COMPARISON OF HAEMODIALYSIS (HD) AND POST DILUTION
HAEMOFILTRATION (HF) ON AN UNSELECTED DIALYSIS
POPULATION

C A Baldamus, W Schoeppe, K M Koch

ZIM, University Hospital, Frankfurt/M., GFR

Summary

In a comparison of post-dilution haemofiltration (HF) with routine haemodialysis (HD) HF was found to be technically feasible and without difficulty as a method of treating end-stage renal failure patients. HF offers the theoretical benefit of a high removal rate of middle molecules at the expense of measured small molecule clearances. The reported improvement in blood pressure and hyperphosphataemia in HF could not be found in our unselected population. The better tolerance to fluid removal during HF may be due to the linear weight loss during treatment but cannot be attributed to constancy in serum osmolality. HF (3 x 20–23L ultrafiltrate/week) seems to be an adequate treatment for small patients. In large, heavy patients without significant residual renal function the ultrafiltration volume has to be increased in relation to body weight. HF was found to be superior to HD in patients with fluid removal problems and frequent hypotensive episodes during HD.

Introduction

Haemofiltration as a method of treating end-stage renal failure patients has been introduced by Henderson [1] and Quellhorst [2]. In selected patients several clinical benefits were reported for HF compared with HD. Hypertension, resistant to dialysis and drugs was reported to be controllable with HF [3,4]. Improvement of hyperphosphataemia [5], of hypertriglyceridaemia [6], of anaemia [2] and of motor nerve conduction velocity [2] were other reported advantages of HF.

In view of these reported clinical benefits the potential of this new treatment of end-stage renal failure has been evaluated in six stable unselected dialysis patients.
Patients and Methods

Patients (3 males, 3 females, age 17–63 years, BW 46–83 kg) had been on regular dialysis for 5–9 months prior to clinical trial. Only one patient had a residual renal function of more than 1ml/min creatinine clearance. Three patients were moderately hypertensive (<180/105 mmHg). Only one patient had a mean interdialytic weight gain exceeding 2 kg (2.8 kg).

The protocol of the study consisted of a 2 months HD control period, followed by a 4 months and longer HF period, followed by 2 months of HD for those patients who were withdrawn from HF.

Patients were dialysed 3 x 6 hr/week on a Gambro Optima dialyser at a $Q_B$ of 200–300 ml/min and a $Q_D$ of 500 ml/min. The dialysate contained 136 mEq/l sodium, 2.5 mEq/L potassium, 3.8 mEq/L calcium, 1.2 mEq/L magnesium, 34 mEq/L acetate, 1.5 mEq/L lactate, 108 mEq/L chloride, and 140 mg/100 ml glucose.

HF was performed with 3 x 20 L infusate/week at an ultrafiltration rate of 60–70 ml/min. A polyacrylonitrile membrane dialyser (Rhône-Poulenc RP 6) and more recently an asymmetric cellulose acetate membrane (Sartorius Haemofilter SM 40003) were used as a filter at a $Q_B$ of 200–300 ml/min. The replacement fluid contained 138 mEq/L of sodium and 35 mEq/L of lactate instead of acetate. Otherwise, it was practically identical with the composition of the dialysate.

Results

During the course of the study, one patient had to be taken off HF after one week because of an increasing allergic reaction, possibly due to the polyacrylonitrile dialyser. Her results have not been included. Another patient was transferred to HD after 4 months of HF because of symptomatic hyperphosphataemia ($PO_4^{3-}$ of 12.1 mg/100 ml, calcium 4.4 mEq/L) with pruritus and red-eye syndrome. The heaviest patient (83 kg) refused to continue HF after 4 months because of deteriorating well-being, weakness and general fatigue. For social reasons two patients returned to HD after 8 months of HF. The oldest patient with a residual renal function of 2.8 ml/min creatinine clearance, still continues HF, after more than one year.

Irrespective of the treatment procedure the mean pre-treatment body weight (BW), $\Delta$ body weight per treatment ($\Delta$ BW), mean pre-treatment MAP and $\Delta$ MAP per treatment did not change significantly (Figure 1).

