Nephrol Dial Transplant (2004) 19: 877–884
DOI: 10.1093/ndt/gfg625

Nephrology
Dialysis
Transplantation

Original Article

Sustained low-efficiency daily diafiltration (SLEDD-*f*) for critically ill patients requiring renal replacement therapy: towards an adequate therapy

Mark R. Marshall[1], Tianmin Ma[1,2], David Galler[3], Alan Patrick Nigel Rankin[3] and Anthony Brendan Williams[3]

[1]Department of Renal Medicine, Middlemore Hospital, Auckland, New Zealand, [2]Renal Centre, Jinan Central Hospital, Shandong, People's Republic of China and [3]Department of Intensive Care Medicine, Middlemore Hospital, Auckland, New Zealand

Abstract

Background. Sustained low-efficiency daily dialysis (SLEDD) is an increasingly popular renal replacement therapy for intensive care unit (ICU) patients. SLEDD has been previously reported to provide good solute control and haemodynamic stability. However, continuous renal replacement therapy (CRRT) is considered superior by many ICU practitioners, due first to the large amounts of convective clearance achieved and second to the ability to deliver treatment independently of nephrology services. We report on a program of sustained low-efficiency daily diafiltration (SLEDD-*f*) delivered autonomously by ICU nursing personnel, and benchmark solute clearance data with recently published reports that have provided dose–outcome relationships for renal replacement therapy in this population.

Methods. SLEDD-*f* treatments were delivered using countercurrent dialysate flow at 200 ml/min and online haemofiltration at 100 ml/min for 8 h on a daily or at least alternate day basis. All aspects of SLEDD-*f* were managed by ICU nursing personnel. Clinical parameters, patient outcomes and solute levels were monitored. Kt/V, corrected equivalent renal urea clearance (EKRc) and theoretical Kt/V_{B12} were calculated.

Results. Fifty-six SLEDD-*f* treatments in 24 critically ill acute renal failure patients were studied. There were no episodes of intradialytic hypotension or other complications. Observed hospital mortality was 46%, not significantly different from the expected mortality as determined from the APACHE II illness severity scoring system. Electrolyte control was excellent. Kt/V per completed treatment was 1.43 ± 0.28 (0.96–2.0). Kt/V_{B12} per completed treatment was 1.02 ± 0.21 (0.6–1.38). EKRc for patients was 35.7 ± 6.4 ml/min (25.0–48.2).

Conclusion. SLEDD-*f* provides stable renal replacement therapy and good clinical outcomes. Logistic elements of SLEDD-*f* delivery by ICU nursing personnel are satisfactory. Small solute clearance is adequate by available standards for CRRT and intermittent haemodialysis, and larger solute clearance considerable. SLEDD-*f* is a viable alternative to CRRT in this setting.

Keywords: acute renal failure; continuous renal replacement therapy; intermittent haemodialysis; urea kinetic modelling; sustained low-efficiency dialysis

Introduction

Sustained low-efficiency daily dialysis (SLEDD) is an increasingly popular renal replacement therapy for critically ill acute renal failure (ARF) patients [1]. The term SLEDD was coined about 3 years ago, although reports of clinical experience with this form of therapy have existed for more than a decade [2,3]. SLEDD has evolved as a conceptual and technical hybrid of continuous renal replacement therapy (CRRT) and intermittent haemodialysis (IHD), with therapeutic aims that combine the desirable properties of each of these component modalities: (i) a reduced rate of ultrafiltration for optimized haemodynamic stability; (ii) low-efficiency solute removal to minimize solute disequilibrium; (iii) a sustained treatment duration to maximize dialysis dose; (iv) intermittency for convenient access to

Correspondence and offprint requests to: Mark R. Marshall, MD, Department of Renal Medicine, Middlemore Hospital, Private Bag 93311, Auckland, New Zealand. Email: mrmarshall@middlemore.co.nz

patients for out-of-unit diagnostic and therapeutic procedures during scheduled down-time.

In general, the modern practice of SLEDD meets most of the therapeutic objectives that led to its original inception [4–9]. SLEDD is able to achieve ultrafiltration goals in patients who are hypotensive or inotrope dependent. The low rates of solute clearance ensure minimal intradialytic urea disequilibrium and equivalence between single and double pool urea kinetic models [10]. Delivered dialysis dose has been shown to be relatively high in comparison to typical IHD regimens, and also much closer to that prescribed [11]. The scheduled down-time is convenient for out-of-unit procedures, and some centres have developed programs of exclusively nocturnal SLEDD to capitalize upon this feature. SLEDD appears to be associated with satisfactory outcomes [7], although more definitive information will become available from impending multicentre prospective randomized trials [The Acute Renal Failure Network Trial (lead investigator P. Palevsky, MD); CRRT *vs* SLEDD—Substudy of the Stuivenberg Hospital Acute Renal Failure Trial (lead investigator R. Lins, MD)]. Finally, several evaluations have shown SLEDD to be less expensive than CRRT, both within the setting of United States heath-care reimbursement structure [12] as well as within a more widely applicable nationalized health-care structure [13].

