SECTION 24

Intermittent Renal Replacement Therapies

CHAPTER 149

Intermittent Techniques for Acute Dialysis

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Objectives

This chapter will:

1. Present the specificity to implement intermittent techniques to treat acute renal failure in the intensive care unit.
2. Review the evidence regarding the effect of the type of dialysis membrane and the dialysis dose on the outcome for the patient with acute renal failure.
3. Discuss the basic principles of prescribing intermittent hemodialysis for patients with acute renal failure, including treatments using sustained, low-efficiency intermittent hemodialysis.

Intermittent hemodialysis (IHD) was the first method available to treat patients with acute renal failure (ARF) in intensive care units (ICUs). In most countries, the use of IHD required a close collaboration with the nephrology team, and the implementation of the technique relied on nephrology practices.[1] Continuous renal replacement therapies (CRRT), therefore, rapidly were accepted by intensivists to enhance ICU independency in the treatment of ARF. In addition, these new methods were thought to improve hemodynamic tolerance and were used widely in most parts of the world.[2] Despite abundant relevant literature over the last 20 years, IHD seems to offer a similar outcome as CRRT for mortality and probably renal recovery.[3–5] Intermittent techniques present some advantages, such as the preservation of patient mobility, the lower exposure to anticoagulants, and the capability to treat several patients a day with one machine. IHD remains widely used in some countries either as the first-line treatment[6] or for patients without hemodynamic instability.[7] Nevertheless, practical aspects have been developed specifically to enhance hemodynamic tolerance and dialysis dose to be adapted to ICU patients. Adaptations must be considered related to blood and dialysate flow, dialysate characteristics, net ultrafiltration, and session duration. New developments to improve efficiency and tolerance tend to become more popular with the use of low-efficiency prolonged IHD, usually called sustained low-efficiency dialysis (SLED) or slow efficiency extended hemodialysis. The chapter explains the specific characteristics to implement intermittent techniques of IHD to treat acutely ill patients with ARF.

PHYSICAL PRINCIPLES

In IHD, molecule removal is driven by a concentration gradient between the vascular and dialysate side of the membrane, using a diffusive mechanism of exchange. This method favors small molecule removal, given their high diffusibility across the membrane, and provides a high efficiency (clearance around 200 mL/min). In a standard way, this method is based on a high dialysate flow (500 mL/min) and needs although a high blood flow (250–300 mL/min). In addition to diffusion a certain amount of convection called "net ultrafiltration" is used during each session to remove an excess of fluids. However, its effect on metabolic control or solute removal is insignificant.

Technical Aspects

The implementation of IHD requires specific equipment: a dialysis machine, a water treatment system, and electrolyte concentrates. Some other aspects may be different from CRRT: vascular access, dialysis membrane, and anticoagulation.

Dialysis Machine

The machine is devoted to the production of the dialysate using the online prepared pure water and the electrolyte concentrates, to the control of the ultrafiltration, and to the monitoring of the treatment. Recent improvements have been implemented in most machines, such as the online monitoring of the ionic dialysance (to monitor the delivered dialysis dose) or blood volume. The machine used in the ICU must be robust, compact, and easy to use.

Pure Water

The microbiologic quality of the prepared water is essential to achieve the best tolerance, including the absence of endotoxin, which may pass through the membrane from the dialysate to the vascular side. Inorganic and organic substances are removed from the water supply to obtain pure water. The water treatment system is composed with filters, a charcoal cartridge, and a reverse osmosis system. The water delivery may occur in three different ways: a central distribution from a specific water treatment system such as in chronic hemodialysis unit, a mobile water treatment incorporated in the dialysis machine, or more recently a batch-delivered system.[8]

Dialysate

The electrolytic composition of the dialysate is attempted to achieve a good electrolytic equilibrium and a good uremic control at the end of the session. The choice of the electrolytic concentrate is paramount. Bicarbonate-based buffer is the standard buffer, given the hemodynamic effects provided by the old acetate-based buffer. For the electrolytic solution, particular attention must be paid to the potassium concentration (from 2 to 3 mmol/L) and the calcium concentration (from 1.25 to 1.75 mmol/L) to avoid dysrhythmia and hemodynamic instability. Their final dialysate concentrations depend on the product used and are provided by the manufacturer. The final sodium concentration (from 140 to 150 mmol/L) and bicarbonate concentration (from 30 to 36 mmol/L), however, can be selected on the dialysis machine and may be modified during treatment. The dialysate flow can be modified in almost all machines (from 300 to 750 mL/min).

