Prolonged Intermittent Renal Replacement Therapy in the Intensive Care Unit

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ABSTRACT

Objective: *To present a review on the use of prolonged intermittent renal replacement therapy in the intensive care patient.*

Data sources: *Articles and abstracts reporting the use of renal replacement therapy.*

Summary of review: *Standard intermittent haemodialysis (IHD) has significant shortcomings in the treatment of the acute renal failure (ARF) of critical illness. These shortcomings include haemodynamic instability, the need to remove excess fluid over a short period of time, the episodic nature of small solute control, the limited ability to achieve middle molecular weight solute control and the episodic nature of acid-base control. Over the last 20 years, these limitations have stimulated the evolution and increased application of continuous renal replacement therapy (CRRT) which provides major biochemical, biological and physiological advantages compared with IHD, although it remains unclear as to whether such advantages translate into a survival advantage. However, CRRT is technically demanding, requires supervision 24 hr per day and is often associated with the need for continuous anticoagulation, which, in some patients, might be undesirable. In some institutions, CRRT changes the nurse to patient ratio from 1:2 to 1:1, an alteration which has cost implications and might affect resource availability for other patients. Accordingly, techniques which prolong the duration of intermittent therapy and avoid the need for 24 hr treatment may offer "best value" in the management of ARF in the intensive care unit (ICU). These techniques will be referred to as prolonged intermittent renal replacement therapies (PIRRT) in this article. They are characterised by several fundamental principles: 1. use of a modified or standard dialysis machines, 2. use of diffusion, convection or any combination of the two, 3. application of a decreased intensity of solute removal compared with IHD, 4. extended duration of treatment beyond the typical 3 or 4 hr of standard IHD (hence the term prolonged) but not beyond an 8 - 12 hr period (hence the term intermittent) and 5. use of "on-line" generation of dialysate or replacement fluid from tap water.*

Conclusions: *Information is now being obtained on the efficacy and safety of PIRRT in the ICU. Several units in Australia have started applying this technology to patient care. It is now important that critical care physicians and nurses become familiar with its principles and practice.* (**Critical Care and Resuscitation 2002; 4: 281-290**)

Key words: Dialysis, haemofiltration, renal replacement therapy, acute renal failure, intensive care, critical illness, multiorgan failure, shock, sepsis, blood purification, uraemia, acid-base, haemodynamics

Acute renal failure (ARF) is a major complication of critical illness. Its incidence in the ICU and the community varies, according to definitions,[1-5] from 5 - 15% of admissions and from 5 - 13 cases/10^5 people/year. The presence of acute renal failure[6] and severe renal failure (defined by the decision to apply renal replacement therapy), appear to contribute to increased mortality *per se* and carry an overall associated mortality of somewhere between 50 and 100%, depending on the patient cohort and centre.[3,4,7,8]

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The treatment of severe ARF with renal replacement therapy (RRT) requires an extracorporeal circulation. The creation of an extracorporeal circulation and its management add complexity to the management of these already very ill patients, who typically have ARF as a manifestation of multiorgan failure. Such complexity is not only costly, in terms of machinery and disposables, but is also demanding in terms of specialised labour. Furthermore, RRT adds a unique series of risks to the patient, which may alter organ recovery and ultimate outcome. It is not surprising that there have been many attempts to improve the safety, efficacy and effectiveness of RRT in this setting.

Until recently, there have been 3 major approaches to RRT: peritoneal dialysis, standard intermittent haemodialysis and continuous renal replacement therapy (CRRT). Each one of these techniques requires some detailed and separate discussion prior to the introduction of the concept of hybrid technology.

Peritoneal dialysis

Peritoneal dialysis (PD) is a well established technique in the management of end stage renal failure (ESRF), particularly in developing countries. The dialysing membrane is the peritoneum and dialysate is provided either by continuous intra-abdominal administration and drainage of dialysate fluid (so-called continuous equilibrating peritoneal dialysis) or by tidal delivery of PD fluids using special machines (so-called tidal peritoneal dialysis). Both these techniques can be applied to the treatment of ARF.[9-11] Particularly in developing countries,[11] their ease of application and low cost provide a potential logistic advantage over other approaches. However, there are major shortcomings with PD including the risk of peritonitis, the diaphragmatic splinting effect of intra-abdominal fluid, the risk of abdominal fluid leaks, the unpredictable fluctuations in glycaemia and the risk of inadequate uraemic and fluid balance control.

