Continuous Renal Replacement Therapy (CRRT) from ground zero

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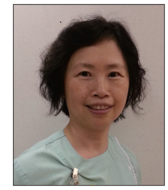

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Continuous renal replacement therapy (CRRT) is a familiar term in the intensive care units (ICU). It is a commonly used procedure to provide renal support to critically ill patients such as those with multi-organ failure. For patients with unstable cardiovascular status, conventional haemodialysis may pose a significant risk. CRRT is mainly a haemofiltration process which can provide renal support with less stress on the body. It is getting increasingly popular in the last 20 years.

The operation of the CRRT machine might look complicated and intimidating. Contrary to its appearance, its underlying principle is simple. The author was involved in its evolution from the beginning ('ground zero') and tracing its developmental history would be interesting and would help the understanding of the procedure.

Problems of the early haemodialysis and the 'dry dialysis'

The development of haemofiltration stemmed from the limitations of haemodialysis in its early days. It was not uncommon to see patients developing hypovolemic shock during haemodialysis. This was related to the hypovolaemia due to removal of accumulated fluid from the patient. Fluid removal was effected by applying a negative pressure on the dialysate side of the dialyser and the water was 'sucked' across the membrane from the blood to the dialysate side down the pressure gradient. The process is technically known as 'ultrafiltration' and the water so removed was called the 'ultrafiltrate'. Normally, as the fluid is removed from the blood compartment, water from the interstitial compartment move into the blood compartment to compensate for the reduced blood volume ('refilling'). If the rate of fluid removal was too fast, the rate of refilling might not be fast enough to compensate and there would be circulating volume depletion with resulting hypotension.

Another difficulty was that haemodialysis has limited ability to remove fluid from the patient over a short period of time. For patients presenting to the renal unit with huge fluid gain, say 4 litres of fluid, removal of such volume in the dialysis span of a few hours can be problematic. One would need to use a large negative pressure to achieve the desired ultrafiltration and this may occasionally cause membrane rupture in the early parallel plate dialysers.

One 'trick' that nephrologists could do in those early days was to clamp the dialysate inlet and connect the outlet to a suction pump with no dialysate flow. The negative pressure so created drew the fluid from the blood to the empty dialysate compartment across the membrane. The fluid in the dialysate compartment and was then drained. After about a litre of fluid extraction, the dialysate flow was reconnected and the normal dialysis resumed (Figures 1 to 3).

Figure 1 The 'dry dialysis' setup. Note the haemodialysis machine was the old batch tank machine

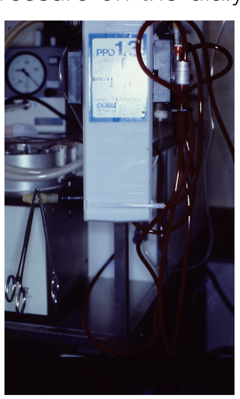

Figure 2 The 'dry dialysis'. Note that the dialysate outlet port was clamped

Figure 3 'Dry dialysis'. Water was removed by a negative pressure pump (left in the picture)

It was found that with such modification, patients could tolerate fluid removal much better. One explanation is that since there was no dialysate, there was no urea removal by diffusion and hence the serum osmolarity was maintained and this maintained the plasma oncotic pressure to facilitate the refilling from the interstitial space.

This procedure was called 'dry dialysis' because there was no dialysate in the dialyser. The term was not logical because without dialysate, the process cannot be called dialysis. The proper technical term was 'isolated ultrafiltration' but nephrologist loved term 'dry dialysis' anyway. The author had done this a number of times for patients with large fluid retention. It was virtually abandoned (and forgotten) when more efficient dialysis techniques such as bicarbonate dialysis and biocompatible dialysers were available. Moreover, newer generation haemodialysis machines had the capacity to perform isolated ultrafiltration with the touch of a button. This was also called 'haemofiltration' because blood was purified by filtering and it paved the way for the development of haemofiltration, haemofiltration-dialysis and CRRT.

