PROTOCOL OF EXTRACORPOREAL PURIFICATION TECHNIQUES

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Method Article

Keywords: intensive care unit, critical care, acute kidney injury, extracorporeal purification techniques, continuous hemodiafiltration, monitoring

Posted Date: July 7th, 2023

DOI: https://doi.org/10.21203/rs.3.pex-2235/v1

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Abstract

Extracorporeal purification techniques (EPT) are complex techniques with a growing application, yet they can induce complications. A standardized approach and strict monitoring of their application are crucial to ensure patient safety. In this protocol, we describe the main indications, modalities, vascular accesses, therapy dosage, and dynamic adjustment for EPT. Additionally, we provide management algorithms that can help professionals to facilitate the adjustment of these therapies, as well as the identification of alarms, understanding of problems, and potential solutions. The application of this protocol and the evaluation of its results through a specific registry and study (DIALYREG) aims to standardize and systematize our clinical practice to improve the quality of care for our patients.

Introduction

Although Graham and Fichz first employed the concept of dialysis in the 19th century, it wasn't until Kramer optimized continuous hemodialysis (CHD) systems in 1977, defined by Scribner in 1960, that CRRT modalities developed. Technological advances have significantly enhanced the effectiveness and safety of Continuous Renal Replacement Therapy (CRRT). With improved depurative efficiency and patient safety, the indications for employing CRRT in intensive medicine have expanded.

Reagents

Equipment

1. **Hemofilter set**: the hemofilter sets that we mainly use in our units are PRISMAFLEX/PRISMAX System M100 set (Factory ID 8353520, Code No. 106697), PRISMAFLEX/PRISMAX System M150 set (Factory ID 8353584, Code No. 109990) and Oxiris Set.

2. **Bacteremia Zero Kit**.

3. **Double-lumen catheter**: we preferably use catheters of 13-14.5 Fr with a "shotgun barrel" geometry. The optimal length will be 24 cm for the femoral location, 15 cm for the right jugular-subclavian, and 20 cm if using the left jugular-subclavian.

4. **Extracorporeal depuration monitor**: we use PrismaflexR or PrismaxR

5. **Dialysis and replacement fluids**: we use PhoxiliumR as the main dialysis and replacement fluid, and PrismaSolR in patients with hyperkalemia despite adequate therapy. If we use citrate anticoagulation, we employ RegiocitR (Citrate 18 mmol/L) on the PBP scale and BiphozylR on the dialysis and replacement scales. The specific characteristics of the fluids that we use are detailed in Table 1.

6. **Corresponding anticoagulation system**: heparin, epoprostenol, or citrate. See specific protocol.
Procedure

1. **Establish the indication:** CRRT provides numerous benefits compared to conventional intermittent hemodialysis (IHD). The most significant advantage of CRRT is the improved hemodynamic stability it offers, making it a suitable alternative to IHD in patients who are unstable. Unlike IHD, which causes abrupt changes in blood volume and electrolyte concentrations, CRRT involves a gradual and continuous elimination of water and toxic metabolites, resulting in better electrolyte management. Additionally, CRRT may improve gas exchange by reducing hydrostatic pressure and improving ventricular filling pressures. It also provides better metabolic control, has a lower extracorporeal volume, reduces complement activation with the use of biocompatible membranes, eliminates interstitial fluid preferentially, and has a low risk of complications. All of these advantages suggest the usefulness of this procedure in the following situations and are resumed in **Figures 1 and 2.**

**Generally accepted:**

1. AKIN stage 3: sudden decrease of renal function (oliguria or anuria) with organic repercussion and fluid accumulation.
2. Non-oliguric renal failure in highly catabolic patients.
4. Situation of fluid overload of any etiology.
5. Fulminant Liver Failure with ARF (consider associating plasmapheresis, hemoadsorption, or MARS in a bridging situation to transplantation).
6. Clearance in some intoxications (lithium, metformin, etc.).
7. Control of body temperature: active warning in severe hypothermia, as well as for cooling patients in selected cases (cardiac arrest, malignant neuroleptic syndrome, etc.).

**Accepted for restricted use (we will preferably use Oxiris®-filter):**

- Improve hemodynamics and respiratory function and potentially improve morbidity, and mortality stopping the progression of multiples organ dysfunction syndrome (MODS) secondary to illness, injury, or infection.

- Regarding the severely injured patient, in our experience, the results are very positive, with a significant improvement in survival. The usefulness of continuous hemofiltration in these cases is based on the “Mediator Theory” and/or the “Hydrostatic Theory” (microcirculation, lymphatic flow).

2. **Set the preferable variant:**

- **Slow Continuous Ultrafiltration (SCUF):** this technical variant is most useful for controlling fluids in situations of fluid overload. The mechanism used in this technique is convection and the flow used for
this technique ranges from 50 to 100 ml/min for blood and 2-5 ml/min for ultrafiltrate, where the main objective is to remove excess fluid.

