Special review

Continuous Renal Replacement Technology: From Adaptive Devices to Flexible Multipurpose Machines

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ABSTRACT

Objective: To review the evolution of technologies in the development of renal replacement therapies.

Data sources: Articles and published reviews on renal replacement therapies.

Summary of review: Continuous arterio-venous haemofiltration (CAVH) was the first continuous renal replacement technique capable of overcoming the traditional haemodialysis-related side effects, making possible the treatment of critically ill patients safely and with less physiological instability. The evolution of technology and the progress experienced in intensive care units (ICUs) has made it possible to start renal replacement therapy programs in the absence of a chronic dialysis facility or a trained nephrological team. Initial limitations and draw-backs of CAVH, stimulated the ICU staff to explore new avenues for better therapy.

Extracorporeal therapies are today a routine experience in the ICUs: continuous renal replacement therapies are a broadly accepted treatment for acute renal failure. Furthermore, alternative indications for extracorporeal blood circulation (e.g. sepsis, liver failure, congestive heart failure, drug intoxications, hyperthermia, immuno-mediated syndromes) are becoming more and more popular. The ideal machine has yet to be completed, but progress has occurred and has opened a new era for critical care nephrology and the further expansion of blood purification technology in the ICU.

Conclusions: Technical advances in renal replacement therapies have increased their functionality (i.e. used in hepatic failure, sepsis, cardiac failure and immuno-mediated syndromes), are easier to operate and have less side-effects compared with their standard extracorporeal counterparts. Further improvements may see them become a routine part in the management of the critically ill patient. (Critical Care and Resuscitation 2004; 6: 180-187)

Key words: Renal replacement therapy, sepsis, multiple organ support therapy
technology supporting the application of CRRT has greatly improved both as far as the hardware and the software are concerned. The trend of this evolution and the potential of CRRT is today growing to a point in which multiple organ support therapy (MOST) is envisaged as a possible therapeutic approach in the critical care setting.3

The birth of continuous arterio-venous haemofiltration (CAVH) and continuous arterio-venous haemodialysis (CAVHD)

CAVH was the first continuous renal replacement technique capable of overcoming the traditional haemodialysis-related side effects, making possible the treatment of critically ill patients safely and with less physiological instability.4 CAVH however, had serious limitations. It required arterial access, with its attendant morbidity,5 and solute clearance was limited by the low rates of ultrafiltration and the pure convective nature of the treatment (10 - 12 mL/min). Technical improvements of CAVH (suction in the ultrafiltrate side, predilution, supplement of counter-current dialysate flow) allowed improved clearances. However, such clearances were at times insufficient to meet the need of severely catabolic patients.6

To overcome such limitations, new filters were designed with increased cross-sectional area and inner hollow fiber diameter, reduced unit length and lower resistance to blood flow. With these measures the phenomenon of filtration pressure equilibrium and easy clotting, due to poorly optimised ultrafiltration profile was diminished.7

Another option explored in those days was the use of highly biocompatible membranes such as AN69S mounted on parallel plate devices (figure 1). These filters, whose design was borrowed from the chronic dialysis setting, presented lower intrinsic resistance (ensuring higher extracorporeal blood flows at a given arterio-venous pressure gradient) and were equipped with a second port in the filtrate compartment so that counter-current dialysate flow could be programmed in the newly conceived CAVHD mode.

From arterio-venous to veno-venous therapies.

The evolution of technology and the progress experienced in intensive care units (ICUs), made it possible to start renal replacement therapy programs in several institutions, even in the absence of a chronic dialysis facility or a trained nephrological team. Initial limitations and draw-backs of CAVH, stimulated nurses and physicians to explore new avenues for better therapy. The logical evolution was to apply a peristaltic pump to the extracorporeal circuit (continuous veno-venous haemofiltration/haemodialysis

The need for this “hardware” evolution from CAVH/D to CVVH/D, was not limited to blood pumps, but was also extended to fluid delivery systems and ultrafiltration control mechanisms to achieve accurate delivery of dialysate or replacement solutions.

With the advent of blood pumps and the feasibility of veno-venous pumped therapies, new technological developments became necessary.

The first step to continuous veno-venous renal replacement therapies (CVVH-CVVHD) was the advent of double lumen catheters.8 The driving force to blood flow resulted from the mechanical action of the roller pumps. Blood flows could finally be programmed and delivered with precision. Nevertheless, the new configuration of the extracorporeal circuit brought with it requirements for new accessories and new safety features that were mostly borrowed from the chronic haemodialysis technology.