At present, the role of SLEDD in the intensive care unit (ICU) is still uncertain in relation to the mainstream options of IHD and CRRT. It would appear that SLEDD is a more than adequate substitute for IHD in most regards. However, the widespread acceptance of SLEDD as a genuine alternative to CRRT is hampered by several factors. First, SLEDD as described in the literature is delivered primarily by—or at least in collaboration with—haemodialysis nurses. This is a familiar and routine arrangement in many ICUs, but often unwelcome in those where renal replacement therapy is managed in-house with CRRT. Secondly, there are aspects of solute clearance specific to CRRT that are of potential benefit to critically ill ARF patients. There are now several reports supporting a relationship between increased small solute clearance and improved outcomes in this population [14–16]. There is little doubt that the greatest solute clearance can be achieved by modalities with continuous rather than intermittent operation, although daily IHD with reasonable treatment duration is able to achieve blood purification that is comparable to most CRRT regimens other than high volume haemofiltration. There is also increasing speculation that facilitated clearance of larger solutes including inflammatory mediators may also be beneficial [17]. The molecular weight of these solutes is above the cut-off for low-flux haemodialysis membranes, and many opinion leaders in the area are advocates of increased convective clearance with suitably porous membranes to maximize their removal [18]. In this regard, the principally diffusive solute clearance during SLEDD as described in the literature may be perceived as a disadvantage.

These issues have led us to modify the archetypal SLEDD prescription for our program. These changes include the development of policies and procedures that enable autonomous treatment delivery by ICU nursing personnel, optimization of (diffusive) clearance for small solutes by somewhat higher blood and dialysate flow rates than previously, and increased (convective) clearance for larger solutes by on-line haemodiafiltration with suitably porous membranes. Our initiative represents a systematic evolution of SLEDD based on current paradigms of treatment. We report on our preliminary technical and clinical experience with this regimen of sustained low-efficiency daily diafiltration (SLEDD-*f*), and benchmark solute clearance data with recently published reports that have provided dose–outcome relationships for renal replacement therapy in the critically ill ARF patient.

Subjects and methods

Data were audited within the Department of Intensive Care Medicine (DICM), Middlemore Hospital, New Zealand. Critically ill ARF patients in this institution who require renal replacement therapy have historically been treated with CRRT. Data were prospectively collected for all patients treated with SLEDD-*f* since the program inception in June 2002, and entered into a single centre prospective Access-based (Microsoft Corporation, Seattle, WA, USA) relational database. Patient data included demographic characteristics, primary and renal diagnoses, illness severity scores, and outcomes. Treatment data included ultrafiltration volumes, patient vital signs, inotrope requirements, and details of SLEDD-*f* prescription. Complications noted by nursing and medical staff were also noted and logged.

SLEDD-f treatments

SLEDD-*f* treatments were performed using the Fresenius 4008S ArRT-Plus on-line haemodiafiltration system (Fresenius Medical Care-Asia Pacific Pty, NSW, Australia). This machine has modules and technical components that are identical and interchangeable with the 4008S model used in the end stage renal disease (ESRD) setting. It does, however, have a refined software interface such that SLEDD-*f* with a range of operating parameters can be chosen at machine start-up. A standard 1.4 m^2 polysulfone high flux haemodiafilter (AV600; FMC-Asia Pacific) was used for all treatments.

SLEDD-*f* operating parameters at our institution have been largely standardized. Countercurrent dialysate flows (QD) were routinely set to 200 ml/min, and on-line haemofiltration (QF) to 100 ml/min in pre-dilution mode. Blood flows (QB) were set to between 250 and 350 ml/min as angioaccess permitted. Default treatment duration was 8 h. SLEDD-*f* treatments discontinued before completion for any reason were restarted only if therapeutic objectives had not already been met. Treatments were performed on a daily or at least alternate day basis. Dialysate purity using the Fresenius 4008 on-line haemodiafiltration system has been validated previously [19,20], and was ensured by regular endotoxin and microbiological testing. Standard dialysate was used with default constituent concentrations (mmol/l) as follows: [Na^+] 143, [K^+] 3.3, [Ca^{2+}] 1.25, [HCO_{3-}] 26.

Anticoagulation was by unfractionated heparin infusion into the extracorporeal blood circuit, to achieve a target activated partial thromboplastin time in the distal blood circuit of 10 s above baseline. Clotting within the haemodiafilter was gauged by changes in dynamic pressures within the extracorporeal circuit, and also by changes in instantaneous haemodiafilter urea clearances (see below).

All aspects of SLEDD-*f* treatment were performed and monitored by nursing personnel from the DICM, including set-up and discontinuation. Haemodialysis personnel with SLEDD-*f* experience were, however, available for trouble-shooting and technical advice.

Patients

Twenty-four patients were treated with SLEDD-*f* over the period June 2002–April 2003. Clinical details are provided in Table 1. APACHE II scores were calculated from physiological measurements obtained during the first 24 h of ICU admission, and expected hospital mortality rates for APACHE II scores calculated using the logistic regression calculations suggested in the original article [21]. Six patients had chronic renal impairment as defined by baseline premorbid serum creatinine levels >0.12 mmol/l. Thirteen patients were anuric. Mean urine output was 1001 ml/day in the remainder. Sixteen patients received concurrently administered nutrition during SLEDD-*f* treatments (7 parenteral, 14 enteral, i.e. 5 received both).

