HAEMOFILTRATION – CRITICAL EVALUATION OF CLINICAL BENEFITS

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Summary

To delineate the worth of chronic HF in end stage renal failure, since 1976 we have treated 9 patients with dialysis-resistant hypertension, 6 patients with dialysis intolerance, 7 patients with hypertriglyceridaemia and 7 patients with polyneuropathy. We found an improvement of polyneuropathy and volume-sodium dependent hypertension and symptoms of dialysis discomfort markedly diminished. No amelioration was detected in anaemia, hypertriglyceridaemia and volume-independent hypertension. Hyperphosphataemia was poorly controlled despite increased amounts of aluminium hydroxide. PTH values increased and renal osteopathy seemed to deteriorate.

Introduction

To elucidate the clinical benefits of chronic haemofiltration (HF) treatment in end stage renal disease, we compared the clinical data with the preceding period on regular dialysis for 15 hours/week. Various investigators have reported an improvement of hypertension resistant to dialysis and drugs [1–3], hypertriglyceridaemia [4,5], anaemia [5], hyperphosphataemia [5,6], polyneuropathy [5,7] and symptoms of dialysis discomfort [3,8]. In view of these reported clinical benefits we have paid special attention to these points.

Patients and Methods

Selection of 19 patients for chronic HF was performed according to symptoms cited above: 9 patients because of dialysis resistant hypertension, 7 patients because of polyneuropathy, 7 patients because of hypertriglyceridaemia and 6 patients because of dialysis discomfort. All patients were on a free diet and supplements of Vitamin D or androgens were not administered routinely. Post-dilution HF was carried out 3 times weekly with an average exchange volume of
20L. Predominantly RP 6 (Rhone-Poulenc, France), Amicon Diafilter 30 (Amicon, Mass. USA) and Berghof polysulfon capillary (Berghof GmbH, Tübingen, FRG) filters were used in automatic volumetric and gravimetric HF machines. Replacement fluid usually contained 140mEq/L Na, 4.0mEq/L Ca, 2.0mEq/L Mg, 111 mEq/L Cl, 35mEq/L acetate.

Results and Discussion

Haematocrit values did not change consistently compared with the preceding dialysis period. Patients requiring transfusions prior to HF had to be transfused at nearly the same intervals to stabilise haematocrit values. Serum ferritin levels followed over a 1 year period were shown to decrease in transfused and non-transfused patients, regardless of the amount of iron administered, possibly leading to a depletion of iron stores in non-transfused patients, whereas siderosis might be prevented in polytransfused patients (Figure 1).

![CHRONIC HF-TREATMENT](chart)

Figure 1. Haematocrit (Hct) values in transfused and non-transfused patients on chronic HF. Patients with liver disease have been excluded. Simultaneous mean monthly iron administration (Fe/Monat) and serum ferritin levels are shown. All values are given in mean ± SD
Pretreatment values of small molecular uraemic solutes in patients treated longer than 1 year increased by 19% to 39% compared with the dialysis period. Total serum calcium decreased 7%, whereas inorganic phosphate increased 4.1% despite a 27% elevation of the dosage of aluminium hydroxide. Compared with the dialysis period, dry body weight was reduced by a mean of 0.5kg during the first months of treatment. Then a steady increase of 1.6kg in males and of 1.4kg in females was noted, presumably due to better food intake.

Assessment of renal osteodystrophy by radiological criteria revealed a trend towards deterioration shown by increased acro-osteolysis, cortical striation and subperiosteal resorption. Bone mineral content however was found to be unchanged as derived from densitometric measurements in the left and right calcaneus (Figure 2).

![Densitometry](image)

**Figure 2.** Bone densitometry in left and right calcaneus followed over a 3 years' period on chronic HF. Values are given in mean ± SD

PTH levels determined by a C-terminal radio immunoassay continuously increased, whilst Vitamin D values stabilised within the normal range after a 4 week supplementation period [9]. Alkaline phosphatase slowly increased, coming to exceed the normal range (Figure 3).

Fat metabolism was studied in control periods with the use of lactate, acetate, and bicarbonate buffer in identical concentrations of 33.75mEq/L. A slight drop of triglycerides during bicarbonate treatment and an increase using lactate or acetate was found but mean values did not show significant differences. Compared
with the preceding HD, HF did not improve hypertriglyceridaemia, though individual deviations were pronounced.

During the same study, the influence of the different buffer substances on metabolic acidosis showed inadequate correction with lactate, satisfactory correction with acetate and compensation with bicarbonate buffer. In the lactate buffer period, serum lactate levels were already elevated above the normal range at the start of treatment (35.7 ± 11.2mg%) and rose during the treatment to 50.8 ± 24.1mg%. Standard bicarbonate values were not significantly different regardless of the buffer substance used (Figure 4).

