

Continuous renal replacement therapy

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Abstract

Acute renal failure refers to sudden deterioration in biochemical and physiological functioning of kidneys and often associated with multi organ failure. Continuous renal replacement therapy (CRRT) holds special significance for the treatment of renal failure due to a variety of factors. It is believed that CRRT helps in restoration of acid-base imbalances and electrolyte abnormalities. Along with that, with gradual solute removal, it ensures haemodynamic stability and prevents the risk of cerebral oedema in neurosurgery patients. Besides this, several studies have supported that CRRT enables practitioners to adjust drug dosages and prevent drug accumulation and overdose. In addition, gradual removal of solutes and metabolic waste products helps to clear inflammatory mediators and ensure adequate nutrition for patients and lead to improved renal recovery. Therefore, this article will discuss the different treatment modalities that encompass CRRT and explore the indications and advantages of CRRT in acute renal failure.

Keywords: Acute renal failure, Continuous renal replacement therapy.

Introduction

Continuous renal replacement therapy (CRRT) is useful in the treatment of acute renal failure (ARF), in the setting of hypotension associated with sepsis, liver disease or cardiogenic shock. CRRT helps in volume management and controls distinct acid-base and electrolyte abnormalities through diffusion and convection.¹ The requirement for CRRT in different regions of the developed world are reported to occur in 5-6% of critically ill patients.¹ Hospital mortality rate of patients with severe ARF has been reported to be around 60%, and of those who survived to go home, 13% were dependent on some form of maintenance renal replacement therapy.²

The term CRRT refers to a technique which allows water and solutes to move across a semi-permeable membrane to support or take over the function of the kidney in the purification of blood and in the maintenance of water and electrolyte balance.³ Diffusion, convection and adsorption are the three mechanisms used for solute removal during CRRT. Diffusion is based on the principle that

molecules and ions flow randomly from an area of higher concentration of solute across a membrane to an area of lower concentration to establish an equilibrium. The speed of diffusion is related to the concentration gradient. Convection is the movement of solutes through a membrane by the force of water. Very large molecules are able to move through, if the flow of water through membrane is fast enough. Process of convection is maximized by using replacement fluid.⁴ Adsorption is the removal of solutes from the blood because they cling to the membrane. It basically refers to the binding of molecules to any surface. Ultra filtration refers to the passage of water through a membrane under a pressure gradient. The rate of ultra filtration depends upon the pressure applied to the filter and on the rate at which the blood passes through the filter. Several treatment modalities can be offered while patients are on continuous renal replacement therapy.

Slow Continuous Ultra filtration (SCUF):

The circuit for SCUF is quite simple. Blood enters the extracorporeal circuit through an access line, passes through the haemofilter, and returns to the patient's circulation via the return line. As the blood passes through the filter, ultra filtration takes place and effluent collects in the effluent bag. Effluent is any fluid that exits the haemofilter and is delivered

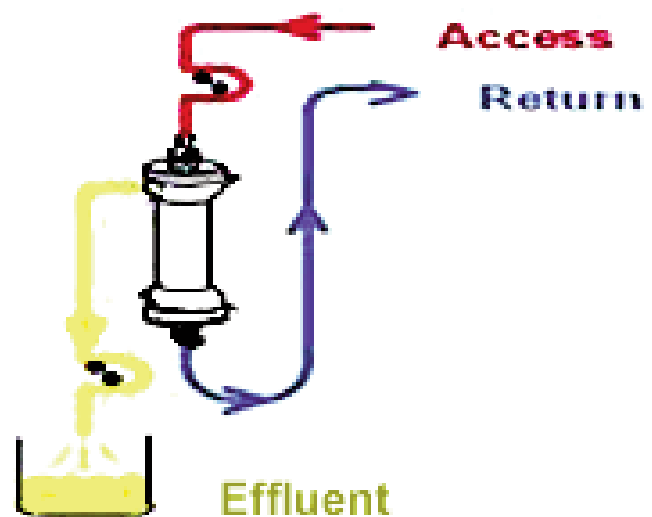


Figure-1: Circuit for slow continuous ultra filtration (SCUF).

to a waste bag. Pumps control blood flow and fluid removal rates. This process is followed by the principle of ultra filtration. No dialysate or replacement fluids are used. However, significant amounts of fluid are removed from the patient. This therapy is quite appropriate for severely hypervolaemic patients. Clinically, practitioners use this therapy to remove fluid from the patient over a short (8-12 hour) time period and then the treatment can be switched to another appropriate therapy.