All critically ill patients with ARF admitted to DICM during the period of observation were planned for SLEDD-*f* as first choice in renal replacement therapy. Of these patients, however, 11 were treated with CRRT instead of SLEDD-*f*. Almost all of these episodes occurred in the 3 months following the SLEDD-*f* program inception, during which time there was a gradual change from CRRT to SLEDD-*f* as nursing skill and education permitted. Only 3 of the 11 patients received CRRT after this run-in period, and these episodes occurred during times when appropriately skilled nurses were not available for SLEDD-*f* (two patients), or during off-site maintenance of SLEDD-*f* machinery (one patient).

Evaluation of solute control

Blood solutes were routinely monitored at the beginning and end of SLEDD-*f* treatments. The blood samples were collected at the end of the treatment by standard stop-flow technique [22]. Kt/V were determined by formal iterative three-point modelling using a standard variable volume single pool urea kinetic model [23]. This model has previously been validated for the determination of dialysis dose during SLEDD [10]. Haemodiafiltration treatment urea clearances were supplied to this model as the average of several instantaneous values determined over the course of the treatment. Calculation was by a conventional mass balance equation modified for haemodiafiltration in pre-dilution mode:

$$Kd = [QB_I * C_I) - (QB_O * C_O)]/\{C_I * [QB_I/(QB_I - QF)]\}$$

where C is urea concentration, QF is haemofiltration rate, Kd is haemodiafilter clearance, QB is blood flow rate, and the subscripts 'I' and 'O' refer to parameters at the haemodiafilter inlet and outlet, respectively. The component of the above equation that accounts for solute clearance by net ultrafiltration is omitted as the rate was set to zero during sampling.

Dialysis dose was also expressed and recorded as equivalent renal urea clearance corrected to a urea distribution volume of 40 l to standardize for body size (EKRc). This

Table 1. Clinical characteristics of patients

Age/Race/Sex	No. of Rx	APACHE II	Inotropes/PPV	Diagnosis	Outcome
72/PI/m	2	18 (32%)	+/+	Septicaemia (pneumonia)	A
45/ PI/f	1	19 (35%)	+/–	Septicaemia, cardiogenic shock	D
75/W/m	2	31 (91%)	+/+	Hypovolaemic shock, acute post-op haemorrhage	A
65/M/m	3	32 (78%)	+/+	Septicaemia (pneumococcal infection)	D
57/W/f	1	24 (67%)	+/+	Septicaemia (meningococcal infection)	D
73/O/m	2	34 (83%)	+/+	Septicaemia (severe acute pancreatitis)	D
55/M/m	2	28 (73%)	–/–	Cardiogenic shock (severe TR, MVR)	D
85/W/m	2	30 (83%)	+/+	Septicaemia (pneumonia)	D
62/W/f	1	20 (53%)	–/+	Septicaemia (infected prosthetic joint)	A
30/PI/f	1	39 (91%)	+/+	Septicaemia (pneumococcal infection)	A
66/W/m	8	27 (63%)	+/+	Septicaemia (pneumonia)	A
66/W/m	4	33 (80%)	+/+	Septicaemia (pancreatitis)	D
30/W/f	7	28 (78%)	+/–	Septicaemia (trauma)	A
30/W/m	1	20 (38%)	–/–	Septicaemia (pneumonia)	A
61/W/f	1	14 (20%)	+/–	Septicaemia (uncertain source)	A
65/W/m	1	35 (91%)	+/+	Myocardial infarction/stroke	D
46/W/f	1	20 (74%)	+/+	Septicaemia (spider bite)	A
60/W /m	1	14 (20%)	+/–	Septicaemia (streptococcal infection)	A
54/Pi/f	8	36 (86%)	+/+	Septicaemia (pneumonia)	A
40/W/ m	2	19 (35%)	–/+	Septicaemia (leptospirosis)	A
84/ W/m	1	30 (73%)	–/+	Septicaemia (pneumonia)	D
62/W/f	1	17 (42%)	+/+	Septicaemia (pneumonia)	D
47/O/m	2	20 (68%)	+/+	Septicaemia/ruptured abdominal aortic aneurysm	D
53/M/f	1	22 (84%)	+/+	Cardiogenic shock, acute post-op haemorrhage	A

Illness severity presented as raw APACHE II score (predicted chance of hospital mortality), calculated as described in the body text. PPV, positive pressure ventilation; PI, Pacific Islander; M, Maori; W, White; O, other; m, male; f, female; A, alive; D, dead; MVR, mitral valve replacement; TR, tricuspid regurgitation.

parameter was determined using a previously published nomogram, which derives EKRc from mean delivered single pool Kt/V per treatment and treatment frequency [24].

Chemical analyses were performed by spectrophotometry using an Abbott Aeroset automated analyzer (Toshiba Pty, Japan). All samples were processed immediately. Coefficients of variation for the measurement of serum urea in our laboratory are 0.0 and 0.5% (intra-assay), and 3.7 and 2.0% (inter-assay) at urea concentrations of 4 and 25 mmol/l, respectively.

