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Prospective Randomized Cross-over Long-term Comparison of Online Haemodiafiltration and Ultrapure High-flux Haemodialysis

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Abstract

Background: The residual uraemic syndrome that is inadequately cleared by diffusion is thought to contribute to the poor outcome of maintenance dialysis patients. Haemodiafiltration combines diffusion and convection in a single therapy, conferring theoretical benefits over haemodialysis. However, only few randomised comparisons have been carried out.

Methods: The prospective crossover clinical evaluation of high-flux ultrapure haemodialysis and online haemodiafiltration included 76 clinically stable patients on low-flux conventional bicarbonate buffered haemodialysis. They were randomized to high-flux haemodialysis or online haemodiafiltration (24 months) and switched to the alternative treatment (24 months).

Results: Removal of urea (Kt/V) and phosphate was significantly greater for online haemodiafiltration than for haemodialysis. Both high-flux haemodialysis and haemodiafiltration were associated with sustained reductions of pretreatment beta 2 microglobulin levels, however, the decrease was greater with haemodiafiltration.

Both modes of renal replacement therapy significantly improved nutritional status and the haematopoietic response to rHu EPO. Under unmatched conditions (sodium and energy balance) haemodiafiltration was associated with a lower number of hypotensive episodes and partial improvement of quality of life. The incidence of death was low in both groups and did not differ among the two modes of renal replacement therapy.

Conclusion: Online haemodiafiltration is a safe, effective and well tolerated therapy for end-stage renal disease patients even in the long run. Whether the dismal mortality rates of unselected end-stage renal disease patients can be changed by online haemodiafiltration remains to be shown in large scale long-term trials.

Key words: online haemodiafiltration, high-flux haemodialysis, dialysis fluid

Introduction

Numerous technical advances of dialysis technology and improvements of medical care have helped end-stage renal disease patients on maintenance haemodialysis (HD) to live better with their disease and allowed older patients to be treated. However, in current patient populations morbidity and mortality rates are still distressingly high. These poor long-term outcomes have led to a renewed interest in alternative renal replacement therapies (RRTs). Online haemodiafiltration (HDF) may confer clinical benefits in terms of solute removal and cardiovascular stability over HD. However, controlled clinical studies reported variable and often conflicting data [3] and a recently published meta-analysis of the published evidence on HDF paradoxically noted an even higher mortality risk with HDF [15].

Currently, the world-wide acceptance of HDF is low, as the production of sterile replacement fluids creates higher costs [18]. On the other hands the benefits of this mode of RRT have not been unequivocally demonstrated. Previous prospective comparisons of HDF with HD have been limited either by sample size, non-ideal control groups, duration of follow up or paucity of outcome data. To favour a more wide spread clinical use of online HDF where it is indicated, further randomized investigations are warranted. This trial compared online HDF with high-flux HD utilising ultrapure dialysis fluid with respect to a number of potential benefits and risks.

Materials and Methods

Study Design

This study was designed as an unblinded, prospective, randomised cross-over single-centre trial of postdilution online HDF and high-flux ultrapure HD. Patients had been treated previously by conventional (low-flux membrane, commercial bicarbonate buffer) HD at the KfH dialysis centre Munich- Laim for at least 6 months. Patients participating in the trial were randomised by coin flip to either online HDF (group A) or to ultrapure high-flux HD (group B) for a period of 24 months. Thereafter, the patients were switched to the other modality of therapy and followed for another 24 months (Fig 1). The study was conducted in accordance with the basic principles of the Declaration of Helsinki and the rules of Good Clinical Practice. The two techniques of extracorporeal renal replacement therapy carried out in the investigations are accepted as alternative routine modes in Germany and approved by legal authorities and ethical committees. For the study no additional blood samples were taken and no measurements were performed other than for