Continuous Venous Haemofiltration (CVVH):

Continuous veno-venous haemofiltration (CVVH) involves convection and ultra filtration mechanisms. Blood enters the extracorporeal circuit through an access line and passes through the haemofilter. The replacement fluids can be delivered either pre or post filter. Solute removal is accomplished by convection and the blood then returns to the patient circulation via the return line. The effluent bag not only contains Ultra filtrate from the patient, but also the replacement fluid volume.

CVVH aims for maximizing convective removal of small and middle molecules. Replacement solutions are used to drive this convective transportation. The standard fluid usage is 25 ml/kg/hr so in average size patient total fluid used is 60-72 litres in 24 hour period to achieve the desired clearance of solutes. Because of its simplicity and efficiency in taking over for the failing kidney, continuous

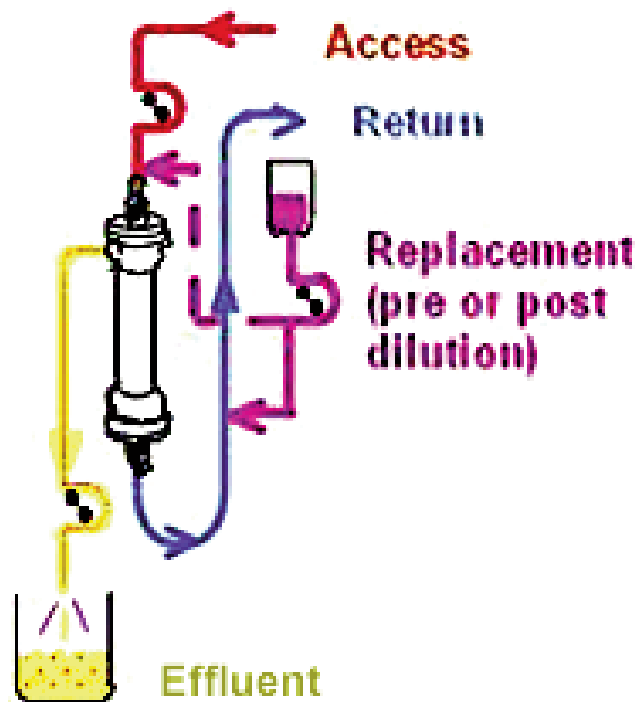


Figure-2: Circuit for continuous venous Haemofiltration (CVVH).

veno venous haemofiltration (CVVH) is widely used to manage acute renal failure.⁵ Pre or Post dilution fluid replacement has its own implications. Pre dilution replacement fluid lowers haematocrit levels thus decreases the risk of clotting and ensures higher Ultra filtration. However, the effluent chemistries do not reflect true plasma solute losses. On the other hand, with post dilutional replacement fluids, there may be a need to increase anticoagulation to prevent filter clotting. A benefit that post-dilution replacement fluid offers is that the effluent characteristics truly indicate the plasma solute losses.

Continuous Venous Haemodialysis (CVVHD)

Continuous veno venous haemodialysis (CVVHD) works on the principle of dialysis and ultra filtration. Blood enters the extracorporeal circuit through an access line, passes through the haemofilter; the dialysate is added on the fluid side of the filter to increase solute exchange by diffusion. The blood then returns to the patient circulation by the return line. The effluent bag not only contains ultra filtrate from the patient, but also the dialysate. Since replacement fluid is not administered with this therapy, ultra filtration rates are lower than with CVVH therapy. Unlike intermittent haemodialysis, it is the dialysate flow rate rather than the blood flow rate that will determine clearances.