The CVVH/D/DF setup, required negative pressure measurement and an alarm along the arterial line before the pump, as well as positive pressure measurement and an alarm along the venous return line. In this line, a bubble trap had to be inserted to prevent air embolism (this was not necessary in CAVH where the circuit operated at positive pressure along the entire length of the system).

The higher blood flows induced higher filtration rates and the possibility to exploit higher clearances because of the increased dialysate flow rates. For this reason roller pumps were applied to the dialysate or fluid replacement delivery section of the circuit, and external scales had to be added to provide sufficiently accurate fluid balance during treatment.

An example of this adaptive technology was the BSM 22 device (figure 2). About 20 years ago, the BSM22 (Hospal, Lyon, France) was the archetype of a CRRT machine derived from a chronic dialysis...
machine (the Monitral). The hardware consisted of a blood roller pump (operational range 30 - 700 mL/min) and a single fluid pump (operational range 100 - 2000 mL/hr). A syringe pump for heparin infusion (continuous or intermittent) was also available. A display showed instantaneous and cumulative treatment parameters (pressure, flows, elapsed time, effective treatment time). The system was sufficiently easy to transport and to operate. It performed slow continuous ultrafiltration (SCUF), continuous veno-venous haemofiltration (CVVH) and continuous veno-venous haemodialysis (CVVHD). It also featured a blood leak detector on the ultrafiltrate/dialysate line, continuous monitoring of the pressure drop across the haemofilter (with a specific alarm in case of “filter clotting” or excessive venous pressure), continuous monitoring of vascular access pressure with a negative pressure alarm, an air/foam detector on the venous line with integrated pump-stop command and a drip-sensor to detect an “empty bag” of replacement fluid/dialysate. This system represented an evolution from the chronic dialysis machine with adjustments oriented towards “continuous use” (roller pumps accuracy, compact and transportable size and specific monitoring).

Nevertheless, its limitations were quite evident: the system did not include a fluid balancing device (the operator had to periodically perform a manual fluid balance) and the machine was not versatile as it did not perform all treatment modalities.

From adaptive technology towards modern CRRT

The benefits induced by this new type of adaptive technology were soon counterbalanced by the gross inaccuracy of the systems and the limited integration between the extracorporeal circuit and the fluid balance devices. Furthermore, the fact that these combined devices were mostly derived from the chronic dialysis world, made continuous and prolonged treatment difficult. Finally, the need to obtain additional information or performing additional functions, induced physician and nurses to include several other devices in this system, which were often poorly integrated, with a final result of a Christmas tree-like effect. Safety and performance were suboptimal. Blood pumps were often inaccurate, circuit tubing were damaged over time, filtration fractions were uncontrolled because of pressure and flow fluctuations, intra-filter hematocrit and platelet count consequently increased beyond safe values and filter clotting typically occurred.

The venous drip chamber (bubble trap) was, and still is, a frequent site of circuit clotting during continuous therapy. Two mechanisms seem to be responsible for clot formation: blood-air interface and blood stagnation in the chamber. Modifications of these chambers, derived from traditional intermittent therapies, appeared necessary in the continuous setting and new chambers without air-blood contact started to be conceived and designed.

Accurate ultrafiltration control is mandatory in modern CRRT. Early machines did not have scales or pumps, and when volumetric pumps started to be used to drive dialysate and ultrafiltrate in and out from the filters, inaccuracies close to 10% were observed: again this apparently small deviation becomes potentially dangerous during continuous therapies. Furthermore, as the membrane started to clot and approach failure, the ultrafiltrate volumetric pump became more inaccurate because of wide fluctuations in the membrane ultrafiltration coefficient.

It soon became evident that an ideal extracorporeal circuit should incorporate continuous pressure measurements and continuous displays of pressures from inlet and outlet lumen of the catheter, inlet and outlet of filter; ultrafiltrate and dialysate ports. This information, integrated with adequate alarms is of crucial importance in allowing ICU staff to maintain filter efficiency and circuit patency, to detect potential sources of clotting and to ensure patient safety.

Another important innovative feature of the ideal integrated system, was a friendly user operator interface. All these requirement were then integrated into a specifically designed CRRT machine project that started to be practically realised in the early nineties. The project was called “Prisma”.

Dedicated CRRT machines: The Prisma machine

The Prisma machine was delivered to the market more than ten years ago; the evolution from its predecessors was immediately evident (figure 3). A compact machine, a large monitor with touch-screen features, four pumps (blood, dialysate, replacement
solution and effluent), three scales (effluent, dialysate and replacement solution), one disposable set with pre-connected AN 69 or PAES (Polyarylethersulfone) filters and fluid circuitry made the machine able to perform a complete range of therapies including SCUF, CVVH, CVVHD, CVVHDF and therapeutic plasma exchange (TPE).

