Treatment of Chronic Uraemia by an Ultrafiltration Kidney—First Clinical Experience

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Summary

Seven patients with chronic renal failure were treated for 74 patient months three times weekly for 4—5 hours each with haemodiafiltration. Eighteen to twenty litres were exchanged per treatment. In spite of an increase in serum urea and creatinine levels all patients are in good condition after 3—18 months. Blood pressure could be normalised in all patients, even if there had been a drug and dialysis resistant hypertension prior to dialfiltration. Nerve conduction velocity and haematocrit values increased. In spite of an amino acid and protein loss of 6.5 and 10 g, respectively, per treatment, symptoms of a depletion syndrome were not observed.

Introduction

The elimination of different retention products by haemodialysis is achieved by a diffusion process, the velocity of which is dependent on the molecular weight of the substances concerned. Thus, substances with a molecular weight of 500—2000 daltons, which have been assumed by Babb et al (1971) to be responsible for uraemic complications, are retained in spite of an adequate dialysis with regard to urea and creatinine removal. In quite a different manner, natural kidneys remove molecules such as creatinine and inulin to the same extent, independent of their molecular weight. Henderson et al (1973) described a filtration and substitution system which corresponds more to the natural kidney than to haemodialysis. Their suggestions encouraged us to perform animal experiments using a diafiltration apparatus, details of which were presented at the EDTA
Conference in 1974 (Rieber et al, 1974). Patients with chronic renal failure were treated by dialfiltration in January 1975 for the first time.

**METHODS**

A diagram of the filtration system is presented in Figure 1. Two hundred to two hundred and fifty ml of blood per minute were pumped into the filter after heparin (1100 U/hour) had been added. A hydrostatic pressure of 200 to 300 mmHg is necessary to produce 70–75 ml of filtrate per minute, the major part

![Diagram of the filtration system](image)

Figure 1. The dialfiltration system. A = arterial blood line; AM = arterial pressure monitor; P₁ = blood pump; Hep = heparin pump; F = filter; FF = ultrafiltrate bottle; P₂ = vacuum pump; M₂ = manometer; B = bubble catcher; M₁ = 'venous' pressure manometer; H = thermostat; P₃ = roller pump; S = substitution fluid; C = clamps; V = venous blood line

of which is replaced by a modified Ringer-lactate-solution (Na⁺ 135, K⁺ 2.0, Ca²⁺ 3.75, Mg²⁺ 1.5, Cl⁻ 108.5 and lactate 33.75 mEq/l). The diluted blood re-enters the body circulation. For filtration the Rhône Poulenc dialyser RP 6 was mainly used, but in some cases an experimental device with cellulose nitrate membranes (Sartorius, Göttingen) was tested (Quellhorst & Flashues, 1971). The filtrate was collected in a bottle connected to a vacuum pump which produced a negative pressure of 200–300 mmHg. Patients were treated three times weekly for 4–4.5 hours each, exchanging about 18 l of extracellular fluid.

Using the described system and banked blood, in vitro studies were performed to determine the clearances of urea, creatinine, EDTA, Vitamin B₁₂ and inulin. Dialfiltration clearances were calculated according to Henderson et al (1973). Substances with a molecular weight smaller than 294 daltons were eliminated by haemodialysis more effectively than by dialfiltration (Table I), whereas larger molecules could be removed to a greater extent by dialfiltration. As the filtrate
TABLE I. Ultrafiltration and Haemodialysis Clearances of Substances with Various Molecular Weights at the Beginning and the end of a Dialysis or Ultrafiltration Procedure (n=15). For ultrafiltration experiments a Rhône Poulenc RP 6, for haemodialysis a Rhône Poulenc RP 5 dialyser was used.