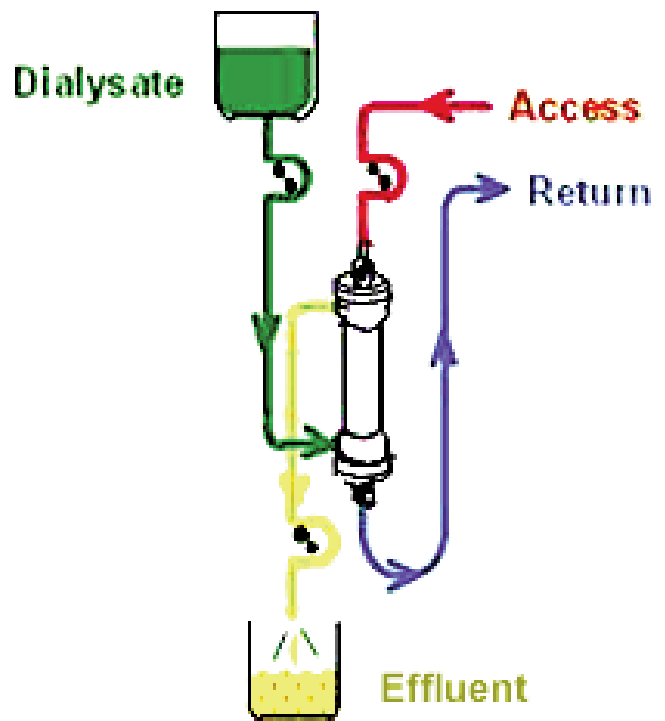


Figure-3: Circuit for continuous venous Haemodialysis (CVVHD).

Continuous Venous Venous Haemodiafiltration (CVVHDF):

Continuous venous venous haemodiafiltration (CVVHDF) works on the principle of dialysis and convection. Blood enters the extracorporeal circuit through an access line, passes through the haemofilter; the dialysate and replacement fluids are added on the fluid side of the filter to increase solute exchange by diffusion and convection. The blood then returns to the patient's circulation by the return line. The effluent bag not only contains ultra filtrate from the patient, but also the dialysate and the replacement fluid. CVVHDF is the therapy that merges the mechanisms of CVVH and CVVHD using both the principles of convection and diffusion. Dialysate functions to remove small molecular weight substances and replacement fluid allow additional convective clearance of middle size molecules. In this therapy, diffusion provides excellent electrolyte and metabolite control, and middle molecules such as TNF, IL-1, cytokines, and mediators of septic shock are cleared by convective transport mechanisms.

In CVVH solutes are removed only by convection, and solute removal is limited by the ultra filtration rate. By adding dialysis to filtration, as in CVVHDF, solutes are removed by both convection and diffusion, increasing the removal of small molecules more than middle-sized and large molecules.^{4,6}

Several factors can be considered for selecting the criteria for the initiation of renal replacement therapy as anuria or oliguria (urine output, 200 ml/12 hours), hyperkalaemia ($K > 6.5$ mmol/l), severe acidaemia (pH < 7.1), azotaemia (BUN < 20mg/dl).⁷ Other criteria for the

