Blood Pressure Response to Hemodialysis

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SUMMARY Blood pressure response to hemodialysis was investigated in 15 patients with end-stage kidney disease; mean arterial pressure was unchanged in five (Group 1) and reduced 10 mm Hg in ten (Group 2). The two groups did not differ significantly with regard to either biochemical values or hemodynamic indices before dialysis, and both sustained comparable reduction in body weight, total blood volume, and cardiac output following dialysis. Heart rate remained unchanged in both. The only significant difference between the two was the response of total peripheral resistance (TPR) to fluid depletion. TPR rose adequately in Group 1 but was unchanged in Group 2 (7.5 ± 2.2 (SE) vs 0.7 ± 1.1 units, p < 0.025) despite equal fall in cardiac output in both (881 ± 212 vs 890 ± 173 ml/m, p > 0.10). Thus, differences in arterial pressure response to fluid loss by hemodialysis could be due to impaired autonomic control of resistance vessels; this abnormality might not be revealed by tests of baroreceptor activity that depend only on heart rate responses to blood pressure variations. (Hypertension 3: 333-339, 1981)

KEY WORDS  * hemodialysis • renal disease, end-stage • kidney • total peripheral resistance • blood pressure variations • hypotension • cardiac output • extracellular fluid volume

UREMIC patients frequently present difficulties in management during hemodialysis, particularly because of severe hypotension in some patients. This has been related either to the magnitude of fluid loss or to the autonomic neuropathy that has been reported in renal insufficiency.1-3 Most studies of that problem have been based on clinical observations and body weight variations; in some, cardiac output has also been determined before and after dialysis. Few investigators, however, have attempted to determine all variables in the same patient to allow more precise analysis, such as the correlation of reduction in blood volume to alterations in cardiac output or the comparison of blood pressure responses among patients with equivalent degrees of fall in output. Further, investigations of baroreceptor sensitivity have been based on the method of Bristow et al.,4 which depends solely on heart response to blood pressure variations. Zanchetti et al.5-6 however, have shown that not all physiological responses to baroreceptor stimulation can be predicated from reflex slowing of heart rate. Conclusions based on heart rate responses alone, therefore, might not apply to reflex modifications of arterial pressure and peripheral resistance in response to fluid loss.

This study was undertaken to determine whether hypotension developing with dialysis was related to the degree of cardiac output reduction or whether it represented an abnormal response of peripheral resistance to the expected reduction of extracellular fluid volume and cardiac output by dialysis.7-8 All attempts were made to ensure equivalent degrees of weight loss with hemodialysis differences among them.

Methods

Patient Population

The study was performed on 15 patients with chronic renal failure who were treated with repetitive maintenance hemodialysis. Care was taken to study only patients without history, clinical or radiological signs of cardiac decompensation or coronary artery disease; also not accepted were patients with markedly increased left ventricular volume (end diastolic diameter > 6.0 cm).
Apart from these requirements, the only criterion for actual enrollment in the study was the possibility of obtaining repeated clear echocardiograms of excellent quality. Of 48 patients who were asked and freely consented to participate, only 15 patients were accepted under this technical requirement.

Blood pressure response to hemodialysis was the basis for classification of patients in two groups: Group 1 included patients whose mean arterial pressure (MAP) was essentially the same (± 10 mm Hg) after dialysis as before. Group 2 included those whose MAP dropped by more than 10 mm Hg following hemodialysis. The choice of that dividing line was based on previous hemodynamic studies of hypertensive patients with upright tilt. Four patients were investigated twice under different conditions of predialysis body weight; none changed groups during the repeat study. Two whose arterial pressure remained stable after the first dialysis behaved similarly after the second, and two who developed hypotension (Group 2) the first time developed it the second time.

Technical Procedures

Cardiac Output

The echocardiogram (Echoview system 80-Picker) was used to determine cardiac output. All patients were examined after at least half an hour of rest, and tracings were obtained either in the supine or in semi-left lateral position. A perfect picture of both septum and posterior wall endocardium was required; left ventricular internal dimensions (left ventricular minor axis) were measured at a plane just below the tip of the mitral leaflets. Pictures and electrocardiogram (Lead 2) were recorded first at a paper speed of 25 and 50 mm/sec, and then a phonocardiogram and carotid pulse tracing were added and the three tracings recorded simultaneously at a paper speed of 100 mm/sec.

