

Patient- and treatment-related determinants of convective volume in post-dilution haemodiafiltration in clinical practice

E. Lars Penne^{1,2}, Neelke C. van der Weerd^{1,2}, Michiel L. Bots³, Marinus A. van den Dorpel⁴, Muriel P. C. Grooteman^{2,5}, Renée Lévesque⁶, Menso J. Nubé^{2,5}, Piet M. ter Wee^{2,5} and Peter J. Blankestijn¹, On behalf of the CONTRAST investigators*

¹Department of Nephrology, University Medical Center Utrecht, Utrecht, ²Department of Nephrology, VU Medical Center, Amsterdam, ³Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, ⁴Department of Internal Medicine, Maasstad Hospital, Rotterdam, ⁵Institute for Cardiovascular Research VU Medical Center (ICaR-VU), VU Medical Center Amsterdam, Amsterdam, The Netherlands and ⁶Department of Nephrology, Centre Hospitalier de l'Université de Montréal, St-Luc Hospital, Québec, Canada

Correspondence and offprint requests to: P. J. Blankestijn; E-mail: p.j.blankestijn@umcutrecht.nl

*See appendix for the list of CONTRAST investigators.

Abstract

Background. Large convective volumes are recommended for online haemodiafiltration (HDF) to maximize solute removal. There has been little systematic evaluation of factors that determine convective volumes in routine clinical practice.

Methods. In the present study, potential patient- and treatment-related determinants of convective volume were analysed in 235 consecutive patients on post-dilution HDF using multivariable linear regression models. All patients (age 64 ± 14 years; 61% male) participated in the ongoing CONvective TRANsport STudy (CONTRAST). Additionally, differences in convective volumes between dialysers were evaluated.

Results. The mean convective volume was 19.4 ± 4.0 L ($\pm$ SD) per treatment, with a large variation between the participating centres (centre means ranging from 13.4 ± 0.9 L to 24.5 ± 0.12 L, $\pm$ SE). The mean filtration fraction of the blood flow was 25.9 ± 3.6 . In the multivariable analysis, factors that were significantly related to convective volume were haematocrit [inversely, regression coefficient (B) = -1.4 ± 0.4 L per 10%], serum albumin (positively, B = 1.0 ± 0.4 L per 10 g/L), blood flow rate (positively, B = 0.4 ± 0.04 L per 10 mL/min) and treatment time (positively, B = 5.1 ± 0.4 L/h). In addition, significant differences between dialysers were observed, likely explained by different operational conditions.

Conclusions. Apart from increasing the treatment time and blood flow rate, convective volumes could be optimized by increasing the filtration fraction in each individual, provided that transmembrane pressures are well within safe limits. The precise role of dialyser characteristics on maximal achievable convective volumes in clinical practice is a topic for further research.

Keywords: albumin; filtration fraction; haematocrit; haemodiafiltration; post-dilution

Introduction

During haemodiafiltration (HDF), diffusive and convective transport is combined to maximize the removal of uraemic toxins. The addition of convective transport leads to enhanced clearance of middle molecular weight (MMW) uraemic toxins. This has been shown most extensively for beta-2-microglobulin (β_2 m), an established MMW marker molecule with a molecular weight of 11.8 kDa [1–4]. Since β_2 m and other MMW uraemic substances have been related to the extremely high cardiovascular mortality and morbidity in patients with end-stage renal disease [5,6], it has been proposed that increased convective transport improves clinical outcome. In fact, HDF has been associated with improved survival in some observational studies [7–9].

High convective volumes have been recommended to maximize MMW solute removal during HDF [10]. Indeed, a positive relationship between the convective volume and the β_2 m reduction ratio during post-dilution HDF has been shown [1,2]. Moreover, in the DOPPS study, high-efficiency HDF (arbitrarily defined as infusion volumes 15–24 L per treatment) appeared to be related to an improved survival, whereas low-efficiency HDF (infusion volume <15 L per treatment) did not [7].

There is currently limited information available concerning the factors that determine maximal convective volumes in post-dilution HDF in routine clinical practice. Obvious factors include treatment time and dialyser blood flow rate [11]. Apart from that, haemoconcentration within the

dialyser leads to high hydraulic and transmembrane pressures and has been recognized as a limiting factor for total convective volumes [12]. Accordingly, a recent study showed a clear inverse relationship between haematocrit levels and the ratio of the total convective volume to treated blood volume [13]. However, a systematic evaluation of these and other patient- and treatment-related factors on achieved convective volumes in routine clinical practice have not yet been performed.

The CONvective TRANsport STudy (CONTRAST) is an ongoing randomized controlled clinical trial comparing on-line (post-dilution) HDF with low-flux (HD) on all-cause mortality and cardiovascular events [14]. As patient and dialysis characteristics are prospectively collected in CONTRAST, this study offers the unique opportunity to identify the determinants of convective volume in clinical practice. We especially aimed to recognize modifiable factors in an effort to optimize HDF treatment.