While representing a definite step forward in the management of CRRT and responding to most of the requirements for a new machine in the field of acute therapies, the Prisma machine has, over time, started to display some of its limitations. In particular, medical and nursing staff performing CRRT have become used to the remarkable advantages offered by the machine, but at the same time, have started to increase the level of demands and performance. On the other hand, some choices made during the original development of the Prisma machine resulted in some rigid constraints of software and hardware itself.

Some of the limitations became of particular importance with the recent development of new therapies and resulted in progress toward a next generation of CRRT equipment. The specific, disposable dedicated set (filter and circuit) with only two surface areas available (0.6 and 0.9 m²), contributed to a certain rigidity of the prescription and performance; the pre-designed circuit with either pre or post-dilution replacement infusion made it impossible to change configuration during treatment; the blood flow range limited to a maximum of 180 mL/min appeared inadequate, especially when high volume therapies were planned. Finally, the initial selection of a technique with a certain degree of complexity (SCUF or CVVH or CVVHD) made impossible to upgrade to another modality in subsequent moments of the treatment. A weight error warning, who allowed clinicians to be aware of eventual scale-pump inaccuracy was not present. The heater for dialysate/replacement fluid warming was never considered as an option All these aspects have recently been reconsidered in light of new scientific evidence and new therapeutic options, and a new machine was developed: the Prismaflex machine (figure 4).

CRRT: The next generation.

Extracorporeal therapies are today a routine experience in the ICUs: CRRTs are a broadly accepted treatment for acute renal failure. Furthermore, alternative indications for extracorporeal blood circulation (e.g. sepsis, liver failure, congestive heart failure, drug intoxications, hyperthermia, anasarca, immunomediated syndromes) are becoming more and more popular despite the absence of solid evidence. A significant effort has been made in order to standardise all these treatments, and prospective randomised control trials to study efficiency and efficacy of disparate therapies for peculiar indications are taking place. Furthermore, the feeling that
extracorporeal therapies may become a therapy for multiple organ dysfunction is increasing and the need for flexible platforms is becoming more evident.

The Prismaflex machine has developed in this enthusiastic environment, designed in the attempt to respond to different unmet clinical needs and complex multitasking functions, while maintaining the classic simplicity and friendly user interface typical of the “family”.

The new Prismaflex is, at first look, elegant and compact although bigger than its previous version (figure 5): it is 167 cm high (vs 147 cm), two and a half times heavier (60 Kg), it features a new and coloured touch screen monitor, five pumps (blood, dialysate/post replacement, pre-blood-pump replacement solution, pre/post-blood-pump replacement solution and effluent) and four scales (effluent, dialysate, replacement and pre blood pump infusion); a disposable set with pre-connected AN 69 or PAES filter and fluid circuitry is available for a complete range of therapies (SCUF, CVVH, CVVHD, CVVHDF, TPE- and haemoperfusion -HP).

The innovative technical solution of two pinch valves (figure 6) provides the possibility of varying the ratio of pre to post dilution, allowing simultaneous pre-post-dilution at different infusion rates. Furthermore, this ratio can be changed during therapy. This feature is important for high volume haemofiltration techniques. Pre or post-dilution mode can also be selected for CVVHDF mode. The available pre-connected kits feature three different surface area dialysers (0.60, 1.00 and 1.40 m²). The filter is positioned such that blood inlet is at the bottom: in this way the priming is optimised with complete de-aeration of filter and blood circuit.

The heparin syringe pump has improved to accommodate different types and sizes of syringes. However an innovative feature is now present in the Prismaflex i.e. the fifth pump. This pump delivers pre-blood-pump (PBP) fluid infusion, and it makes possible to implement citrate anticoagulation (figure 7). The design of this feature, in fact, allows citrate infusion just after the connection between the arterial access and the blood line.

The blood pump is bigger than in the earlier version and it allows blood flows within a range of 10 - 450 mL/min (depending on the set in use). Fluid flow rate range is adjustable between 0 - 8000 mL/hr for each pump, but only the total of all fluid exchanges (dialysate, replacement, pre blood pump infusion) can
Figure 6. Pinch valve are designed to easily switch from pre dilution (or post dilution) hemofiltration to various percentage (10 - 90%) of mixed pre and post dilution.

Figure 7. Pre blood pump delivers replacement solution after the connection between the arterial access and the blood line.

go up to 8 litres per hour. Moreover if a pre-blood pump replacement solution is used, the blood pump is able to automatically adjust its rotational speed in order to maintain the set blood flow, which otherwise would be relatively decreased by the scaling down factor induced by the pre-blood pump speed.

