Regional anticoagulation with citrate for continuous renal replacement therapy (CRRT) is increasingly applied in intensive care patients. The reason for this popularity is the high incidence of bleeding in patients receiving heparins for anticoagulation of the CRRT circuit. While using citrate, CRRT can be applied without increasing the patient’s risk of bleeding.

After the first reports of Mehta and Ward [1], a wide variety of citrate systems for CRRT have been described: for continuous venovenous hemodialysis (CVVHD), pre- and postdilution continuous hemofiltration (CVVH), continuous hemodiafiltration (CVVHDF) and for different doses of CRRT (1.5 to 4 L/h) [summarized in the electronic supplemental material of reference 2]. Studies compete in the degree of safety, feasibility and flexibility. However, none of the systems has proven superiority and none of the proposed systems can attain perfect acid-base control using one standard citrate-, replacement- or dialysis solution. Each protocol has its own rules to correct metabolic acidosis or alkalosis, hypo- or hypercalcemia, depending on the modality and the solutions in use. Each has its specified composition of dialysis and replacement fluids.

In this issue, Vervloet and Nurmohamed present their method of citrate-based CVVH for predilution and their ongoing randomized controlled trial comparing circuit survival with this citrate method to heparin-based CVVH in patients without an increased risk of bleeding [3]. The protocol is derived from the Pallson method [4]. It uses an isotonic predilution replacement fluid of which citrate is an integral component. The study is important for further justification of the clinical use of citrate.

Citrate-based CVVH: pre- or postdilution?

Which aspects are important comparing this predilution method to the postdilution option as used in many centres in the Netherlands [5]. The postdilution protocol uses a hypertonic tri-sodium citrate solution, and, depending on prescribed ultrafiltrate flow, one or two different replacement fluids: a buffer free low sodium solution and a bicarbonate buffered solution.

Simplicity

The predilution system strikes by its simplicity, because the citrate is integrated in the replacement fluid. Thus anticoagulation and (buffer) replacement are combined in one solution; however, separate calcium supplementation is still required. To increase simplicity replacement flow and blood flow have a fixed relation and post-filter ionized calcium is not measured for fine tuning of anticoagulation. The postdilution method is more complex, because two different replacement fluids are often needed, especially for the higher dose.

This method also has a fixed relation between citrate- and blood flow, obviating post-filter calcium measurements.

Flexibility

The predilution system is less flexible to adjust acid-base balance, because the buffer supply is fixed, depending on predilution and ultrafiltrate flow.

The postdilution system provides maximal flexibility to adjust acid-base derangement. It is better equipped for severely acidic and septic patients. In these patients, the lower dosed predilution system is expected to give a less effective control of metabolic derangements.

Safety

Safety of citrate systems primarily depends on the local protocol and the user’s ability to adhere to the protocol. Safety further depends on the CRRT device. Safety will rise enormously with the modern CRRT devices, coupling citrate flow to blood-, ultrafiltrate- and replacement- or dialysate flow.

The citrate solution in the predilution protocol is isotonic, which is less dangerous in case of inadequate use. The hypertonic trisodium solution used for some of the postdilution protocols can be life-threatening if inadvertently used outside the setting of CRRT.

Circuit survival

A further pro of the predilution system is that circuit survival is expected to be longer, because hemoconcentration in the filter is less, due to predilution, but also to the lower hemofiltration dose.

In the postdilution method, hemoconcentration is higher and circuit survival will consequently be shorter. The risk of clotting is also increased in the venous chamber, if calcium containing replacement fluids are used. In the near future, a commercial calcium-free solution becomes available. It is expected that this fluid will increase circuit survival.

CRRT dose and survival

A major drawback of the predilution method is that the attained CVVH dose is lower than the presently recommended for CRRT, namely 35 ml/kg/h [6-8]. This dose is associated with a lower mortality compared to a dose of about 20 ml/kg/h in two randomized controlled trials [7,8]. With the described predilution system, a dose of 31 ml/kg/h can be attained for a 70 kg person; however, for a 100 kg person dose is limited to 22 ml/kg/h. It is not known whether the above mentioned benefits of the predilution methods weigh against the lower dose in terms of mortality.

The postdilution method can attain a dose of 40 ml/kg/h for a 100 kg person. With adjustment of the protocol, higher doses can be obtained if desired for severely septic patients.
Costs
Due to the lower dose and the expected longer circuit life, costs of the predilution method are less. However a cost-effectiveness analysis should include the entire intensive care treatment, including the possible benefits of a higher CRRT dose on the recovery of organ failure and survival.

Conclusion
Differences between methods are far-reaching and not without clinical consequences. Up to now there are no randomized controlled trials showing that either method is best. It is of utmost importance that the clinician understands the two methods and their differences for taking a well-considered decision and making his nurses familiar with the method. Safety of citrate-based CRRT will further increase if citrate is integrated in the hard- and software of the emerging CRRT devices.

References