Con-Current versus Counter-Current Dialysate Flow during CVVHD. A Comparative Study for Creatinine and Urea Removal

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Key Words

CRRT · ICU · Haemofiltration · ARF · Dialysate · Counter-current

Abstract

Background: Dialysate fluid connection to the membrane in continuous dialysis may affect solute clearance. Although circuit connections are routinely made counter-current to blood flow in intermittent dialysis, no study has assessed the effect of this dialysate fluid flow direction on removal of small solutes creatinine and urea during treatment using continuous veno-venous haemodialysis (CVVHD). **Aims:** To assess if dialysate flow direction during CVVHD affects small solute removal. **Methods:** This ethics-approved study recruited a convenience sample of 26 adult ICU patients requiring continuous dialysis to assess urea and creatinine removal for con-current vs. counter-current dialysate flow direction. The circuit was adjusted from continuous veno-venous haemodiafiltration to CVVHD 20 min prior to sampling with no fluid removal. Blood (b) and spent dialysate fluid (f) were taken in both concurrent and counter-current fluid flow at 1 (T1) and 4 (T4) hours with a new treatment. Blood flow was 200 ml/min. Dialysate flow 33 ml/min. Removal of urea and creatinine was expressed as the dialysate/plasma concentration ratio: U_f/b and C_f/b respectively.

Data lacking normal distribution are presented as median with 25th and 75th interquartile ranges (IQR), otherwise as mean with SD and assessed with the independent t test for paired data. $p < 0.5$ was considered significant. **Results:** Fifteen male patients were included with a median (IQR) age of 67 years (52–75), and APACHE II score 17 (14–19) with all patients meeting RIFLE criteria 'F'. At both times, the counter-current dialysate flow was associated with higher mean (SD) dialysate/plasma concentration ratios: T1 0.87 (0.16) vs. 0.77 (0.10), $p = 0.006$; T2 0.96 (0.16) vs. 0.76 (0.09), $p < 0.001$ for creatinine and T1 0.98 (0.09) vs. 0.81 (0.09), $p < 0.001$; T2 0.99 (0.07) vs. 0.82 (0.08), $p < 0.001$ for urea. **Conclusion:** Counter-current dialysate flow during CVVHD for ICU patients is associated with an approximately 20% increase in removal of small solutes creatinine and urea.

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Study Background

Solute removal during continuous veno-venous haemodialysis (CVVHD) is achieved by exposure of blood to dialysate fluid across a semi-permeable membrane [1–4]. The circuit set up for this technique can establish blood

and fluid flow as concurrent with direction alignment, or as counter-current and opposing direction (see figure 1) [5, 6]. The counter-current approach is used for intermittent haemodialysis to provide maximum diffusive gradient as fresh dialysate fluid is continuously exposed to solute-laden blood [2, 3], and appears to have been adopted from the beginning of dialysis in the 1950s where a blood-filled circuit was immersed in a salt bath [7, 8]. During modern dialysis the blood flow (e.g. 300 ml/min) and fluid (300–500 ml/min) flow rate is faster when compared to continuous techniques such as CVVHD(F) [3] and with a higher solute removal rate.

This aspect of circuit set up is also used in CVVHD(F), despite the dialysate flow rate being approximately 10% of a dialysis treatment and much slower (e.g. 33 ml/min commonly) [9]. During CVVHD(F), the blood flow rate is frequently 150–200 ml/min, and with a slow dialysate flow as described, blood and fluid exposure time is longer and diffusion of solutes limited by the slower fluid flow rate. The limitation is due to a long dwell time, where the diffusive gradient between blood and dialysate fluid is closed quickly and diffusion is not sustained, as the gradient between blood and fluid is not replenished [10].

This prolonged diffusive time suggests that the circuit could be set up as con-current or counter-current without affecting small-solute clearance efficiency and there would be no benefit of either set up.

In a practical setting, priming, preparing and use of the CRRT circuit are easier with concurrent flow for dialysate fluid (blood and fluid path aligned), because gas and air bubbles will be removed from the membrane efficiently as they continuously flush to the top of the membrane (fig. 1) when the membrane is placed in a machine clamp or holder in the vertical [4].

