Mean arterial pressure was 98 mm Hg before haemodialysis and remained unaffected by it. The THR and CRCO\textsubscript{2} were normal before haemodialysis and were not significantly altered following haemodialysis. The mean (SD) resting end-tidal carbon dioxide increased from 4.5 (0.6) kPa before haemodialysis to 4.8 (0.4) kPa afterwards (Table I, \( P<0.05 \)). Urea concentrations were significantly reduced and the haemoglobin blood pH increased after haemodialysis (Table II).

### Discussion

Our results indicate that in patients with chronic renal failure, MCA FV, dynamic pressure autoregulation and CRCO\textsubscript{2} remain within the range described for healthy subjects.\textsuperscript{6–9} In addition, we have shown that haemodialysis results in a significant decrease in MCA FV (Table I), but no significant changes in dynamic pressure autoregulation or CRCO\textsubscript{2}. However, despite the decrease in MCA FV after haemodialysis, it remained within the normal range of 56 (12) cm s\textsuperscript{-1}.\textsuperscript{7}

A decrease in MCA FV following haemodialysis has also been shown in a previous study.\textsuperscript{3} The most likely

### Table 1

<table>
<thead>
<tr>
<th>Pre-dialysis</th>
<th>Post-dialysis</th>
<th>( P )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP (mm Hg)</td>
<td>98 (16)</td>
<td>99 (17)</td>
</tr>
<tr>
<td>MCA FV (cm s\textsuperscript{-1})</td>
<td>57 (10)</td>
<td>46 (13)</td>
</tr>
<tr>
<td>THR</td>
<td>1.29 (0.13)</td>
<td>1.36 (0.10)</td>
</tr>
<tr>
<td>( F'\text{CO}_{2} ) (kPa)</td>
<td>4.5 (0.6)</td>
<td>4.8 (0.4)</td>
</tr>
<tr>
<td>CRCO\textsubscript{2} (% kPa\textsuperscript{-1})</td>
<td>21.7 (8.3)</td>
<td>20.9 (3.8)</td>
</tr>
</tbody>
</table>

### Table 2

<table>
<thead>
<tr>
<th>Pre-dialysis</th>
<th>Post-dialysis</th>
<th>( P )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (g dl\textsuperscript{-1})</td>
<td>11.7 (0.9)</td>
<td>13.1 (1.8)</td>
</tr>
<tr>
<td>( Pa_{\text{CO}_{2}} ) (kPa)</td>
<td>4.7 (0.7)</td>
<td>5.1 (0.6)</td>
</tr>
<tr>
<td>pH</td>
<td>7.35 (0.05)</td>
<td>7.41 (0.05)</td>
</tr>
<tr>
<td>Urea (mmol litre\textsuperscript{-1})</td>
<td>23.9 (7.4)</td>
<td>8.7 (1.6)</td>
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exploration for this decrease is a reduction in cerebral blood flow. Gotlieb and colleagues confirmed a reduction in cerebral blood flow after dialysis. Cerebral blood flow may be altered by many factors including blood pH, arterial carbon dioxide, haematocrit, urea, mean arterial pressure, stroke volume and cardiac output. Mean arterial pressure was not affected post-haemodialysis in our study, but Gadegbeku and colleagues reported a decrease in stroke volume and cardiac output of around 20% after haemodialysis, even though blood pressure remained unchanged. Arterial and end-tidal carbon dioxide were slightly increased after dialysis (Table 1), which probably represented respiratory compensation as a result of relative alkalinization of blood. Arterio-venous shunting of blood during haemodialysis could also have contributed. The reduction in MCA FV after dialysis could also have been as a result of the increase in blood viscosity with an associated increase in oxygen carrying capacity, and the clearance of acids and urea, as suggested by previous workers.

Davenport and colleagues found a close relationship between mean arterial pressure and intracranial pressure in patients with acute haemoteral failure and concluded that cerebral pressure autoregulation was impaired. Auto-nomic nerve dysfunction is a common problem in patients with chronic renal failure, and an impaired sympathetic response to volume removal has been demonstrated. So far, cerebral vascular reactivity (dynamic pressure autoregulation or CRCO2) has not been reported in patients with chronic renal failure. The THR test for dynamic pressure autoregulation and CRCO2 have been validated as markers of cerebral vascular reactivity. The THR was 1.29 before dialysis in this study (Table 1). In previous studies, healthy volunteers had mean THR values of 1.26 (0.13) and 1.20 (95% confidence limits 1.17 and 1.24), respectively. After haemodialysis, there was a trend towards an increase in the THR (Table 1); post-hoc power analysis suggests that the small increase in THR (1.29–1.36) could reach statistical significance on recruiting 30 patients to the study. However, we would not regard this increase as clinically significant. Moreover, all our patients had a THR, before and after haemodialysis, within the normal range: in particular, none of them had a THR that would indicate impaired dynamic pressure autoregulation (i.e. <1.09).

In normal subjects, on average, MCA FV could be expected to change by 22% with each kPa change in $F_eCO_2$. The mean change in our patients was 21.7% before and 20.9% after dialysis, indicating normal reactivity. Kuwabara and co-workers found a decrease in CRCO2 in anaemic patients with chronic renal failure. The mean haemoglobin concentration in their patients was only 8.6 g dl−1. Cerebral resistance vessels would therefore be more likely dilated, and a reduced response to carbon dioxide could be expected. Since the introduction of erythropoietin, renal patients are now seldom this anaemic.

The presence of altered cerebral vascular reactivity would have implications for cerebral perfusion during anaesthesia and intensive care. Patients with chronic renal failure present for surgery that can be related or unrelated to their renal failure. Furthermore, these patients often undergo haemodialysis before surgery. Our results are reassuring that cerebral vascular reactivity remains intact in these patients. However, we studied patients with chronic renal failure who had stable, controlled blood pressure and had no history of neurological disease. Therefore, it is not possible to extrapolate our findings to patients with acute renal failure, to those who are haemodynamically unstable, or those with neurological pathology.

We conclude that dynamic pressure autoregulation and CRCO2 remain intact in patients with chronic renal failure. Haemodialysis decreases MCA FV significantly, but is not associated with significant changes in either dynamic pressure autoregulation or CRCO2.

References