Theoretical Kt/V for vitamin B12 (Kt/V_{B12}) were approximated using the method described by Leypoldt *et al.* [25]. Accordingly, haemodiafilter clearances were calculated for each treatment from the haemodiafilter mass transfer-area coefficient for vitamin B12 (equal in this case to 215.8 ml/min for the AV600), and ultrafiltration rate. As described in the original article, the assumption of a constant ratio between distribution volumes for vitamin B12 and urea permits Kd_{B12} per treatment to be expressed as a fractional clearance Kt/V_{B12}.

Results

Patient outcomes

All results unless otherwise stated are presented as mean ± standard deviation (range). Observed patient hospital mortality was 45.8%. Hospital mortality ratio and 95% confidence intervals (calculated by dividing the observed by expected mortality [26]) was 0.72 (95% CI 0.47–1.00). Patient mean arterial pressure pre-SLEDD-*f* was 87.1 ± 13.7 mmHg (65–112), and post-SLEDD-*f* was 85.9 ± 14.0 mmHg (67–135). The median number of concurrently administered inotropes per patient pre-SLEDD was one, and this did not change post-SLEDD although increased inotrope dose was transiently required during four treatments. No patients developed threatening intradialytic hypotension, and none needed *de novo* institution of inotropes during SLEDD-*f*. Prescribed ultrafiltration volume for all treatments was 2.2 ± 1.6 (0.0–6.0) l, and achieved ultrafiltration for all (completed and prematurely discontinued) treatments was 1.9 ± 1.5 (0.0–6.0) l. Core temperature pre-SLEDD-*f* was 37 ± 0.7°C (36–39.1), and post-SLEDD-*f* was 37.2 ± 0.7°C (36.1–39.4). There were no episodes of haemorrhage related to anticoagulation, intradialytic arrhythmia or death during SLEDD-*f*.

The 11 patients treated with CRRT rather than SLEDD-*f* did not differ significantly in illness severity or outcomes when compared to the study cohort. APACHE II score was 25.9 ± 6.4 (16–36), and hospital mortality ratio was 0.76 (95% CI 0.38–1.15).

Treatment outcomes

A total of 56 SLEDD-*f* treatments were performed. QB was 283 ± 41 ml/min (range, 200–350). All SLEDD-*f* treatments were performed on a daily basis other than for two patients, in whom treatment on an alternate day basis was deemed to have achieved therapeutic objectives by the treating physician. A total of 17 treatments were prematurely discontinued for primarily extracorporeal blood circuit clotting (16 treatments), with one due to persistent vascular access difficulties. The duration of prematurely discontinued SLEDD-*f* treatments was 5.0 ± 1.5 h (2.0–7.0). Heparin anticoagulation was used for 43 treatments: 1716 ± 1110 (0–4000) IU loading dose, 776 ± 309 (100–1500) IU/h maintenance dose. Activated partial thromboplastin time in these patients was 39 ± 13 s (26–90). Thirteen treatments were performed without anticoagulation because of thrombocytopaenia or coagulopathy; seven of these went to completion.

Table 2. Serum chemistries pre- and post-SLEDD-*f*

	Pre-SLEDD-*f*	Post-SLEDD-*f*
Sodium	134.6 ± 2.96 (125.0–143.0)	135.1 ± 1.7 (132.0–141.0)
Potassium	4.4 ± 0.8 (3.0–6.2)	4.3 ± 0.6 (3.2–6.3)
Urea	19.6 ± 10.5 (7.0–64.7)	7.3 ± 3.6 (6.9–21.0)
Creatinine	0.34 ± 0.16 (0.1–0.7)	0.16 ± 0.07 (0.05–0.49)
Bicarbonate	20.5 ± 5.0 (12.0–31.0)	23.3 ± 2.7 (17.0–29.0)
Magnesium	1.0 ± 0.2 (0.4–1.5)	0.8 ± 0.1 (0.7–1.3)
Ionised calcium	1.2 ± 0.1 (1.2–1.3)	1.5 ± 0.6 (1.2–1.7)
Phosphate	1.3 ± 0.6 (0.5–3.1)	0.8 ± 0.3 (0.3–1.6)
Albumin	23.4 ± 5.6 (8.0–39.0)	24.5 ± 5.5 (8.0–38.0)

All units in mmol/l apart from serum albumin (g/l).

Solute control

Electrolytes pre- and post-SLEDD-*f* are shown in Table 2. Kt/V per completed treatment was 1.43 ± 0.28 (0.96–2.0). Kt/V_{B12} per competed treatment was 1.02 ± 0.21 (0.6–1.38). EKRc for patients was 35.7 ± 6.4 ml/min (25.0–48.2). Figure 1 illustrates these observed EKRc for each patient as a function of QB, and also models EKRc in each case to provide EKRc values for hypothetical SLEDD-*f* schedules that involve treatments being performed on less than a daily basis. One patient is excluded from this figure due to insufficient data acquisition.