In 1990, Davenport et al. [6] reported the effect of dialysate flow direction during continuous arterio-venous haemofiltration (CAVHF), concluding that counter-current flow direction of the dialysate solution yielded a greater clearance of small molecules compared to concurrent flow. This early version of CRRT required an arterial and venous cannulation, and blood flow was unknown and variable with the critically ill [6].

We previously reported computational modelling for the effect of dialysate flow configuration during CVVHD with replication of common blood and fluid flow settings [11]. This modelling revealed superior solute removal for counter-current flow configuration but did not account for the in-vivo effects of blood and membrane interac-

Fig. 1. Blood and dialysate flow concurrent; gas bubbles escape to waste pathway when placed in the vertical.

tions such as polarisation, protein layering, clotting, and pores size reduction with plugging, and the effect of gravity when the membrane is aligned vertical and hydrostatic pressures change with dialysate fluid flow.

Since the only in-vivo report published by Davenport et al. [6] in 1990, no further study has been identified to assess this aspect of circuit set up despite the introduction of continuous veno-venous haemo(dia)filtration (CVVHDF or CVVHD) with faster blood and dialysate flow rates to those assessed by Davenport et al. [6]. CRRT is now associated with blood and fluid pump-controlled machines, with set and fixed reliable flow delivery and with new membranes developed over the last 25 years. We now report the findings from a small in-vivo clinical evaluation for the effect of dialysate flow direction during CVVHD with current-day technology.

Hypothesis

We aimed at testing the hypothesis that concurrent dialysate flow during CVVHD would be no different compared to the counter-current flow for small solute removal of creatinine and urea.

Methods

Trial Design

We performed a prospective trial in a convenience sample of adult ICU patients with assessment during CVVHD modes. Two centres participated in the study – Austin Hospital (H1) ICU, Melbourne Australia and St. Bortolos Hospital, Vicenza, Italy (H2). Our study was approved by the relevant ethics committees, which waived the need for informed consent.

Setting and CRRT Modality

Both H1 and H2 ICUs involved had been using CRRT for over 25 years. A convenience sample of adult patients was recruited with diagnosed acute renal failure (RIFLE criteria 'F' [12]) and assessed during CVVHD via the Infomed HF 440 machine in Australia (Infomed, Geneva, Switzerland) or the Multifiltrate machine (Fresenius Medical care, Bad Homburg, Germany) in Italy. CVVHD was the technique and mode used during study sampling. All patients were treated with CVVHDF, and when samples were taken, any fluid substitution and ultrafiltration was turned off for 20 min prior to remove any effect of these fluids and provide CVVHD only. In H1, dialysate fluid was commercial Baxter Accusol bicarbonate added CRRT fluid (Baxter Health Care, Zurich, Switzerland) and Duosol™ bicarbonate-buffered haemofiltration solutions (B. Braun Melsungen, Germany) or PrismaSol (Gambro, Lund, Sweden) in H2. Any fluid removal was set to zero during the sampling periods. The dialysate fluid rate was 33 ml/min and blood pump speed was at 200 ml/min during sampling. Anticoagulation was determined by the existing ICU protocols for CRRT, and when used was given as 5–10 IU/kg/h of unfractionated heparin. When postoperative or surgical bleeding was of concern in these patients, no anticoagulation was used at the discretion of the prescribing ICU doctor.

Samples for urea and creatinine were taken from both the spent dialysate and the circuit blood (pre blood pump) at the same time, and after centrifuge were sent to the local hospital biochemistry pathology. In order to assess the effect of time during treatment, samples were taken at hour 1 (Time 1 = T1) and 4 (Time 2 = T2) after a new treatment and circuit were started in each patient. Solute removal across the membrane during diffusion was measured by calculation of the dialysate/blood plasma ratio for creatinine and urea (C_b/f and U_f/b respectively). As blood and fluid flow was fixed and no pre-dilution or added ultrafiltration was prescribed during sampling, this ratio calculation is a reasonable approach to measuring the movement of these small solutes across the membrane during each fluid flow direction.

Demographic data for the patient were retrieved from patient records and entered to a simple spreadsheet database.