In the ICUs of developed countries, issues of cost are easily overcome by the need to achieve solute clearances that can reliably control uraemia in truly hypercatabolic patients with a large body mass index and multiorgan failure. The mean urea clearance achieved with tidal peritoneal dialysis is 10.6 mL/min[11] and is clearly insufficient to control solute concentrations in the setting of ARF and the multi-organ dysfunction syndrome (MODS). It is no surprise, therefore, that PD has been virtually abandoned in the treatment of ARF in the ICUs of developed countries. In a recent prospective survey (unpublished) of the treatment of ARF in 846 ICU patients in Australia, Europe and North America, none were treated with PD. More importantly, in a recent randomised controlled trial, PD has been shown to triple the mortality of ARF in the ICU[12] and to increase the cost of care per life saved in a developing country. PD can no longer be justified in the ICU patient.

Standard intermittent haemodialysis

The term standard intermittent haemodialysis (IHD) refers to intermittent haemodialysis as is typically applied to the care of patients with ESRF. This typically means second daily dialysis treatment, a treatment duration of 3 - 4 hr and a target Kt/V of > 1 per session (although this is often not formally measured). Standard IHD as currently applied to ESRF patients is an effective mode of treatment, which prevents death and can ensure survival for several years. Furthermore, the relative short duration of treatment ensures patient rehabilitation and their ability to function relatively well during the non-dialysis time. Unfortunately, such standard IHD is "unphysiologic".[13-15] The shortcomings include accelerated atherosclerosis, bone disease, increased risk of sepsis, anemia, increased risk of bleeding and amyloid accumulation. These shortcomings are even more obvious in the short-term when the technique is applied to critically ill patients with ARF in whom the benefit of short treatment time and the ability to return to the normal activities of daily living are irrelevant. In such patients, IHD induces major physiological complications at all levels when compared with continuous renal replacement therapies. They include haemodynamic instability, inadequate uraemic control, poor electrolyte control, limited acid-base control, limited control on calcium and phosphate balance, episodic potassium control, inadequate water control, episodic tonicity control and poor intravascular volume control.[15-19] Furthermore, the use of IHD imposes several limitations on caloric and protein intake further disadvantaging critically ill patients.[15] Finally, the rapid solute shifts induced by standard IHD induce significant changes in cerebral water, participating in the pathogenesis of the disequilibrium syndrome and increased intracranial pressure in patients at risk of, or with, cerebral oedema.

Given all of these major shortcomings of IHD, the last 20 years have seen the progressive rise of CRRT as the dominant technique of artificial renal support in the ICU, especially in Australia. These changes have occurred without randomised controlled studies to support the view that CRRT improves survival but are sustained by randomised controlled evidence that renal recovery is significantly improved by the application of CRRT instead of IHD.[20]

Continuous renal replacement therapy

The development of CRRT seems to have resolved

many of the physiological problems associated with the delivery of artificial renal support in the ICU.[15,18] Indeed, CRRT is associated with haemodynamic stability, unlimited control of fluid balance, the ability to allow unlimited nutritional support, the ability to achieve excellent small solute control, the ability to correct or prevent many electrolyte abnormalities and the ability to control body temperature.[15,18] More recently a randomised controlled study has shown that increasing the CRRT dose might even increase survival in ICU patients with ARF.[21] The potential benefits of increasing the dose of ultrafiltration might partly derive from the possible effect of CRRT on the humoral mediators of sepsis, which are adsorbed by the filtering membrane during convective treatment and may be directly removed by the convective process itself.[22-29]

These considerations have led investigators to apply increasing amounts of haemofiltration to the treatment of septic patients with ARF.[30,31] Thus, CRRT has evolved along 2 lines: on the one hand it is now the dominant form of artificial renal support in developed countries and, on the other hand, it is developing in the direction of a more general approach to blood purification, which seeks to go beyond the simple concept of RRT and move into the concept of multi-organ support therapy (MOST). In a paradoxical sense, as CRRT establishes its territory and develops dedicated technology, some of its limitations might become apparent.

