CLINICAL EXPERIENCE WITH HAEMOFILTRATION

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Summary

Five hundred and sixty-nine haemofiltrations have been done in 8 patients using the Berghof-capillary membrane, the RP-6 and the Amicon XM 50 membrane. An automated haemofiltration system has been developed for iso-volumetric replacement of diafiltrate by a modified Ringer solution, containing lactate or acetate as buffer. Pretreatment BUN and creatinine levels rose by 10—25%, uric acid decreased by 7% after half a year of treatment. Diafiltrate volumes of 21L per single treatment were exchanged. Amino acid loss averaged 3.22 g per treatment. Middle molecular peaks in diafiltrate samples eluted by Sephadex G 15 chromatography had varying heights in different patients. During a single haemofiltration planimetrically determined areas between 1029 and 2538 daltons decreased in two patients to 49% and 63% respectively. Malignant hypertension showed an improvement after 3 months of treatment. Markedly elevated serum triglyceride levels decreased when using lactate or bicarbonate-containing substitution fluids and rose again with acetate-containing fluid.

Introduction

Haemofiltration is a form of membrane filtration applied to the separation of metabolic products, water and electrolytes from the high molecular weight substances and cells in blood. Asymmetric porous membranes are best. The membrane cut-off is closely predicted by the diameter of the pores. When applying a hydrostatic pressure, plasma water is filtered1, which contains all molecules with a molecular weight below the membrane cut-off in the same concentration as found in the blood.

Methods

We used three different membranes: the Berghof capillary membrane with a cut-off at 15000 daltons made from aromatic polyamide with a surface area of
1.0 m²; the RP-6 Polyacrylonitrile membrane and the Amicon XM 50 capillary membrane made from polysulfone with a membrane area of 0.55 m².

We have developed a haemofiltration system in which dialfiltrate is replaced by an identical volume of sterile, balanced electrolyte solution using a spheroidal body separated into two equal compartments by a thin elastic membrane². Two different, modified Ringer solutions, one containing 33.75 mval lactate, the other 31.75 mval acetate as buffer, were used.

Mean dialfiltration volumes of 60 ml/min for the Berghof-capillary membrane and the RP-6, 90 ml/min for the XM 50 membrane were found when replacement solution was given into the venous line (postdilution) and when optimal working conditions were obtained with a blood flow of 300 ml/min and a transmembrane pressure of 300–350 mmHg. During a 5–6 hour haemofiltration procedure a mean dialfiltrate volume of 20.98 ± 1.93 L was exchanged (N = 50). Eight patients (4 females, 4 males) who had been on regular haemodialysis treatment for 2–34 months, were subjected to haemofiltration because of uncontrollable hypertension or hyperlipoproteinaemia. The longest period of haemofiltration treatment was 13 months, the shortest 2 months, representing a total of 44 treatment months. The 569 haemofiltrations were done 48 times with the Berghof-capillary membrane, 505 times with the RP-6 membrane and 16 times with the XM 50 membrane.

Results

In comparison with conventional dialysers³ with the same membrane surface, we demonstrated lower clearance values for small molecules like urea and creatinine, and higher values for larger molecules like uric acid and phosphate. For the XM 50 membrane, clearance rates of about 90 ml/min for small solutes are similar to conventional dialysers with the same surface area.

Our studies showed an increase in the plasma clearance rates parallel to the rise in dialfiltration volumes and in correlation with blood flow rates in the extracorporeal circuit⁴,⁵. Working with a blood flow of 300 ml/min and a transmembrane pressure of 300–350 mmHg, plasma clearance rates for the RP-6 membrane were found to be: for BUN 96.0 ± 5.7 ml/min, creatinine 67.2 ± 7.1 ml/min, uric acid 67.4 ± 6.7 ml/min, inorganic phosphate 64.4 ± 4.0 ml/min, inulin 60.4 ± 1.8 ml/min. Using the Berghof-capillary membrane the following plasma clearances were obtained: BUN 59.6 ± 1.1 ml/min, creatinine 58.4 ± 3.1 ml/min, uric acid 56.8 ± 1.7 ml/min, inorganic phosphate 53.2 ± 7.1 ml/min, inulin 32.1 ± 0.9 ml/min. Clearance values for BUN, creatinine, uric acid and phosphate are 13.1–17.4%, and for inulin 46.9% lower than with the RP-6 membrane. This phenomenon may be caused by a flow-dependent secondary protein layer which leads to a variation in the original membrane characteristic, augmented by the 600 μ inside diameter of the capillary⁵.