Discussion

SLEDD treatments using a variety of operating parameters have been described in the nephrology literature for more than a decade [3–9,27,28], although most of the earlier reports were provisional and only a few of these earlier programs appear to have had significant longevity. SLEDD is still, at the present time, not yet a mature therapy with widespread acceptance, and opinion leaders in the field continue to be somewhat polarized toward either CRRT or IHD as the standard of care for their critically ill ARF patients. The shortcomings and disadvantages often ascribed to SLEDD are in general those that have been also ascribed to IHD, and include the lower clearance rates of small and particularly large solutes in comparison to CRRT.

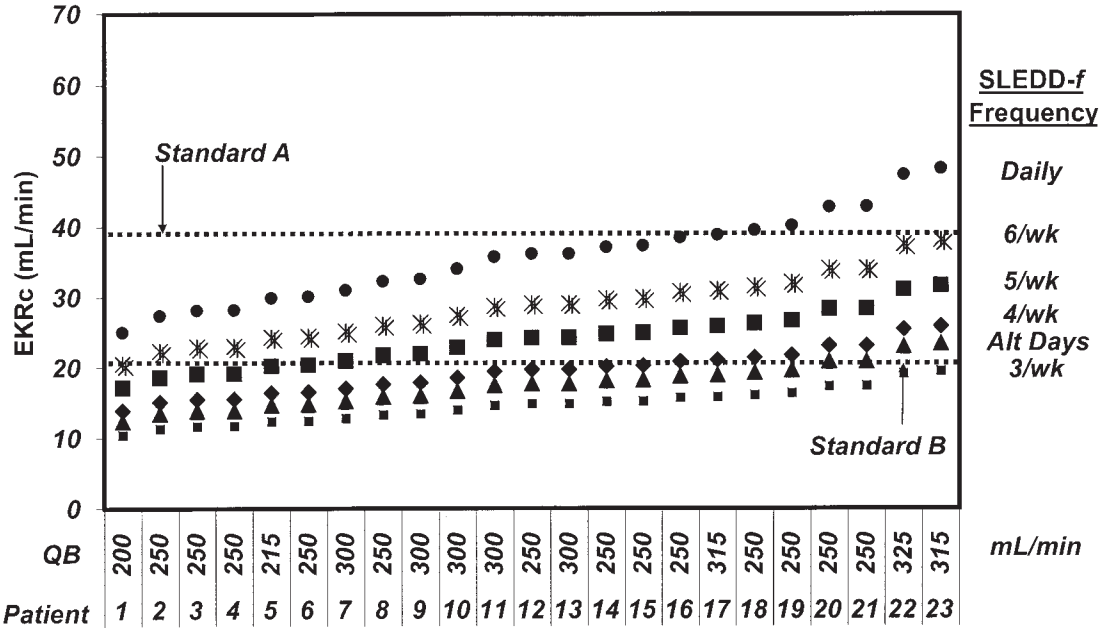

Fig. 1. EKRc for patients who had completed at least one SLEDD-*f* treatment. These are presented as a function of QB, and also modelled in each case to provide values for hypothetical SLEDD-*f* schedules that involve treatments being performed on less than a daily basis. The dotted lines indicate EKRc associated with superior outcomes in two recent studies (Standard A, CRRT delivering a clearance of 35 ml/kg/h [16]; Standard B, IHD delivering a single pool Kt/V of 0.92 per treatment at a frequency of 6.2 per week [15]).

Table 3. EKRc from other published series of SLEDD or SLEDD-*f*

Reference	SLEDD or SLEDD-*f* regimen QD/QF (ml/min)	QB (ml/min)	Membrane surface area (m^2)	Schedule	EKRc
6	70/–	70	1.3	Daily, 18 h	36.8[a]
10	100/–	200	1.8	5–7/week, 12 h	31.9[b]
28	30–80/50	150–200	1.0	Daily, 10 h	16.4–26.0[c]
29	100/–	200	1.8	Daily, 12 h	29.8[d]
30	300/–	200	2.0	Daily, 6–8 h	25.1[e]

[a]Original reported urea kinetic values converted to EKRc by method of Casino and Marshall [39].
[b]Original reported EKR values corrected to a urea distribution volume (V) of 40 l, and corrected for urea non-steady state by method of Casino and Marshall [39].
[c]Reported Kt/V from 0.6 to 1.0, converted to EKRc by nomogram method [24].
[d]Simulated data, original reported EKR values corrected to a V of 40 l.
[e]Original reported EKR unable to be corrected to a V of 40 l.

The study of small solute clearance in this setting is unfortunately confounded by lack of consensus as to the best expression for dose quantification. Purely from the perspective of solute removal, EKRc provides the most realistic description of the effect of any intermittent therapy upon solutes and allows comparison of both dose and dose–outcome relationships for all renal replacement therapies in critically ill ARF patients. This parameter can be applied to clinical data that have recently been presented in this population. Ronco *et al.* [16] optimized patient outcomes in their series with a CRRT regimen employing a substitution rate of 35 ml/kg/h (EKRc = 39 ml/min assuming V = 0.6 × body weight). Schiffl *et al.* [15] reported more recently in a controversial study that patient outcomes were better in those receiving daily as opposed to alternate day IHD. The daily dialysis group received an average Kt/V of 0.92 per treatment, at an average frequency of 6.2 times per week (EKRc = 20.7 ml/min using the nomogram method).