Nine patients have been subjected to chronic HF because of dialysis resistant hypertension. Three of these patients did not improve, but the others responded and antihypertensive drugs could be markedly reduced. It has been speculated that improvement of autonomic neuropathy during HF was the cause of the improvement of hypertension [2]. Dopamine β-hydroxylase (DBH) activity at the start of treatment was found to be subnormal in all patients, without essential differences between the hypertensive (19.3 ± 21.2 i.U.) and the normotensive (26.5 ± 31.4 i.U.) group. Long term observations did not reveal significant changes in either group. From this observation it may be concluded that changes in DBH values, as far as DBH reflects sympathetic activity, are not essential for an improvement in dialysis resistant hypertension. The normalisation of blood pressure regulation in responding patients is probably due to salt and water withdrawal without major symptoms.

Symptoms of dialysis discomfort (e.g. headache, vomiting, blood pressure drop, muscle cramps) were markedly reduced in HF as opposed to HD, especially in those patients who were selected for this reason. In our opinion this results from reduced fluctuation of serum osmolality and an increase of peripheral resistance [3,10,11]. Rapid osmotic fall during HD in contrast with HF leads to
a shift of water into the intracellular space and may interfere with vasomotor adaptation [12]. In HF intravascular volume reduction is followed by an increase of peripheral resistance and venous pooling of blood is avoided, possibly due to release of catecholamines. This explanation is supported by the intra-individual comparative measurements of DBH, which increased more rapidly and to a greater extent during HF [13].

In all patients polyneuropathy was evaluated by means of sequential measurements of motor nerve conduction velocity in the nervus peroneus of the left leg. In 7 patients reduction of MNCV was detected, 4 of these patients disclosed clinical signs of severe polyneuropathy. Repeated measurements of MNCV showed an improvement in 6 patients, paralleled by clinical amelioration of symptoms; 1 failed to respond (Figure 5).

In conclusion, HF improved polyneuropathy, volume-dependent hypertension and markedly diminished symptoms of dialysis discomfort. HF was found to be ineffective in respect of improvement of anaemia, hypertriglyceridaemia or cor-
Figure 5. Motor nerve conduction velocity (MNCV) in the n.peroneus of the left leg in 7 patients subjected to chronic HF because of neuropathy.

Rection of volume-independent hypertension. Hyperphosphataemia is poorly controlled despite increased amounts of aluminium hydroxide; PTH increases and renal osteodystrophy seems to deteriorate.

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Open Discussion

KRAMER (Göttingen) You mentioned in your paper that your patients on haemofiltration had a better tolerance of fluid withdrawal as compared to those on haemodialysis. It is, however, of critical importance for the purpose of comparison whether effective fluid withdrawal was performed in a controlled manner also during haemodialysis. My question: did you use a machine for controlled fluid withdrawal and if so, what type of machine did you use?

SCHNEIDER In those comparative groups a control system was used and scales with balancing. So the fluid withdrawal was exactly the same.

JONES (London) Did you use any criteria other than measurement of DBH for assessing autonomic neuropathy? What is the evidence for your statement that haemodialysis is accompanied by a movement of water into cells?

SCHNEIDER To your first question: the peripheral neuropathy was evaluated by means of nerve conduction velocity measurements. We have no measurements about autonomic neuropathy.

JONES I thought you said that during haemodialysis there was a movement of water into cells. Now I understood that this in fact is reversed, that water tends to leave cells with sodium during haemodialysis.

SCHNEIDER This is our interpretation because we found that the intracellular space was more rapidly contracted in haemofiltration and the explanation for this might be that cell water moves outside and in haemodialysis we thought that the water would go inside the cells and would explain this.

BERGSTRÖM (Stockholm) I would like to ask you by which method you assess the middle molecule levels in your patients. The reason I ask you is that we now know that there are at least 12 different peptides which make up the middle molecule fraction so if you use a crude non-specific separation method you may not exclude that some of the middle molecule peptides are influenced by haemofiltration.

SCHNEIDER We use the Sephadex gel chromatography.

BERGSTRÖM So that is a very unspecific method I would say.

FOURNIER (Amiens) Our findings fully support your statement that haemofiltration worsens hyperparathyroidism. Since in our patients calcium balance was always positive we have no explanation for this worsening. Have you checked that with a uniform concentration of 4mEq/L of calcium in the substitution fluid all your patients have always been in positive calcium balance? In our experience a few patients may need 4.5mEq/L of calcium in the substitution fluid to be in a positive calcium balance.

SCHNEIDER Professor Fournier, we know this problem and I do not have any explanation for this and we are very worried about it, because Professor Schäfer has not found this, so I cannot explain this. To the second point I think the calcium balance was always positive.