Serum levels of uraemic solutes during half a year of haemofiltration treatment rose for BUN and creatinine to 10–25% above previous values, whilst uric acid decreased by 7%.

Mean extractions in the dialfiltrate in 50 procedures were calculated to be: BUN 16.45 g, creatinine 1.99 g, uric acid 1.2 g and inorganic phosphate 0.83 g.
Protein loss into the dialfiltrate is negligible using the Berghof capillary membrane, about 10 g are lost with the RP-6 and the protein loss is 12–14 g with the XM 50 membrane.

Amino acid loss in the dialfiltrate during a single haemofiltration procedure averages 3.22 g (N = 5) and is not higher than the loss usually found in conventional dialysis. Separation of amino acids in the dialfiltrate by gel column filtration shows concentrations similar to the serum values (Figure 1).

![Aminosäureauscheidung im Dialfiltrat (N=4)](image)

Figure 1. Mean total amino acid loss (N = 4) in dialfiltrate during a single treatment. Mean dialfiltrate volume: 20.2 L. Mean duration of dialfiltration: 5.5 hours

Normalisation of the serum amino acid pattern in one patient after half a year of haemofiltration treatment was observed, in association with better control of accelerated hypertension and an increase of body weight.

Because of the high inulin clearances the expected major advantage of haemofiltration compared with conventional dialysis lies in the elimination of so-called middle molecules. We were able to detect in dialfiltrate samples, solutes in the middle molecular range (403–2538 daltons) by Sephadex G 15 gel chromatography. Chromatograms of 7 patients compared with a healthy control show different altitudes of the middle molecular peaks. Of interest is the area from 1029–2532 daltons, in which we detected three different spots of ninhydrine positive substances by thin layer chromatography (Figure 2).

At the end of a single five hour haemofiltration the planimetrically determined area between 1029–2532 daltons decreased in two patients to 49% and 63% respectively, and rose to 64% and 68% by the start of the following treatment. A longer term study in one patient showed after 6 weeks values of 57% compared with the beginning of treatment (Figure 3).
Figure 2. Sephadex G 15 chromatography of dialfiltrate samples of 7 patients at the beginning of haemofiltration treatment. For comparison, chromatogram of a healthy control is shown. Thin line shows UV absorption at 254 nm, thick line at 280 nm. Molecular weights of standard substances are indicated: I=Insulin A-chain 2532 daltons; A=Angiotensinamide 1029 daltons; P=Peptide (Val-Ala-Ala-Phe) 403 daltons.
Figure 3. Sephadex G 15 chromatogram of a patient with Alport’s Syndrome and severe polyneuropathy. From top: First treatment at the beginning, first treatment at the end, second treatment at the beginning, 18th treatment at the beginning. Arrows show molecular weight of standard substances: I=Insulin A-chain 2532 daltons; A=Angiotensinamide 1029 daltons; P=Peptide (Val-Ala-Ala-Phe) 403 daltons; UA=Uric acid 168 daltons
Clinical Response

Hypertension

Five patients (two females, three males) were admitted to the haemofiltration programme because of uncontrolled hypertension on regular haemodialysis and antihypertensive medication. Three patients showed a distinct drop in blood pressure after a mean treatment period of three months, and the antihypertensive medication could be reduced in two patients.

This drop in blood pressure was not observed in all patients. One patient with uncontrolled hypertension and severe neuropathy with markedly impaired nerve conduction velocity (N. peroneus), showed no improvement during nine months of haemofiltration until Minoxidil was added to the medication.