Limitations of continuous renal replacement therapy

Although physiologically better than standard IHD, CRRT has several limitations. First it has to operate for 24 hr a day and places great demand on ICU nursing expertise. In addition, CRRT limits patient mobility, especially when the recovery phase begins. This is undesirable for it may have adverse effects on the delivery of physiotherapy, increase the need for sedation and decrease the amount and quality of sleep. Anticoagulation is often needed (60 - 80% worldwide) which potentially exposes the patient to the risk of bleeding. In patients who are lactate intolerant, the administration of lactate-buffered replacement fluids may generate significant hyperlactatemia and acid-base derangements[32-35] through the effects of lactate accumulation on the strong ion difference.[35] In such patients, CRRT has to be carried out with sterile bicarbonate-buffered replacement fluids[36,37] or dialysate at a cost of approximately $370 (AUD) per day. If patients with severe sepsis and lactate intolerance, are required to have high volume haemofiltration (HVHF), the costs would escalate further to approximately $40 (AUD) per hr and become almost prohibitive. Finally, during CRRT one patient requires one machine, while during IHD two or more patients might be treated with one machine over a 24 - 48 hour period.

So CRRT, like IHD, has shortcomings, which suggest that further improvements in the technology of artificial renal support might become necessary to optimise the care of critically ill patients with ARF. One such technological development might be represented by the so-called hybrid techniques.

Hybrid techniques

These techniques of artificial renal support initially represented a way of readjusting the dose of IHD to the needs of critically ill patients with ARF.[38] The first theoretical goal of these techniques was to attenuate or remove the haemodynamic effects of intermittent treatment by removing solvent and solute over a longer period of time thus avoiding rapid solute shifts and/or intravascular volume depletion. The second theoretical goal was to improve the dialysis dose in these highly catabolic patients with the understanding that dialysis dose may be an important determinant of outcome.[19,21] Thus the first defining technical and practical aspect of hybrid therapy was - dialysis machines would be used for treatment. The second defining feature was - therapy should be intermittent. The third defining feature was - therapy should be prolonged to achieve significantly longer session times that go beyond the typical 3 - 4 hr periods.

To describe such prolonged treatment sessions, terms such as “extended” or “sustained” have been used. We consider that the appropriate term should be prolonged intermittent renal replacement therapy (PIRRT). The fourth defining feature was - the mode of solute control should be diffusive, hence the use of the term dialysis instead of filtration. Finally the fifth defining but not entirely ubiquitous feature was - the application of a dialytic intensity (expressed as urea clearance in mL/min) below the typical intensity applied in standard IHD or in the treatment of well patients with ESRF.

The terms “slow” or “low-efficiency” have been used to describe this change in dialytic intensity. According to these defining features, hybrid techniques have been described by such expressions as sustained low-efficiency dialysis (SLED) or slow extended dialysis or slow continuous dialysis (if applied for long uninterrupted periods of time) or extended daily dialysis (if applied with daily frequency). These terms clearly illustrate the fact that once the stereotyped approach to IHD for ARF has been broken and flexibility embraced, then treatment becomes extraordinarily variable in all of its defining features (e.g. intensity, duration, frequency, technology and mode of solute removal). Such variability has particularly affected the mode of solute removal in our unit where convection has also been

applied. Thus any term involving the word dialysis (diffusive clearance) does not fully capture the choices available, while the expression renal replacement therapy does.

Practical features and experience with prolonged intermittent renal replacement therapy

The most extensive published experience with PIRRT techniques has been with the approach described as sustained low-efficiency dialysis (SLED) embraced by the group at the University of Arkansas Medical Sciences Center.[39,40] Only 3 other centres have published data on the clinical application of hybrid technology and approaches to the treatment of ARF,[41-43] but the extent of their experience and analysis of urea kinetics has been less extensive. The SLED treatment approach has now been described in 37 critically ill patients for a total of 175 treatments.[40] These patients were all treated in the ICU, many required inotropic drugs and most were receiving mechanical ventilation at the time of the intervention. The mean APACHE II score at admission was 27.8 with an expected mortality of approximately 70%.

At the inception of the program, treatment was scheduled during the day to allow ICU nursing staff to become familiar with the technology. Once familiarity and ease of operation were established, more than 75% of treatments were initiated in the evening between 4 and 12 pm and delivered overnight with the result that treatment duration was on average of 10.4 hr. This represents a clear change from standard IHD. The machine used for SLED was the Fresenius 2008H machine (Fresenius Medical Care North America, Lexington, MA, USA) and was set up by the dialysis nurse. Subsequent operation and 'trouble shooting' was a shared responsibility, with ICU nurses responsible for the management of simple problems, monitoring and documentation, and the dialysis nurse 'on-call', for the management of more significant technical problems. Dialysis nurses were also responsible for the training of ICU nurses and for the discontinuation of treatment. Prescription of therapy was by the nephrology team after discussion with the ICU medical staff.

