5th International Fluid Academy Days: Conference App
November 26–28, 2015, Hilton Congress Centre, Antwerp, Belgium

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5th International Fluid Academy Days: Live blog by Adrian Wong @avkwong November 26–28, 2015, Hilton Congress Centre, Antwerp, Belgium

The SPLIT trial does not answer all questions regarding balanced solutions vs "normal" saline. Posted Oct 17, 2015 - 580 views - 6 Likes - 2 Comments

Normal (so-called physiologic) saline, still one of the most employed intravenous crystalloid solutions, presents a high, *non-physiological*, content of Cl– (and Na+), and has long been known to induce, as a side-effect of its liberal administration, hyperchloremic metabolic acidosis. Recently, in October 2015, the SPLIT trial (the 0.9% Saline vs Plasma-Lyte 148 for Intensive Cate Unit Fluid Therapy), the first large randomized controlled trial comparing the clinical effects of two different types of crystalloids, has been finally published (http://jama.jamanetwork.com/article.aspx?articleid=2454911). In this double-blind, cluster randomized, double-crossover trial, conducted in 4 ICUs in New Zealand, 2278 ICU patients in need for crystalloid fluid therapy were enrolled to receive either 0.9% NaCl or Plasma-Lyte 148, as a balanced solution, according to an alternating block of 7-weeks for each specific ICU. The study was designed to evaluate the proportion of patients with acute kidney injury (AKI) during the first 90 days after enrollment as the primary outcome, and to assess several clinically relevant endpoints as secondary outcomes. In contrast to the hypothesis, the authors observed an identical proportion of patients developing AKI in the two groups of treatment (9.6% in the balanced solutions group vs. 9.2% in the 0.9% NaCl group), as well as a similar use of renal replacement therapy, and in-hospital mortality.

Although the trial has been conducted and analyzed with a rigorous methodology (internal validity) and represents a very important step ahead in the field, it also has some important limitations, which leaves some major questions unanswered:
Normal saline should be called abnormal saline due to its unphysiologic Na+ and Cl- properties

- First, this study was a feasibility study and therefore sample size and power calculations were not possible. As discussed previously, *"normal"* saline can be referred to as *"abnormal unphysiologic"* saline due to its physiologic abnormality. The fact that not all "balanced" solutions are equal, also raises questions about generalisability of the SPLIT trial results: the differences between Plasma-Lyte and other solutions make it difficult to extrapolate the results obtained with Plasma-Lyte to other balanced solutions.
- Second, the study population included was composed, for its vast majority, of post-operative patients, after elective surgery (mainly cardiovascular), with small incidence of co-morbidities (and relatively low APACHE II score), other sub-groups (like sepsis and trauma) all had small numbers of patients included (less than 5%).
- Third, more than 90% of patients were exposed to intravenous fluids before enrolment and the majority of pre-enrolment fluid was balanced crystalloid.
- Fourth, only low volumes of NaCl (namely a median of 2 liters per entire ICU stay) were used, and as such this cannot be seen as a resuscitation strategy as patients with septic shock may require 4-6 liters of crystalloid, patients with severe diabetic ketoacidosis may need up to 6-8 liters and patients with trauma even more than 10 liters. The study does not reveal whether larger volumes (> 2 L) of normal saline are equivalent to Plasma-Lyte, nor does it clarify whether hyperchloremic metabolic acidosis is safe.
- Fifth, data on renal biomarkers was not available (cost issues) so we cannot answer the question whether or not hyperchloremic metabolic acidosis causes AKI.
- Sixth, primary outcome data was not available in 7.5%.
- Seventh, there was a major bias (unblinding) given the fact that use of 0.9% NaCl is associated with hyperchloremic acidosis, two-thirds of clinician were able to correctly identify the study fluid type.
- Finally, the effects of the two treatments on plasma Cl– concentration have not been measured, making it therefore impossible to assess the potential role in the deterioration of renal function during fluid therapy.

As the authors concluded, these findings, whereas showing a neutral effects of the two strategies in post-operative patients, leave unsolved the potential effects of intravenous balanced solutions in high-risk populations, more exposed to fluid therapy and at risk of AKI. We have to congratulate the authors for having performed this excellent study in order to solve the question whether or not hyperchloremic metabolic acidosis is related to AKI. The bottom-line is that the study does provide reassurance that in elective surgery and moderately sick critically ill patients, giving up to a maximum of 2L 0.9% NaCl (during the entire ICU stay) results in no increased risk of AKI compared with Plasma-Lyte 148. However, although this study is well designed with excellent internal validity, it adds little if nothing to our understanding of large-volume resuscitation in severely unstable critically ill patients. More data and studies are needed to solve this question.

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