Hyperlipoproteinaemia

Two patients were admitted to the haemofiltration programme because of marked hyperlipidaemia (type IV according to the Fredrickson classification). Mean plasma triglyceride levels in the preceding six months on regular dialysis were found to be 1160mg/100ml and 550mg/100ml, serum cholesterol 250mg/100ml and 350mg/100ml respectively. We observed a distinct drop in triglyceride levels when using a lactate-containing substitution fluid. This effect was reversed by using an acetate-containing substitution fluid, especially in those patients who initially had a marked hypertriglyceridaemia (Figure 4).

Figure 4. Behaviour of serum triglycerides in 5 patients on haemofiltration treatment with lactate and with acetate substitution fluid.
One patient (RA, female) who showed rising triglyceride values even with lactate substitution was admitted to the haemofiltration programme because of malignant hypertension and severe malnutrition. With better control of hypertensin, food intake and body weight rose to nearly the same extent as the triglyceride levels.

One patient (WA, female) is an excellent example of the interaction of serum triglyceride values and buffer substances. During lactate substitution following dialysis with acetate-containing dialysate, triglycerides showed a marked decline to nearly normal values, followed by continuous elevation after a change to acetate-containing fluid, which was again reversible when using bicarbonate in the substitution fluid.

The mechanisms influencing triglyceride levels during haemofiltration treatment are not yet known. Henderson proposes the elimination of a lipoprotein-lipase-inhibitor as a major factor, whilst recently, we proposed the elimination of glycerol as a possible factor, but as we could show with the XM 50 membrane, there is insufficient loss of glycerol and mono-, di- and triglycerides into the dialfiltrate to explain the normalisation of serum triglycerides.

The observation that serum triglyceride levels in patients with disordered fat metabolism are dependent upon the alkali equivalent used in the substitution fluid, may explain the good results with haemofiltration found by other observers who used lactate. For the moment we suggest that the influence of haemofiltration upon hypertriglyceridaemia depends on the buffer substance used.

Conclusions

The clinical studies shown above have been made with patients who suffered from resistant hypertension or hyperlipoproteinaemia uninfluenced by previous regular dialysis. Hypertension improved in all but one patient during haemofiltration; hyperlipoproteinaemia showed a marked decline using lactate- or bicarbonate-containing substitution fluid.

Despite rising serum creatinine and BUN values during haemofiltration treatment, subjective improvement was experienced by all patients. It is unfair to draw comparisons between haemofiltration and dialysis because this was a highly selected group of patients. In cases of uncontrollable hypertension, haemofiltration seems to be superior to conventional dialysis.

Acknowledgments

The development of the Berghof capillary membrane has been supported by BMFT, Nr. MT 216 A.

References

1. Schläge, R (1964) Stofftransport durch Membranen, Darmstadt
Open Discussion

CAMBI (Parma) If phosphate clearances are very similar with haemofiltration and haemodialysis, can you logically explain the differences in predialysis values of phosphate in haemofiltration patients versus haemodialysis patients considering also that the phosphate rebound one hour after dialysis is very large?

SCHNEIDER We think that phosphate clearance rates are higher in haemofiltration treatment than in haemodialysis but we have not shown the phosphate levels during the half-year’s treatment because of the decreasing amounts of aluminium binders taken by the patients.

WALLS (Leicester) You demonstrated nicely the disappearance of middle molecules of certain peaks in your ultrafiltration technique, but you did not say what happened to the patients with peripheral neuropathy.

SCHNEIDER We measured the nerve conduction velocity even in old patients, and especially in those who had markedly impaired nerve conduction velocity, but we have seen no improvement as yet.

PARSONS (London) Could I ask you if you measured the acetate levels and triglyceride levels in your patients? Were those patients who had the high triglyceride levels the ones who showed the highest plasma acetate levels?

SCHNEIDER We did not measure the acetate levels.