During SLED, the default dialysate flow was set at 100 mL/min and the blood flow at 200 mL/min (estimated urea clearance 70 to 100 mL/min). A 12-hour duration of treatment was generally applied for, and prescribed, either daily or second daily according to clinical judgement of patient needs. A loading dose of heparin was generally given at the start of treatment followed by a continuous infusion into the circuit aiming for an APTT of 1.5 times normal. Online dialysate was generated with a bicarbonate proportioning system using tap water treated with a reverse osmosis system. The chosen dialysate flow allowed the entire treatment to occur without the need for replacement. Dialysate composition was varied according to clinical needs but the default dialysate contained a potassium of 4 mmol/L, a bicarbonate of 35 mmol/L and a calcium of 1.25 mmol/L. Low flux polysulfone filters were used for treatment. This is worthy of note for the quality of dialysate in the absence of additional filtration would most likely have been less than adequate and exposure to a high-flux filter would have induced back filtration of such dialysate into the patient.[44]

Clinical results with sustained low efficiency dialysis

In the experience of Marshall and colleagues, the application of SLED as described above resulted in excellent haemodynamic tolerance with a steady mean arterial blood pressure (MAP) and heart rate. Body temperature was also unaltered. However, half of the patients receiving inotropic support required an increase in dose, with the median increase being 66.7%. Twenty out of 145 treatments were associated with one or more episodes of hypotension (defined by the need for a fluid bolus of 250 mL or the need to readjust ultrafiltration goals). The problem was such that 11 treatments had to be stopped. Post-SLED MAP was 49 mmHg in these treatments. Prescribed ultrafiltration per treatment was 3 L and delivered ultrafiltration was 2.8 L per session. In nine patients, urea kinetics and removal were studied in detail. Total urea nitrogen removal was a mean of 28.6 g/treatment and double pool Kt/V for urea was 1.36. Significant decreases in a variety of solutes were achieved.

In addition, because the duration of treatment was limited, less heparin was used than would have been expected with CRRT. In fact, another study comparing extended dialysis with CRRT[41] showed a reduction in heparin use with SLED, while achieving similar ultrafiltration goals. Extracorporeal blood circuit clotting occurred in 38 SLED treatments. Nine of these were restarted. Bleeding complicated 2 out of 145 treatments with an episode of haemorrhagic tamponade occurring within 48 hr of bypass surgery and an episode of major gastrointestinal bleeding occurring 6 hr after initiation of SLED in a man with unrecognised upper gastrointestinal ulceration. In 2 patients, SLED was used in response to failure to achieve solute control with IHD; in the other 23 patients, the indication for SLED was the presence of haemodynamic complications during a trial of IHD. In 12 patients, SLED was performed because the clinicians felt that IHD would not be haemodynamically tolerated. The time averaged concentration (TAC) for plasma urea nitrogen in a subgroup of these patients, who received careful assessment of urea nitrogen kinetics revealed a mean intradialytic TAC of 47.3

mg/dL. With a mean pre-SLED blood urea nitrogen of 76.9 mg/dL. No information was provided on the mean TAC for blood urea nitrogen between SLED sessions. The estimated intensity of clearance delivered was a mean of 77.9 mL/min.

Other investigators have applied more "high-efficiency" dialytic therapy[41] in the treatment of 25 ICU patients for a total treatment of 367 days. These patients underwent dialysis during daylight hours for 6 to 8 hours (median 7.5 hr) using a blood flow of 200 mL/min and a dialysate flow of 300 mL/min. This prescription would be expected to deliver a urea clearance of 150 - 180 mL/min and a Kt/V of approximately 1.4 in an 80 kg man. The mean ultrafiltration was 400 mL/hr versus 126 mL/hr during CVVH. Importantly, this type of more intensive extended dialysis with the inevitable need to remove fluid more rapidly was associated with an incidence of hypotensive episodes of 0.13 events/hour versus 0.06 events/hour during CVVH and with a vasopressor use of 0.08 events/hour vs 0.03 events/hour during CVVH.[41] These observations suggest that CRRT remains the physiological "gold standard" for RRT in the ICU.