Vascular Access

For the treatment of ARF in the ICU, double-lumen catheters are used instead of single-lumen catheters. The latter requires a dialysis machine able to deliver dialysis using the mode "single needle" but is associated with higher recirculation, decreasing the delivered dialysis dose. The best insertion site providing the higher blood flow is the right jugular vein, but femoral access still remains the emergency site and is associated with the lower rate of acute complication during insertion. Concerning the rate of nosocomial infection or catheter dysfunction between jugular and femoral access, recent data seem to challenge the usually reported higher rate of infection or catheter dysfunction with femoral access.[9,10] The subclavian access should be avoided, considering the high rate of venous stenosis after dialysis catheter insertion. Usually the use of an arteriovenous fistula in chronic renal failure patients is discouraged in the ICU, considering the risk of infection, the risk of low cardiac output, and the lack of experience of the ICU nurse. Use of the long-term cuffed catheter may be considered after the acute phase in a stable patient, but the occurrence of systemic infection usually leads to catheter removal. The diameter of the catheter is important to consider to obtain a good blood flow with acceptable pressures. In this setting, 12 Fr seems to be the minimal inner diameter.

Dialysis Membrane

Unmodified cellulosic membranes have a low molecular permeability and a low ultrafiltration coefficient compared with modified cellulosic or synthetic membranes (polysulfone, polymethylmethacrylate, polyacrylonitrile, polyamide). In addition, they are well known to activate the inflammation (complement and leukocytes activation) that is described as "bioincompatibility" properties. This induces hemodynamic impairment and may induce pulmonary and kidney damage. Randomized studies of the survival of acute renal failure patients in intensive care according to the type of membrane used[11,12] do not yield a definitive conclusion because of the small total number of patients studied and conflicting results. However, meta-analyses suggest excess mortality with Cuprophan membranes, at the limit of significance.[13]

Unmodified cellulosic membranes are no longer recommended in ARF. No study has reported any significant difference for major outcome between modified cellulosic or synthetic membranes as well as between different synthetic membranes. Concerning the molecular permeability or the ultrafiltration coefficient, no study has demonstrated that high-permeability or high-flux membranes are useful to treat ARF. The surface of the membrane is usually between 1.3 and 1.6 m^2. High-flux membrane and high surface may provide retrofiltration, increasing the risk of infectious complication.

Anticoagulation

One of the major advantages of IHD is the lesser need for anticoagulation compared with CRRT. Some authors have reported that IHD may be used without any anticoagulation but usually for short duration.[14] New membranes (heparin coated) have been proposed to be used without anticoagulation after a priming with heparin. Recent studies did not show any advantage.[15] Unfractionated heparin remains the historic anticoagulant in IHD. Several other options may be used,[16] including low-molecular-weight heparin, regional citrate anticoagulation, heparinoids, hirudin, or prostacyclin. Regional heparinization with protamine infusion is no longer recommended given the systemic anticoagulation usually observed. Heparinoids and hirudin may be used for heparin-induced thrombocytopenia. Regional citrate anticoagulation also may be used when heparin is contraindicated or for patients at high risk of bleeding.

Advantages and Limits in the Intensive Care Unit

The high efficiency achieved with IHD is responsible for a rapid decrease of the concentration gradient, leading to a decrease in the removal rate that limits the amount of solute removed. This explains why IHD is used discontinuously, usually during 4 to 6 hours every day or every other day. This high efficiency and the short duration of each session explain some important limits of IHD:

- The refilling of urea from the interstitial space to the vascular compartment is limited during the session and occurs soon after the end of the treatment. Given the high extravascular volume of urea distribution, we observe a significant increase of serum urea after each session that is called urea rebound. This phenomenon limits IHD efficiency.
- The rapid exchange of solute induces high and fast osmolality variations during the treatment. These variations involve the vascular compartment and may induce

hemodynamic instability as well as cellular edema particularly deleterious for the brain.
- The fluid balance control requires high ultrafiltrate rate, considering the short session duration that may influence hemodynamic impairment.