The left ventricular end-diastolic diameter (EDD) was measured at the peak of the R wave of the electrocardiogram; the left ventricular end-systolic diameter (ESD) was measured at the onset of the second sound. Ten beats were measured by two independent observers, and the average of these values was used. The left ventricular end-diastolic (EDV) and end-systolic (ESV) volume were calculated by the D3 formula; and stroke volume by subtraction (SV = EDV – ESV). Heart rate (HR) was measured from the electrocardiogram, and cardiac output (CO) calculated as the product of stroke volume times heart rate; values were normalized for body surface area (BSA) to give the cardiac index (CI).

Dynamic measurements of the left ventricle by echocardiography have been evaluated in many studies: a good correlation was repeatedly reported between stroke volume derived from echocardiography and that determined by dye dilution, Fick method, or angiography. provided that there was no left ventricular asynergy. As noted by Linhart et al., echocardiography was particularly accurate when used for follow-up of cardiac changes over a relatively short period of time, with the patients being their own controls. Further, patients with markedly enlarged left ventricular end-diastolic diameter (EDD > 6 mm) were not enrolled in the study to avoid inaccuracies in calculating ventricular volume in these cases.

Volume Determinations

Before hemodialysis, plasma volume (PV) was measured after a half-hour of rest supine, using human serum albumin (RISA) and a 10-minute equilibration period. Total blood volume (TBV) was calculated from plasma volume and simultaneously determined hematocrit (mean value of four different samples — microhematocrit method), with appropriate correction factors for the difference between total body and large vessel hematocrit. After dialysis, changes in plasma volume were calculated from the volume determined before dialysis and the post-dialysis hematocrit values, assuming that there was only minimal loss of red cell mass during the procedure.

Alterations in extracellular fluid (ECF) were estimated from the change in body weight associated with the procedure; the decrease in weight was shown by de Planque et al. and Omvik et al. to be due to ECF loss in short-term dialysis studies.

Biochemical variables were assessed using the following determinations before and after hemodialysis: BUN, serum creatinine, electrolytes, calcium, and phosphorus.

Blood pressure was determined by auscultation with the patient at rest in the supine position; recorded were the systolic blood pressure at phase I of Korotkoff sounds, and the diastolic at their disappearance (phase V). Values reported represent the average of two separate readings.

Study Protocol

All patients were studied in a quiet room on an outpatient basis and under exactly the same conditions before and after dialysis. After they had rested supine at least 30 minutes, plasma volume, hematocrit, and other blood tests were obtained as well as the echocardiogram. The same procedure was repeated on that same day, after a 5-hour hemodialysis. All forms of medications (usually alphamethyldopa, hydralazine, or propranolol) were discontinued 1 week before the study; no patient received blood transfusion, colloid infusion, or saline solution during the procedure except for 300 ml of isotonic saline solution used to prime the extracorporeal circulation of the artificial kidney. Hemodialysis was performed for 5 hours using a Travenol CF 1500 instrument with the following standard dialysate concentrations: Na+ = 135 mEq/liter; Cl− = 99 mEq/liter; K+ = 2 mEq/liter; Mg++ = 1.5 mEq/liter; glucose = 2000 mg/liter; acetate = 38 mEq/liter; and Ca = 3.5 mEq/liter. The flow rate was maintained at 500 ml/min and the transmembrane pressure between 200 to 250 mm Hg, with blood flow...
rate kept between 200 to 225 ml/min during the whole procedure.

Values obtained were expressed as average ± one standard deviation. Statistical significance of differences was calculated by standard methods.21

**Results**

Patients in both groups were found to be similar with respect to age, sex, race, and blood pressure level before hemodialysis (table 1); their renal disease was of varied etiology, but there was no obvious difference in that regard between two groups. However, the mean duration of chronic hemodialysis was significantly different, averaging 13.0 ± 9.7 months in Group 1 and 38.6 ± 33.4 months in Group 2 (p < 0.05), and there was a wide range of values in both groups. The biochemical variables determined before dialysis were not statistically different between the two groups (table 2). With regard to hemodynamic variables, total blood volume, cardiac index, total peripheral resistance, and mean arterial pressure before dialysis appeared somewhat higher in Group 2, but none of these differences from Group 1 were statistically significant (table 3).