Technical requirements for prolonged intermittent renal replacement therapy and costs

Water production "on line" – Technical issues

A recent development by Fresenius Medical Care is the ARrT 4008S plus machine. This machine is the one used for SLED in our unit and it represents the technology which is bringing PIRRT into the Australian clinical arena.[45,46] This machine represents the "latest model" and a significant advance for such therapy. It can also perform all modes of renal replacement therapy and produces fluid for replacement "on-line". This dialysis-based machine incorporates a single fluid pump and an internal fluid 'balancing' chamber for the management of dialysate and/or fluid replacement in HDF or CVVH mode (Figure 1). This ONLINEplus™ pump module delivers ultrapure substitution fluid or dialysate complying with requirements of the European pharmacopoeia (1997) standard for sterility of infusion solutions.

The satisfactory preparation of tap water to this standard requires a reverse osmosis and filtering process before use and mandates the need for a cycle of maintenance and quality testing. This aspect of machine use is a major difference to the use of commercially prepared plasma water replacement and dialysate solutions during CRRT, and requires extremely careful attention by users. The preparation process requires not only the elimination of water contaminants, heavy metals and dirt, but the mixing of additive substrates such as electrolytes and bicarbonate before heating.

Finally, adequate filtering of the fluid is required to ensure that the fluid produced is microbiologically safe and endotoxin free. The resultant fluid produced in this way at the bedside has been reported to be more sterile than comparative commercial solutions .[47-49]

The process of water purification is as follows.

1. *Soft water production and filtration*: Tap water supply must be assessed initially for the presence of bacteria, heavy metals and the degree of 'hardness'. A filtration and water 'softening' process may be part of major hospital water supply system. The softening process required removes ions such as calcium and magnesium by a sodium containing cation exchange resin.
2. *Preparation for reverse osmosis*: Tap water first flows into three membrane filters in series involving;
   a. a 10 micron filter removing granulates, sand and large particles,
   b. activated charcoal for carbon, chloramines and chlorine adsorption and removal of organic contaminates,
   c. a 1 micron filter for removal of any carbon particles.

   This filtered water then enters the reverse osmosis unit. This can be a small portable device next to the bed or be a "master" unit supplying many outlets.
3. *Reverse osmosis*: The purpose of this step is to remove 90 - 99 % of univalent and divalent ions by forcing the water through a cellulosic and synthetic membrane (~ 5 microns) at a pressure exceeding water osmotic pressure. The subsequent permeate or reverse osmosis water should also be 100% free of dissolved organic contaminants with a molecular weight above 100 daltons.
4. *Preparation of dialysate*: The ultra-pure water requires the addition of electrolytes, glucose and bicarbonate from a concentrate obtained from commercially prepared bottles utilised for each treatment. The potassium, sodium and bicarbonate content can be easily adjusted during treatment via the machine screen interface.
5. *Post reverse osmosis treatment:* Polysulfone filtration membranes are used. As a final water preparation step, the water is passed through 2 Diasafe® 2.2 M^2 Polysulfone® membranes. This process ensures the water is 'ultra-pure' or can be considered to have less than 1 colony forming units per mL and less than 0.03 endotoxin units per mL. This level of microbiological safety has been the subject of several clinical evaluations validating this technique.