For these reasons, specific adaptations from nephrologic practices have been proposed and evaluated to improve efficiency and hemodynamic tolerance in ICU patients. Guidelines from French scientific societies (intensive care, anesthesiology, nephrology, and pediatrics) have been provided recently in a practical point of view regarding adaptation and settings to use IHD in acutely ill patients.[17]

Specificity of Intermittent Hemodialysis Use in Intensive Care Units

In the acutely ill, ARF is usually part of a multiple organ failure syndrome with hemodynamic impairment. In this population, the main objectives are the metabolic control and the good hemodynamic tolerance to avoid any further damage to the kidney and other organs.

Metabolic Control and Dialysis Dose

The dialysis adequacy has been recognized as a strong prognostic factor in chronic IHD for at least two decades. There is accumulating evidence to support the link between the dialysis efficacy and the outcome for the treatment of ARF in ICU. One major unresolved issue is the target dose able to provide a better outcome. In IHD, the study from Schiffl et al.[18] showed that daily dialysis (six sessions per week, mean session duration 3 hr 20 min) significantly improved the patient's survival compared with alternate-day sessions (three sessions per week, same mean duration). This study presented several shortcomings, especially in the alternate-day group. The net ultrafiltration was around 1 L/hr during IHD session compared with approximately 400 mL/hr in the other group. Unsurprisingly, the alternate-day group experienced more frequent hypotensive episodes (25 ± 5% vs. 5 ± 2%), more frequent oliguria (73% vs. 21%), and a worsening of the organ failure score. In addition, even in the daily group, the delivered dose was lower than standard dose used in chronic dialysis.

A recent prospective randomized multicenter study challenges the role of a high delivered dialysis dose in ARF.[19] The authors randomized 1124 patients with ARF and at least one nonrenal organ failure or sepsis to receive intensive or less-intensive renal replacement therapy. Patients were assigned to IHD if hemodynamically stable and CRRT or SLED if hemodynamic impairment was present. Intensive treatment was IHD or SLED six times per week or 35 mL/kg/hr for CRRT, and less-intensive treatment was IHD or SLED three times per week or CRRT 20 mL/kg/hr. In the less-intensive group assigned to IHD, sequential dialysis could be used to control the fluid balance (ultrafiltration alone on days when dialysis was not performed). In IHD the prescribed dose based on formal urea kinetic modeling (Kt/V) derived from chronic hemodialysis patients was 1.2 to 1.4, which is the target recommended to improve outcome in patients with chronic renal failure. They found no differences between the two groups regarding 60-day survival, renal recovery, duration of renal support, and rate of organ failure. No definitive comparison can be drawn between this study and the other because the control group (less-intensive treatment) received a treatment definitively more intensive than the control group from Schiffl et al.[18]

When considered in a meta-analysis, these studies do not show that a higher dialysis dose was superior in terms of mortality or dependence on chronic dialysis.[20] It is not, however, possible to conclude that the dialysis dose has no impact on the prognosis of intensive care patients, but rather that there is a minimum dose, used in the control arm of these three studies, above which increase provides no further benefit. The French guidelines recommend a minimal dose based on the control group from the VA/NIH study[17]: "In intermittent RRT the minimum delivered dose of dialysis should probably be 1) three sessions per week of at least 4 hours with a blood flow >200 mL/min and a dialysate flow >500 mL/min, or 2) a Kt/V index >3.9 per week, or 3) maintenance of a predialysis urea concentration of 20 to 25 mmol/L."

After the initiation, these goals have to be adjusted in light of the patient's progress. An increase of the dialysis dose is required in certain clinical circumstances, such as life-threatening hyperkalemia, severe metabolic acidosis, and tumor lysis syndrome.

