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Fluid management in continuous renal replacement therapy

Abstract

The purpose of intravenous fluid administration is to increase cardiac output. Excessive fluid administration can lead to accumulation of interstitial fluid, worsening hypoperfusion and hence develop organic dysfunction. Therefore, fluid overload is a poor prognostic factor for hospitalized patients and those admitted to the Intensive Care Unit (ICU). A resuscitation strategy divided in four phases has been described; the last phase consists in the elimination of those fluids that have been administrated in the previous phases. When fluid overload is complicated by acute kidney injury renal replacement therapy may be used for this purpose. A successful fluid treatment of a patient depends on a proper, accurate and frequent evaluation, and in the correct understanding of the basic principles and clear objectives of the treatment. In the continuous renal replacement therapy, the rate of the fluid eliminated can be adjusted safely according to each patient needs and it allows additional support of other complications. The ideal strategy to guide the elimination rate is unknown. This review presents the basic principles for an optimum fluid management in the continuous renal replacement therapy.

Keywords: acute kidney injury, fluid overload, renal replacement therapy, fluid accumulation, intensive care unit, critical care

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Abbreviations: AKI, acute kidney injury; ICU, intensive care unit; FO, fluid overload; FB, fluid balance; CRRT, continuous renal replacement therapy; IV, intravenous; IHD, intermittent hemodialysis; Q_{UF}, ultrafiltrate; Q_B, blood flow; TMP, transmembrane pressure; Q_{NET-UF}, net ultrafiltration rate; IB, integral balance

Introduction

Acute kidney injury (AKI) is one of the most frequent complications for critically ill patients admitted to Intensive Care Unit (ICU).[1] Often, patients with AKI suffer from concomitant fluid overload (FO),[2] especially those whom hemodynamics, and pulmonary or cardiac function are altered, as these factors influence Fluid Balance (FB). Around 10-20% of these patients will require extracorporeal support, such as Continuous Renal Replacement Therapy (CRRT).[3] In this context, the management of the fluid balance (hydric status) should be based on accurate and frequent evaluations of the static and dynamic parameters of perfusion, monitoring clinical evolution, a proper understanding of the basic principles of blood filtration with CRRT, in addition to clear objectives of treatment. Advantages for CRRT include better achieved nutrition, drugs and blood products administration as needed, meanwhile maintaining solutes and fluid homeostasis.[4] We ought to review the basic principles and recent evidence of fluid management during CRRT.

Fluid management

Intravenous (IV)fluid therapy is a common strategy used to improve organ perfusion in hospitalized patients.[5,6] A recent observational study showed that the most common indications for IV fluid administration in ICU are: hypotension, increase in the vasopressor drugs doses, hypovolemia, oliguria, sepsis, low mean arterial pressure and heart rate increase.[7] The theorical purpose of administration of IV fluids is to increase the stress volume, augmenting the gradient between the mean systemic pressure and the right auricular pressure, improving the venous return.[8] In patients situated in the ascending limb of the Frank Starling curve, increasing venous return will result in an increase of the cardiac output.[9] However, in critically ill patients these occurs in a short margin of action.[10] Also, excessive administration of fluids associated with an increased capillary permeability provoke leak into interstitial space, further affecting tissue perfusion. Being realistic, less than 50% of the patients that receive IV fluid therapy will increase cardiac output (classified as responders).[7,9]

Fluid therapy stages

When we face a patient, who may benefit from IV fluid therapy, at least 3 queries must be evaluated. Which are the actual objectives of fluid therapy? Which will be the parameters to identify the need for volume administration? How will you evaluate the effect of the administrated volume?[11] With those questions in mind, a novel strategy organized in 4 phases has been described. The duration and specific characteristics of every phase depend on each patient´s clinical condition or evolution, and also static and dynamics variables to evaluate volume response.[5] These phases are Resuscitation, Optimization, Stabilization, and Elimination (ROSE).[10]

Resuscitation intends to replete intravascular volume as soon as possible. In *Optimization* phase, a comprehensive approach to all aspects of management is completed. *Stabilization* may be the stage to initiate organic support, fostering neutral fluid balance and optimizing nutrition (enteral or parenteral). Lastly, in *Elimination*, the accumulated volume during previous stages should be removed avoiding unnecessary intravenous fluids or actively eliminated by medical or mechanical means.[10] These phases are related with each other, so it is possible to step back to any one of them depending on clinical evolution and patient´s requirements. For further details see Table 1.