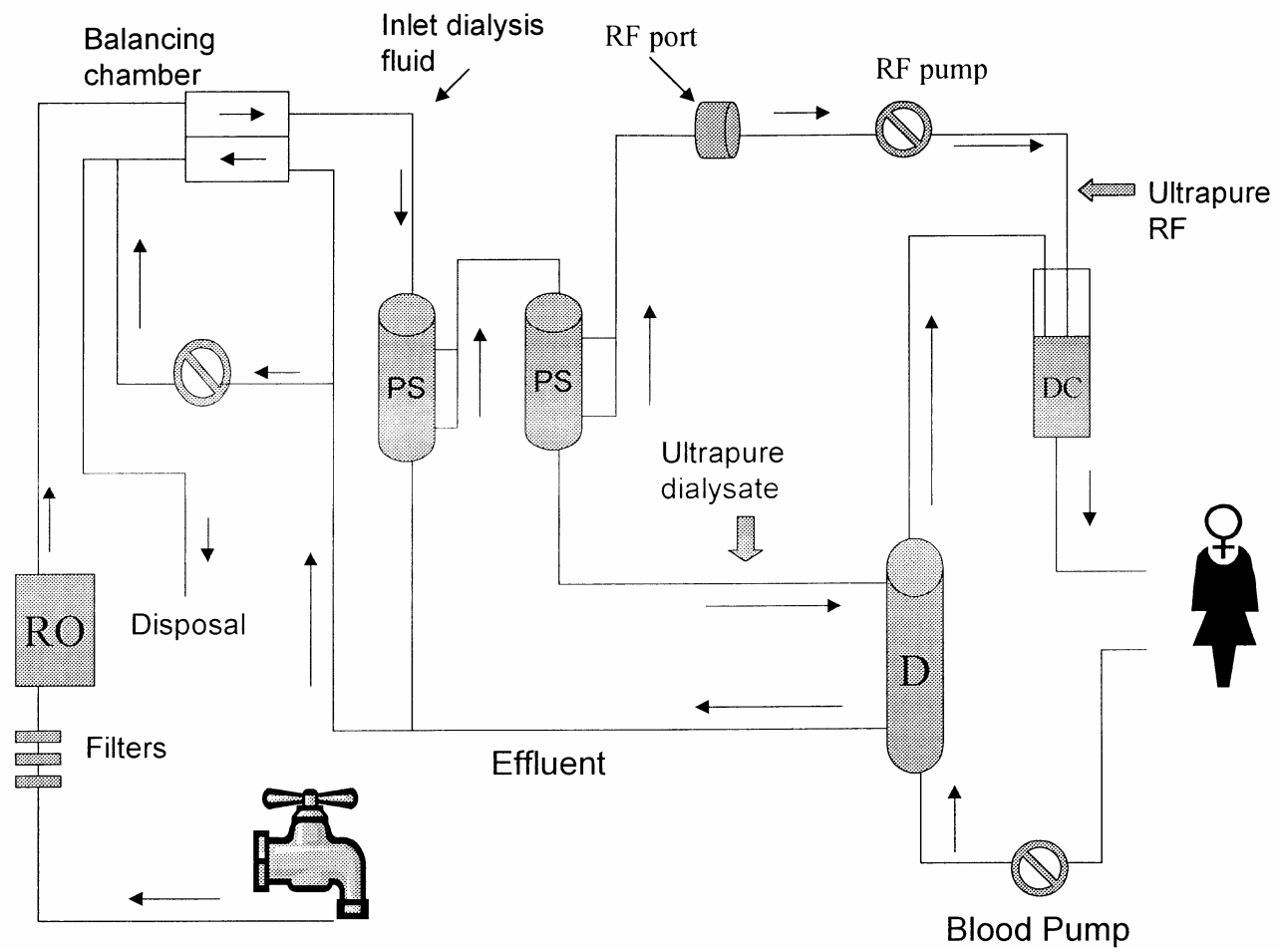

Figure 3. Diagram presenting the technical features of the ARrT 4008S plus machine circuit used for prolonged intermittent renal replacement therapy at the Austin and Repatriation Medical Centre. Water from the hospital water supply enters a series of three filters for additional purification before entering the reverse osmosis (RO) unit. From there, through a balancing chamber, it is mixed with concentrate and double filtered through polysulfone® filters (PS) to become ultrapure dialysate. Then it can be used as dialysate, passed through the non blood compartment of the dialyser (D) and returned as effluent for disposal. An ultrafiltration pump will regulate net fluid loss. Alternatively, the ultrapure fluid can pass through a replacement fluid (RF) port and then pumped (RF pump) into the drip chamber (DC) as substitution fluid. In this situation there may or may not be dialysate flow (pure convection or mixed convection/diffusion). Overall fluid balance is determined by the setting of the effluent pump.

Testing and maintenance

Water produced using this process as well as water obtained from the tap pre-treatment must undergo chemical, microbiological, chlorine/chloramines and endotoxin assessment on the basis of a regular schedule. On initial use of this technology this may be weekly in order to establish a true baseline. Following this initial process, assessment of water 'quality' should follow a set schedule. Such verification of water quality is a paramount safety feature of SLED.

