PART III

DIALYSIS: Haemodiafiltration

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TREATMENT OF SEVERE HYPERTENSION IN CHRONIC RENAL FAILURE BY HAEMOFILTRATION

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Summary

Thirteen patients with chronic renal insufficiency who had been transferred from haemodialysis to haemofiltration treatment because of dialysis and drug resistant hypertension (10 with high plasma renin activity) showed normalisation of blood pressure during a treatment period of 8 months, after which only one patient required antihypertensive drug therapy. During the first period blood pressure drop paralleled body weight loss and after 3–4 weeks blood pressure remained normal in spite of an increase in body weight. In the course of the second phase the effect of fluid withdrawal on blood pressure was directly proportional to the blood pressure at the beginning of the procedure. Adaptation of baroreceptor function must be assumed. In contrast to haemodialysis, haemofiltration did not influence the inulin space. Because of the reduced removal of small molecular substances compared with haemodialysis, extracellular osmolarity was kept stable during haemofiltration. Withdrawal of even large amounts of fluid was sustained without collapse reactions or signs of orthostatic dysregulation.

Introduction

In contrast to haemodialysis or peritoneal dialysis, water and electrolyte removal is achieved in haemofiltration by a filtration process in the course of which solutes are excreted by means of convective transport, a process similar to that used by the natural kidney to eliminate metabolic waste products. Besides favourable effects on calcium, phosphate and lipid metabolism which have been discussed elsewhere\(^1\) this new method permits exact control of ultrafiltration. Moreover, both body sodium content and extracellular volume can be independently influenced in a predictable manner. Soon after haemofiltration (diafiltration, haemodiafiltration) had been introduced into the clinical treatment of chronic renal failure (CRI) the question arose as to whether treatment of severe hypertension could be improved by the better control of sodium and water balance. Indeed, favourable effects on blood pressure regulation in hypertension
could be shown in the first patient treated by haemofiltration for CRF. A larger number of patients have now been introduced into the haemofiltration programme and this has allowed evaluation of the haemodynamic effects of haemofiltration.

**Patients and Methods**

Since 1974, 15 patients have been treated on a regular haemofiltration programme (Table I). Eight patients were suffering from chronic glomerulonephritis, 4 from chronic pyelonephritis, 2 from diabetic nephropathy and one from polyanarteritis nodosa. Fourteen patients had been previously treated by haemodialysis, generally after an initial period of peritoneal dialysis treatment. During 172 patient months, 2,408 haemofiltration procedures were performed. With the exception of one patient who was suffering from polyanarteritis nodosa, residual glomerular filtration, calculated according to Babb et al.3, was in the range of 2 to 5 ml/min.

Severe hypertension was the cause of the transfer from haemodialysis to haemofiltration treatment in 13 patients. In 10 of these very high plasma renin levels were recorded during the haemodialysis period (pre-dialysis supine 48 ± 12 ng/ml/h, post-dialysis 92 ± 22 ng/ml/h), the mean pre-dialysis plasma sodium concentration being 132 ± 3.5 mEq/L. The haemofiltration system previously described4 was used, applying ‘post-dilution’ (ie replacement of the filtrate after the filter). The composition of the substitution fluid was: Na⁺ 138 mEq/L, K⁺ 2.0 mEq/L, Ca²⁺ 3.75 mEq/L, Mg²⁺ 1.5 mEq/L, Cl⁻ 111.5 mEq/L, lactate 33.75 mEq/L. In 20 haemofiltration procedures lactate was replaced by acetate.

Patients were treated three times weekly for 4–5 hours each, exchanging about 20 L of body fluid during one procedure. In 6 haemodialyses and 6