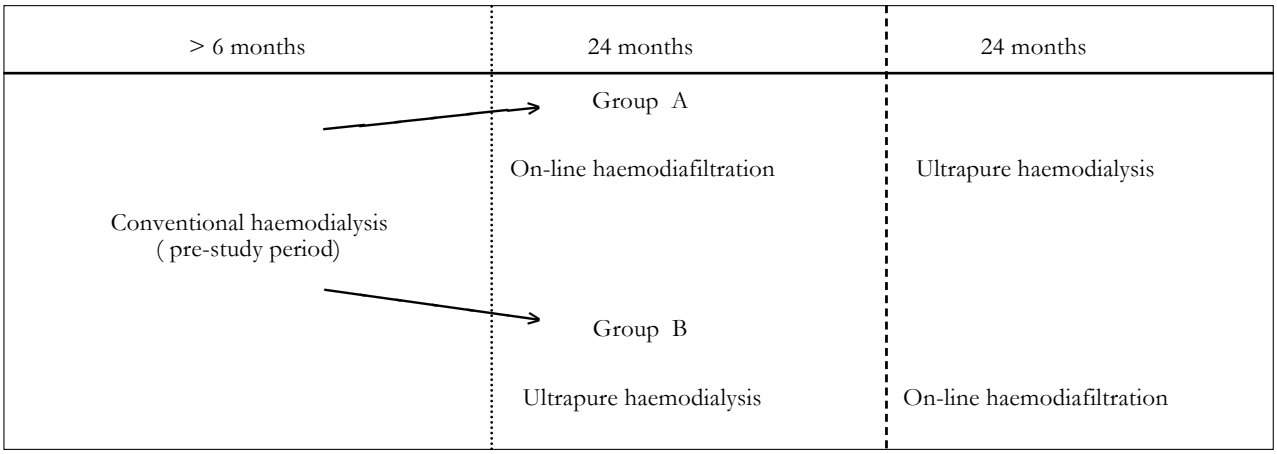

Fig 1. Design of the prospective randomized crossover study.

routine extracorporeal therapy.

Written informed consent was obtained from all participants before the investigations. Prospective defined endpoints of the comparison were calcium phosphate homeostasis, nutritional status, anaemia, cardiovascular stability and quality of life.

Patients

Seventy-six clinically stable ESRD patients (42 men, 34 women, ages 32 to 78 years) who had been on thrice weekly conventional HD for at least 6 months (duration of HD 9 to 280 months, mean 45 months) and who had a permanent blood access capable of delivery of a blood flow rate of at least 250 ml/min were recruited for the study.

Patients with a malignancy, severe co morbidity (heart failure NYHA class III-IV, liver cirrhosis, chronic inflammatory or infectious diseases, diabetic foot, and dementia) were not eligible. Five patients refused to participate in the study. However, patients were not pre-selected according to cardiovascular co morbidity, nutritional status or degree of anaemia or any other biochemical parameter. None of the patients had received either ultrapure high-flux dialysis or online HDF prior to the study. During the 48 month study period, the attending nephrologists determined the patients dialysis prescription according to the usual clinical standards and estimated the postdialytic dry weight by clinical acumen, blood pressure (sphygmomanometer), other signs and symptoms of hypervolemia or dehydration and chest X ray. If necessary the diameter of the inferior vena cava was measured by ultrasound. The usual management of long-term dialysis patients according the guidelines of EBPG was employed , i.e. no further restrictions or guidelines were imposed. The patient´s individual pharmacotherapy was continued, changes, if necessary, were documented.

Renal Replacement Therapies

Dialysis machines with volumetric control of ultrafiltration were used to perform conventional HD, high-flux HD utilising ultrapure dialysis fluid and online HDF (MTS 4008 and MTS 4008 H, respectively, Fresenius Medical Care, Bad Homburg, Germany)

Conventional HD was performed with low-flux polysulfone dialyser membranes (F 6, Fresenius Medical Care, Bad Homburg ,Germany) and commercial bicarbonate buffered dialysis fluid. Regular microbiological monitoring of the commercial dialysate was performed at 3 to 6 months intervals. Bacterial contamination of commercial dialysis fluid was 0-1500 colony forming units (CFU) per ml (median 165 CFU per ml). High-flux ultrapure HD and online HDF utilised single use high-flux polysulfone dialysers (F60 and F 80, respectively, polysulfone, Fresenius Medical Care, Bad Homburg, Germany).Ultrapure dialysis fluid was produced by one step ultrafiltration with an endotoxin absorbing polysulfone membrane , sterile substitution fluid by two step ultrafiltration with an endotoxin absorbing polysulfone membrane (Diasafe ; Fresenius Medical Care, Bad Homburg, Germany). None of the filtered dialysis fluid samples contained colony forming units or measurable endotoxin concentrations.