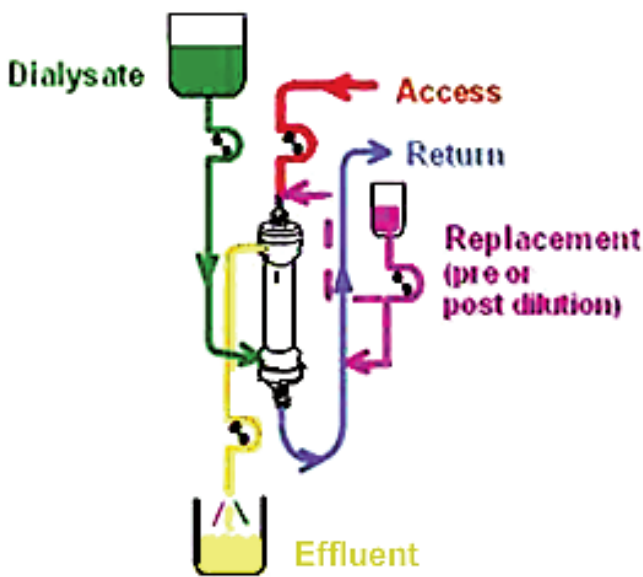


Figure-4: Circuit for continuous venous venous Haemodiafiltration (CVVHDF).

initiation of replacement therapy could be clinically significant organ oedema (particularly lung), uraemic encephalopathy, uraemic pericarditis, uraemic neuropathy/myopathy, hyperthermia or drug overdose with a dialyzable product.^{3,7} There is no consensus in the medical community on when to start CRRT. The decision to start CRRT depends on individual patient's condition.

CRRT requires the placement and maintenance of a vascular access. Most often a double lumen vascath is inserted to aid in the process. Internal jugular and femoral veins are different sites that can be used. Subclavian site is usually avoided due to high risk of subclavian vein stenosis. However, the selection for appropriate site depends on the patient's condition. For example a femoral catheter could not be a very good choice for a patient with ascites due to increased intra abdominal pressure.

CRRT proves to be effective in acute renal failure as it helps to maintain electrolyte and acid base balance. It corrects renal acidosis by clearing acids and other metabolic waste products. Along with that, it ensures adequate nutrition and clears inflammatory mediators. CRRT offers better control of metabolic acidosis and serum electrolyte levels compared to IHD. However, due to the high phosphate clearance and the simultaneous initiation of nutritional support, hypophosphataemia may develop during CRRT and thus should be monitored and treated.¹ Another study supports that acid base imbalance can be corrected and sustained more effectively using CRRT due to the continuous supply of buffer contained within the dialysate and/or replacement fluid.⁸ CRRT also removes excess fluid volume. Fluid overload is controlled more effectively using CRRT especially in the setting of haemodynamically unstable patient. The advantage of CRRT is that the composition of replacement fluid and dialysate can be modified easily and lower rate of blood flow promotes cardiovascular stability. The use of CRRT is now an established primary treatment modality for renal replacement as conventional IHD increases the frequency of hypotensive episodes in haemodynamically unstable patients.⁷ Besides this, a slower blood flow speed than conventional IHD allow the rate of fluid removal during CRRT to be achieved over a longer period of time and along with the use of biocompatible membranes, reduce the incidence of haemodynamic instability. In addition, the CRRT therapy ensures adequate mean arterial pressure (MAP) and prevents cardiovascular complications. Along with that, CRRT has positive effects in patients who are at risk of increased intracranial pressure such as neurosurgical patients, patients with encephalitis or meningo-encephalitis or hepatic encephalopathy. Since, the solutes are removed slowly and gradually during CRRT, therefore, it prevents the risk of cerebral oedema. In addition, CRRT has been demonstrated to prevent the surges in

intracranial pressure associated with intermittent therapies that can perpetuate further injury.¹ As many antibiotics are excreted through the kidneys, the antibiotic doses may have to be reduced or discontinued because of nephrotoxicity. The critically ill patient with renal failure is at risk for drug accumulation and overdose, but also for under dosing, that may be life-threatening.⁴ However, physicians can plan effective antibiotic regimen when patients are started on continuous renal replacement therapy. Therefore, the principles of drug removal during CRRT need to be clearly understood.⁴ Therefore, deliberate attention is required from the physician and pharmacologist while prescribing and adjusting drugs appropriately.