Hemodynamic Tolerance

Hypotension during IHD remains a serious problem in ICU patients, occurring for approximately 30% of all sessions in cases of multiple organ dysfunction syndrome. This complication is of multiple origins, hypovolemia (fluid removal during the priming and during treatment), sodium and water loss (osmolality variation), and vascular vasodilation. Most of the studies published in ICU patients, reporting a high incidence of hypotension, used settings directly derived from chronic renal failure patients. Taking into account specificity of ICU patients, particular settings may dramatically improve the hemodynamic tolerance of IHD. It has been reported that high dialysate sodium concentration may reduce sodium loss at the initiation and osmolality variation during treatment. Mild dialysate hypothermia also may contribute to the better tolerance by the preservation of vascular tone. These positive effects have been reported by Schortgen et al.,[21] showing that specific settings significantly decreased the hypotension rate during treatment and the rate of any intervention to maintain arterial pressure. These aforementioned settings (Box 149.1) were saline priming with isovolemic connection, application of a high dialysate sodium concentration, mild hypothermic dialysate, and low ultrafiltration rate. Recent prospective randomized studies using optimized settings in IHD illustrate the tolerance improvement.[22,23] New technologic developments are available to improve hemodynamic tolerance: blood volume monitoring with online hematocrit or hemoglobin measurement, sodium or ultrafiltration profiling, and blood temperature monitoring. It could be useful in ICU patients, but data are sparse for this population.

Different Modalities

Several modalities can be used combining diffusion, convection with different session frequency, or duration.

Conventional Intermittent Hemodialysis

This modality is derived directly from the use in chronic dialysis units. The sessions are performed on a daily or alternate-day basis.

BOX 149.1

Guidelines to Improve Hemodynamic Tolerance Using Intermittent Hemodialysis

Guidelines to Apply Systematically
- Use synthetic membranes
- Use isovolemic connection
- Sodium conductance ≥ 145 mmol/L
- Dialysate temperature ≤ 37°C
- Minimal duration: 4 hr

Guidelines for Unstable Patients
- Sequential dialysis without ultrafiltration at the start
- Dialysate temperature set at 35°C

Complementary Guidelines
- Stop vasodilators
- Adapt ultrafiltration flow rate to the hemodynamic
- Define closely ultrafiltration needs

Data from Schortgen F, Soubrier N, Delclaux C, et al. Hemodynamic tolerance of intermittent hemodialysis in critically ill patients: Usefulness of practice guidelines. *Am J Respir Crit Care Med.* 2000;162:197–202.

Sequential Intermittent Hemodialysis

Ultrafiltration and diffusion are not performed simultaneously during the same session. Usually, ultrafiltration is performed alone to manage the fluid balance; thereafter diffusion is used alone. In end-stage renal disease patients experiencing hemodynamic instability during IHD, this modality has been reported to improve the hemodynamic tolerance.

Sustained Low-Efficiency Dialysis

The principle of this method is to decrease the solute clearance and to maintain the treatment over prolonged periods of time. Different terminology has been proposed in the literature: prolonged intermittent renal replacement therapy, extended daily dialysis, and sustained low-efficiency dialysis. The principal characteristic of these therapies is the prolonged treatment time and the low efficiency to permit slow removal of fluids with better hemodynamic tolerance and enhanced molecule removal. Usually, the dialysate and the blood flow rate are decreased (respectively 100 mL/min and 200 mL/min), and the session duration is increased (8 to 12 hours).[24,25] The lower clearance induces a lower solute removal rate and a lower decrease of the concentration gradient. Therefore the refilling from the interstitium to the vascular bed is enhanced, and given the prolonged duration of the treatment, the effective solute removal (i.e., efficiency) is increased. The hemodynamic tolerance has been reported equivalent to CRRT.[25] The Genius system from Fresenius (Fresenius Medical Care Germany, Bad Homburg, Germany) is devoted to the SLED, even if the machine may provide standard IHD.[8]

Key Points

1. Intermittent hemodialysis performed three or four times per week is a common modality for treating patients with acute renal failure.
2. A target delivered dose of dialysis must be determined, and specific settings must be used to provide the target dose.
3. Evidence to support the use of specific dialysis membranes or higher doses of dialysis to improve patient outcomes remains limited.
4. Intermittent hemodialysis can be used to treat hemodynamically unstable patients with acute renal failure if applied with specific settings or as sustained low-efficiency dialysis (SLED).

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