All therapies were performed thrice per week for 4 to 5 hours (mean 254 + 25 min); blood flow rates ranged from 250-350 ml/min (288 + 19 ml/min), but for each patient a fixed rate was used throughout the study. Dialysis flow rate was set at 500 ml/min. The volume of substitution fluid was 4.5l per hour of HDF session. The sodium, potassium, calcium and bicarbonate concentration of the dialysis fluid had been adapted to the individual patient's need during the pre-study period of conventional HD. The temperature of the dialysis fluid was fixed for each patient individually at 36.5-37.5 °C. The sodium concentrations remained unchanged for each participant throughout the study.

Data Collection and Laboratory Analysis

Clinical study parameters

Body weight and pressure recordings were performed at the beginning and the end of each treatment session throughout the study.

Biochemical tests

Pre treatment blood samples were drawn immediately

after access needle insert, post treatment blood samples were taken from the arterial line after decreasing the blood flow rate to 80 ml/min. Predialysis concentrations of routine biochemical parameters (calcium, phosphate, urea) were measured at recruitment and at 6 week intervals by auto analyzer methods. Beta-2 microglobulin was determined at recruitment and at 6 months intervals by nephelometry, serum albumin concentrations by the bromocresol green method and CRP concentrations by super sensitive immuno nephelometric assay. Single pool Kt/V was calculated from pre-and post treatment urea concentrations according to the second generation Daugirdas formula.

Nutritional status
The nutritional status of the patients was characterized by determinations of postdialytic dry body weight and mid-arm muscle circumference at recruitment and at 12 months intervals as described previously [17], and by measurements of serum albumin concentrations.

Anaemia control
Haematological parameters (blood count, ferritin and transferrin saturation) were determined at 6 week intervals using routine laboratory methods. All patients received intravenous human recombinant erythropoietin (alpha or beta erythropoietin) thrice per week. Recommended target haemoglobin levels were 10-11 g/dL. Ferritin levels were kept above 300 ng/ml and transferrin saturation above 30 %. Erythropoietin doses were changed by max 25 % as required to maintain the target levels.

Hypotensive episodes
Cardiovascular stability was judged by the number of hypotensive episodes, defined by a systolic blood pressure reduction of 30 mmHg in normotensive or hypertensive patients or by a drop of less than 30 mmHg in hypotensive patients combined with clinical symptoms necessitating intervention (changes in posture, saline infusion).

Quality of life
Disease related quality of life was determined after 52 weeks of each study period using the Kidney Disease Questionnaire (KDQ). The KDQ determines quality of life in five dimensions: physical symptoms, fatigue, depression, relationship with others and frustration.

Statistical methods
Data are expressed as mean ± SD or as median and range. Comparisons of continuous variables between the two study groups were conducted with the Student unpaired t-test if the parameter in question was distributed normally or with its nonparametric equivalent (Mann-Whitney U test) if not. Discrete categorical variables were compared either with the use of the chi-square test or Fisher's exact test. Comparisons of continuous variables through time were made with the use of the analysis of variance for repeated measurements, statistical analyses were restricted to baseline, 12 and 24 months. All data analyses were performed using the SAS statistical software packages. P values less than 0.05 were considered statistically significant.

RESULTS

PATIENT OUTCOME

Demographic characteristics
Thirty eight patients each were randomly assigned to online HDF treatment (group A) or high-flux ultrapure HD therapy (group B). The two study groups did not differ significantly regarding age, distribution of gender and causes of ESRD, time on dialysis or percentage of patients with oliguria at the start of the cross-over comparison (Table 1).

Drop-outs
Thirty-five patients of group A completed the two year study period on online HDF. One patient had died of severe infection, one patient was transferred to another dialysis centre, and another patient received a kidney transplant. The following 2 years on high-flux HD were completed by thirty-one patients of group A. One patient died from myocardial infarction, two patients received a kidney transplant and one patient was transferred to another center.