### TABLE 1. **Clinical Data on Hemodialysis Patients Studied**

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Race</th>
<th>Diagnosis</th>
<th>BP before dialysis (mm Hg)</th>
<th>Duration dialysis (mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>49</td>
<td>F</td>
<td>O</td>
<td>GN</td>
<td>158/90</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>38</td>
<td>M</td>
<td>B</td>
<td>Nphscl</td>
<td>172/84</td>
<td>12</td>
</tr>
<tr>
<td>3</td>
<td>69</td>
<td>M</td>
<td>W</td>
<td>Undeter</td>
<td>174/74</td>
<td>7</td>
</tr>
<tr>
<td>4</td>
<td>65</td>
<td>F</td>
<td>W</td>
<td>GN</td>
<td>148/70</td>
<td>30</td>
</tr>
<tr>
<td>5</td>
<td>29</td>
<td>M</td>
<td>W</td>
<td>ChPyelo</td>
<td>165/105</td>
<td>11</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>163/85</td>
<td>13</td>
</tr>
<tr>
<td>(17.1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(11/14)</td>
<td>(9.7)</td>
</tr>
<tr>
<td>Group 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>23</td>
<td>M</td>
<td>W</td>
<td>Nphscl</td>
<td>210/142</td>
<td>10</td>
</tr>
<tr>
<td>7</td>
<td>62</td>
<td>M</td>
<td>B</td>
<td>GN</td>
<td>224/104</td>
<td>22</td>
</tr>
<tr>
<td>8</td>
<td>60</td>
<td>M</td>
<td>B</td>
<td>Nphscl</td>
<td>200/80</td>
<td>28</td>
</tr>
<tr>
<td>9</td>
<td>68</td>
<td>F</td>
<td>W</td>
<td>Undeter</td>
<td>190/94</td>
<td>10</td>
</tr>
<tr>
<td>10</td>
<td>57</td>
<td>F</td>
<td>B</td>
<td>GN</td>
<td>179/88</td>
<td>48</td>
</tr>
<tr>
<td>11</td>
<td>59</td>
<td>M</td>
<td>B</td>
<td>GN</td>
<td>202/77</td>
<td>34</td>
</tr>
<tr>
<td>12</td>
<td>56</td>
<td>F</td>
<td>W</td>
<td>Polycyst</td>
<td>174/93</td>
<td>44</td>
</tr>
<tr>
<td>13</td>
<td>52</td>
<td>F</td>
<td>W</td>
<td>GN</td>
<td>221/89</td>
<td>108</td>
</tr>
<tr>
<td>14</td>
<td>28</td>
<td>M</td>
<td>W</td>
<td>ChPyelo</td>
<td>145/80</td>
<td>80</td>
</tr>
<tr>
<td>15</td>
<td>21</td>
<td>M</td>
<td>W</td>
<td>HydNeph</td>
<td>158/96</td>
<td>2</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>190/94</td>
<td>38.6</td>
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<tr>
<td>(17.6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(27/19)</td>
<td>(33.4)</td>
</tr>
</tbody>
</table>

**Abbreviations**: O = Oriental; B = Black; W = White; GN = glomerulonephritis; Nphscl = nephrosclerosis; Undeter = undetermined; ChPyelo = chronic pyelonephritis; Polycyst = polycystic kidney disease; and HydNeph = hydronephrosis.

### TABLE 2. **Biochemical Data on Hemodialysis Patients Studied**

<table>
<thead>
<tr>
<th>Biochemical test</th>
<th>Before</th>
<th>After</th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN (mg%)</td>
<td>105</td>
<td>58.8</td>
<td>90.5</td>
<td>46.7</td>
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<tr>
<td>Serum creatinine (mg%)</td>
<td>18.3</td>
<td>12.2</td>
<td>14.3</td>
<td>8.9</td>
</tr>
<tr>
<td>Serum sodium (mEq/liter)</td>
<td>142</td>
<td>138</td>
<td>136.5</td>
<td>136</td>
</tr>
<tr>
<td>Serum potassium (mEq/liter)</td>
<td>5.3</td>
<td>4.1</td>
<td>5.9</td>
<td>4.3</td>
</tr>
<tr>
<td>Serum bicarbonate (mEq/liter)</td>
<td>21.3</td>
<td>24.0</td>
<td>20.4</td>
<td>22.9</td>
</tr>
<tr>
<td>Serum chloride (mEq/liter)</td>
<td>103</td>
<td>99.8</td>
<td>99.0</td>
<td>97.9</td>
</tr>
<tr>
<td>Serum calcium (mg%)</td>
<td>9.2</td>
<td>11.7</td>
<td>9.5</td>
<td>11.2</td>
</tr>
</tbody>
</table>