Chemical testing of tap and manufactured water

This should occur annually unless changes occur to the system, water supply or component performance. Analysis of water samples should be performed by a chemistry laboratory able to measure contaminant concentrations to AAMI standards (USA 1998).

Free chlorine/chloramines testing. This testing applies to filter water after it has passed through the carbon filter and before it enters the reverse osmosis unit. This should occur daily and before each treatment. Bedside test strip analysis is available for this purpose.

Microbiology testing. This testing applies to reverse osmosis unit and substitution fluid. It should occur weekly to monthly depending upon results. It requires that dialysate specimens be sent to the microbiology laboratory for culture.

Endotoxin testing. This should occur monthly to 3 monthly depending upon results. A suitable laboratory able to assess fluids for the presence of bacterial

endotoxin should perform such tests (LAL assay).

Satisfactory results from the above quality assurance program will only be achieved if appropriate maintenance of equipment is also done. The major maintenance requirement is changing of the water filters at regular intervals (e.g. Diasafe® Polysulfone® filters after 3 months or after 100 treatments). The machine must also undergo a daily flush and hot disinfection and sterilisation procedure. This can be a semi-automated procedure on a programmed time clock in the machine. This process uses a commercial acid solution preparation fitted to the machine ready for the procedure and requires monitoring and replacement when empty. A diagram of the ARrT 2008S Plus machine is presented in Figure 1.

Costs of SLED compared with CRRT

Cost comparisons can take many approaches. However, the circuit tubing, membrane and components used for CRRT are very similar in cost to the total tubing membrane and fluids additives used for PIRRT. If each system supported one patient for a 24 hr period, there would be no difference in cost.

However, it is important to note that PIRRT could be applied to 2 patients over a 24 hour cycle potentially achieving further savings. Assuming a one machine for one patient for one day arrangement, the essential cost difference emerges from a comparison of the cost of fluids obtained either 'on line' during PIRRT or from commercially prepared bags for CRRT. This could be performed over differing time intervals, but, in our setting, when considering the use of commercially prepared bicarbonate solutions alone, one CRRT machine uses approximately $15,000 (AUD) of these solutions annually. The Fresenius ARrT 2008S *plus* and reverse osmosis water production system costs approximately $7,500.00 (AUD) annually to maintain. This is in addition to the costs of fluids and additives of $45 (AUD) per treatment. Provided the machines/treatments are utilised for the same hours of use in an ICU, PIRRT is approximately half the treatment cost.

The production cost of ultra pure water prepared via a central reverse osmosis system is cheaper than that from a portable bedside unit. However the considerable building and development required for a central system may take many years of use to recoup and makes cost comparison difficult.

Although portable water purification systems can be acquired, PIRRT in the form described above is, in our opinion, impossible or logistically prohibitive in hospitals without fixed water treatment systems (essentially all private hospitals in Australia).

Prolonged intermittent renal replacement therapy in Australia

More than a dozen patients treated with PIRRT have now been reported in abstract form in Australia.[45,46] Thus, it is early days in the evolution and application of this technology in our country. Several observations, however, can be made. The first unique feature of PIRRT in Australia compared with the USA is that it has not involved renal units and, like CRRT, has developed under the control of intensivists and critical care nurses. This is an important feature because we now have multiskilled individuals as intensivists prescribing dialysis, performing bronchoscopies, tracheostomies, transoesophageal echocardiograms and inserting intra-aortic balloon counterpulsation devices. As these technical activities have been, and still are, considered part of the realm of other specialties, we need to be careful in their application. Without documented due care and quality assurance programs, major mishaps might occur during PIRRT, which could easily expose intensivists and intensive care nurses to legal action.

The second unique feature is the use of ultra pure replacement fluid.[45] Such use is not novel and has been applied to >1 million dialysis treatments in Europe alone.[47-49] Nonetheless, it is relatively untested in patients with ARF, although at least one unit in Hong Kong has been using it for some time (Dr. Ian Tan, personal communication). Again, attention needs to be paid to ensure microbiological purity. In this regard, it is worthy of note that endotoxin contamination of commercially available replacement fluid is, on average, greater than that of ultrapure water.[47-49]