Thirty-four patients of group B completed the two-

Table 1. Demographic characteristics of patient groups at randomization. Data are given as mean (± SD) or median (range)

	All patients	Group A	Group B
Number of patients	76	38	38
Age (years)	62 (10)	63 (9)	59 (10)
Gender (M/F)	42 / 34	22 / 16	20 / 18
Cause of ESRD			
Glomerulonephritis	22	10	12
Hypertensive Nephropathy	18	10	8
Diabetes mellitus	15	7	8
Polycystic Kidney Disease	8	5	3
Chronic Tubulointerstitial Nephritis	7	2	5
Unknown	6	4	2
Time on HD (months)	26 (9-280)	25 (9-280)	28 (9-253)

year study period on high-flux ultrapure HD, 2 patients died from cardiovascular events and 2 patients received a kidney transplant. Of the remaining thirty-four patients thirty completed the 2 year study period on online HDF. Two patients died from vascular complications and 2 patients received a kidney transplant.

No patient was withdrawn due to intolerance of online HDF. Drop outs were not replaced. The intention to treat analysis revealed no difference in mortality among the two modes of renal replacement therapy.

Dialysis dose

Throughout the study single pool Kt/ V urea values were significantly higher in patients receiving online HDF than in patients treated with different HD prescriptions. There were no significant differences in mean dialysis doses among patients receiving conventional (prior to randomization) or ultrapure high-flux HD (during the study).

Calcium phosphate metabolism

Average pre-treatment concentrations of calcium and iPTH (pre-study period : 18.8 ± 9.2 pmol/l; high-flux HD 19.4 ± 10.1 pmol/l; HDF 17.8 ± 9.8) did not differ between the three treatment modalities. However, haemodiafiltration therapy resulted in both groups (A and B) in significantly lower phosphate levels at unchanged doses of phosphate binders compared with high-flux HD.

Beta 2 microglobulin

Pre-treatment beta 2 microglobulin concentrations were significantly lower in patients receiving high-flux ultrapure HD or HDF compared to conventional HD. The reduction of pre-treatment beta 2 microglobulin concentrations was more pronounced in patients on HDF than in high-flux HD patients (Tables 2 and 3).

Inflammation, anaemia and nutrition

Compared with CRP levels obtained during conventional HD both high-flux ultrapure HD and online HDF were associated with significant decreases in low grade micro-inflammation. Pre treatment serum CRP levels did not differ between patients receiving ultrapure high-flux dialysis and patients treated with online HDF.

Haemoglobin concentrations for patients on pre-study conventional HD or patients randomized to

Table 2. Urea kinetics, pre treatment phosphate and beta-2-microglobulin levels in patients receiving different renal replacement therapies (RRT). Data are given as mean (± SD).

Mode of RRT	Kt/V urea	Serum phosphate (mg/dl)	Serum beta-2-microglobulin (mg/L)
Group A			
CHD	1.3 (0.1)	4.8 (0.5)	34 (3)
HDF 12 months	1.6 (0.1)*	4.1 (0.2)*	20 (4)*
HDF 24 months	1.6 (0.2)*	4.2 (0.3)*	22 (4)*
UHD 12 months	1.3 (0.2)	4.7 (o.4)	28 (2) #
UHD 24 months	1.3 (0.1)	4.9 (0.5)	29 (2) #
Group B			
CHD	1.3 (0.1)	4.9 (0.5)	39 (2)
UHD 12 months	1.2 (0.2)	5.0 (0.4)	26 (1) #
UHD 24 months	1.3 (0.1)	4.8 (0.3)	25 (2) #
HDF 12 months	1.6 (0.1)*	4.3 (0.2)*	20 (2)*
HDF 24 months	1.6 (0.2)*	4.2 (0.3)*	21 (4)*

CHD: conventional (low-flux, commercial dialysis fluid) haemodialysis
UHD: high-flux ultrapure dialysis fluid haemodialysis
HDF: online haemodiafiltration
* $P < 0.05$ vs corresponding values in patients treated with CHD or UHD,
# $P < 0.05$ vs corresponding values in patients treated with CHD or HDF

Table 3. Urea kinetics, pre-treatment serum phosphate and beta-2-microglobulin levels at the end of the pre-study period (CHD), ultrapure haemodialysis (UHD) after 24 months and online HDF (24 months). Data are given as mean (± SD).