Early haemofiltration-the CAVH (continuous arterio-venous haemofiltration) and CVVH (continuous veno-venous haemofiltration)

The discovery that the 'isolated ultrafiltration' (removal of water by a pressure gradient without dialysis) was better tolerated generated much interest in the nephrology circle, for patient tolerance was a very important consideration. In the early isolated ultrafiltration, one would need to use a suction pump. This was because the membrane in the early dialyser was made of cuprophane derived from plant cellulose cell walls. The natural pore size would allow small molecules like urea, potassium, water etc to pass through but not the larger molecules like plasma proteins. Due to the limited size of the pores, the rate of water removal was not high and for patients with large volume of fluid to be removed, a large negative pressure was necessary. This could pose a problem because early dialysers, being made of flat membrane, could not stand high transmembrane pressure.

With the improvement in polymer technology in the plastic industry, synthetic membrane was available. The pore size could be made larger and hence the rate of water removal can be increased. Such membrane can be used to replace the cuprophane membrane of a usual dialyser. It was found that water could be removed with relatively low transmembrane pressure and it was said to have a high 'ultra-filtration coefficient'. It was called a 'haemofilter' to distinguish it from the usual dialysers.

Such 'haemofilters' became available in 1980's in Hong Kong. Its overall size was small and can be held with the palm of a hand (Figure 4). Its synthetic membrane has large pores to allow easy passage of the fluid. Because of the high ultra-filtration coefficient, the pressure of the blood flowing inside the hollow fibres would be sufficient to drive water from the blood across the membrane without the aid of negative pressure. The set-up was simple that no machine was needed. In its simplest form, a catheter was inserted into the femoral artery and the blood was returned through another catheter into the femoral vein. The patient's blood was driven by the pressure from the femoral artery to the haemofilter and back to the body by the femoral vein (Figure 5 and 6, the CAVH setup). The water (ultrafiltrate) was drained into 'urine meter' and the volume measured and recorded. Uraemic toxins such as urea and acids were removed along with the ultrafiltrate and the fluid removed could be partially replaced with substitution fluid. The process of toxin removal was slow but was better tolerated by the critically ill patients. Since the efficiency was low, the process had to be continued for several days.

Figure 4 A small size haemofilter

Figure 5 CAVH setup

Figure 6 CAVH closeup

In this procedure, no external power was needed and it was known as continuous arterio-venous haemofiltration CAVH (Figures 5 and 6). It was especially useful in those ICUs with no haemodialysis facility to treat acute renal failure. CAVH kits were available in which all the necessary materials (haemofilter, blood line, catheters, fluid collection box etc.) were packed into a kit. In

Figure 7 A CAVH kit

the 1980's, the author used to have one such kit in the boot of his car in case he was called to treat patient in a hospital with no dialysis facilities (Figure 7). [1]

Since puncture of the femoral artery was somewhat traumatic and posed some risks, attempts were made to obtain the blood flow from one femoral vein and return through another one. Later double lumen catheters were available and only one venous puncture was needed. Since the pressure in the femoral vein was low, a blood pump was needed and the modified procedure was then called continuous veno-venous haemofiltration (CVVH) (Figures 8 and 9).

The CVVH with dialysis-the CVVHD

The CVVH provide a safe form of renal support in critically ill patients. It was good for fluid removal (such as the treatment of acute pulmonary oedema) but the rate of removal of uraemic toxin was slow. One way to augment the rate of toxin removal was to run dialysate in the dialysate compartment with an infusion pump so that some uraemic toxins can be removed by diffusion across the membrane to the dialysate. A convenient source of the dialysate was the dialysis fluid used in continuous ambulatory peritoneal dialysis because it was widely available in 2 litre bags. The author has used this method with the dialysate running at the rate of 999 ml/hour, the maximum rate of the infusion pump. The dialysate flow rate of one litre per hour was slow in comparison with 30 l/hour in standard haemodialysis. It would augment the efficiency but it added to the complexity of the procedure. (Figure 10 the CVVHD, note that dialysate was delivered to the haemofilter with an infusion pump, the right one in the picture.)