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**TABLE I. Diagnosis, Previous Treatment, Duration of Haemofiltration Treatment, Mean Body Weight and Mean Food Intake in 15 Patients on a Regular Haemofiltration Programme**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of patients</th>
<th>Pre-treatment (Months X)</th>
<th>Procedures</th>
<th>Haemofiltration</th>
<th>Residual Renal Function Pre (ml/min)</th>
<th>Post (ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chr.GN</td>
<td>8</td>
<td>26.5 HD 3.8 PD</td>
<td>1,288</td>
<td>92(1-27)</td>
<td>3.7 ± 0.09</td>
<td>2.9 ± 0.41</td>
</tr>
<tr>
<td>Chr.PN</td>
<td>4</td>
<td>12.4 HD – PD</td>
<td>644</td>
<td>46(4-26)</td>
<td>2.9 ± 0.15</td>
<td>2.1 ± 0.11</td>
</tr>
<tr>
<td>Diabetic N</td>
<td>2</td>
<td>8.6 HD 7.9 PD</td>
<td>196</td>
<td>14(6-8)</td>
<td>4.9 ± 0.27</td>
<td>3.9 ± 1.54</td>
</tr>
<tr>
<td>Panart.Nod.</td>
<td>1</td>
<td>– HD 18.5 PD</td>
<td>280</td>
<td>20</td>
<td>8.1</td>
<td>2.1</td>
</tr>
<tr>
<td>15 patients</td>
<td></td>
<td>2,408 procedures</td>
<td>172 patients months</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mean Body Weight: 68.5 ± 6.43 kg

Diet
Protein 104 ± 22.8 g/die
Calcium 1.4 ± 0.85 g/die
Phosphorus 1.54 ± 0.97 g/die

NaCl 8.9 ± 3.34 g/die

3,373 ± 729 Cal/die
Results

Regardless of the plasma renin activity at the beginning of the treatment, blood pressure was normalised in 6 patients within 3 months, and in 11 patients within 5 months of the start of haemofiltration treatment. After a treatment period of 8 months, blood pressure had been normalised in all patients except one, who needed antihypertensive therapy. At that time plasma renin activity was only slightly increased (pre-treatment supine 8.4 ± 5.3, post-treatment 12.5 ± 8.16 ng/ml/h). In the patients showing a normalisation of blood pressure within three months, mean arterial blood pressure paralleled the fall in body weight during the first three week period. The blood pressure then remained in the normal range in spite of an increase in body weight.

In 1000 haemofiltration and 1000 haemodialysis procedures we have tried to correlate body weight loss per treatment and the decrease of systolic blood pressure, with the systolic blood pressure at the beginning of the procedure. The regression slopes calculated for the groups of different pre-treatment blood pressure are shown in Figure 1. For haemofiltration it was found that the higher the pre-treatment blood pressure, the more it could be influenced by a given body fluid withdrawal. For haemodialysis the correlation was not so close.

In the course of a single haemofiltration large amounts of fluid could be removed and blood pressure could be normalised without any collapse reaction, regardless of the use of lactate or acetate as buffer in the substitution fluid. In contrast to haemodialysis, pulse rate rose only slightly and orthostatic collapse reactions after the end of the treatment were not observed.

Figure 2 shows the changes of inulin space, body weight and mean arterial blood pressure in the course of a single haemofiltration compared with haemodialysis. In spite of a significant drop in body weight and a decrease in blood pressure, the inulin space shows only insignificant changes during haemofiltration and for a period of 18 hours after its termination. In haemodialysis, however, inulin space is reduced significantly in spite of a smaller decrease in body weight. With the exception of the buffers lactate and acetate the electrolyte content of the substitution fluid and dialysate did not differ. In spite of this, a decrease of plasma osmolarity during haemodialysis could be observed whereas plasma osmolarity remained stable during haemofiltration (Figure 3).

Discussion

Severe hypertension due to CRI was brought down to normal in 12 out of 13 patients who had been selected for this treatment because of drug and dialysis resistant high blood pressure. This effect, also described by Henderson and co-workers\(^6\), was not influenced by the plasma renin activity at the start of the
Figure 1. Decrease of systolic blood pressure (Δ BP syst) in relation to the decrease of body weight and pre-treatment blood pressure during a haemofiltration or haemodialysis procedure (n = 1000 haemofiltration and 1000 haemodialysis procedures)
Figure 2. Inulin space, body weight and mean arterial blood pressure (MAP) at the beginning and end of haemofiltration or haemodialysis and 6 and 18 hours afterwards (n=6 haemofiltration and 6 haemodialysis procedures)