Patients and methods

Patients

In the present study, we included 256 consecutive HDF patients from 26 dialysis centres (24 Dutch centres, 1 Norwegian and 1 Canadian centre) who were enrolled in the CONvective TRANsport STudy (CONTRAST, ISRCTN38365125) and had completed 6 months of follow-up. Patient and dialysis characteristics at the 6-month visit were used for the present analyses. Twenty-one patients were not treated with HDF at the 6-month study visit because of vascular access problems (5 patients), unavailability of substitution fluids (3 patients) or other reasons (13 patients). Analyses were therefore restricted to 235 patients.

Before randomization in the CONTRAST trial, all patients were treated with low-flux HD (two or three times per week, for at least 2 months) with a minimum dialysis urea $Kt/V \geq 1.15$ and age ≥ 18 years. Main exclusion criteria were (1) treatment with high-flux HD or haemo(dia)filtration in the preceding 6 months, (2) severe non-compliance and (3) life expectancy < 3 months due to non-renal disease. The study was conducted in accordance with the Declaration of Helsinki and good clinical practice guidelines and was approved by the institutional review board of each participating centre. Written informed consent was obtained from all patients prior to randomization.

HDF prescription

Online HDF was performed in the post-dilution mode, using one of the dialysers as summarized in Table 1. The target convective volume was arbitrarily set at 6 L/h (or 100 mL/min). According to the CONTRAST protocol, the filtration fraction should not exceed 33%. The operator's user manual of the FX-class dialysers (Fresenius Medical Care, Bad Homburg, Germany) recommends that 25% of the blood flow should be the maximum substitution flow. The manual of the Polyflux dialysers (Gambro Corporation, Lund, Sweden) does not give specific advice on maximum filtration fraction.

Treatment times were fixed at baseline and could only be increased if the dialysis urea $spKt/V$ were below 1.2. Sterile and non-pyrogenic substitution fluids were produced by ultrafiltration of the ultrapure dialysate. Ultrapure quality was defined as bacterial counts < 0.1 colony forming unit per mL (CFU/mL) and endotoxin levels < 0.025 endotoxin units per mL (EU/mL). The microbiological water quality of the dialysis fluid was regularly monitored. Anticoagulation was performed with low molecular weight heparin before treatment. All routine patient care, e.g. metabolic control, was performed according to the guidelines of the Quality of Care Committee of the Dutch Federation of Nephrology. The following dialysis systems were used for online HDF: 4008/5008 ONLINE (Fresenius), AK 100/200 ULTRA (Gambro) and DBB05 (Nikkiso, Tokyo, Japan) dialysis systems. At the time of analysis, the dialysis frequency of the patients was two times per week in 6.4% ($n = 15$), three times per week in 93% ($n = 218$), four times per week in 0.4% ($n = 1$) and six times per week in 0.4% ($n = 1$).

Data collection

Demographical data and data on medical history, including diabetic state, previous cardiovascular disease (CVD), vascular access and time on renal replacement therapy (RRT) were collected at the CONTRAST baseline study visit. All other data were collected at the 6-month study visit, including blood pressure level, body mass index (BMI) and various parameters of dialysis adequacy and prescription (treatment time, blood flow rate, intradialytic weight loss and infusion volume). Blood samples were collected before the start of a dialysis session for determination of haemoglobin, haematocrit, thrombocytes and serum albumin. All laboratory assessments were analysed in the laboratories of the participating centers by standard laboratory techniques.

The infusion volume (L per treatment) represents the amount of substitution fluid infused directly downstream of the dialyser (post-dilution). The convective volume (L per treatment) was calculated by the sum of the intradialytic weight loss and the infusion volume per treatment and reported as the mean value of three consecutive dialysis treatments (i.e. 3 different days). The convective flow rate represents the convective volume per minute (mL per min). The filtration fraction (FF in%) is defined as the ratio between the convective flow rate and the dialyser blood flow rate. High-efficiency HDF was defined as a total infusion volume of ≥ 15 L per treatment [7]. Blood pressure (BP, in mmHg) was registered both as pre-dialysis systolic BP (SBP) and diastolic BP (DBP) and as the mean of pre- and post-dialysis values of 3 consecutive dialysis days. The reported blood flow rates represent the flow rates as displayed by the dialysis machines. Body mass index (BMI) was calculated by weight (kg) divided by the square of height (m^2).

Data analysis

Data were reported as proportions or as means with standard deviation (SD) or standard errors (SE) when appropriate. To study the independent relationship of each variable with convective volume, we used multivariable linear regression analysis. We entered all patient- and dialysis-related variables in a multivariable model that showed a univariable relationship with the convective volume using a cut-off P -value < 0.15 . In addition, haematocrit, blood flow rate and treatment time were entered in the multivariable model up front. The multivariable model was adjusted for dialyser type and dialysis machine, to correct for possible differences between dialysers, dialysis-operating procedures and centre effects.

In a separate analysis, differences between dialysers were evaluated. Mean values of all characteristics that were significant in the multivariate regression model were reported for each dialyser category. Convective volumes were reported both unadjusted and after multivariable adjustment. Results were considered statistically significant when $P < 0.05$ (two-tailed). We used the SPSS software for all analyses (version 16.0.1; SPSS Inc. Headquarters, Chicago, Illinois, USA).