CRRT can lead to some complications. Anticoagulation in CRRT can lead to cause systemic bleeding episodes. Vigilant care is directed to look for the signs and symptoms of occult or fresh bleeding.^{9,10} Moreover, the patient's haemoglobin levels are checked as per the institutional policy and patient's condition. Besides this, the dialysate and replacement fluids are kept at room temperature and administration of large volumes of room temperature fluids can cause hypothermia. Fluids containing bicarbonate cannot be warmed as warming can convert bicarbonate into carbon dioxide bubbles. Therefore, general warming interventions are required. On the other hand, patients may get infection because of this invasive procedure. So, nursing care is focused on maintaining asepsis. Another complication that may occur during CRRT is the development of emboli.¹⁰ Specific attention is paid while priming and CRRT circuit is routinely checked for the presence of air to prevent air embolus.

Continuous Renal Replacement Therapy (CRRT) versus Intermittent Haemodialysis (IHD); Comparison and Contrast:

Intermittent haemodialysis (IHD) is commonly used for the treatment of renal failure. High blood flow rate (200-500 ml/minute) and high dialysate flow rate (500-800 ml/minute) can be used in order to achieve high solute clearances over a short period of time.¹¹ On the other hand, CRRT is most frequently used in patients who are haemodynamically unstable and can not tolerate IHD, usually because of sepsis or cardiac problem. It is rightly believed that CRRT is associated with a significantly higher mean arterial pressure (MAP). Along with this, the need to escalate inotropic or pressor support is decreased while patients are on CRRT as compared to IHD.¹² However; patients on CRRT modality are prone to continuous anticoagulation and hypothermia that might adversely affect the outcome. Several clinical trials support that CRRT is associated with a significantly increased risk of recurrent filter clotting and bleeding tendencies as compared to IHD.¹³ Besides this, IHD

is cost effective and cheaper as compared to CRRT. The training expenditure and resource management in terms of equipment are low with IHD. On the other hand, CRRT requires a specialized equipment and training of staff, additional supplies (especially replacement fluids), and consumes greater health care resources than IHD. A recently published randomized trial of intermittent haemodialysis versus CRRT demonstrated that even the sickest of patients could be safely treated with intermittent haemodialysis given the significantly higher cost of CRRT.¹⁴ Pannu, et al performed a systemic review of 30 randomized control trials and 8 prospective cohort studies in 2008 and concluded that there is no difference in survival between CRRT and IHD, and there was no evidence that either CRRT or IHD was superior for reducing mortality. Although cohort data suggests a lower risk of hypotension among CRRT recipients.¹⁴ Despite apparent advantages over intermittent therapies in unstable patients, superiority of CRRT with respect to mortality or recovery of renal function has not been demonstrated.¹² The research findings also reflect that the creatinine clearance and blood urea nitrogen levels also do not differ significantly when compared in both the therapies. As the solute clearance depends on the dialysis prescription and the operational characteristics; it is also possible to increase clearances in CRRT by adjustment of the ultra filtration rate and dialysate flow rate. In contrast, if IHD techniques are operational at maximum capability, it is difficult to enhance clearances except by increasing the size of the membrane or the duration of therapy. In general, IHD techniques are limited by available time, and in catabolic patients it may not be possible to achieve a desired level of solute control even by maximizing the operational characteristics.¹⁵

This still remains a controversial issue. The decision to use CRRT or IHD in patients with ARF is mainly based on the physician preference at the particular point in time and patient's assessment findings such as electrolyte and acid-base status, uraemia, nutritional requirements, urine output, haemodynamic status, and the clinical condition of each individual patient. A practical approach could be to consider both, IHD and CRRT as complementary therapies that can be interchangeably utilized in ARF patients according to individual patient's needs. It is anticipated that a multidisciplinary approach will bring more advancement in this complex field.

A large randomized controlled trial and further meta analysis is recommended to explore further advantages and disadvantages and practical implications of various treatment modalities of CRRT and IHD. More extensive research is required to identify which therapy is more appropriate and applicable based on different patient's co morbid and patient's diseases process.

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