

Acute Dialysis Quality Initiative

Workgroup 7

Fluid Composition and Management

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Introduction

The composition of the dialysate and/or substitution fluid, as well as the modality of its administration, are important parts of adequate CRRT management. In particular, the choice of a buffer has elicited a considerable amount of interest in the literature. Less data are available on other components or on the required bacteriological quality of CRRT fluids. Whether the pre-dilution mode of hemofiltration is preferable and how fluid balance should be managed is also a matter of controversy.

Fluid Composition

What should the composition of replacement fluid and dialysate be?

There is general consensus that replacement fluid and/or dialysate should contain a buffer and electrolytes in concentrations aiming for physiological levels and taking into account preexisting deficits or excesses and all inputs and losses. In most situations, replacement fluid should contain physiological concentrations of electrolytes except for those that are protein-bound.¹⁻² Most commercially available solutions do not contain phosphate and phosphate supplementation is generally required at some stage during CRRT.³⁻⁴ Customized solutions will be required in patients with some electrolyte imbalances.⁵ Frequent monitoring of serum electrolytes is imperative during CRRT.

Does the use of a supraphysiological sodium concentration in the dialysate or replacement solution improve hemodynamic stability or prevent increases of ICP?

There is no CRRT data examining whether the use of supraphysiological concentrations of sodium may improve hemodynamics or outcome in head injury.

Should the dialysate and/or substitution fluid contain glucose and how much?

Although physiological concentrations of glucose in the dialysate or substitution fluid are probably preferable to prevent or compensate for extracorporeal losses, glucose-free solutions may be acceptable if

extracorporeal losses are accounted for in the nutritional regimen. The supra-physiologic glucose concentrations in some dialysis or substitution fluids usually result in excessive glucose intake and hyperglycemia and should be avoided.⁶⁻¹⁰

Summary: Most commercially available CRRT solutions contain physiological electrolyte concentrations and are able to reestablish electrolyte homeostasis provided some phosphate supplementation is given (level V). Supra-physiological glucose levels result in excessive glucose intake and hyperglycemia (level V).

Recommendations for clinical practice: The dialysate or substitution fluids used during CRRT should contain physiological concentrations of electrolytes, except in patients with extreme imbalances (Grade E). Supra-physiological glucose levels should be avoided (Grade E).

Recommendations for future research: Future research should establish the effect of supraphysiological sodium concentration on hemodynamics or on the control of intracranial hypertension.

Fluid Administration

How should replacement fluids be administered (pre-filter versus post-filter, other considerations)?

Maximum efficiency of post-dilutional hemofiltration/hemodialfiltration is limited by the maximum acceptable value of filtration fraction and by the maximal blood flow that can be delivered by the access. Since higher ultrafiltration rates are allowed with pre-dilution, solute clearances can be increased but this requires an increase in replacement fluid as well as more porous membranes. At much higher ultrafiltration rates, such as in high volume CVVH, a larger surface area will be needed. However, for the same ultrafiltration rate, pre-dilution results in a reduction in solute clearance because of dilution of solutes at blood entry into the filter. At conventional flow rates (of 2 L/h or less), pre-dilution results in a nearly 15% decrease in urea clearance. Therefore additional ultrafiltration volume and replacement fluid are required to achieve similar clearances.¹¹⁻¹⁴

Does predilution enhance filter patency or diminish anticoagulation need?

Pre-dilution fluid replacement is believed to enhance filter patency during CRRT and/or to diminish anticoagulation needs (Level V). However, further studies in this area are required. At present, pre-dilution can be considered as an adjunct to the anticoagulation regimen.