Results

The mean age of the patients was 64 ± 14 years, and 61% were male (Table 2). The mean convective volume was 19.4 ± 4.0 L ($\pm$ SD) per treatment (range 6.7–28.2 L) and the mean filtration fraction was $25.9 \pm 3.6\%$ (range 11.2–36.8%). The blood flow rate was 333 ± 44 mL/min. Seventy-eight percent of the patients were treated with high-efficiency HDF defined as infusion volumes ≥ 15 L (i.e. convective volume ≥ 17 L, assuming mean intradialytic weight loss of 2 L). The pre-defined target convective volume of ≥ 6 L/h was reached in 43 of the 235 patients (18%). These 43 patients had lower haematocrit levels [37 ± 0.3 versus $34 \pm 0.6\%$ ($\pm$ SE, $P < 0.001$) in the remaining patients], higher albumin levels (38 ± 0.5 versus 36 ± 0.3 g/L, $P = 0.002$) and were treated with higher blood flow rates (384 ± 5 mL/min versus 322 ± 3 , $P < 0.001$). In 10 of the 26 centres, the target convective volume of ≥ 6 L/h was reached in none of the patients. In two centres, the target was reached in all patients. Centre means of convective volume ranged from 13.4 ± 0.9 L to 24.5 ± 0.12 L ($\pm$ SE) per treatment (Figure 1).

Table 1. Characteristics of dialysers for HDF

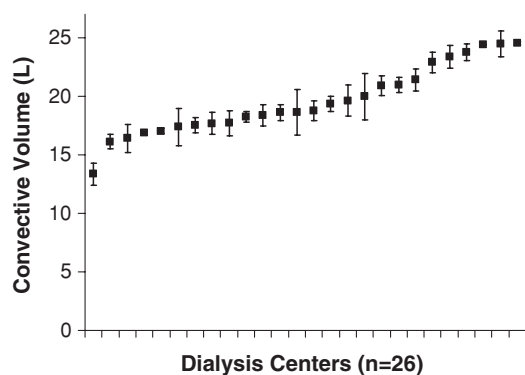
Company	Dialyser	Membrane material	Effective surface area (m ²)	Fibre inner diameter (µm)	UF coefficient ^a (mL/h/mmHg)	Effective fibre length (mm)
Fresenius medical care	FX80	Polysulfone	1.8	185	59	225
Fresenius medical care	FX100	Polysulfone	2.2	185	73	225
Fresenius medical care	Optiflux F 200NR	Polysulfone	2.0	200	56	280
Gambro corporation	Polyflux 170H	Polyarylethersulfone/ polyamide	1.7	215	70	270
Gambro corporation	Polyflux 210H	Polyarylethersulfone/ polyamide	2.1	215	85	270

^aUF coefficients as given by the manufacturer, measured *in vitro* at 37°C with bovine blood (Ht = 32% and protein = 60 g/L).

Table 2. Patient characteristics of 235 chronic HDF patients

	Mean ± SD or %
Male	61
Age (years)	64 ± 14
Body mass index (kg/m ²)	25 ± 4.5
History of cardiovascular disease	44
Diabetes mellitus	26
Time on renal replacement therapy (years)	3.6 ± 4.1
Systolic blood pressure (mmHg)	141 ± 20
Diastolic blood pressure (mmHg)	72 ± 12
Vascular access:	
Fistula	78
Graft	18
Central venous catheter	4
Haemoglobin (mmol/L)	7.4 ± 0.8
Haematocrit (%)	36 ± 4.3
Thrombocytes (× 10 ⁹ /L)	227 ± 73
Serum albumin (g/L)	36 ± 4.5
Treatment time (min)	225 ± 24
Blood flow rate (mL/min)	333 ± 44
Intradialytic weight loss (L per treatment)	1.9 ± 0.9
Infusion volume (L per treatment)	17.5 ± 3.8
Convection volume (L per treatment)	19.4 ± 4.0
Convective flow rate (mL/min)	86.1 ± 16
Filtration fraction (%)	25.9 ± 3.6

To convert haemoglobin from mmol/L to g/dL multiply by 1.61. To convert albumin from g/L to d/dL divide by 10.

**Fig. 1.** Mean convective volumes per dialysis centre. Bars represent SE of the means.

Patient-related factors

In the univariable analysis, male sex, body mass index, serum albumin, haemoglobin and haematocrit were related to the convective volume. Age, a history of cardiovascular disease, diabetic state, dialysis vintage, blood pressure

Table 3. Determinants of convective volume in post-dilution HDF: univariable and multivariable linear regression analysis