**Before** = before hemodialysis; **after** = after hemodialysis. None of the differences between the two groups was significant.
Changes induced by hemodialysis are summarized in Table 4. Extracellular fluid loss was not significantly different between the two groups, 1857 ± 346 ml in Group 1 vs 2225 ± 628 ml in Group 2; p < 0.10. Similarly, none of the differences in volume or systemic flow was significant at the 0.05 confidence level: TBV decreased by 387 ± 181 ml in Group 1 vs 483 ± 370 ml in Group 2; and the cardiac index fell by 881 ± 189 ml/min/m² in Group 1 and by 890 ± 173 ml/min/m² in Group 2. In contrast, change in total peripheral resistance (TPR) was significantly (p < 0.025) different between the two groups; TPR increased by 7.5 ± 2.23 units in patients with stable blood pressure while it barely changed in Group 2 (+0.7 ± 1.2 units) despite the 0.9 liter/m fall in cardiac index. The change in mean arterial pressure (ΔMAP) was correlated with the change in peripheral resistance (y = 1.06 (ΔTPR) — 18.51, r = 0.511; fig. 1); no significant correlation was found between ΔMAP and changes in cardiac index (r = 0.118).

Heart rate did not change significantly in either group, although mean arterial pressure fell by more than 10 mm Hg in the second group (from 129 to 106 mm Hg) (table 3).

### Discussion

Severe hypotension during hemodialysis can occur in some patients despite careful attention to fluid balance. As the fall in blood pressure is usually controlled by infusion of saline or colloid solutions, the initial hypothesis naturally related hypotension to hypovolemia. Kim et al. reported that patients who became hypotensive during dialysis started with a 14% lower blood volume than others who maintained a stable arterial pressure; this was confirmed in a small group of patients by Lilley et al. Although initial hypovolemia might be a factor in some patients, it is obviously not the only one. In the studies reported, values for total blood volume overlapped markedly among individual patients; in our study, predialysis total blood volume was not statistically different between those who developed hypotension following hemodialysis and those with stable blood pressure (table 3). If anything, it tended, in fact, to be larger in the patients who developed hypotension. Moreover, the hemodynamic variable directly related to arterial pressure is cardiac output, which was significantly reduced by dialysis in both groups of patients.
HYPOTENSION AND HEMODIALYSIS/Chaignon et al.

Figure 1. Hemodynamic changes following hemodialysis. Change in mean arterial pressure (ΔMAP) correlated significantly (y = 1.06x - 18.51, r = 0.511, p < 0.02) with changes in total peripheral resistance (ΔTPR, Graph A) but not with changes in cardiac index (ΔCl, Graph B) (r = 0.118).

Reduction was probably related to the volume loss, but that relationship is not a simple one, since it could be influenced by a number of variables including, among others, rapidity of volume change, level of cardiac performance, and redistribution of intravascular volume. Cardiac performance was not found either by ourselves or by others to be significantly altered by hemodialysis, while hypovolemia could be compensated for by vasoconstriction. In the final analysis, arterial pressure following dialysis will depend on both the net effect of fluid depletion on cardiac output and the response of peripheral resistance vessels to the fall in output.

For a precise evaluation of factors involved in post-dialysis hypotension, a step-by-step analysis is therefore needed of those factors linking volume variations to changes in blood pressure. This analysis must depend on actual determination of the variables involved (blood volume, cardiac filling, cardiac output, and arterial pressure) because of the errors inherent in extrapolating from one index to another. Thus, blood volume contraction does not necessarily lead to similar changes in cardiac output, and peripheral pooling of blood can play a more important role in determining venous return than the absolute amount of plasma volume lost. In our patients, both blood volume and cardiac output fell equally in those with post-hemodialysis hypotension and in those with stable arterial pressure (table 4). This naturally means that the difference between the two groups was related to an altered response of peripheral resistance. These results are in accordance with invasive hemodynamic studies of hypotension during hemodialysis. The hemodynamic responses to ultrafiltration differ from those following dialysis, however, the difference in techniques could not explain the differences between our two groups of patients since both had exactly the same procedure (conventional hemodialysis with combined ultrafiltration) with similar duration of dialysis and degree of ultrafiltration.

