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EDITORIAL

Balanced solution versus saline in critically ill patients: a new piece to the puzzle!

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Almost all critically ill patients receive intravenous fluids and this therapy is often the first-line treatment to optimize the hemodynamic condition. This common therapy is far from being innocuous. In particular, administration of large volumes of saline as resuscitation or maintenance fluid carries the risk of developing an hypernatremic and hyperchloremic metabolic acidosis, acute kidney injury, and might worsening patients' outcome [1]. The use of balanced solutions (BS) may avoid these adverse effects and would result in a lower rate of renal replacement therapy or persistent renal dysfunction than the use of saline [2].

Recently, four large trials with controversial results evaluated the effect of balanced crystalloids versus saline on patient-centered outcomes in critically ill patients [2–5]. When fluid composition was monitored early before admission to the intensive care unit (ICU), the use of BS was beneficial [2, 3], but when this was monitored only after ICU admission, no difference could be demonstrated [4, 5]. In a secondary analysis of the multicenter, randomized BaSICS trial [4] comparing balanced crystalloids with saline in critically ill patients, Zampieri et al. [6] were able to show that the patients who received balanced crystalloids before and after randomization had a reduced mortality compared to patients that only received saline.

In an article published in this issue [7], Zampieri and colleagues continued their investigation by carrying out a new post-hoc analysis of the original BaSICS study. They attempted to answer two questions: is the volume of fluid infused more determined by patient characteristics or local practices and is there a "dose–response" for the potential benefit provided by BS? They analyzed 10.505 patients, from 53 "effective" sites after lumping sites that recruited fewer than 20 patients. First, they found that basic predictors of filling, such as admission type, vasopressor use and heart rate, explained only a small part of the variance in fluid use during the first three days, whereas the site of enrolment explained it better. Second, and even more importantly, the results support a better prognosis with BS for septic patients who received more fluid, without being able to clearly define a threshold value. Accordingly, a benefit of BS was found for sites with high fluid administration, particularly for septic patients.

This study is the result of a secondary analysis of the BaSICS multicenter randomized trial, which included a large number of critically ill patients, enabling such an analysis. Over 5000 patients admitted to the ICU and over 3000 patients alive on day three were analyzed in each group. Thus, the results can be considered valid despite the fact that this is a post hoc study with multiple statistical manipulations.

The main finding of this study was the beneficial effect of BS over saline in septic patients when higher volumes were administered and is in line with a recently published cluster-randomized trial [8]. The benefit of BS in septic patients has already been reported in secondary trial analyses [6, 9, 10] and its dose–response effect suggested in a retrospective study [11]. The present study supports the idea that the benefit of BS is more potent in septic patients, and in case of large volumes infused. Indeed, the risk of hyperchloremic metabolic acidosis should appear only when such large volumes are infused, suggesting that the choice of fluid should be personalized depending on the amount of fluid that is required [12]. However, it is also possible that the infusion of smaller amounts of

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saline might also cause harm that does not have a clinical manifestation.

Typically, BS should be preferred to saline for hemodynamic stabilization in septic patients in whom the hypovolemic component of circulatory failure is strong, such as in case large fluid losses, peritonitis or pancreatitis, bearing in mind their detrimental effect in traumatic brain injury [2]. It is perhaps because the comparison of BS vs. saline was not performed in such specific patients that large RCTs could not show any difference in mortality, as confirmed by a recent meta-analysis [13]. In any cases, it must be borne in mind that resuscitation with large volumes of fluid carries other risks than hyperchloremic acidosis and acute kidney injury. Whatever the type of fluid, fluid accumulation is clearly associated with worse outcomes, especially in septic patients [14]. The present study focuses not only on the type of fluid used, but also on the volume infused.

In conclusion, the analysis published here adds a new stone to the edifice of resuscitation management in critical situations, but it should prompt further randomized studies for confirmation. This is not the final round, as the game continues.

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