Determinant	Univariable model		Multivariable model	
	B	95% CI	B	95% CI
Sex (male)	1.8	0.7–2.8 [†]	0.47	–0.16–1.1
Age (years)	0.0	–0.04–0.03		
BMI (kg/m ²)	0.14	0.03–0.25 [†]	0.028	–0.04–0.09
History of CVD	–0.14	–1.2–0.90		
DM	0.67	–0.50–1.8		
Time on RRT (years)	0.01	–0.1–0.1		
SBP (mmHg)	0.0	–0.03–0.02		
DBP (mmHg)	0.01	–0.03–0.06		
Vascular access (Fistula)	–0.3	–1.5–1.0		
Haemoglobin (mmol/L)	–0.89	–1.5 to –0.28 [†]		
Haematocrit (%)	–0.18	–0.30 to –0.06 [†]	–0.14	–0.22 to –0.07 [†]
Thrombocytes (× 10 ⁹ /L)	–0.003	–0.01–0.004		
Serum albumin (g/L)	0.19	0.07–0.3 [†]	0.10	0.02–0.18 [†]
Treatment time (min)	0.09	0.07–0.10 [†]	0.09	0.07–0.10 [†]
Blood flow rate (mL/min)	0.05	0.04–0.06 [†]	0.04	0.03–0.05 [†]

The multivariable model was adjusted for dialyser and for dialysis system.
[†]*P* < 0.05.

*R*² of the multivariable model = 0.71.

B reflects the change of the total convective volume (in L per treatment) related to one unit increment of the determinant.

(either measured as pre-dialysis DBP and SBP or as the average of pre- and post-dialysis values), vascular access and thrombocyte levels did not show an association with the convective volume (Table 3). In the multivariable analysis, serum albumin was positively and haematocrit was inversely related to the convective volume. Male sex and BMI were no longer significant in the multivariable model. In Figures 2 and 3, the relationships between albumin and haematocrit with the convective volume are depicted after multivariable adjustments.

Treatment-related factors

Blood flow rate [B = 0.04 L per mL/min (95% CI 0.03–0.05, *P* < 0.001)] and treatment time [B = 0.09 L per min (95% CI 0.07–0.10, *P* < 0.001)] were positively related to the convective volume in the multivariable model (Table 3).

Table 4. Comparison of dialysers

	European centres [§] FX80	FX100	Polyflux 170H	Polyflux 210H	Canadian centre Optiflux F 200NR
<i>N</i> (patients)	57	34	46	78	17
<i>N</i> (centres) [#]	8	4	7	14	1
Dialysis system					
4008/5008	53 (93%)	17 (50%)	6 (13%)	11 (14%)	17 (100%)
AK 100/200	4 (7%)	1 (3%)	37 (78%)	59 (76%)	0 (0%)
DBB05	0 (0%)	16 (47%)	3 (7%)	8 (10%)	0 (0%)
Haematocrit (%)	38 ± 0.6	36 ± 0.8	37 ± 0.7	36 ± 0.4	33 ± 1.0 ^{a,b,c,d}
Serum albumin (g/L)	37 ± 0.5	38 ± 0.8	33 ± 0.6 ^{a,b,d,e}	36 ± 0.5 ^b	37 ± 0.6
Blood flow (mL/min)	301 ± 4.5	325 ± 6.5 ^a	322 ± 5.1 ^a	356 ± 4.0 ^{a,b,c}	372 ± 10.3 ^{a,b,c}
Treatment time (min)	231 ± 3.2	208 ± 4.7 ^{a,c,d}	227 ± 3.0	229 ± 2.3	215 ± 5.2 ^d
Unadjusted convective volume (L per treatment)	17.9 ± 0.4	16.6 ± 0.8	18.8 ± 0.5 ^b	20.9 ± 0.4 ^{a,b,c}	23.8 ± 0.7 ^{a,b,c,d}
Filtration fraction (%)	25.8 ± 0.4	24.6 ± 0.9	25.7 ± 0.4	25.6 ± 0.3	29.9 ± 0.6 ^{a,b,c,d}
Adjusted convective volume [†] (L per treatment)	18.2 ± 0.4	18.7 ± 0.5	19.5 ± 0.4 ^a	19.8 ± 0.3 ^a	22.2 ± 0.6 ^{a,b,c,d}

Mean ± SE or *n* (%).

[§]24 Dutch and 1 Norwegian dialysis centres.

[#]More than one dialyser can be used per centre.

[†]Adjusted for: dialysis system, haematocrit, albumin, blood flow rate and treatment time.

^a*P* < 0.05 versus FX80; ^b*P* < 0.05 versus FX100; ^c*P* < 0.05 versus Polyflux 170H; ^d*P* < 0.05 versus Polyflux 210H; ^e*P* < 0.05 versus Optiflux F 200NR.

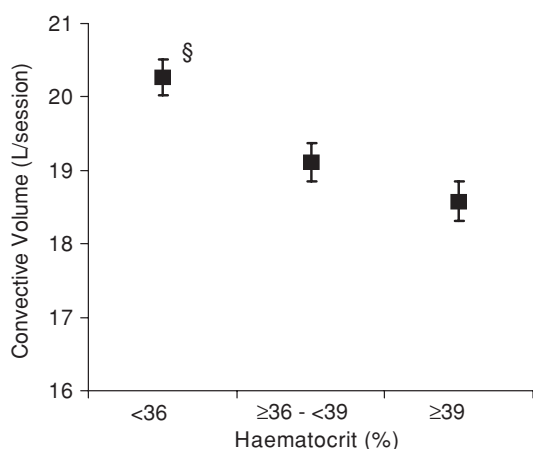


Fig. 2. Relationship between haematocrit and convective volume, adjusted for dialysis system, type of dialyser, serum albumin, blood flow rate and treatment time. Haematocrit levels in tertiles, bars represent SE. §versus 2nd tertile: *P* = 0.002; versus 3rd tertile: *P* < 0.001.