Data Analysis

Data lacking normality of distribution are presented as median with interquartile range (25 and 75%) or mean with SD when normally distributed using the Wilcoxon signed-rank paired *t* test. $p < 0.5$ was considered significant.

SPSS (IBM, Chicago, IL, USA, version 18.0) software was used for all data analysis.

Results

Twenty-six patients were included in the study with the first dialysis treatment assessed for each. This included 15 males with a median age of 67 years (52–75), median APACHE II score 17 (14–19), and all patients met RIFLE criteria 'F'. These and other demographic data are displayed in table 1.

At both times, counter-current dialysate flow was associated with higher dialysate/blood plasma concentra-

tion ratios: mean (SD) creatinine at T1 0.87 (0.16) vs. 0.77 (0.10), $p = 0.006$; T2 0.96 (0.16) vs. 0.76 (0.09), $p < 0.001$ and for urea T1 0.98 (0.09) vs. 0.81 (0.09), $p < 0.001$; T2 0.99 (0.07) vs. 0.82 (0.08), $p < 0.001$. For all samples, combining data for both times: creatinine 0.92 (0.17) vs. 0.76 (0.10), $p < 0.001$ and for urea 0.99 (0.08) vs. 0.81 (0.08), $p < 0.001$. Not all solute removal increased during counter-current flow. One patient sample at H2 reflected a decrease in both C_b/f and U_f/b during counter-current flow; 0.93 to 0.81 and 0.98 to 0.78, respectively and 1 C_b/f at T4 also decreased; 0.92 to 0.83. At H1 4 C_b/f samples at T1 and one at T4 also decreased during counter-current flow, but no greater than 0.06 during T1 and 0.05 at T4. These data are displayed in figure 2 for creatinine and in figure 3 for urea at both sampling times, T1 and T2.

Discussion

Data from our study failed to support the hypothesis that removal of small solutes creatinine and urea during CVVHD would be no different with concurrent dialysate fluid flow. Removal of these small solutes was approximately 20% greater when the dialysate fluid flow was counter-current to the blood flow. This difference is significant and suggests this approach be used for CVVHD and would represent five hours of treatment time advantage per day or any 24 h period with continuous function of a treatment. In a practical setting, this circuit set up is more difficult to prepare when the fluid flow is in the reverse direction (downwards) to the blood flow (upwards), as gas bubbles within the membrane casing will not be flushed into the waste pathway during use; they will accumulate at the highest vertical point or distal end of the membrane.

These findings are consistent with those of the Davenport study in 1990 [6] when a more simple CAVHF circuit was assessed using a low-resistance flat-plate dialyser in three critically ill patients and concluded both creatinine and urea removal, expressed as ml/min, was greater using the counter-current method. In this study, the dialysate flow rate was 16.6 ml/min or half the rate we used, and it is important to acknowledge that the blood flow and ultrafiltrate rates were variable in CAVHF and that the filtrate was on free drainage without any mechanical pumps controlling the treatment. The authors reported that there was a greater volume of ultrafiltrate produced during counter-current flow, but this was not statistically significant and probably did not affect the benefit found using counter-current fluid flow.

Fig. 2. Con- and counter-current creatinine clearance ratio for T1, T2 and all data.

Fig. 3. Con- and counter-current urea clearance ratio for T1, T2 and all data.

Table 1. Patient demographic data: con-current vs. counter-current dialysate flow study