The results of our study (shown in Figure 1) and others (shown in Table 3) demonstrate that SLEDD and SLEDD-*f* provide a greater dose of dialysis than daily IHD, when the latter is performed with operating parameters that are typical in this setting [6,7,28–30]. Our study demonstrates that SLEDD-*f* can provide small solute clearance comparable to that provided by a regimen of CRRT with a substitution fluid rate of 35 ml/kg/min. As also shown in Figure 1, QB > 300 ml/min during SLEDD-*f* was not unexpectedly associated with a greater dialysis dose.

Interest in the removal of larger solutes arises from recent studies that have demonstrated a correlation between levels of various circulating pro-inflammatory cytokines and outcomes for critically ill patients. It has therefore been hypothesized that their increased

clearance may be of clinical benefit, and most investigators have tried to achieve this with blood purification strategies that utilize increased convection. However, the sieving coefficient (proportionality constant between the rate of solute movement and fluid movement across the membrane) of these mediators is frequently well below 1, and their mass removal by convection using conventional CRRT is probably trivial in comparison to their endogenous clearance [31,32]. In addition, the non-specific nature of CRRT also results in the simultaneous removal of anti-inflammatory cytokines, which may be detrimental. To date, *in vivo* studies have not been able to consistently demonstrate a sustained fall in a range of circulating cytokine levels as a result of their attempted extracorporeal removal. In addition, it is now apparent that a predominantly adsorptive mechanism is responsible for the cytokine removal that does occur, resulting in an approximately 10-fold higher removal in comparison to convection alone [33].

Our data demonstrate that SLEDD-*f* provides a considerable degree of convective clearance, although the Kt/V_{B12} from our study are much less than Kt/V for urea. Operational SLEDD-*f* is therefore less effective than CRRT for the removal of larger as opposed to small solutes. However, SLEDD-*f per se* is equally well suited for membrane adsorption, which is dependent less on ultrafiltration than on membrane composition and structure; an open pore structure and hydrophobic membrane is generally more conducive to adsorption [34]. This hypothesis is supported by a recent study showing SLEDD to be at least as efficacious as continuous haemofiltration in modulating endotoxin induced TNF-α production [35]. Our theoretical approach to larger solute clearance is a limitation of this study, and there are plans for future research in our laboratory, which will compare measured larger solute clearance during a number of modalities including high flux SLEDD, SLEDD-*f* and conventional CRRT. However, based on the theoretical data presented, an increase in either QF or treatment duration could be easily included as part of the routine operation of SLEDD-*f* to provide a similar amount of convective clearance as CRRT.

A comment on SLEDD and SLEDD-*f* machinery is relevant. The first machines to be used for these therapies were batch dialysate systems that were cumbersome and labour-intensive compared to the new generation of increasingly user-friendly and therefore more popular CRRT machines [3,36,37]. Currently, the most commonly used machine for SLEDD is the Fresenius 2008H with low dialysis flow option (QD = 100 ml/min). This option was originally developed for overnight home dialysis, and requires substantial hardware changes since the gear pumps cannot be adjusted to deliver accurate QD over the entire range between 50 and 1000 ml/min. Therefore, all low dialysate flows with the 2008H are delivered by the gear pump at a default rate of 300 ml/min. The regulation of QD falls entirely to the volumetric balancing chambers, and if dialysate is delivered to the balancing chambers at a rate greater than prescribed QD, it is then recirculated around the gear pump via a pressure limited overflow valve [38].

This machine has been part of the technical opportunism responsible for the modern re-emergence of SLEDD. However, it is unavailable outside of North America and other machines have been used elsewhere. The low dialysate flow rate during SLEDD requires either batch dialysate delivery, or single pass machinery that includes specific regulatory features within the ultrafiltration system, and appropriately calibrated gear pumps. The largest reported programs of SLEDD have used a QD as low as 100 ml/min, although other published experience has established that a QD up to 300 ml/min can be used without compromise in haemodynamic stability.

The majority of conventional IHD machines are able to fulfil these operational requirements, and even the use of on-line haemodiafiltration for SLEDD-*f* can be achieved with standard factory machinery. Dialysis equipment manufacturers are unlikely to provide in the future specialized lines of machines expressly for SLEDD or SLEDD-*f*, although it is probable that these options will become routinely available as part of a universal platform that can also be used for IHD in the ESRD and ARF settings, and even conventional CRRT. At the present time, there are also opportunities to utilize other aspects of dialysis machinery from the ESRD setting that may have alternative but important applications for critically ill ARF patients. For instance, the machines utilized in our centre are currently being fitted with on-line clearance monitors that will be used primarily to detect filter clotting rather than quantify dialysis dose.

With regard to treatment delivery, our program is the first to our knowledge in which the full operational responsibility for SLEDD-*f* treatment delivery is assumed by ICU nurses. Our experience has in general been positive. As expected, it has been difficult for some staff to familiarize themselves with conceptually new machinery, although most have been able to attain a degree of proficiency sufficient to manage treatments without hands-on assistance from haemodialysis personnel. The on-line haemodiafiltration used for SLEDD-*f* in our centre undoubtedly results in additional procedural complexity for the personnel administering the treatment, and preference could be given to the SLEDD (without filtration) if logistic difficulties were hampering acceptance of these therapies into the ICU. In our experience, however, there have been no instances to date of compromised care as a result of technical shortcomings in the ICU nurse managing the SLEDD-*f* treatment.