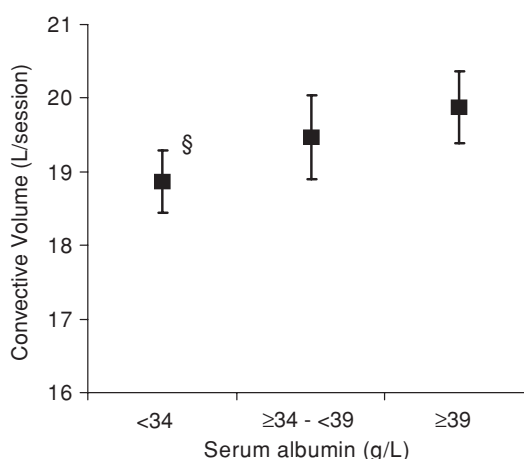


Fig. 3. Relationship between serum albumin and convective volume, adjusted for dialysis system, type of dialyser, haematocrit, blood flow rate and treatment time. Albumin levels in tertiles, bars represent SE. §versus 3rd tertile: *P* < 0.05.

In Table 4, the different prescribed dialysers are compared. FX80 dialysers were prescribed in 24% of the patients, FX100 dialysers in 20%, and Polyflux 170H and 210H dialysers in 20% and 33%, respectively. Optiflux F 200NR dialysers were prescribed in 7% of the patients, all from one single centre. Three patients (1%) used alternative dialysers and were excluded from the multivariable analyses. Haematocrit and serum albumin levels, treatment times, blood flow rates and convective volumes were all different between the dialysers (Table 4). When dialysers of similar materials were compared (FX100 versus FX80 and Polyflux 210H versus Polyflux 170H), blood flow rates were significantly higher in the patients treated with the largest dialysers (i.e. FX100 and Polyflux 210H). However, after multivariable adjustment (including adjustment for blood flow rate), convective volumes were not significantly dif-

ferent between FX100 and FX80 dialysers and between Polyflux 210H and Polyflux 170H dialysers (Table 4). The highest convective volumes were achieved in the patients using Optiflux F 200NR dialysers (all from one centre). In these patients, the haematocrit level was significantly lower ($33 \pm 1.0\%$ versus $37 \pm 4.2\%$, *P* < 0.002) and the filtration fraction was higher ($29.9 \pm 0.6\%$ versus $25.5 \pm 0.2\%$, *P* < 0.001) in comparison with patients using other dialysers.

Discussion

To the best of our knowledge, the present study is the first in which patient- and treatment-related determinants of convective volume were systemically evaluated in a large

group of patients on post-dilution HDF in clinical practice. We observed higher convective volumes in patients with low haematocrit and/or high serum albumin levels. Dialysis treatment time and blood flow rate were identified as treatment-related determinants of the convective volume. Apart from that, we found considerable differences in convective volume between centres, which could only partly be explained by patient or treatment characteristics.

The mean convective volume of 19.4 ± 4.0 L per treatment in the present study is comparable to the 18 to 23 L achieved in most other studies in patients on post-dilution HDF [1,3,9,13]. In few small studies, post-dilution infusion volumes up to 30 L per treatment have been reported [4,15]. In these studies, especially mean blood flow rates were much higher (400 mL/min) as compared to 333 mL/min in the present study. At the time of the conception of the study, it was unclear which amount of convective volume could be considered adequate or sufficient. The target volume was arbitrarily set at 6 L/h. More recently, the DOPPS data became available, indicating that volumes of ~ 17 L per session (15 L infusion + 2 L net weight loss) and higher were associated with survival benefit [7]. To date, these are still the only data relating volume to clinical outcome. The pre-defined treatment target of 6 L/h was achieved in only 18% of the patients. However, 78% of the patients were treated with volumes of 17 L per session and higher.

Patient-related factors

Blood viscosity has been recognized as an important limiting factor of convective transport [12]. Post-dialyser haematocrit values rise up to 54% during treatment [16], which together with a comparable rise in plasma protein levels may reduce the hydraulic permeability of the dialyser. As a consequence, the resistance to flow in the dialyser will increase, and eventually, clotting of dialyser fibres may occur [17]. In line with this notion, we and others [13] found an inverse relationship between the pre-dialysis haematocrit level and convective volume. The optimal haematocrit level for dialysis patients remains to be established, but for post-dilution HDF values should not exceed treatment targets. In the present study, 52% of the patients had haemoglobin levels above the current KDOQI target of 7.4 mmol/L (12 g/dL), which may have contributed to suboptimal convective volumes.