Summary: Pre-dilution appears desirable to enhance the achievable ultrafiltration rate (this may be especially important in high volume CVVH). Recommendations for clinical practice: Pre-dilution may be considered in patients with frequent filter clotting (Grade E) or, in combination with post-dilution, when extracorporeal clearance is limited by the achievable blood flow (Grade E). Recommendations for future research: Comparison of equipotent (i.e. with similar creatinine clearance) pre-and post-dilution treatments should establish whether the supplementary costs for fluids associated with pre-dilution treatment are outweighed by a higher filter life or a lower anticoagulant requirement. Further clinical studies should also

establish the maximal clearances achievable for different solutes at high ultrafiltration rates (e.g. high volume CVVH) using pre-dilution vs. post-dilution or a combination of both.

Buffer Composition

What metabolizable anion should be used and under what circumstances?

Both lactate and bicarbonate ions are used in replacement fluid and dialysate for CRRT. Controlled (though not all randomized) trials have shown that during CRRT lactate or bicarbonate buffered solutions have a similar efficacy for correction of metabolic acidosis¹⁵⁻²⁰ Lactate levels are generally higher with lactate solutions and might confuse the interpretation of blood lactate levels. Whether this hyperlactatemia is associated with morbidity is not clear. Potential concerns are hemodynamic compromise,¹⁹ increased urea generation^{16,21} or cerebral dysfunction.²¹ This hyperlactatemia can be expected to be more pronounced if lactate-buffered solutions are used during high volume hemofiltration.

Are bicarbonate-buffered solutions better than lactate-buffered solutions during CRRT?

Lactate-based solutions have been warned against in patients with lactic acidosis²²⁻²³ and in those who manifest lactate-intolerance, arbitrarily defined as a rise of 5mmol/l or more during CRRT with lactate-based solutions.²⁴ Both groups are at risk for worsening acidosis because of insufficient conversion of lactate to bicarbonate in the face of ongoing bicarbonate losses. Although a worsening of acidosis with lactate solutions in patients with hepatic failure has only anecdotally been described during CRRT²⁵ and during intermittent hemofiltration,²⁶⁻²⁸ careful monitoring of acid-base status is recommended in these patients. Conversely, the benefit of bicarbonate administration in patients with lactic acidosis has been questioned. A full discussion of this issue is beyond the scope of this text. In any case, the CRRT treatment itself allows one to avoid some of the ill-effects (hypervolemia and hypernatremia) of bicarbonate infusion.

Can acetate or citrate be used as a buffer during CRRT in critically ill patients?

There is insufficient data to evaluate the use of acetate-buffered solutions in CRRT. However, limited evidence does not support its use compared to lactate or bicarbonate.^{17,19} Citrate, used for regional anticoagulation during CRRT, is metabolized to bicarbonate, each citrate ion producing three bicarbonate ions. The efficacy of sodium citrate as a buffer has not been sufficiently studied and both metabolic alkalosis and worsening of acidosis during citrate CRRT has been described.²⁹⁻³¹ However, lactic acidosis has been successfully treated by continuous hemodialfiltration using citrate.³²

What should be the buffer concentration in the dialysate/substitution fluid?

The buffer load should compensate for deficits, for losses in the buffer process and for extracorporeal losses and should therefore usually be supra-physiologic.

Should the buffer concentration be higher in patients with permissive hypercapnia?

Patients with permissive hypercapnia might need more buffer for the correction of acidosis although the administration of buffer might theoretically lead to a further increased CO₂ production and worsening of acidemia (as a result of limited CO₂ elimination).

Summary: Both lactate and bicarbonate are able to correct metabolic acidosis in most CRRT patients (level II). Worsening of acidosis has been noted when lactate was used in patients with lactic acidosis or liver failure (level V). The use of citrate, mostly not titrated on pH but on coagulation parameters, has been associated with both metabolic alkalosis and metabolic acidosis (level IV). Recommendations for clinical practice: Lactate is an effective buffer in most CRRT patients (Grade C). Bicarbonate is preferred in patients with lactic acidosis and /or liver failure (Grade C) and in high volume hemofiltration (Grade E). When citrate is used as anticoagulant, no other buffer should be administered, but monitoring of pH is required (Grade E) (*see also workgroup 6*). Recommendations for future research: Further studies comparing lactate and bicarbonate in high volume hemofiltration are required. Rigorous pH monitoring should be performed during CRRT with citrate in order to define the clinical situations where this approach can result in dangerous deviations of acid-base homeostasis. Optimal acid-base management of patients with permissive hypercapnia requires further investigation.

