



## Fluid care, Consensuses and Debates

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### **Editorial**

Fluid administration in critically ill patients is continued to be a source of intensive clinical trials and debate. Despite great hope and enthusiasm, early goal-directed therapy (EGDT) protocols did not show any superiority over usual fluid care in two randomized control trials including; the Protocolized Care for Early Septic Shock (PROCESS) and the Australian Resuscitation in Sepsis Evaluation trial [1]. The third multi-centric trial in which 1260 patients receive EGDT versus usual care, concluded that EGDT was less cost-effective with no significant increment in health-related quality or decrement of adverse event [1-3]. Type of administered fluid is also a matter of disagreement. Current data did not support the superiority of colloid solutions over crystalloids in patients with circulatory shock, and interestingly some colloids such as hetastarch (hydroxyethyl starch [HES]) increases the risk of acute kidney injury (AKI) and bleeding. Patients with septic shock are particularly more susceptible to those complications [4, 5]. The Saline (normal saline) versus Albumin Fluid Evaluation (SAFE) trial found an elevation of intracranial pressure in a subset of patients with traumatic brain injury who received albumin. Although this condition is counterintuitive. It could be explained by impaired micro vascular integrity resulting in extravasation of big molecules and subsequent exacerbation of brain edema [6]. In a recent study on patients with severe sepsis volume expansion by albumin was associated with lower mortality compared with saline-treated group [7]. The result of other new trials are in favour of albumin versus saline in severe septic shock although they only considered the 90 days mortality and proving this superiority needs future exploration [8]. Yuns et al demonstrated a lower risk of AKI in intensive care unit (ICU) patients when they are resuscitated with balanced crystalloids instead of saline (normal saline). (3). In a retrospective study of patients with sepsis, Raghunathan et al found higher mortality in those who received saline compared with balanced solutions [9, 10]. Bellomo et al in a double-blind, cluster-randomized, double-crossover study investigated the risk of Crystalloid Solution Versus Saline on AKI in

ICU patients. There was no difference in AKI rates within 90 days of enrolment between two groups. Although saline group received low volume (<2 liter) of this solution [3]. In a newly published article by Leticia Kawano-Dourado et al, they concluded low- versus high-chloride content of intravenous fluid did not affect the mortality and need for RRT in critically ill patients [5, 11].

Sodium chloride solution, or normal saline (saline) has been the most commonly administered intravenous fluid. The chloride concentration of saline (154 mmol per liter) is higher than plasma (94 - 111 mmol per liter). The chloride concentration in lactated Ringer solution is 109 mmol/liter, and in Plasma-Lyte A is 98 mmol/ liter both are more similar to human plasma and for these reason they are considered balanced crystalloids [5, 9, 11]. Saline is considered a potential generator of hyperchloremic metabolic acidosis, on the other hand, balanced solutions that are hypotonic relative to extracellular fluid could be associated with metabolic alkalosis [5]. In recently published results of two trials, balanced crystalloids resulted in a lower mortality or need for RRT in critically ill patients, but the benefit was not obvious in non-critically ill patients [9, 11].

During the past half century, the use of intravenous fluids are mainly based on physiological principles rather than being emerged from clinical trials [3]. The considered toxic effect for saline such as hyperchloremia and chloride-induced tubule-glomerular feedback and consequent GFR decline are also emerged from mechanistic explanations.

However, evidences that are against saline are also derived from post-hoc analyses of large data sets, and they are not coming from prospective and controlled trials [5, 9]. With above considerations, none of the currently used resuscitation fluids are “physiological,” the ideal fluid for resuscitation in the ICU remains unclear and still evidences do not supporting the avoidance of normal saline [11, 12]. It is defenceless but defensible.

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