Resuscitation stages	Resuscitation	Optimization	Stabilization	Elimination
Patient characteristics	• Severe hypotension • Hypoperfusion	• Hypoperfusion • Vasopressorneeds	• No hypoperfusion • Stable or decreasing vasopressor dose	• No evidence of hypoperfusion for 12 hours
Goals of treatment	Priority correction of hypotension and hypoperfusion	Improve cardiac output and oxygen delivery	Neutral Fluid Balance	Negative Fluid Balance
Fluid strategy	• Fluid challenges • Early vasopressor initiation	• Evaluate fluid responsiveness • Fluid only to responders	• Restrictive fluid administration	• Diuretics • RRT • CRRT
Evaluation variable	Shock etiology, US	PLR, VCI, BLUE protocol, FALLS, PPV, SVV, PiCCO®, SGC, FATE, Lactate	IAP, RPP, BLUE, FALLS, SVV, PPV, PiCCO®, FATE	PIA, PPR, BLUE, SVV, PPV, PiCCO®, FATE

Abbreviations: RRT, renal replacement therapy; CRRT, continuous RRT;USG, ultrasonography; PLR, passive leg raising;VCI, vena cava index; BLUE, bedside lung ultrasound in emergency protocol; FALLS, fluid administration limited by lung sonography protocol; PPV, pulse pressure variation; SVV, systolic volume variation; SG, Swan Ganz catheter; FATE, Focus assessed transthoracic echocardiography protocol; IAP, intraabdominal pressure; RPP, renal perfusion pressure

Fluid overload

Measuring fluid balance and fluid overload

FB is defined as the difference between the amount of fluid intake and the amount of fluid lost (Formula 1). The cumulative balance is the algebraic addition of the FB in a specific period (i.e. since hospital admission).[5,12] Estimate of FB must be done at least every 24 hours, or more frequent depending of hospital protocols and the specific area were the patient is admitted. It is suggested that the reevaluation should be done periodically and the results of this evaluation should trigger corresponding actions.[13] FO is expressed as percentage and is calculated dividing the FBby the baseline body weight and multiplying by 100 as shown in Formula.[14,15]

Formula 1: $FluidBalane = Intake(L) - Outtake(L)$

Formula 2: $Fluidoverload = \frac{Cumulativebalance\ (L)}{baselinebodyweight\ (kg)} x100$

Physiopathology effects of the fluid overload

A possible deleterious consequence of excessive IV fluid administration during *Resuscitation* could be worsening of tissue hypoperfusion and dysfunction of enzymatic cellular systems, which can lead to complete metabolic unbalance as well.[16]

The liberal IV fluid administration can cause increased intra-abdominal pressure that further compromises renal and/or hepatic perfusion.[16] At the same time, these effects are potentiated in encapsulated organs like liver and kidneys, because interstitial pressure increases, affecting negatively local blood flow.[17]

Other undesirable effects of the FO include dysfunction in all the systems and organs, like brain, hepatic, pulmonary, myocardia, intestinal, renal, and interstitial and skin edema.[10] The percentage of FO associated to poor clinical results is 10 to 20%,[18,19] some of these are: more days of mechanical ventilation, longer stay in ICU, and higher mortality.

Volume control with CRRT

In patients with AKI, is particularly important to prevent FO during IV fluid management (despite of which resuscitation phase the patients is in).[20] NICE (National Institute for Health and Care Excellence) guidelines suggest avoiding the free administration of IV fluids in patients who develop AKI, mainly those with oliguria.[21] In the cases with poor control of FB as result of AKI, possibilities include restricting fluid therapy, administrate diuretic drugs and/or start CRRT.22,23 Threshold to initiate CRRT in patients with oliguria must be lowered, as in those patients with multi organ failure, acute respiratory distress syndrome or in patients with brain edema and elevated intracranial pressure who benefit from neutral FB and strict electrolyte control.[24,25]

The indication to start CRRT is usually evaluated in cycles of 24 hours, unless the patient requires something different. Studies suggest that reaching a FO higher than 10-20% before CRRT is associated to higher risk of death.[26] Although most clinical research on the time of initiation of CRRT has been focusing on classic renal biomarkers like serum creatinine or based on the clinical definition of AKI,[27-31] FO percentage could be important, mainly along special circumstances like diuretic resistance or when metabolic complications due to diuretics exist.[18] No study has evaluated different FO thresholds to start CRRT, but increasing evidence support the importance of considering cumulative FB to start CRRT, mainly in children.[32-34]

The decision to begin a therapy to mechanically remove fluid further involve choosing the right modality, the one that can achieve the desire goals. The options include intermittent hemodialysis (IHD), selective ultrafiltration, low or very low efficiency dialysis, peritoneal dialysis and CRRT.[20] The factors that must be considered to make the decision comprise the amount of fluid to be removed, the mandatory anticipated fluid administration, the actual outtake, the probability of the renal function recovery, the cumulative FB, the hemodynamic status, the resuscitation phase, the adequate rate to remove volume excess, the need for solute removal, electrolytic homeostasis, uremic control and even the available resources at the hospital.[35] CRRT offer