The effluent pump nominal set range is 0 - 10000 mL/hr. This is clearly designed to meet the needs of high volume haemofiltration (HVHF). The Prismaflex software controls fluids flows by an accurate pump-scales feedback: 30 g per hour is the accepted error for each pump and an alarm warns the operator if this limit is exceeded. When the therapy is interrupted by a pressure alarm, it automatically restarts if the pressure level normalises within few seconds (i.e. during coughs or inadvertent line kinking). Scales are designed as four parallel sliding “drawers” positioned below the monitor, and are able to shift-out and allow easy and work-safe collection of fluid bags (figure 8).

Figure 8. Scales design facilitates bags change, and decreases nurse workload.

The never-ending issue of de-aerating chamber clots has been challenged by an innovative design: the chamber is connected to a pressure sensor (different from other four “Prisma-like” pressure pods) which is able to adjust chamber blood level by means of a pump; a reversed cone inside the chamber makes the blood run into the return line with a whirling movement, which reduces stagnant flows; furthermore when replacement solution is rein fused postfilter, it is poured directly on top of de-aeration chamber, in order to create a fluid layer between air and blood (figure 9). The touch-screen shows pressures and flows in the first page. A complete fully coloured graphs and event list is displayed in other
history pages (figure 10). A suitable card allows the downloading of data into laptop computers.

Figure 9. The reverse cone placed inside the de-aeration chamber reduces flow stagnation while the postfilter reinfusion avoids blood air interface.

At the time of writing, some features are still in progress: each scale will be able to carry up to 10 litres of fluid; a new blood-line warmer is going to be implemented; a “dosage” calculator will allow the operator to be aware about the clearance performed by the treatment; the upgrading to “higher” modalities is still absent but in progress.

Figure 10. Coloured pressure graph is a useful tool to visualise filter and circuit state.

In the dialysis department and ICU of St. Bortolo Hospital, Vicenza, we tested a Prismaflex prototype and performed the first alpha-trials of the new hardware. The trials were divided into three steps: in vitro runs, short “intermittent” dialysis and continuous therapies. During the tests we evaluated software usability, touch screen and graphic tools interface, clearance parameters, pressure pods (by using external Labview measures), scales accuracy (by weighing bags and timing the bag change intervals), disposable lines and filters sets. We performed the very first in vitro tests with milk, which shares some physical properties with blood (viscosity, superficial tension). We achieved confidence with the new system and some already interesting data: pump segment delivered a blood flow close to the nominal set value for up to 24 hours, even at blood flow rate up to 250 mL/min: during in vitro tests, the measured flow error was only 2% (SD ± 0.5).

In vivo 4 - 8 hours intermittent sessions performed in the dialysis department were 5 for CVVHD, and 5 for CVVHDF. Continuous treatments were 15 in number and performed in each modality (5 as CVVH, performed either pre or postdilution, or mixed, 5 as CVVHD, 5 as CVVHDF performed pre or post). Dialysate/replacement flow rates were speeded up to 6 L/hr during intermittent therapies, in order to achieve an adequate Kt/V, and maintained at about 2 L/hr during CRRT. All treatments delivered the expected efficiency according to the prescribed schedule. No major clinical problem occurred, nor side effects. Graphical user interface, colour touch screen, on-screen schematics and stepwise on-line help allowed a error-proof handling of the machine and a correct and easy use of the machine (programming, alarms interpretation, graphics visualisation). We measured balance and weight loss errors during all treatments: the first were less then 0.5% (SD ± 0.1) while the second were never more then 8 g/hr during continuous treatments. No major clots were observed in the de-aeration chamber during 8 - 24 hour runs.

So far we have been impressed by the remarkable scale accuracy (a major issue during HVHF) and by the general performance of the machine. The difficult task of evolving the hardware while keeping the user-friendly approach, appeared to have been successfully achieved.

Some shortcomings of the old model have been overcome: the range of fluxes now available is widened and the flexibility is greatly improved. Some other weak points are still present: the warmer is still optional; buffer batteries are not provided; each bag requires a single connection and no mixing is possible between bags. Nurses may be required to change three or even four bags in three or four different moments because of the single bag connection policy. The new machine is heavy and bigger than the old Prisma, although it is sufficiently easy to transport.

The new machine, is the latest arrival as equipment for CRRT. The fact that machines are today designed to work either in a nephrological or a intensive care setting, is the best proof that the multidisciplinary approach to
critically ill patients with renal dysfunction has become a reality. The process of developing an ideal machine has yet to be completed, but actual progress has occurred and has opened a new era for critical care nephrology and the further expansion of blood purification technology in the ICU.

REFERENCES