Number	Age	Sex	APACHE II	Indication	Diagnosis	Access site	Anticoagulation
1	81	Male	12	AKI	ARF, sepsis	L int j	Heparin
2	24	Female	14	AKI	Confusion state in liver disease	L fem	Heparin
3	68	Male	18	AKI	Subdural haemorrhage and SAH	R fem	None
4	43	Female	16	AKI	Hepatic failure	R fem	None
5	58	Female	31	AKI	AKI	R fem	None
6	20	Female	6	AKI	Liver failure (paracetamol overdose)	L fem	None
7	66	Male	20	AKI	Liver trx	R fem	None
8	68	Male	33	AKI	Septic shock in AML	R int j	None
9	44	Female	24	AKI	Fulminant hepatic failure, AKI	L fem	Heparin/protamine
10	70	Male	24	AKI	Bradycardia cardiac arrest	R int j	Heparin
11	67	Male	19	AKI	Bowel obstruction, post decompression	L int j	None
12	59	Female	15	CKD	Complication after cardiac surgery	CVC fem	Heparin
13	78	Male	20	AKI	Respiratory disease	CVC fem	None
14	46	Male	14	AKI	Drug toxication	CVC fem	None
15	75	Female	19	AKI/CKD	Pulmonary edema	CVC fem	LMWH
16	52	Female	14	CKD	Immuno-rejection after kidney transplant	CVC fem	LMWH
17	75	Female	11	AKI	Sepsis	CVC fem	None
18	74	Male	17	CKD	Sepsis	CVC fem	None
19	64	Male	14	AKI	Head trauma	CVC fem	LMWH
20	49	Female	15	CKD	Delayed dialysis	CVC fem	Heparin
21	69	Male	16	AKI	CPB and septic shock	CVC fem	LMWH
22	80	Female	18	AKI	CKD	CVC fem	None
23	75	Male	15	CKD	ESRD with complications	Graft	LMWH
24	73	Male	16	AKI/CKD	Cardiogenic shock, CKD	CVC fem	Clexane
25	85	Male	19	AKI/CKD	Emergency abdominal aortic surgery	CVC fem	None
26	61	Male	19	AKI/CKD	Diabetes unstable	CVC fem	LMWH

LMWH = Low molecular weight heparin; AKI = acute kidney injury; CKD = chronic kidney disease.

The hydraulic, flow and pressure mechanics within the CRRT membrane is complex and has been described from in-vitro work using dye injection and sequential radiological imaging to better understand the flow distribution in the blood and dialysate compartments and then the relationship between these two for clearance efficiency [13]. The findings of this work contribute mostly to membrane design and build. However, this work proposed that a mismatch between blood and dialysate flow distributions within the membrane occurs, with preferential flow in the central core fibres and this does influence diffusive exchange. Our study did not assess the distribution of blood flow within the membrane during clinical use; however, this is a phenomenon that may occur equally in both concurrent and counter-current flow. However, it may explain why in some of our samples, the clearance of creatinine was not greater in counter-current flow where 4 samples at H1 and 5 at H2 revealed a decrease in solute clearance ratio with a bias for this change at 4 h representing some effect of membrane clotting or protein laying with outer fibre occlusion. One creatinine and urea sample in a patient at T1 at H2 was decreased during counter-current flow, suggesting that this could be a sampling error. All other measurements where the Cb/f was decreased were at H1 during counter-current flow were for creatinine only. The difference or decrease was not significant at no greater than 0.06 but was unexpected and did not reflect the 20% benefit found across all samples.

There are other aspects of within membrane mass transport and movement of solutes such as the non-uniformity of blood and dialysate flow with mismatch, the effect of gravity when a membrane is positioned vertical, the pressure that is greater in the fluid compartment at the base [11] and the effect of different flow rates [14], which may have influenced our findings. However, our study was an in-vivo experimental design using the same protocol for technique and sampling in each centre.

Strengths and Limitations

Our study is the first report investigating this question since 1990 and was conducted in 2 centres with multiple sampling for new treatments at 2 time points. This is important because many advances and changes have been made with CRRT provided by purpose-built machines and new higher permeability membranes. Our findings will provide useful guidance for clinical use of CRRT and set up of the circuit, where counter-current dialysate fluid flow provides a significant clinical advantage for small solute removal. However, the mode used was only assessing the effect of diffusion in CVVHD and did not consider the additional influence of convective fluid and solute removal in CVVHDF, as this is probably the most common technique used worldwide [9, 15]. However, it could be assumed that convection added to counter-current fluid flow would also increase solute clearance at the same rate for both concurrent and counter-current circuits. This could be the basis of a future study to assess the effect of convection during CVVHDF.

Conclusions

Counter-current dialysate flow during CVVHD for ICU patients is associated with an increase of approximately 20% in diafiltrate/plasma creatinine and urea ratio. This suggests that when using CVVHDF, counter-current fluid flow provides a treatment benefit of approximately five hours when compared to the concurrent flow over a 24 h day with continuous use.

Disclosure Statement

The authors for this paper have no disclosures or competing interests associated with this research and publication.

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