- **Continuous Hemofiltration (CVVHF):** the main difference from the previous technique is the need for replacement (pre- or post-filter). This way, we can balance the volume loss to the patient’s need, achieving high clearance and strict volume control. The physical mechanism used is convection. For molecules with a sieving coefficient close to one, the clearance achieved is equal to the volume of UF generated.

- **Continuous Hemodialysis (CVVHD):** diffusion is the main physical mechanism, exposing the blood to a dialysis bath through the membrane, resulting in the diffusion of low molecular weight molecules. As a result, the dialysis fluid passes through the filter only once, its composition is not altered and it achieves the highest diffusion capacity. The dialysate at the outlet of the filter is almost 100% saturated with urea, achieving a diffusive clearance of 20-25 ml/min at a flow rate of 20-25 ml/min. The passage of water through the membrane is small, so volume replacement will not be necessary, and the UF produced corresponds to the patient’s weight loss. The flows used for this technique range from 100 to 150 ml/min for blood, 10-25 ml/min for dialysis fluid, and 2-4 ml/min for UF.

- **Continuous Hemodiafiltration (CVVHDF):** it is a combination of the two previous techniques and is also a very commonly used EDT in the ICUs of our country.

3. **Prepare the hemofilter:**

   - Follow the assembly instructions for each monitor.

   - Always perform the system assembly with gloves, after having performed the necessary hand washing. Extreme asepsis.

4. **Select vascular access:**

   - Individualize in each case, with the right femoral access being preferred initially. The right jugular route is the one that provides more flow and may be necessary when using high therapy doses (first choice). In compliance with the Zero Bacteremia protocol, in which our Services are involved, the right jugular route can be used as the first choice, assessing risks and benefits in each patient.

   - Double-lumen catheter, 13-14.5 Fr; preferably with a "shotgun barrel" geometry. The optimal length will be 24 cm for the femoral location, 15 cm for the right jugular-subclavian, and 20 cm if using the left jugular-subclavian.

5. **Connect the hemofilter to the patient:**

   - We will perform simple or double connection, depending on the patient’s profile (double connection in the hemodynamic unstable patient). In the simple connection, only the arterial route is connected initially, and the purging fluid is eliminated to the collection bag before connecting the venous light of the circuit. In the double connection, both lights of the circuit are connected simultaneously.
6. **Choose anticoagulation mode:**
   - See specific protocol.

7. **Set initial treatment parameters:**
   - Initial blood flow: 150-250 ml/min (which will be modified based on therapy and the flow achieved with the chosen catheter route).
   - Filtration fraction <20%, which will require adjusting blood flow and greater use of diffusion. In some cases, pre-filter replacement could be considered.
   - Initial modality: CVVHDF (at 50%), with post-filter replacement.
   - Replacement: our Services have two commercial replacement fluids (Prismasol\textsuperscript{R} and Phoxilium\textsuperscript{R}). Although both can be used safely, we recommend using Prismasol\textsuperscript{R} only in patients with hyperkalemia despite adequate therapy (>5 mEq/L). For the remaining patients, Phoxilium\textsuperscript{R} is a better-balanced solution. If we use citrate anticoagulation, we employ Regiocit\textsuperscript{R} (Citrate 18 mmol/L) on the PBP scale and Biphozy\textsuperscript{R} on the dialysis and replacement scales. The specific characteristics of the fluids that we use are detailed in Table 1.
   - Anticoagulation according to specific protocol.
   - For high-volume "pulses" we will use the CVVHF modality, with mixed replacement (1/3 pre-filter and 2/3 post-filter).

8. **Monitoring the CEPT circuit:** current CRRT monitors provide us with information on the essential parameters for effectively, efficiently, and safely implementing therapies. The Prismaflex\textsuperscript{R} and Prismax\textsuperscript{R} monitors, as they allow entering the patient's weight and hematocrit, will provide us with reliable on-screen information on dose, PTM, and filtration fraction, making its calculation unnecessary in most cases.
   - **Flows:** the clinician, according to the needs of each clinical situation and therapeutic modality sets their values.
     - **Blood flow rate (ml/min.):** flow rates from 50 ml/min to 450 ml/min can be programmed. Their pattern will depend on the chosen therapy type and the vascular access possibilities.
     - **Replacement fluid flow rate (ml/h):** set based on the required convection dose (ml/kg/h) in therapy.
     - **Dialysis fluid flow rate (ml/h):** set based on the required diffusion dose in therapy.
     - **Anticoagulant flow rate (ml/h):** set based on the concentration of the anticoagulant administered and the need for system anticoagulation.
Ø Patient fluid removal (ml/h): set according to the desired fluid balance. It is part of the administered convection dose.

Ø Pre-blood pump fluid flow rate (ml/h): used in regional anticoagulation with citrate.

Ø Effluent flow rate (ml/h): flow resulting from the addition of replacement fluid, dialysis fluid, and patient fluid removal flows.

· Pressures: their monitoring allows us to identify and locate alterations in the system to offer an appropriate response. It is more useful to assess the trend of their values throughout the treatment than to infer conclusions from their punctual values.