Autonomic nervous dysfunction has often been postulated as an important complication of uremia; but its testing was limited to such indirect tests as Valsalva maneuver, baroreceptor sensitivity, and reflex sweating. However, this dysfunction seemed common among uremic patients and was not apparently related to hypotension because many of these patients with dysfunction did not have a blood pressure decrease following dialysis. This conclusion is open to question because of the tests used; for this particular question they can only supply "indirect" information. Conclusions regarding autonomic dysfunction in the case of arterial pressure response to dialysis are based on a study of vascular responses to an equivalent stimulus (reduction in output). In this study, the two groups of patients had equal weight loss following hemodialysis as well as equivalent hypovolemia and similar fall in cardiac index (table 4). This brought out more clearly the basic difference between the two, namely, the response of calculated peripheral vascular resistance to fluid depletion. The results implied some abnormality at one or several points along the reflex arcs originating from either the high or low pressure-sensitive areas.

Compared to other tests of baroreceptor function, TPR response to fall in venous return seems the more direct index to assess autonomic capacity to maintain a stable arterial pressure in response to hemodialysis. Its use disclosed an abnormality that would have been undetected if the study had been restricted to heart rate response to fluid depletion or blood pressure drop. The lack of change in heart rate in both patient groups
raises important questions. In both groups, those with and without effective blood pressure control after dialysis, heart rate did not change significantly; this observation confirms previous studies that described a fixed heart rate in spite of blood pressure variations in patients with end-stage renal disease and led to the suggestion of depressed baroreceptor reflexes. However, this component of the reflex did not allow, either in our study or that of Lazarus et al., the differentiation of patients with stable arterial pressure from those with hypertension following dialysis. In contrast, the component based on TPR response clearly differentiated between the two, indicating that tests based on heart rate alone do not describe the whole spectrum of autonomic dysfunction.

Dissociation between heart rate and peripheral resistance responses to baroreceptor stimulation has been reported in other conditions. A reason for that dissociation is sometimes evident, as the partial sparing of cardiac nerves in early stages of idiopathic orthostatic hypotension, but it can also defy current interpretations. In patients with end-stage renal disease, some factors could be responsible for the relative unresponsiveness of heart rate to fluid loss. Diminished sensitivity to atropine has been reported in uremic patients; the anemia and metabolism disturbances in uremia could blunt the range of heart rate response to blood pressure variations. However, final explanations for different responses of different segments of the cardiovascular system must await the elucidation of all possible pathways involved in reflex control of arterial pressure. Recent studies have stressed the role of cardiopulmonary receptors in control of arterial pressure. Changes in biochemical data was significant difference in clinical, hemodynamic, or biochemical aspects before dialysis between the two groups (table 2). However, the chronicity of hemodialysis was longer in the second group; whether that is involved in the incidences of autonomic nervous dysfunction remains purely speculative.

In summary, altered reactivity of peripheral resistance to a fall in cardiac output appeared an important cause of postdialysis hypotension. This abnormality could not be identified by baroreceptor tests based on heart rate alone. This is not to say that hypotension following hemodialysis cannot in some instances be due to excessive fluid loss or to cardiac depression by reduced preload; the results indicate that, even when these factors are controlled, hypotension can develop. The reduction in blood pressure is then due to diminished compensatory vasoconstriction, which had no relation in this group of patients to their heart rate response to fluid loss. The lack of resistance response could also be due to diminished responsiveness of the vessels because of alterations in calcium, angiotensin, or other humoral factors. Obvolously, studies dissecting the various components of the efferent limb are needed to localize the disturbance either in the neural limb or in the vascular end organ.

The practical implication of this study is that some patients on hemodialysis cannot accommodate the reduction in cardiac output induced by this procedure, and hence suffer an excessive fall in blood pressure. This can be avoided by reducing the fall in output either by avoiding excessive fluid removal (which is not always possible) or by combining hemofiltration with hemodialysis. Fluid removal by the latter procedure induces venoconstriction and central relocation of blood volume, which help mitigate the effect of hypovolemia on cardiac output.

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