Figure 3. Changes of plasma osmolarity and loss of body weight during haemofiltration and haemodialysis (n=20 haemofiltration and 20 haemodialysis procedures, X ± SD, Student’s t-test)
treatment and was confirmed in 6 patients, who, because of very high plasma renin values, had been proposed for bilateral nephrectomy. During the first 3-4 weeks of treatment the normalisation of blood pressure seemed to be volume dependent. After this period blood pressure remained in the normal range in spite of an increase in body fluid. During the second phase a positive correlation existed between the blood pressure at the start of the procedure and the effect of the removal of different volumes of body fluid. The same degree of dehydration led to a considerable decrease of blood pressure in severe hypertension, but did not influence blood pressure in normotensive patients. Changes in baroreceptor function, as assumed by Henderson, would explain this reaction.

In contrast to haemodialysis, patients did not show any signs of orthostatic hypotension after haemofiltration. Even after the withdrawal of large amounts of body fluid, symptoms of a dysequilibrium syndrome were absent.

Recently a decrease of myocardial contractile force, and vasodilatation have been reported as a consequence of acetate administration. It could be argued that the lack of collapse reactions in haemofiltration compared to haemodialysis was due to the use of lactate instead of acetate. We therefore replaced lactate by acetate in 20 haemofiltration procedures. In these, too, the circulatory system remained stable and collapse reactions, which are commonly observed during and after ultrafiltration in haemodialysis, did not occur.

Whereas ECV was considerably reduced by haemodialysis it remained stable in haemofiltration, despite a considerable degree of dehydration. As changes in the amount of body solids during the course of the procedure may be neglected, it would appear that ultrafiltration in haemodialysis mainly reduces the extracellular space, whereas fluid withdrawal in haemofiltration influences intracellular space, leaving extracellular space almost unchanged. An explanation for this behaviour may be the constancy of extracellular osmolarity during ultrafiltration, perhaps as a consequence of its minor effect on the elimination of small osmotically effective molecules.

According to our results haemofiltration is a very effective method for the treatment of patients with severe hypertension who have not responded to dialysis and drug therapy. Exact control of ultrafiltration and negligible changes of extracellular osmolarity are the main causes for the lack of collapse reaction which makes this method useful, especially in older patients with hypertension, or hypotensive patients suffering from fluid overload.

References

1 Quellhorst, E, Schuenemann, B and Doht, B (1977) 10th Annual Contractors' Conference, Bethesda, Ma

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Open Discussion

CAMBI (Parma) Did you try the effect of increasing the sodium concentration in the infusion solution of the patients that had better results, to the range of 140–142, in order to exclude the influence of sodium on the pathogenesis of hypertension in these patients? Secondly, can you tell us the predialysis values of phosphate?

QUELLHORST At the beginning of our haemofiltration programme we used a substitution fluid with a sodium concentration of 143 mEq/L and the reaction of the circulatory system was the same as we saw in patients treated with a substitution fluid containing 138 mEq/L. There was no difference in the mean blood pressure. Serum phosphate concentrations were about 4 to 5 mg/dl in the haemofiltration group and about 6 to 8 mg/dl in the haemodialysis group. But our haemofiltration group does not receive aluminium hydroxide therapy.

SHALDON (Montpellier) I don’t quite understand how during a haemofiltration period you can maintain your extracellular space constant during weight loss and yet reduce it during a haemodialysis period. Is this due to a differential clearance of inulin by the two procedures?

QUELLHORST We have used ¹⁴C method for the measurements of the inulin space and have determined the loss of inulin in ultrafiltrate, dialysate and urine. By this means an uncontrolled loss of inulin would be detected.

LULU (Kuwait) You said it takes about six months just to control the blood pressure in your method. How often have you resorted to nephrectomy in cases of malignant hypertension complicated by heart failure or very severe retinopathy because of the time factor.

QUELLHORST There was no need to perform bilateral nephrectomy in our patients. During the first six month period of treatment we had to administer antihypertensive drug therapy in most patients, guanethidine etc, but after this period we could stop the drug therapy.

DEANE (New York) May we have a little more information about how you did the measurement of extracellular fluid by inulin space, because I believe in the original report the equilibration time for inulin was given as 3 to 5 hours.

QUELLHORST The inulin prime was given about 3 hours before the beginning of the haemofiltration procedure.