The argument can be made that it might be safer to avoid convection altogether during PIRRT. However, if high-flux filters are used (as is currently the case), one would be performing so-called high-flux dialysis when using diffusive therapy. Such high-flux dialysis is associated with the phenomenon of back-filtration where dialysate water moves into the blood compartment of the filter in its distal half, effectively delivering up to 2 L/hr of dialysate water via a "third membrane" into the patient at standard dialysate flows.[44] Thus, either way, (i.e. diffusion or convection), ultrapure water is delivered in large quantitites to the patient. The final observation is that the dose has been variable from prescribed clearances in the range of 80 - 100 mL/min[45] to perhaps 150 - 180 mL/min.[46]

Different doses, like mode of treatment, have different implications, not only in terms of urea clearances but also in terms of solute movement rate, changes in cerebral water, loss of nutrients and haemodynamic effects. More information is needed on these aspects of therapy before we can make rational choices on "best

dose" and "best mode". Nonetheless, the lower dose was associated with excellent haemodynamic stability as highlighted by the evolution of blood pressure with treatment as well as the stable requirements of vasopressor therapy.

Comments on the clinical use of intermittent renal replacement therapy

Although the experience with PIRRT is somewhat limited, several comments appear justified at this time. The first is that, in general, the application of PIRRT is a welcome development in acute dialysis. If it represents the beginning of a paradigm shift in the provision of intermittent RRT to critically ill patients with ARF, then it is particularly welcome. Finally, if it achieves the demise of standard intermittent IHD, which has already been seriously injured by the arrival of CRRT, then it should be hailed as a major success. The second observation is that, while the use of PIRRT may still offer haemodynamically unsuitable therapy to some ICU patients, it should offer much better therapy than IHD to non-ICU ARF patients. In such patients, the use of stereotyped standard IHD techniques may delay renal recovery and a shift to PIRRT would most likely be a significant improvement.

The third observation is that PIRRT has some shortcomings too and that its application should be considered with great caution in a significant proportion of ICU patients, who require substantial vasopressor support (especially when the significant removal of fluid is in prospect), are at risk of cerebral oedema or require careful fluid management. These patients should receive CRRT. The fourth observation is that PIRRT need not become another stereotyped technique like IHD. In each patient, the prescription of solute removal, dose and ultrafiltration rate should not occur at the beginning of the session and immutably be held until haemodynamic trouble occurs and triggers rearrangements. Such treatment goals should instead be constantly reviewed and readjusted. For this reason, we favour treatment during the day, rather than at night. Indeed treatment during the day has been our practice at the Austin and Repatriation Medical Centre from the inception of our PIRRT program.

A further observation is that PIRRT is unlikely to be an ideal therapy in acutely ill patients recently admitted to the ICU with haemodynamic instability, shock and multiorgan failure or with cerebral oedema or at risk of cerebral oedema (rapid solute control induced by relatively high solute clearances are contraindicated in these patients). In these patients, the treatment of choice is, and will probably remain, CRRT. However, once recovery takes place, vasopressors have been weaned and the patient is moving well into the reparative phase of his/her illness, PIRRT may offer important advantages, while still maintaining adequate uraemic and volume control and avoiding haemodynamic instability. Such advantages include the use of bicarbonate as buffer, decreased nursing workload, increased patient mobility and decreased nocturnal patient manipulation. These effects may translate into better acid-base control, night time rest for the patient, decreased need for sedation and more effective physiotherapy. These practical and physiological advantages may turn out to be clinically important. Thus, to draw a parallel with mechanical ventilation, PIRRT may turn out to be the renal equivalent of pressure support ventilation: a technique to facilitate the patient's return to spontaneous function and subsequent weaning. Whether PIRRT can be more than that will remain uncertain until more clinical research is undertaken.

Conclusions

Standard IHD remains an imperfect therapy in the treatment of ARF in the ICU patient. Indeed, in developed countries, it has been largely replaced by CRRT over the last 10 years. However, CRRT has several features that may not make it an ideal therapy for these patients at all times. The emergence of so-called hybrid techniques such as PIRRT represents a welcome addition to the intensivist's armamentarium and may offer "best value" as a weaning technique from CRRT in recovering patients who are haemodynamic-ally stable. As such, PIRRT might improve patient mobility, decrease nursing workload, improve night time rest and allow unimpeded renal recovery without the additional haemodynamic and solute accumulation insults that are typically seen with standard IHD.

Although much work needs to be done in the area of critical care nephrology and much more experience needs to be obtained and published, it seems advisable for a unit with a large burden of ARF patients to become familiar with the technology and gain independent experience in its use.

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