Ø Inlet or arterial pressure (P1): it has a negative value. It informs us about the state of the arterial lumen of the catheter, the pre-blood pump segment of the circuit, and changes in blood flow velocity.

Ø Prefilter pressure (P2): it has positive values (normally the highest in the system). It informs us about the state of the filter and is modified by variations in blood flow and alterations in the venous segment of the system.

Ø Post-filter, return, or venous pressure (P3): it has positive values. It informs us about the situation of the venous segment, the venous branch of the catheter, and the retrograde of the state of the filter. It is modified by variations in blood flow.

Ø Effluent pressure (P4): is the pressure in the effluent compartment. It depends on blood flow, the number of permeable capillaries, and the programmed ultrafiltration flow. It can take positive or negative values. If positive, it means that the filter adequately responds to ultrafiltration requirements, and if negative, it cannot offer us the required performance.

Ø Transmembrane pressure (TMP): pressure gradient that must be generated between both sides of the membrane to obtain the required ultrafiltration volume. Values close to 200 mm Hg indicate imminent coagulation of the system or problems obtaining the required ultrafiltration. A similar meaning would be given by a value higher than 0.5 in the resistance to blood flow (Pcap-Pven/Blood flow). The filter should be changed when the evolving TMP reaches 200 mmHg (to avoid filter clotting and the consequent loss of the patient's blood), and every 72 hours in any case (maximum life of the blood pump segment).

Ø Filtration fraction (FF): percentage of serum that we ultrafilter from the total plasma that passes through the system per unit of time. This value is expressed as a percentage, and its recommended value is less than 25%.

9. Surveillance, controls, ad maintenance:

· Related to the catheter:

  · Insertion and care following the Bacteremia Zero premises.
- Perform washes with saline at all disconnections. If the connection to the filter is expected to last more than 6 hours, heparinize the lumens (9cc of 0.9% saline solution + 1cc of 1% heparin) according to the catheter's indication (priming volume of each line).

- Monitor the patient's correct position, avoiding bending or tight lines.

  Related to the technique:

  - Aseptic technique when handling circuit lines and sterility of dialysis fluids.

  - Samples can be taken from the circuit itself (arterial line port before the blood pump) by applying an antiseptic solution previously, and it is not necessary to discard the sample.

  - In the mobilization of these patients, the use of a crane (hygiene) may be recommended and/or adjusting filter requirements (decreasing FF) during mobilization to avoid continuous therapy stops that favor coagulation.

  - Early detection of signs of coagulation and preparedness to act.

  - Avoid lumen inversion ("recirculation"). If performed, it will not last more than 6 hours. A medical evaluation will be requested to evaluate the catheter change.

  Anticoagulation: see specific protocol.

  Monitor the patient's temperature: caloric energy loss is common, as with any extracorporeal circuit. Always use the Prismaflex or Prismax monitor heater. If necessary, use active patient warming with blankets. In some cases, allowing the patient to cool may be of interest.

  Recommended controls (in addition to usual requests): patient coagulation study 6 hours after starting the technique, and complete coagulation study every 24 hours. Capillary blood glucose every nursing shift, at least. Phosphorus and Urea every 24 hours. Trace elements every 72 hours (every 24 hours when using citrate). Fluid balance and electrolyte replacement depend on each patient. Adjust therapy following the algorithm in Figure 3.

**Troubleshooting**

Alarms are fundamental safety elements of the system. Those that can represent a risk to the patient, such as air detection or disconnection of the lines, stop the implementation of therapy. The most common alarms and issues that occur in these therapies as well as their possible solutions are detailed in Table 2.

**Time Taken**

- Preparation of the hemofilter: 15-20 minutes
Selection of vascular access and catheter insertion: 15 minutes

Decisions involving the indication for the therapy, selection of modality, dosage, anticoagulation, and monitoring with dynamic adjustment require variable time depending on the complexity of the clinical scenario.

**Anticipated Results**

About half of critically ill patients will suffer acute kidney injury and 20% will require CEPT within the first week of admission in ICU. This situation is associated with a mortality rate of 50%. The accomplishment of best practices in the management of these techniques is essential to improve outcomes in a highly vulnerable population. Also, the increasing incidence of AKI treated with CEPT and the improvements in security and depurative efficiency of the therapies has promoted an expansion of the indications and technical modalities of CEPT in Critical Care. It has also forced us to deepen our knowledge in this setting and to give specific training to all the professionals involved in its management.

The standardization of EPT allows for their management to be carried out in a homogeneous and systematic way. For this reason, it promotes a safe and high-quality environment in the care of critically ill patients. We consider that the application of this protocol and the recording of the data obtained from its implementation would allow us to analyze the epidemiological characteristics of patients receiving CEPT, to detect and correct problems in the application of these therapies, and to identify the advantages and disadvantages of different anticoagulation strategies. All these benefits have been demonstrated through our DIALYREG study.

**References**


**Supplementary Files**

This is a list of supplementary files associated with this preprint. Click to download.

- GPTable1.pdf
- GPTable2.pdf
- GPFigure1.pdf
- GPFigure2.pdf