Urea ($p<0.005$) and creatinine ($p<0.05$) increased significantly from HD to HF (Figure 2). Urea ($p<0.01$) fell significantly when patients were transferred to HD again; the accompanying decrease of creatinine was not significant. Calcium did not change significantly, whereas phosphate increased in all patients when they were transferred from HD to HF ($p<0.01$) and it fell ($p<0.001$) when patients changed to HD again (Figure 2).

Pre-treatment serum osmolality increased from 295 ± 8.9 mOsm/kg in HD to 313 ± 13 in HF ($p<0.005$), and fell again to 303 mOsm/kg ($p<0.01$). However, the pre- to post-treatment change in osmolality was identical in HD (11.6 ± 7 mOsm/kg) and HF (11.4 ± 4 mOsm/kg).
Figure 1. The mean pre-treatment body weight (BW), the mean Δ BW per treatment, the mean pre-treatment arterial blood pressure (MAP) and the mean pre- to post-treatment change in MAP (Δ MAP) are given for each single patient. Symbols for patients are identical to those used in Figure 2.
Figure 2. The mean pre-treatment serum levels of urea (U), creatinine (Cr), calcium (Ca) and phosphate (PO₄⁻) are given for each single patient. Symbols for patients are identical to those used in Figure 1.
Figure 3. The ultrafiltration volume \( V_{1/2} \), necessary to reduce the concentration of a substance evenly distributed in total body water (TBW = 62 ± 6.5% BW) is calculated in correlation with BW. The regression line \( V_{1/2} = 0.42 \times BW \) is shown with its standard deviation (shadowed area). The measured \( V_{1/2} \) for serum urea of 11 patients with different BW are given as open circles.
Compared with HD, hypotensive episodes during treatment were less frequently observed during HF. This was most evident in one hypertensive patient who suffered from symptomatic blood pressure drops in 33% of all haemodialysis runs compared with 16% of all HF treatments. The incidence of muscle cramps during treatment was higher in HF (31%) than in HD (14%). This symptom increased especially in those patients who already suffered from cramps during HD.

Kinetic studies on small molecule removal during HF revealed that the decrease in serum urea concentration per volume ultrafiltrate was identical at an ultrafiltration rate of 60 ml/min to that at 90 ml/min. From the decrease of serum urea concentration during a HF treatment, the individual ultrafiltration volume necessary to reach a 50% reduction in serum concentration ($V_{1/2}$) was determined. As can be seen from Figure 3, $V_{1/2}$ was significantly correlated with body weight ($V_{1/2} = 0.47 \times BW - 3.03$, $r = 0.92$, $p < 0.001$).

Discussion

The technique of post-dilution haemofiltration was introduced as a method of treating end-stage renal failure patients by Henderson [1] and Quellhorst [2]. The technique of HF, especially with automatic balancing machines (Sartorius Haemoprocessor) is safe and easy to learn and to control.

The most evident clinical benefit of HF compared with HD in this study was the better tolerance to fluid removal, indicated by fewer hypotensive episodes during HF. This has been attributed to a constant serum osmolality during HF whereas during HD a pre- to post-treatment change of about 15 mOsm/kg was observed [4]. In steady state conditions at comparable metabolic urea generation rates during HD and HF, the amount of solvents removed during treatment should be the same in HD and HF, although because of different clearance rates the serum urea concentration is higher in HF than in HD. Therefore using dialysate and HF replacement fluid of comparable osmolalities, the pre- to post-treatment decrease in serum osmolality should be identical to HD and HF. Accordingly, identical serum osmolality changes were found during HD (11.6 mOsm/kg) and during HF (11.4 mOsm/kg).

One possible explanation for improved control of hypertension, as reported for HF [2-4] might be easier fluid removal and thus easier achievement of ‘body dry weight’. According to this concept it is not surprising that we did not see an improvement in blood pressure in the three hypertensive patients, since BW was kept constant throughout the study. Another reason for persisting hypertension might be that all three patients belonged to the nonresponder group in regard to dopamine-β-hydroxylase activity, as described by Henderson [3].