Serum albumin was positively related to the convective volume, although its contribution was limited (1 L per treatment increase of convective volume per 10 g/L albumin, Table 3). It is likely that higher colloid osmotic pressures in patients with high serum albumin levels enhance plasma refill rates, thus allowing more convective transport [18]. Alternatively, increased platelet aggregation [19] or reduced red cell deformability [20] in patients with hypoalbuminaemia may limit the convective volume. On the other hand, high protein levels may decrease membrane permeability by increasing the thickness of the protein layer on the membrane [17]. However, total protein levels were not measured in this study. Likely, the beneficial effects of high albumin on the convective volume are the result of opposite factors. It is therefore unclear whether albumin levels higher than the range in this study would still be benefi-

cial. Nevertheless, paying attention to the nutritional and inflammatory state in patients with low albumin levels may contribute to high convective volumes and may, more importantly, improve clinical outcome [21].

Treatment-related factors

Apart from treatment time and blood flow rate, the dialyser type was related to the convective volume, also after multivariable adjustments. However, the present study was not designed to investigate differences between dialysers. A reliable comparison between dialysers can only be made in relation to the applied transmembrane pressure. Since transmembrane pressures were not assessed, it is unknown whether maximal tolerable and safe transmembrane pressures were applied in all patients. In contrast, the large differences in convective volumes between centres suggested that HDF was not performed at maximal transmembrane pressures in several centres. Nevertheless, it can be hypothesized that the design of the dialyser plays a role on maximal achievable convective volumes. Dialyser characteristics such as fibre length or fibre diameter have substantial effects on the pressure profile [22–24], which could influence maximal convective transport. In addition, the membrane type may have an effect on the water permeability. Recently, it has been shown that almost similar synthetic high-flux dialysers may be different in terms of middle molecule removal and solute trapping [25]. Finally, a large surface area may allow higher blood flow rates and could therefore be beneficial to optimize exchange volumes. The precise role of the above-mentioned dialyser characteristics in clinical practice needs further evaluation.

The user manual of some manufacturers recommends that the filtration fraction should not exceed 25%. However, the present study demonstrates that higher filtration fractions are tolerated in many patients. For example, the mean filtration fraction in the Canadian centre was 30%. It should be noted that an increase of the filtration fraction from 25% to 30% has substantial effects on the total convective volume. During a regular HDF session (treatment time 4 h, blood flow rate 350 mL/min), a 5% increase of the filtration fraction leads to an increase of the convective volume of 4.2 L.

To improve convective volumes in post-dilution HDF in clinical practice, the treatment time and blood flow rate should be increased first if possible. Then, the filtration fraction should be increased within the limits of safe transmembrane pressures, taking into account haematocrit and protein levels and possibly also dialyser characteristics.

Limitations and strengths

All patients participated in a randomized trial and satisfied predefined inclusion criteria, which may have limited the generalizability of the results. On the other hand, the inclusion criteria were meant to include the average chronic HD patient, and all patients were randomly allocated to HDF treatment. Furthermore, the data for this study were not specifically collected to investigate determinants of convective volume. For example, the indication to prescribe a certain dialyser to a patient was unknown. It is possible that

larger dialysers were more often prescribed for patients with lower convective volumes in an effort to improve treatment. Moreover, transmembrane pressures were not assessed, limiting the possibilities to compare different dialysers. Effects of dialyser characteristics on convective volumes should be evaluated in specifically designed prospective studies. Finally, it should be noted that the definition of filtration fraction (i.e. filtered fraction of the blood flow) as frequently used in clinical practice is theoretically incorrect, since it does not take into account differences in haematocrit level. Ideally, the fraction of the plasma flow should be used instead. However, this is not very practical in everyday clinical practice. The strengths of this study were the large number of patients, allowing for multivariable comparisons, and the prospective and standardized data collection.

Optimizing convective volumes may be of clinical relevance and has been recommended by the European Best Practice Guidelines [10]. Moreover, data from DOPPS suggest that infusion volumes should be at least 15 L per treatment in order to improve clinical outcomes with online HDF [7]. Whether the differences within the observed range of convective volumes in the present study are of any clinical relevance is currently unknown. The CONTRAST study may provide data to answer that question.

Conclusion

The present study suggests that a sufficient treatment time and/or blood flow rate are a prerequisite to achieve convective volumes that are presently considered adequate [7]. In addition, attention should be paid to current haemoglobin treatment targets and the nutritional and inflammatory state, since convective volumes may be attenuated by high haematocrit or low albumin levels. The precise role of dialyser characteristics on maximal achievable convective volumes is a topic for further research. The data suggest that within the haematocrit range of this study, which represents everyday clinical practice, filtration fraction could be higher than recommended by some of the manufacturers. As minor changes of the filtration fraction have substantial effects on the total convective volume, the maximal tolerable filtration fraction for each individual patient should be assessed for treatment optimization.