Our experience suggests that SLEDD-*f* can provide excellent clinical and metabolic outcomes in these critically ill ARF patients. Small solute clearance is adequate by available standards, and large solute clearance significant. SLEDD-*f* can be delivered autonomously in the ICU by in-house nursing personnel in a similar manner to CRRT, which is logistically attractive to many units, particularly outside of North America. It is

difficult to predict the future role of SLEDD-*f* in ICUs, given the already divergent practice patterns within the nephrology and critical care communities. The results of upcoming appropriately designed and powered clinical studies will better determine the clinical role and benefit of SLEDD and SLEDD-*f* in relation to other modalities available for the critically ill ARF patient.

Acknowledgements. The authors would like to thank the following personnel at Fresenius Medical Care—Asia Pacific for their advice and technical assistance; Dr F. Woods, K. Eggleton RN, V. Wilson RN, R. Walker and A. Ferencz. The authors acknowledge the assistance and perseverance of all the medical and nursing personnel at DICM, and recognize the following individuals for their help in establishing the SLEDD-*f* program; S. Mann RN, Dr B. Barry and Dr C. Simpson.

Conflict of interest statement. None declared.

References

1. Vanholder R, Van Biesen W, Lameire N. What is the renal replacement method of first choice for intensive care patients? *J Am Soc Nephrol* 2001; 12 [Suppl 17]: S40–S43
2. Kihara M, Ikeda Y, Shibata K *et al*. Slow hemodialysis performed during the day in managing renal failure in critically ill patients. *Nephron* 1994; 67: 36–41
3. Hombrouckx R, Bogaert AM, Leroy F, De Vos JY, Larno L. Go-slow dialysis instead of continuous arteriovenous hemofiltration. *Contrib Nephrol* 1991; 93: 149–151
4. Kielstein J, Kretschmer U, Ernst T, Hafer C, Haller H, Fliser D. Slow low efficient daily dialysis (SLED) as renal replacement therapy for acute renal failure in the intensive care unit: Combination of superior detoxification and excellent cardiovascular tolerability in severely ill patients [Abstract]. *Nephrol Dial Transplant* 2003; 18 [Suppl 4]: 667
5. Vasquez E, Vera E, Yee J, Osman-Malik Y. Safety and effectiveness of sustained low efficiency dialysis (SLED) as CRRT in critically ill patients with acute renal failure (ARF) [Abstract]. *J Am Soc Nephrol* 2002; 13: 236A
6. Lonnemann G, Floege J, Kliem V, Brunkhorst R, Koch K. Extended daily veno-venous high flux haemodialysis in patients with acute renal failure and multiple organ dysfunction syndrome using a single path batch dialysis system. *Nephrol Dial Transplant* 2000; 15: 1189–1193
7. Marshall M, Golper T, Shaver M, Alam M, Chatoth D. Sustained low-efficiency dialysis for critically ill patients requiring renal replacement therapy: Clinical experience. *Kidney Int* 2001; 60: 777–785
8. Kumar V, Craig M, Depner T, Yeun J. Extended daily dailysis: A new approach to renal replacement therapy for acute renal failure in the intensive care unit. *Am J Kidney Dis* 2000; 36: 294–300
9. Schlaeper C, Amerling R, Manns M, Levin NW. High clearance continuous renal replacement therapy with a modified dialysis machine. *Kidney Int* 1999; 56 [Suppl 72]: S20–S23
10. Marshall MR, Golper TA, Shaver MJ, Alam MG, Chatoth DK. Urea kinetics during sustained low-efficiency dialysis in critically ill patients requiring renal replacement therapy. *Am J Kidney Dis* 2002; 39: 556–570
11. Marshall M, Shaver M, Alam M, Chatoth D. Prescribed versus delivered dose of sustained low-efficiency dialysis (SLED) [Abstract]. *J Am Soc Nephrol*. 2000; 11: 324A
12. Alam M, Marshall M, Shaver M, Chatoth D. Cost comparison between sustained low efficiency hemodialysis (SLED) and continuous venovenous hemofiltration (CVVH) for ICU patients with ARF [Abstract]. *Am J Kidney Dis* 2000; 35: A9
13. Ma T, Walker R, Eggleton K, Marshall M. Cost comparison between sustained low efficiency daily dialysis/diafiltration (SLEDD) and continuous renal replacement therapy for ICU patients with ARF [Abstract]. *Nephrology* 2002; 7: A54
14. Paganini EP, Tapolyai M, Goormastic M *et al*. Establishing a dialysis therapy/patient outcome link in intensive care unit acute dialysis for patients with acute renal failure. *Am J Kidney Dis* 1996; 28 [Suppl 3]: S81–S89
15. Schiffl H, Lang S, Fischer R. Daily hemodialysis and the outcomes of acute renal failure. *N Engl J Med* 2002; 346: 305–310
16. Ronco C, Bellomo R, Homel P *et al*. Effects of different doses in continuous veno-venous haemofiltration on outcomes of acute renal failure: A prospective randomised trial. *Lancet* 2000; 356: 26–30
17. Schetz M. Non-renal indications for continuous renal replacement therapy. *Kidney Int* 1999; 56 [Suppl 72]: S88–S94
18. Ronco C, Brendolan A, Bellomo R. Continuous versus intermittent renal replacement therapy in the treatment of acute renal failure. *Nephrol Dial Transplant* 1998; 13 [Suppl 6]: 79–85
19. Weber C, Groetsch W, Schlotter S, Mitteregger R, Falkenhagen D. Novel online infusate-assisted dialysis system performs microbiologically safely. *Artif Organs* 2000; 24: 323–328
20. Vaslaki L, Karatson A, Voros P *et al*. Can sterile and pyrogen-free on-line substitution fluid be routinely delivered? A multicentric study on the microbiological safety of on-line haemodiafiltration. *Nephrol Dial Transplant* 2000; 15 [Suppl 1]: 74–78
21. Knaus W, Draper E, Wagner D, Zimmermen J. APACHE II: A severity of disease classification system. *Crit Care Med* 1985; 13: 818–829
22. Sherman R, Kapoian T. Recirculation, urea disequilibrium, and dialysis efficiency: Peripheral arteriovenous versus central venovenous access. *Am J Kidney Dis* 1997; 29: 479–489
23. Sargent J, Gotch F. Principles and biophysics of dialysis. In: Jacobs C, Kjellstrand C, Koch K, Winchester J, eds. *Replacement of Renal Function by Dialysis*. Kluwer Academic Publishers, Dordrecht, The Netherlands: 1996; 34–102
24. Casino F, Lopez T. The equivalent renal urea clearance: A new parameter to assess dialysis. *Nephrol Dial Transplant* 1996; 11: 1574–1581
25. Leypoldt JK, Cheung AK, Carroll CE *et al*. Effect of dialysis membranes and middle molecule removal on chronic hemodialysis patient survival. *Am J Kidney Dis* 1999; 33: 349–355
26. Morris J, Gardner M. Calculating confidence intervals for relative risks (odds ratios) and standardised ratios and rates. *Br Med J (Clin Res Ed)* 1988; 296: 1313–1316
27. Kihara M, Ikeda Y, Shibata K *et al*. Slow hemodialysis performed during the day in managing renal failure in critically ill patients. *Nephron* 1994; 67: 36–41
28. Van Malderen P, De Rijck L, Vermaut M *et al*. Intermittent venovenous haemodiafiltration in critically ill patients with acute renal failure. *EDTNA-ERCA Journal* 1998; 24: 19–20
29. Liao Z, Huang Z, Cui X, Goa D, Kraus M, Clark W. Dose capablilites of renal replacement therapies in acute renal failure (ARF) [Abstract]. *J Am Soc Nephrol* 2002; 13: 237A
30. Depner T, Craig M, Hu K, Kumar V, Tarne J, Yeun J. Solute kinetics during extended daily hemodialysis in the intensive care unit (ICU) [Abstract]. *ASAIO J* 1999; 45: 185
31. Sieberth HG, Kierdorf HP. Is cytokine removal by continuous hemofiltration feasible? *Kidney Int* 1999; 56 [Suppl 72]: S79–S83
32. Lonnemann G, Linnenweber S, Burg M, Koch KM. Transfer of endogenous pyrogens across artificial membranes? *Kidney Int* 1998; 53 [Suppl 66]: S43–S46
33. De Vriese AS, Colardyn FA, Philippe JJ, Vanholder RC, De Sutter JH, Lameire NH. Cytokine removal during continuous hemofiltration in septic patients. *J Am Soc Nephrol* 1999; 10: 846–853