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flexibility to abord all these goals. For example, the amount and rate of volume to remove can be simply and safety adjust depending on each patient needs.[36]

Basic principles of volume extraction with CRRT

Concepts can be confused in CRRT, so it's important to clarify some concepts. The ultra-filtrate (Q_{UF} hemofiltration or filtration) is the plasma water that cross the semipermeable membrane into the effluent bag and drags along solutes below the membrane cut-off; that is, those solutes with molecular weight below the pore size. This water may be partially or totally replaced by substitution fluid. Hence, the mechanisms slowly attempts to shift blood concentrations to those of the fluid substituted (CRRT solutions);[35] most of the commercially available solutions are similar to normal plasma electrolyte concentrations. The rate of shift may be influenced by the intrinsic properties of the filter, the filter ultrafiltration rate (which depends on the ultrafiltration rate and the surface area of the membrane), and some operative parameters such as the blood flow (Q_B) and the transmembrane pressure (TMP).[37] The net ultrafiltration rate (Q_{NET-UF}) is the difference between plasma water filtered and plasma water replaced. In other words, the $Q_{NET-UF}$is defined as the volume of fluid removed per unit of time by the machine and reflects upon patient body weight lost. In clinical practice, $Q_{UF}$is defined as the substitution rate (Q_R) in the CRRT machine, in addition to the fluid eliminated from the patient (Formula 3).

Formula 3: $Q_{UF} = Q_{NET-UF} + Q_R$

Integral balance strategy

Integral Balance (IB) is the management strategy of combining FB and the Q_{NET-UF}.[35] The ideallycontrolled FB during CRRT needs to considerate not only the Q_{NET-UF} reported by the machine, but to integrate FB modified by residual diuresis, bleeding or diarrhea; other IV incomes like parenteral nutrition or transfusions. In an opposite case, these factors could lead to FO or excessive losses. This is IB, which must be constantly evaluated and act in consequence to achieve the patient's hydric status goal.[35]

The IB goal is centered to the clinical needs of the patient and in the evolutive stage of the disease. To achieve the IB per hour two methods have been described. In the A method (most common),[35] the Q_{NET-UF} is changed on the CRRT machine and may be variated even every hour. We need to keep in mind, if the effluent volume is modified, the solute clearance will vary (i.e. dose). In the B method, the Q_{NET-UF} remains constant, while Q_R change to achieve a FB goal.[38] In the latter, Q_R could be introduced by machine´s pumps into the circuit lines of CRRT, or intravenously by a central or peripheric line installed in the patient.[35] These hybrids strategies should be considered in order to get the patient's goal. The A method allows FB calculations for longer periods and is well-known by most hospital teams, but by changing Q_{UF} the solute clearance is modified and the filtration fraction changes.[39] In the B method, clearance remains constant and independent of the FB, but this method demands frequent recalculation and to consider every income and outcome due to high misbalance risk.

Prescription

Cardiovascular tolerance is another variable that determines the rate of elimination of the volume overload. It had been recognized that a rate under 13ml/kg/h of Q_{NET-UF} lower the risk of hemodynamic intolerance. The ideal strategy to guide the ultrafiltration during Stabilization and *Elimination* phases is uncertain and several factors may influence the vascular refilling from interstitial space.[38] A common strategy dictates that a neutral FB could be maintained avoiding further fluid accumulation while the patient persists hemodynamically unstable. Once this instability resolves, progression of Q_{NET-UF} as tolerated clinically, while avoiding secondary complications like deterioration of hemodynamic state, or organ dysfunction. Fluid removal can be optimized and adapted by continuous monitoring of hemodynamic targets, as does resuscitation.[9] Is essential to identify if cardiac output decrease below the patient´s needs, as this may be the first signal of intolerability in removal rate. Usually, reducing the Q_{NET-UF} to allow vascular refilling to occur solves the problem.

Conclusion

The FO is a poor prognosis factor for hospitalized patients in the ICU. A value over 10-20% is associated to longer ICU stay, longer time of mechanical ventilation and higher mortality. FO should be avoided as much as possible by an accurate and precise hydric status evaluation with clear goals for IV fluid treatment. When hemodynamic goals of treatment have been reached, optimization of FB usually requires the removal of extra fluid. CRRT is an exceptional tool for the FB control if required by patient´s condition. The ideal strategy for fluid removal is uncertain, but it must be centered on physiopathologyand biologic principles of the patient and treatment.

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Conflicts of interest

The authors have no conflict of interests to declare.

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