<table>
<thead>
<tr>
<th>Substance</th>
<th>Mol.Wt.</th>
<th>Ultrafiltration Begin</th>
<th>Ultrafiltration End</th>
<th>Haemodialysis Begin</th>
<th>Haemodialysis End</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea</td>
<td>60</td>
<td>64±8.4</td>
<td>59± 9.5</td>
<td>121±7.4</td>
<td>104±5.1</td>
</tr>
<tr>
<td>Creatinine</td>
<td>113</td>
<td>62±7.5</td>
<td>57± 7.1</td>
<td>98±9.5</td>
<td>88±9.1</td>
</tr>
<tr>
<td>EDTA</td>
<td>294</td>
<td>61±3.4</td>
<td>54± 3.1</td>
<td>37±4.9</td>
<td>22±4.5</td>
</tr>
<tr>
<td>Vitamin B₁₂</td>
<td>1355</td>
<td>59±6.2</td>
<td>50± 4.9</td>
<td>25±3.1</td>
<td>12±2.1</td>
</tr>
<tr>
<td>Inulin</td>
<td>5000</td>
<td>61±4.4</td>
<td>41± 3.7</td>
<td>9±1.6</td>
<td>3±0.5</td>
</tr>
</tbody>
</table>

flow and the inulin clearance were in the same range, the sieving coefficient for inulin must be 1.

PATIENTS

Since the beginning of 1975 seven patients between 33 and 65 years have been treated for 3 to 18 months. During 74 patient months 1,016 ultrafiltration procedures were performed. The patients suffered from chronic pyelonephritis (2 patients), chronic glomerulonephritis (3), polyarteritis nodosa (1), diabetic nephropathy (1), the GFR ranged from 1.8 to 6.6 ml/min (mean 4.3 ml/min). Prior treatment had been chronic haemodialysis (4 patients), chronic peritoneal dialysis (2) and conservative (1).

RESULTS

Mean values of urea, phosphate and haematocrit levels of the first and the last month of treatment are demonstrated in Figure 2, blood samples being taken at the beginning of dialfiltration. Nerve conduction velocity (N. peronaeus) was measured at the same time. In most patients serum urea levels increased (from a mean of 146 to 162 mg/dl) in the same way as did serum creatinine concentrations (from 12.9 to 14.1 mg/dl). Serum phosphate levels decreased, so that after 3 to 4 months aluminium hydroxide therapy could be stopped in 6 patients. Serum calcium levels increased slowly to 10–11 mg/dl. Haematocrit values slowly decreased during the first months of treatment, especially in those patients who were transferred from chronic peritoneal dialysis. After 3 to 4 months haematocrit increased in all patients and reached higher levels than at the beginning of treatment. No patient received blood transfusions, but iron was administered up to an amount of 2 g/year. Whereas glucose tolerance and serum choles-
Figure 2. Mean values of serum urea, serum phosphate, haematocrit and nerve conduction velocity in the first and the last month of a 3 to 18 months ultrafiltration period.

Values were not changed, a statistically significant decrease in serum triglyceride levels could be observed (284 ± 18.5 to 221 ± 13.1 mg/dl). The metabolic acidosis was not fully compensated by dialfiltration. But pH could be augmented from 7.319 ± 0.015 to 7.388 ± 0.011 and standard bicarbonate rose from 16.8 ± 1.2 to 19.9 ± 0.6 mEq/l, pCO2 remained nearly constant at 31.7 ± 0.75 and 31.5 ± 0.6 mmHg (n=14). The plasma amino acid concentration at the beginning and the end of dialfiltration and in the ultrafiltrate was measured in 10 procedures after a fasting period of 12 hours using a method previously described (Rieger et al, 1974). As demonstrated in Figure 3 amino acid loss was mainly dependent on the plasma concentration and independent of the molecular weight. During a 5-hour dialfiltration period a mean amino acid loss of 6.5 ± 1.2 g could be calculated. At the beginning of the dialfiltration period 5 patients suffered from severe hypertension. In 2 patients (polyarteritis nod., chr.PN) bilateral nephrectomy...
Figure 3. Amino acid loss during a single ultrafiltration procedure
had been proposed because of a dialysis and drug-resistant high blood pressure. After a dialfiltration period of 4 to 6 months normal blood pressure was achieved in all patients (Figure 4) in spite of an unchanged mean body weight gain between the dialfiltration procedures. No antihypertensive therapy was necessary. A reduction of body weight up to 5 kg per 4 hours was well tolerated, muscle cramps or collapse reactions never occurred.

