Intensive Care Med (2017) 43:1907–1909
DOI 10.1007/s00134-017-4956-0

FOCUS EDITORIAL

Focus on fluid therapy

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Introduction

Fluid therapy is a mainstay intervention in critically ill patients [1].

Recent years have given us a slightly clearer picture of the clinical practice for this simple yet complex intervention. Previous point prevalence studies have shown that clinical practice is, with some variation, quite simple [2–4]. The indications for intravenous fluid administration relate mainly to low blood pressure, high plasma lactate and low urinary output. Thus, only a small minority of patients may have advanced haemodynamic tools, e.g. echocardiography, to guide their fluid therapy. The fluids used are mainly crystalloid solutions, both saline and buffered solutions, and if a colloid is used, it is albumin [2, 3, 5]. While this practice may be well within the current evidence base, the observations raise some questions.

Are blood pressure, lactate and urinary output good indications for fluid therapy?

Few data exist on the effects of fluids on the clinical markers of hypoperfusion. The recent CLASSIC feasibility trial on fluid restriction in ICU patients with septic shock after initial resuscitation, who had received the initial 30 mL/kg of fluid, provides the first randomised data [6]. During the first 24 h after randomisation, the fluid restriction group received significantly less fluid than the standard care group [6], but noradrenalin doses, lactate and urinary outputs were similar in the two groups [7]. Importantly, all exploratory patient-important outcome measures favoured fluid restriction over standard care and worsening of kidney injury did so with statistical significance [6].

These data add to those of two recent meta-analyses of randomised trials, the results of which indicate no benefits of more vs. less fluid [8, 9]. The meta-analysis of the early goal directed therapy trials showed no effect of the protocol resulting in more fluids given vs. usual care in patients with septic shock [8]. The meta-analysis on conservative vs. more liberal fluid strategies after the initial management of patients with sepsis or acute respiratory distress syndrome (ARDS) showed no significant effect on mortality, but reduced time on mechanical ventilation with conservative fluid strategies [9]. While the Surviving Sepsis Campaign guideline still promotes continued fluid therapy after initial resuscitation based on improvements in the circulatory makers [1], we may question if more fluid leads to any sustained improvement in these markers and, more importantly, in patient outcomes.

Why are the advanced haemodynamic tools not used to guide fluid therapy?

Surprisingly, central venous pressure (CVP) was the most frequently used single marker in ICU patients receiving fluid therapy in the FENICE study [2], in spite of recommendations against its use to guide fluid therapy [10]. A recent analysis of a pooled dataset comprising CVP values of 1148 patients confirmed the low predictive power of CVP for fluid responsiveness [11]. Thus, experts promote more advanced tools, but, overall, the evidence supporting the use of these tools is of low quality in critical care [12].

Some methods do appear to have proof-of-concept such as the passive leg-raising method for the prediction of fluid responsiveness [13]. However, other methods have not been properly validated for monitoring, e.g. cardiac output measurements by echocardiography [14]. Taken together, there is no high-quality evidence indicating improved patient care and outcomes with the use of any haemodynamic tool in critically ill patients.

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Table 1 Important questions we need to answer to improve fluid therapy in critically ill patients

What are the indications for fluids during shock?
How should we give fluids—as a bolus or a continuous infusion?
What is the safe range of volumes? And how does this differ between patient groups?
Do the predictors of fluid responsiveness have a role in clinical practice?
Can we transfer fluid strategies that appear to be efficacious and safe in the developed part of the world to the developing part?
Can we transfer fluid strategies that appear to be efficacious and safe in adult patients to paediatric patients?
Should we give intravenous fluids as maintenance or to force diuresis?
Are buffered solutions preferable to saline? If so, in all patient groups?
Which buffer is preferable? Does it differ between patient groups?
Is albumin beneficial in any patient groups? If so, is it worth the cost?
What are the long-term consequences of the choices of volume and type of fluid on, e.g., quality of life and chronic organ dysfunction including the brain and kidney?

Does the choice or rate of fluid matter?

A network meta-analysis assessed whether different types of fluid impacts in the use of renal replacement therapy (RRT) by direct and indirect comparisons using data from randomised trial in patients with sepsis [15]. Hydroxyethyl starch solutions increased the use of RRT as compared to both saline and buffered crystalloid solutions. For all other comparisons, both direct and indirect, the results were less clear, but there were no major differences in the use of RRT with albumin vs. crystalloids or with saline vs. buffered crystalloids solutions. The point estimates for gelatine vs. albumin or crystalloid did suggest increased use of RRT with gelatine, but these results were not statistically significant [15].

As crystalloids appear to be safe and the most frequently used fluid type, the question now is whether we shall use saline or buffered solutions for critically ill patients. The best trial until now, the cluster randomised SPLIT trial, indicated no differences in rates of acute kidney injury (AKI) with the use of saline or gluconate/acetate-buffered crystalloid in 2278 mainly surgical patients in four ICUs in New Zealand [16]. This may contradict the results of a before and after study done in a single ICU that restricted the use of chloride-rich fluids and observed reduced rates of AKI at extended follow-up [17]. However, there may have been subgroups of patients in the SPLIT trial who had a different intervention effect than the full cohort, i.e. those acutely admitted [18]. In a post hoc analysis excluding elective surgical cases, the point estimate for mortality favoured buffered crystalloids over saline (relative risk 0.87, 95% CI 0.66–1.14) [18]. Obviously, we need better data, and two very large RCTs are now randomising ICU patients to saline vs. gluconate/acetate-buffered crystalloid in Brazil and Australasia. These trials will, however, not answer which buffer is preferable, e.g. lactate vs. acetate, in the crystalloids we give to critically ill patients.

Taken together, recent years have resulted in major advances and safer fluid therapy resulting in improved outcomes in critically ill patients. However, many clinically important questions remain to be answered (Table 1), even simple ones such as the rate of fluid administration (bolus vs. maintenance). We in the critical care community must work together to answer these questions. If so, we will continue to improve the care and outcomes of our patients.

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Compliance with ethical standards

Conflicts of interest
The Dept. of Intensive Care, Rigshospitalet has received support for research from Fresenius Kabi, CSL Behring and Ferring Pharmaceuticals.

Received: 28 September 2017 Accepted: 30 September 2017
Published online: 5 October 2017

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