Renal replacement therapy	Kt/V urea	Serum phosphate (mg/dl)	Serum beta-2-microglobulin (mg/l)
CHD	1.3 (0.1)	4.9 (0.5)	37 (3)
UHD	1.3 (0.2)	4.9 (0.4)	27 (0.2)#
HDF	1.6 (0.2)*	4.2 (0.3)*	21 (3)*

* $p < 0.05$ vs. data obtained during ultrapure or conventional HD
# $p < 0.05$ vs. data obtained during conventional HD

Table 4. Microinflammation and response to rHu EPO in the two study groups. Data are given as mean (± SD).

Mode of RRT	CRP (mg/dl)	Haemoglobin (g/dl)	EPO dose (IU/kg/week)
Group A			
CHD	1.2 (0.3)	10.3(0.4)	86 (14)
HDF 12 months	0.5 (0.3)*	10.4(0.3)	66 (10)*
HDF 24 months	0.5 (0.3)*	10.5(0.3)	64 (10)*
UHD 12 months	0.6 (0.2)*	10.5(0.3)	66 (12)*
UHD 24 months	0.4 (0.2)*	10.4(0.2)	68 (12)*
Group B			
CHD	0.9 (0.3)	10.2(0.3)	94 (15)
UPD 12 months	0.5 (0.2)*	10.5(0.4	70 (10)*
UPD 24 months	0.5 (0.2)*	10.3(0.3)	68 (12)*
HDF 12 months	0.6 (0.1)*	10.4(0.4)	66 (12)*
HDF 24 months	0.5 (0.2)*	10.5(0.3)	70 (12)*

* $P < 0.05$ versus corresponding parameter during pre-study conventional haemodialysis.

Table 5. Response to rHu EPO at the end of therapy with different renal replacement techniques. Data are given as mean (± SD).

	CRP (mg/dl)	Haemoglobin (g/dl)	Epo Dose (IU/kg/week)
CHD	1.1(0.3)	10.3(0.3)	90(14)
HDF	0.5(0.3)*	10.5(0.3)	66(12)*
UHD	0.5(0.2)*	10.4(0.2)	69(12)*

* $P < 0.05$ vs corresponding parameter at the end of the pre-study phase

Table 6. Parameters of nutritional status in the two study groups. Data are given as mean (± SD).

Renal replacement therapy	Body weight (kg)	U MAC (cm)	Serum albumin (g/dl)
Group A			
CHD	72 (10)	25 (2)	3.6 (0.1)
HDF 12 months	74 (12)*	28 (2)*	3.8 (0.2)*
HDF 24 months	75 (10)*	29 (1)*	3.8 (0.2)*
UHD 12 months	75 (9)*	29 (2)*	3.9 (0.2)*
UHD 24 months	74 (10)*	28 (1)*	3.9 (0.3)*
Group B			
CHD	74 (12)	24 (3)	3.4 (0.2)
UHD 12 months	76 (9)*	26 (2)*	3.8 (0.2)*
UHD 24 months	77 (10)*	26 (3)*	3.9 (0.2)*
HDF 12 months	78 (11)*	27 (1)*	3.8 (0.2)*
HDF 24 months	77 (9)*	26 (2)*	3.8 (0.2)*

* P 0.05 vs corresponding value in the pre-study period.

high-flux HD and online haemodiafiltration did not differ nor did they show any significant change over the time. However, the dose of erythropoietin necessary to maintain target haemoglobin levels was 24 % less in patients treated with ultrapure high-flux HD or 27% less in patients on online haemodiafiltration than in patients on conventional HD. EPO doses did not differ among high-flux dialysis patients and patients on HDF (Tables 4 and 5).

Average dry body weight, upper mid-arm muscle circumference and serum albumin concentrations were all significantly higher in patients on high-flux HD or online HDF than in patients undergoing conventional HD. The means of the nutritional parame-

Table 7. Parameter of nutritional status at the end of the pre-study period and after 2 year ultrapure haemodialysis or online haemodiafiltration

RRT	Body weight (kg)	U MAC	Serum albumin
CHD	73 (12)	25 (3)	3.5 (0.2)
HDF	76 (10)*	28 (3)*	3.8 (0.2)*
UHD	77 (10)*	28 (2)*	3.9 (0.3)*

*P < 0.05 vs corresponding parameter obtained at the end of the pre-study period.

ters did not differ among patients treated with ultrapure dialysis or with online HDF (Tables 6 and 7).