Physical Properties of Replacement Fluid and Dialysate

Should the substitution fluid and/or dialysate be warmed?

The large volumes exchanged during CRRT result in a decrease of body temperature. The extent of this decrease depends on the length of the circuit (AV versus VV), on blood flow, replacement rate and/or dialysate flow rate, on body weight and on presence or absence of intact autoregulatory mechanisms to preserve core temperature (shivering versus sedation and/or paralysis).³³⁻³⁵ CRRT-induced hypothermia may mask the presence of fever making body temperature an unreliable marker of inflammation and infection in this population. It is not clear in which patients the net effect of CRRT-induced hypothermia is harmful (e.g. reduction of heat shock response) or beneficial (e.g. reduced VO₂, hemodynamic stability, cerebral protection). The hypothermia-induced reduction of the metabolic rate may offset the effect of extracorporeal heat loss on caloric balance.

Do CRRT fluids need to be sterile?

Since replacement fluid is directly administered to the patient's circulation, it must be sterile. Whether or not dialysate should be sterile or even "ultra-pure" (see table 1 for differences) depends on the occurrence of back-filtration and/or back-diffusion of cytokine-inducing substances. Although no clinical studies have shown the presence of back-diffusion or back-filtration during CRRT, both might theoretically occur.³⁶⁻³⁸ Back-filtration depends on the pressure profiles and membrane hydraulic permeability. With regard to

back-diffusion, due to their higher adsorptive capacity, synthetic high-flux membranes allow less diffusive transfer of cytokine-inducing substances than low- and high flux cellulosic membranes (although differences may exist between synthetic membranes).³⁹⁻⁴² In ESRD hemodiafiltration with back-filtration has been shown to be associated with increases of IL-6 and CRP compared with a modified hemodiafiltration modality without back-filtration but this is the only study showing clinical relevance of this phenomenon.⁴³

Table 1: Definitions of water and dialysate quality

Classification	Bacterial growth cfu/ml	Endotoxin EU/ml	Cytokine induction
AAMI, dialysate	2000	5	+
AAMI, water	200	5	+
Tap water	100	0.25	+
Ultra-pure	0.1	0.03	-
Sterile	10 ⁻⁶	0.03	-

AAMI = Association for the Advancement of Medical Instrumentation. Endotoxin 5EU/mL = 1mg/mL (detection limit of LAL assay = 0.03EU/mL). Cytokine induction measured with bioassay in which human donor blood is incubated in vitro with dialysate (detection limit 0.15-0.25EU/mL = 30-50pg/mL endotoxin. Adapted from Lonnemann⁴⁴ with permission.

Is on-line production of substitution fluid for CRRT safe and feasible?

The technical requirements for on-line production of substitution fluids are specific. Only one clinical study shows the feasibility of this procedure during CRRT (without evaluating the safety).⁴⁵ Other techniques for dialysate generation have been described.¹⁵ Extensive evaluation of the safety of on-line hemofiltration has only been done in ESRD.⁴⁶⁻⁴⁷

Summary: Most patients undergoing CRRT show a decrease of body temperature, the clinical consequences of which are ill-defined. Whereas the use of sterile substitution fluid is imperative, the bacteriological requirements for CRRT dialysate are less clear, except in high flux dialysis where dialysate should probably be sterile because of back-filtration (level V). Recommendations for clinical practice: Although reductions of body temperature below 35°C should probably be avoided (Grade E), available data do not allow us to make recommendations on whether CRRT fluids should be warmed. Whether less than ultrapure dialysate is safe in critically ill patients with ARF is also not clear. Recommendations for future research: Further studies are needed to address the clinical consequences of thermal energy loss during CRRT, perhaps using calorimetry with warmed or non-warmed solutions. The safety of on-line production

of, or use of less than ultra-pure, dialysate in CRRT should be evaluated, particularly its possible contribution to systemic inflammation.