Acknowledgements. CONTRAST is financially supported by a grant from the Dutch Kidney Foundation (Nierstichting Nederland grant C02.2019) and unrestricted grants from Fresenius Medical Care (The Netherlands) and Gambro Lundia AB (Sweden). Additional support was received from the Dr E.E. Twiss Fund, Roche, The Netherlands, the International Society of Nephrology/Baxter Extramural Grant Program and the Dutch Organization for Health Research and Development (ZonMW grant 17088.2802). We would like to acknowledge all patients and medical staff that participated in this project.

Conflict of interest statement. None declared.

Appendix

Contrast investigators. In Canada: M Dorval, Dr Georges-L Dumont Regional Hospital, Moncton; and R Levesque,

St-Luc Hospital, Montreal. In The Netherlands: MG Koopman, Academic Medical Center, Amsterdam; CJ Konings, Catharina Hospital, Eindhoven; WP Haanstra, Dialysis Clinic Noord, Beilen; P Vos, Dianet Dialysis Centers, Utrecht; T Noordzij, Franciscus Hospital, Roosendaal; GW Feith, Gelderse Vallei Hospital, Ede; M van Buren, Haga Hospital, The Hague; JJ Offerman, Isala Clinics, Zwolle; EK Hoogeveen, Jeroen Bosch Hospital, 's Hertogenbosch; F de Heer, Maasland Hospital, Sittard; PJ van de Ven, Maasstad Hospital, Rotterdam; TK Kremer Hovinga, Martini Hospital, Groningen; W Bax, Medical Center Alkmaar, Alkmaar; JO Groeneveld, Onze Lieve Vrouwe Gasthuis, Amsterdam; AT Lavrijssen, Oosterschelde Hospital, Goes; AM Schrander-Van der Meer, Rijnland Hospital, Leiderdorp; LJ Reichert, Rijnstate Hospital, Arnhem; J Huussen, Slingeland Hospital, Doetinchem; PL Rensma, St Elisabeth Hospital, Tilburg; Y Schrama, St Franciscus Gasthuis, Rotterdam; HW van Hamersvelt, University Medical Center St Radboud, Nijmegen; WH Boer, University Medical Center Utrecht, Utrecht; WH van Kuijk, VieCuri Medical Center, Venlo; MG Vervloet, VU Medical Center, Amsterdam; and IM Wauters, Zeeuws-Vlaanderen Hospital, Terneuzen. In Norway: I Sekse, Haukeland University Hospital, Bergen.

References

1. Lin CL, Yang CW, Chiang CC *et al.* Long-term on-line hemodiafiltration reduces predialysis beta-2-microglobulin levels in chronic hemodialysis patients. *Blood Purif* 2001; 19: 301–307
2. Lornoy W, Becaus I, Billioux JM *et al.* On-line haemodiafiltration. Remarkable removal of beta2-microglobulin. Long-term clinical observations. *Nephrol Dial Transplant* 2000; 15: 49–54
3. Ward RA, Schmidt B, Hullin J *et al.* A comparison of on-line hemodiafiltration and high-flux hemodialysis: a prospective clinical study. *J Am Soc Nephrol* 2000; 11: 2344–2350
4. Maduell F, Navarro V, Cruz MC *et al.* Osteocalcin and myoglobin removal in on-line hemodiafiltration versus low- and high-flux hemodialysis. *Am J Kidney Dis* 2002; 40: 582–589
5. Cheung AK, Rocco MV, Yan G *et al.* Serum beta-2 microglobulin levels predict mortality in dialysis patients: results of the HEMO study. *J Am Soc Nephrol* 2006; 17: 546–555
6. Vanholder R, Argiles A, Baurmeister U *et al.* Uremic toxicity: present state of the art. *Int J Artif Organs* 2001; 24: 695–725
7. Canaud B, Bragg-Gresham JL, Marshall MR *et al.* Mortality risk for patients receiving hemodiafiltration versus hemodialysis: European results from the DOPPS. *Kidney Int* 2006; 69: 2087–2093
8. Jirka T, Cesare S, Di BA *et al.* Mortality risk for patients receiving hemodiafiltration versus hemodialysis. *Kidney Int* 2006; 70: 1524–1525
9. Panichi V, Rizza GM, Paoletti S *et al.* Chronic inflammation and mortality in haemodialysis: effect of different renal replacement therapies. Results from the RISCVID study. *Nephrol Dial Transplant* 2008; 23: 2337–2343
10. Tattersall J, Martin-Malo A, Pedrini L *et al.* EBP guideline on dialysis strategies. *Nephrol Dial Transplant* 2007; 22: ii5–ii21
11. Maduell F. Optimizing the prescription of hemodiafiltration. *Contrib Nephrol* 2007; 158: 225–231
12. Pedrini LA, De Cristofaro V, Pagliari B *et al.* Mixed predilution and postdilution online hemodiafiltration compared with the traditional infusion modes. *Kidney Int* 2000; 58: 2155–2165