Cardiovascular stability and mode of treatment.

Recordings of pre-dialysis blood pressure values revealed no statistically significant differences between the groups. (mean values : pre-study period 142/ 84 mm Hg, HD 138/ 82 mm Hg, HDF 137/82 mm Hg) Blood pressure did not change significantly over time, nor did the patient groups differ in the number of antihypertensive drugs compared to their pre study treatment. Hypotensive episodes necessitating intervention occurred rarely with all treatment modalities, however, online HDF was associated with an even lower number of hypotensive events (0.4 ± 0.3 events per month per patients in patients on online haemodiafiltration vs. 1.1 ± 0.8 events per month per patient in patients on ultrapure high-flux HD; $p < 0.05$)

Quality of life

The patients in the two treatment groups had similar perceptions of their quality of life. The patients assessment of their physical symptoms showed a sustained improvement during treatment with online HDF, but no change of this dimension with the other modes of therapy (3.8 (0.3) vs. 4.8(0.3); $P < 0.05$). None of the other dimensions of the Kidney Disease Questionnaire showed a change during the course of the study.

Discussion

Post-dilution online HDF is the most commonly used convective renal replacement therapy in clinical practice. The results of this long-term, prospective, randomized trial indicate that routine post-dilution online HDF is an efficient, safe and well tolerated extracorporeal therapy for current ESRD patients even when it is used long-term. Possible clinical benefits of online HDF are thought to be the result of the higher solute removal capacity of small and medium sized uraemic toxins. Furthermore, online HDF combines the use of high-flux synthetic membranes and ultrapure dialysis fluid purity and thereby improves the biocompatibility of the procedure. Another benefit may be due to mode-inherent effects of HDF on thermal balance preventing cardiovascular instability. Therefore, for a direct comparison of HD and online HDF it is essential to use the same membrane type and high microbiological quality of dialysis fluid under identical conditions. Using a cross –over design this study compared online HDF and high-flux HD with ultrapure dialysis fluid over periods of 2 years each to minimize seasonal or carry-over effects.

The superior efficacy of solute removal by online HDF has been confirmed by a number of studies and validated in various patient populations [12]. Accordingly, urea removal as measured by single pool Kt/V was 23 % higher for patients on online HDF than for HD patients in this study. Despite the fact that the results of the HEMO study [6] did not show any positive impact of higher dialysis dose (1.3 vs. 1.7) nor of membrane flux (low vs. high) on the mortality of dialysis patients, heavy weight patients may not reach a Kt/V of at least 1.3 and may be easier provided adequate dialysis doses with online HDF. Another advantage of HDF compared to HD is the improved removal of phosphate, which remains however limited with all modalities. Measurable reductions of hyperphosphataemia were noted in some [19, 22], but not all studies [21]. However, control of phosphate levels required the use of oral phosphate binders in all studies as was true for this study population and HDF induced changes in iPTH concentrations were not noted. Thus, the clinical relevance of HDF induced changes in hyperphosphataemia remained obscure. Another issue is the removal of beta-2 microglobulin which was shown in post-dilution HDF to exceed that in high-flux HD in a number of acute-effects studies, particularly when the substitution volumes were greater than 60 ml/min [12]. Confirming previous data, in the current study mean pre-treatment beta 2 microglobulin concentrations were reduced by 43 % during HDF and by 27 % during high-flux HD compared to conventional HD with impermeable low-flux dialyser membranes and these differences were maintained over the 2 year period. These effects cannot be attributed to differences in residual renal function since the majority of patients (24/34 patients of the high-flux group and 23/ 35 of the HDF group) were anuric at the end of the treatment period. The remaining patients had a mean residual creatinine clearance of 4.7 (± 1.2) after two years of ultrapure high-flux HD and 4.9 (± 1.4) after 2 years of online HD.