Muscle cramps did occur more frequently in HF than in HD. One possible explanation could be the more severe acidosis in HF, which was inadequately corrected during treatment (pre pH 7.30 ± 0.05, post pH 7.37 ± 0.03) with lactate-containing (35 mEq/L) replacement fluid. This is supported by the fact that the patient with the highest incidence of muscle cramps during HF had the lowest mean pre-treatment pH of all our patients (pH 7.24 ± 0.054).
Hyperphosphataemia is reported [2,5] to decrease during HF to a level at which phosphate-binders could be drastically reduced or even withdrawn. This could not be confirmed by the present study. Pre-treatment serum phosphate levels increased during HF in all patients and decreased when patients were transferred to HD again. One patient had to be withdrawn from HF because of symptomatic hyperphosphataemia. He had secondary hyperparathyroidism and his PTH values did not change significantly from HD to HF.

HF offers the theoretical benefit of a high removal rate of ‘middle molecules’ [7] at the expense of measured small molecule clearances, indicated by a significant increase in serum urea and creatinine concentrations in HF (Figure 2). This increase was most evident in heavy patients. If one considers low molecular weight molecules as contributing to uraemic toxicity, one might speculate that the heaviest patient, who was withdrawn from HF because of lack of well being, general fatigue and weakness, suffered from insufficient treatment. To predict the effect of treatment and to standardise treatment in regard to small molecule removal, the ultrafiltration volume necessary to reduce serum urea levels to 50% ($V_{1/2}$) was measured for patients of different BW (Figure 3). $V_{1/2}$ was found to be correlated with BW ($V_{1/2} = 0.47 \times \text{BW} - 3.03$). This regression line was practically identical with that calculated for a substance evenly distributed in measured total body water, assuming a one compartment model ($V_{1/2} = 0.42 \times \text{BW}$). Total body water, determined by tritium-labelled water was found to be $62 \pm 6.5\%$ of BW. From these results it is easy to calculate the ultrafiltration volume necessary to reach the desired reduction in pre-treatment serum urea level.

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Open Discussion

QUELLHORST (Hann. Münden) You may have noticed that our results on haemofiltration presented here last year are quite different. Concerning hypertension, are you justified in stating that haemofiltration does not correct hyper-
tension if you do not see any change of blood pressure in 6 patients with only slightly increased blood pressure at the start of treatment? In our group, the patients' blood pressure was substantially higher at the start of haemofiltration.

BALDAMUS In our study body weight was kept constant throughout the study whereas in most published cases, body weight decreased during the initial haemofiltration period. So I would assume that one major factor in blood pressure regulation would be that it is easier with haemofiltration than with haemodialysis to reach the 'dry body weight' of the patient.

QUELLHORST Concerning phosphate metabolism, did your patients get vitamin D metabolites and did you correct the calcium balance for the fluid removal from the patient?

BALDAMUS Patients were on phosphate-binders and on vitamin D therapy during the haemodialysis as well as the haemofiltration period. The calcium balance was positive during haemofiltration.

ANDREUCCI (Naples) We started five months ago post-dilutional haemofiltration and up to now we have similar results. Cramps can be reduced by increasing the concentration of sodium in the reinfusion solution. Secondly, we did not find any improvement in hypertension, but our patients can reduce their weight during haemofiltration much better than during dialysis. They realise this, so they come to the unit overweight more and more of the time. I do not know whether you find the same or is this just a characteristic of Neapolitan people?

BALDAMUS I think that improvement of hypertension is one of the main benefits claimed for haemofiltration. To find out whether the effect on blood pressure is due to easier fluid removal during haemofiltration or to the haemofiltration treatment per se, a controlled study needs to be performed, in which the body weight of the patient has to be kept constant throughout the haemofiltration period.

FOURNIER (Amiens) We confirm your data about the absence of effect of haemofiltration on hyperphosphataemia and on high blood pressure on the basis of personal observation and the observations of three other French-speaking dialysis centres. As suggested by Quellhorst one point is the critical importance of calcium balance and we advise a substitution fluid with a calcium concentration greater than 70 mg/dl to prevent a negative calcium balance. If you do not, you have a prohibitive increase in the risk of bone disease on long term treatment.

CAMBI (Parma) We recently presented at the 1978 ASAIO meeting our results concerning recirculation dialysis with 40 litres of dialysate and standard dialysers. The results so far are similar to or better than with haemofiltration as far as control of blood pressure and cramp. We think consequently that the main problem should be related to the water and electrolyte balance and not to anything that has to do with the so-called larger molecular fraction.