13. Joyeux V, Sijpkens Y, Haddj-Elmrabet A *et al.* Optimized convective transport with automated pressure control in on-line postdilution hemodiafiltration. *Int J Artif Organs* 2008; 31: 928–936
14. Penne EL, Blankestijn PJ, Bots ML *et al.* Effect of increased convective clearance by on-line hemodiafiltration on all cause and cardiovascular mortality in chronic hemodialysis patients—the Dutch CONvective TRANsport STudy (CONTRAST): rationale and design of a randomised controlled trial [ISRCTN38365125]. *Curr Control Trials Cardiovasc Med* 2005; 6: 8
15. Pedrini LA, De Cristofaro V. On-line mixed hemodiafiltration with a feedback for ultrafiltration control: effect on middle-molecule removal. *Kidney Int* 2003; 64: 1505–1513
16. Spalding EM, Pandya P, Farrington K. Effect of high haematocrit on the efficiency of high-flux dialysis therapies. *Nephron Clin Pract* 2008; 110: c86–c92
17. Henderson LW. Biophysics of ultrafiltration and hemofiltration. In: Jacobs C, Kjellstrand CM, Koch KM, Winchester JF (eds). *Replacement of Renal Function by Dialysis*. Dordrecht, The Netherlands: Kluwer 1996; 114–145
18. Rodriguez M, Llach F, Pederson JA *et al.* Changes in plasma oncotic pressure during isolated ultrafiltration. *Kidney Int* 1982; 21: 519–523
19. Kim SB, Chi HS, Park JS *et al.* Effect of increasing serum albumin on plasma D-dimer, von Willebrand factor, and platelet aggregation in CAPD patients. *Am J Kidney Dis* 1999; 33: 312–317
20. Joles JA, Willekes-Koolschijn N, Koomans HA. Hypoalbuminemia causes high blood viscosity by increasing red cell lysophosphatidylcholine. *Kidney Int* 1997; 52: 761–770
21. Levin NW, Kotanko P. Improving albumin levels among hemodialysis patients. *Am J Kidney Dis* 2006; 48: 171–173
22. Ronco C, Orlandini G, Brendolan A *et al.* Enhancement of convective transport by internal filtration in a modified experimental hemodialyzer: technical note. *Kidney Int* 1998; 54: 979–985
23. Ronco C, Brendolan A, Lupi A *et al.* Effects of a reduced inner diameter of hollow fibers in hemodialyzers. *Kidney Int* 2000; 58: 809–817
24. Sato Y, Mineshima M, Ishimori I *et al.* Effect of hollow fiber length on solute removal and quantification of internal filtration rate by Doppler ultrasound. *Int J Artif Organs* 2003; 26: 129–134
25. Ouseph R, Hutchison CA, Ward RA. Differences in solute removal by two high-flux membranes of nominally similar synthetic polymers. *Nephrol Dial Transplant* 2008; 23: 1704–1712

Received for publication: 18.3.09; Accepted in revised form: 11.5.09

Nephrol Dial Transplant (2009) 24: 3499–3504

doi: 10.1093/ndt/gfp312

Advance Access publication 25 June 2009

Safety and efficacy of percutaneous insertion of peritoneal dialysis catheters under sedation and local anaesthetic

Scott Henderson, Edwina Brown and Jeremy Levy

Imperial College Kidney and Transplant Institute, Imperial College Healthcare NHS Trust, Du Cane Road, London, W12 OHS, UK

Correspondence and offprint requests to: Jeremy Levy; E-mail: j.levy@imperial.ac.uk

Abstract

Background. Success of peritoneal dialysis (PD) is partially dependent on the ease of insertion of the catheter. We have been inserting PD catheters percutaneously in a majority of our patients under local anaesthetic and sedation by physicians, and detail here the outcomes for 283 catheters inserted in this manner, and 150 patients with surgical catheter insertion by laparotomy or laparoscopy.

Methods. Data were collected prospectively on all patients having PD catheters inserted between 1999 and 2008, including success of insertion, complications and infections.

Results. A total of 283 catheters were inserted percutaneously using a Seldinger technique under sedation and local anaesthesia, and 150 surgically under general anaesthetic. Eighty-six percent of the percutaneous catheters and 66% surgical catheters were first catheters. No major complications occurred. In 7% of the percutaneous patients and 5% surgical patients, the procedure failed or was abandoned. Poor initial drainage occurred in 21% insertions but resolved in most cases and resolved dialysate leak in 6%. Wound infections or peritonitis occurred in 9% and 4% of

percutaneous insertions. Only 13% of patients could not use their catheter at 1 month after percutaneous insertion, and 83% of the patients remained on PD using the original catheter at 6 months.

Conclusions. Percutaneous PD catheter insertion was associated with a very low complication rate and high primary success rate, and was highly efficient in use of resources and avoided the need for general anaesthesia.

Keywords: dialysis access; peritoneal dialysis; peritonitis

Introduction

Peritoneal dialysis (PD) remains an important dialysis modality. In the UK, 20% of new patients starting dialysis opt for PD, and PD represents 44% of all dialysis modalities in New Zealand [1]. Peritoneal dialysis avoids the need for vascular access, is a home-based therapy and may reduce

Copyright of Nephrology Dialysis Transplantation is the property of Oxford University Press / UK and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.