Clinical Practice of Fluid Balance

How should fluid balance be achieved?

Fluid removal can be achieved with all CRRT techniques.⁴⁸ The hourly ultrafiltrate volumes required to deliver these therapies are larger with continuous hemofiltration/hemodiafiltration than either SCUF or continuous hemodialysis. Because of the removal and replacement of greater amounts of fluids, the risk of fluid balance errors (negative or positive) might theoretically be greater during hemofiltration or hemodiafiltration than during hemodialysis (level V). All fluid intake and output should be considered in CRRT fluid balance.

Is fluid management better achieved with AV versus VV systems? What is the role of integrated balancing systems?

All systems can effectively manage fluid balance. The potential for excessive ultrafiltration and negative fluid balance is greater with VV than with AV systems, because hypotension makes the latter self-limiting.⁴⁹ Similarly, in the absence of frequent monitoring or an integrated fluid balance system, unrecognized decreases in ultrafiltration caused by either hypotension (AV) or filter clotting (AV, VV) may result in fluid overload. Adaptive use of intravenous fluid pumps for CRRT may be associated with errors of 5% or more.⁵⁰⁻⁵³ Thus, it is imperative that fluid balance be monitored and adjusted continuously when such equipment is used in CRRT. Superior safety or efficacy of integrated fluid balancing systems over carefully monitored non-integrated systems is clinically unproven.⁵³ The use of integrated fluid balancing systems decreases nursing workload and potentially improves acceptance of CRRT. In children, fluid balance should be monitored hourly during CRRT even when using an integrated fluid balancing system, since there is little margin for error, and operational accuracy has not been definitively established in this population.

What should be the parameters to guide fluid balance?

There is no consensus on the optimal tools and parameters to assess volume status and systemic perfusion in critically ill patients.⁵⁴⁻⁵⁵ Clinical judgment integrating a variety of data continues to be the best guide to fluid balance prescription during CRRT.

Does fluid balance affect outcome?

Volume overload is associated with adverse outcomes in a variety of critical illness populations, including CHF, postoperative, ARDS, and septic shock patients.⁵⁶⁻⁵⁹ Data from a single small prospective randomized controlled trial found improved outcomes (duration of mechanical ventilation, ICU length of stay) in critically ill patients with pulmonary edema managed with negative fluid balance titrated according to

extra-vascular lung water measurement.⁶⁰ CRRT has been shown to effectively remove fluid in critically ill patients with volume overload, improving a variety of physiologic parameters in the presence or absence of renal failure.^{56,61-67} Fluid removal by CRRT (or by other techniques) has not been proven to improve short-term or long-term clinical outcomes.

Summary: No specific method has been demonstrated to be better in terms of efficacy or safety for fluid balance control during CRRT. Integrated fluid balancing systems have important, albeit theoretical, advantages. While there is no evidence that fluid removal per se improves outcome in critically ill patients with or without ARF, there is (level III) evidence that volume overload is associated with adverse outcomes. Limited (level II) data suggests that maintaining negative fluid balance decreases ICU length of stay in patients with acute lung injury.⁶⁰ Recommendations for clinical practice: Volume overload should be avoided (Grade D) especially in patients with acute lung injury (Grade C). Since adaptive use of intravenous infusion pumps for CRRT has been shown to risk significant errors in fluid balance, these systems should be discouraged when devices specifically designed for CRRT are available (Grade D). Recommendations for future research: Future studies should establish the operational accuracy of CRRT systems in clinical use, particularly in children. The potential role of newer techniques such as blood volume monitors⁶⁸ needs to be further explored. Fluid management is a neglected area of investigation in the CRRT literature. Future studies should document a variety of physiologic parameters and outcomes to assess the importance of these variables in determining the impact of CRRT, and guide subsequent development of CRRT fluid balance strategy guidelines for clinical and protocolized research use.

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