Machine controlled haemofiltration and CRRT

The advantage of CVVH and CVVHD was that they were (relatively) well-tolerated even in critically ill patients and no special equipment was needed. However, it was very labour intensive as the attending nurses have to measure the ultrafiltration output, the urine output and then calculate the rate of the substitution fluid every hour. In addition, they had to take care of the extra-corporeal circulation, monitor the pressure in the arterial and venous chambers, the anticoagulation and the dialysate flow etc. (in CVVHD). These were in addition to the already heavy ICU routines.

Since the procedures involved in CVVHD were straight forward and mechanical (though tedious), there were attempts to perform them with a computer. A machine was built in which the weight of the fluid removed (ultra-filtrate) was continuously monitored, the data was fed into a microprocessor (the heart of a computer) which would calculate the substitution fluid rate and then control the built-in fluid pump to replace the fluid. There were also blood warmers, dialysate pumps, replacement pumps in addition to the blood pumps and heparin pumps to monitor the extra-corporeal circulation parameters like a haemodialysis machine. It was found that such machines could reduce the workload of the nursing staff considerably. Since it is not exactly a dialysis process and it needs to be carried on for a few days, it was called continuous renal replacement therapy.

Figure 8 The blood pump used in CVVH

Figure 9 CVVH setup. Note the complexity

Figure 10 CVVHD. Note the infusion pump (right) delivering dialysate to the haemofilter

Disadvantages of CRRT

The introduction of the CRRT greatly reduced the amount of work by the attending staff. However, the setting up of the machine was a bit complicated and the staff needed special training. The machines and the consumables are expensive. It had to be done continuously for a few days and ICU stay was needed. There were also problems associated with prolonged anticoagulation. As a result, the cost of CRRT is high.

Another alternative is to perform slow low efficacy dialysis (SLED) **daily** instead of continuously. The efficiency of the dialysis set low so as to reduce the stress to the patient. It is also well-tolerated but the cost is much lower than CRRT. There may be no need for ICU stay and the cost would be further reduced. Initial data showed that both methods yielded similar result but more trials are needed for a definitively comparison of the pros and cons (Figure 12, SLED).

Conclusion

The 'dry dialysis' was the humble starting point of the present day CRRT which was made possible by modern industrial technology. Hemofiltration was made possible with the development of the polymer membrane technology and CRRT was facilitated by the microprocessor technology. However, the feedback of the clinicians was essential in its success.

CRRT is mainly for the short term management of acute unstable renal failure patients using haemofiltration. Another application of the technique was to prevent long term dialysis complications in chronic stable renal failure patients. This is another advance in the renal replacement technology and it is not covered in this short article.

Q&A **Self-assessment questions**

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Answer these on page 27 or make an online submission at: www.hkmacme.org
Please indicate whether the following statements are true or false.

1. Continuous renal replacement therapy is a commonly used procedure to provide renal support to critically ill patients with multi-organ failure in ICU.
2. Patients could develop hypovolemic shock easily in early haemodialysis.
3. 'Dry dialysis' provides a stable environment in which water from the interstitial compartment can easily move into blood compartment for refilling since serum osmolarity was maintained.
4. A suction pump was needed in early CAVH to create a negative pressure in the dialysate compartment in order to draw the fluid from the blood.
5. The availability of double lumen catheters facilitated the procedure from CAVH to CVVH.
6. The membrane in the early dialyser was made of cuprophane which derived from cell membranes.
7. The natural pore size of cuprophane is big enough to allow large volume of water to be removed in the process.
8. Polymer technology in haemofilter enabled uremic toxins to be removed efficiently with relatively low transmembrane pressure.
9. CVVHD is the augmentation of uremic toxin removal by running dialysate in the dialysate compartment at a slow speed with an infusion pump.
10. The introduction of the CRRT machine made the process less labour intensive since some of the decision is made by the microprocessor.

Figure 11 The CRRT setup. Note the patient has multi-organ failure requiring a ventilator

Figure 12 The patient on SLED, only intermittent dialysis was needed

References:

1. CP Ho. Continuous Arterio-venous haemofiltration (CAVH) – a new tool in critical care therapy. *Journal of the HKMA*, vol 38, 4, 1986.