There is no doubt that both high-flux HD [8, 9] as well as online HDF postpone clinical complications of AB amyloidosis. Using data from the Lombardy Register, Locatelli et al [10] reviewed 6440 patients and found that the relative risk of carpal tunnel syndrome surgery was 44 % lower in patients treated with haemodiafiltration or haemofiltration compared to conventional HD. Nakai et al. [14] analyzed 1196 patients treated with various modes of RRT to describe the most effective mode of extracorporeal therapy for

the reduction of the incidence of dialysis-related amyloidosis. When the risk for the worst therapeutic effect (low-flux conventional HD) was defined as 1, the risk for patients using high-flux HD was 0.49 , whereas the risk for online haemodiafiltration was 0.013. However, all of these studies demonstrated that circulating beta 2 microglobulin concentrations remained significantly above normal and found no correlation between beta microglobulin levels and clinical signs of dialysis related amyloidosis. Moreover, Baz et al found retrospectively that low flux ultrapure dialysis resulted in a significantly lower rate of carpal tunnel syndrome than HD utilising commercial (potentially contaminated dialysis fluid) [1]. Taken together, these observations indicate that biocompatibility of dialysis may be more important than the flux of the membranes. The findings of the HEMO study, that serum beta 2 microglobulin levels predict mortality in dialysis patients, are of greater clinical importance. Using time dependent Cox regression models, the authors found that the mean cumulative pre dialysis serum beta 2 microglobulin levels but not the dialyser beta 2 microglobulin clearance were associated with all-cause mortality, after adjustment of residual kidney urea clearance and number of pre study years on dialysis. The data support the potential value of beta- 2 microglobulin as a marker to guide chronic HD and the view that improved survival may be the consequence of removal of other solutes with molecular weights similar to that of microglobulin [4].

Both study groups had elevated CRP levels at recruitment. Previous studies have shown that microinflammation may impair the haematopoietic response to rHu-EPO [7, 16]. This study demonstrates an improved correction of renal anaemia despite lower EPO doses in patients switched from conventional to high-flux ultrapure HD or to online HDF. These findings are in accordance with other randomized studies. Noteworthy, Wizemann and colleagues compared low flux dialysis to HDF and suggested no benefit of online HDF on anaemia [21]. However, in the latter study all patients received treatment with the same ultrapure fluid. In the present study, there were no differences in the haematopoietic response among high-flux HD and online HDF.

At recruitment, there were no statistically significant differences in the parameters chosen to characterize nutritional status (body weight, mid-arm circumference, serum albumin) in the patients randomized for 2 years therapy either with HDF or HF, but improved nutritional status could be documented in patients undergoing treatment with filtered dialysis fluid compared to patients receiving conventional HD. The improved biocompatibility and decreased production of inflammatory cytokines may be major mediators of the changes in the nutritional parameters [17]. This interpretation is corroborated by the findings of Wizemann et al, that in patients randomised to receive either low-flux ultrapure HD or online HDF [21]. These authors did not observe a difference in dry weight or plasma albumin concentrations after two years.

Under unmatched conditions (sodium and energy balance) HDF was associated with a lower number of hypotensive episodes. The lower hypotension rates for HDF found in my study may be, at least in part, due to a more positive sodium balance as shown by other authors, who reported that these modes generally remove less sodium than HD [11]. Moreover, according to other investigators, changes in core temperature leading to vasodilatation may also play a role for the altered haemodynamic response[5, 13]. However I cannot argue in favour of these observations as effects of energy balance or sodium balance were not measured in this study.

There have been no studies suggesting that HDF is detrimental, but there is little concrete evidence of a significant benefit on morbidity and mortality. Most investigations were severely underpowered, reported a low mortality rate due to selection of less sick patients and suffered from an insufficient observation period. The Dialysis Outcomes and Practice Pattern Study, a prospective , observational study of a large dialysis population, reported that patients treated with HDF had a 23 % improved survival compared to patients on HD. When these patients were divided into groups according to the amount of convection applied, the survival benefit was statistically significant and independent of Kt/V in the group receiving the largest volume of convection (14-24 l/per session) [2]. Improved quality of life by HDF was observed in this study as well as in an investigation by Ward [20].

High volume online haemodiafiltration techniques mark a step towards coming closer to the native kidney function. The pattern of acceptance will change as positive outcome data from ongoing long term trials accumulate, abating concerns of the higher costs compared to conventional or ultrapure high-flux HD.

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