34. Goldfarb S, Golper TA. Proinflammatory cytokines and hemofiltration membranes. *J Am Soc Nephrol* 1994; 5: 228–232
35. Lonnemann G, Bechstein M, Linnenweber S, Burg M, Koch KM. Tumor necrosis factor-α during continuous high-flux hemodialysis in sepsis with acute renal failure. *Kidney Int* 1999; 56 [Suppl 72]: S84–S87
36. Kudoh Y, Shiiki M, Sasa Y, Hotta D, Nozawa A, Iimura O. Slow continuous hemodialysis—new therapy for acute renal failure in critically ill patients—Part 2. Animal experiments and clinical implication. *Jpn Circ J* 1988; 52: 1183–1190
37. Kudoh Y, Iimura O. Slow continuous hemodialysis—new therapy for acute renal failure in critically ill patients—Part 1. Theoretical considerations and new technique. *Jpn Circ J* 1988; 52: 1171–1182
38. Stragier A, Backus G, Concepcion D *et al.* EDTNA/ERCA dialysis technology Journal Club 2001/2002 Summary. *EDTNA-ERCA Journal* 2002; 28 [Suppl]: 60–67
39. Casino F, Marshall M. EKRmb—Simple and accurate quantification intermittent hemodialysis (IHD) dose in acute renal failure (ARF) patients by a mass balance method [Abstract]. *J Am Soc Nephrol* 2002; 13: 249A

Received for publication: 22.7.03
Accepted in revised form: 22.10.03