**DISCUSSION**

In the system proposed by Henderson et al (1975) the substitution fluid was introduced into the extracorporeal circuit before the blood entered the filter. Sixty to seventy litres of sterile fluid were needed. Without influencing the effectiveness we could reduce the amount of dilution fluid per dialfiltration to 18–20 l by means of substitution beyond the filter. As previously reported by us (Rieger et al, 1974) no adverse reaction involving haemolysis, blood cell damage or hypofibrinogenaemia was observed. In contrast to Henderson et al (1975) we used lactate instead of acetate as buffer without any complication,
even in diabetics. Since patients are loaded with 675 mEq of lactate within 4 hours, bicarbonate would be preferred in severe liver failure. All patients were recommended to control the sodium, potassium and water intake. As protein was not restricted, most patients showed an increase in serum urea concentration. Even high levels of urea and creatinine were tolerated well. Haematocrit values and nerve conduction velocity increased slowly. The molecular cut-off was determined by Man et al (1973) for the polycrylonitile membrane of the RP 6 dialyser to be in the range of 40,000 daltons. The ‘pores’ of the cellulose nitrate membrane are passed by substances with a molecular weight up to 20,000 daltons. When these membranes are used the loss of substances necessary for life has to be observed carefully. Initially a greater depletion of amino acids than with haemo- or peritoneal dialysis (Bergström et al, 1972; Held et al, 1974) was feared. This did not occur, however. An amino acid loss of 6.5 g and a protein loss of about 10 g per dialfiltration were tolerated. Serum protein concentration remained stable in all patients. Even in patients with dialysis and drug resistant hypertension blood pressure could be normalised by dialfiltration. As there was no correlation between blood pressure and body weight loss, other factors, not only withdrawal of extracellular volume, must be responsible for the normalisation of blood pressure (Henderson et al, 1975).

Haemodiafiltration has proved to be an effective and simple method for the treatment of chronic uraemia. Avoidance of dialysis fluid and exact control of ultrafiltration result in a higher degree of security. Diafiltration combined with adsorption or other methods of detoxification may be a further step in the development of a wearable artificial kidney.

Acknowledgment

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References

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Open Discussion

CHAIRMAN (SHALDON, Montpellier) Thank you Dr Quellhorst for the very stimulating paper on the first large clinical experience with ultrafiltration. I was interested to note that you confirm the observations of Lee Henderson that blood pressure control was much facilitated by this technique. I wonder in the light of Dr Bergström’s observation whether you would revise your opinion as to why you were able to control the patients’ blood pressure more easily.

QUELLHORST We can confirm the observation of Henderson, for we saw normalisation of blood pressure in all patients, even in those patients for whom bilateral nephrectomy had been proposed because of intractable high blood pressure. There was no correlation between blood pressure depression and extracellular volume or body weight of patients.

CHAIRMAN You were taking off fluid without changing the serum osmolality, were you not?

QUELLHORST We did not change the osmolality.

CHAIRMAN Therefore you might reach the stage of more effective true dry weight without having any symptoms. That is the suggestion I was making.

PERRONE (Pontoise) At Pontoise we are treating four patients by the same technique, and one of those patients had very bad haemostatic function. After only three months of ultrafiltration treatment his haemostatic function has much improved. Did you observe any similar improvement in the haemostasis of your patients?

QUELLHORST No, we did not observe it.

DAVISON (Leeds) Could I ask if there was any change in the residual function of your patients after one year’s treatment, or did they all still have a creatinine clearance of 2.6–4 ml/min?

QUELLHORST No, they did not have any change in their renal function.