

## RESEARCH NEWS

# To balance or not to balance: we are still left in a SPLIT

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**Keywords** - saline, buffered, balanced, fluids, crystalloids, critically ill, acute kidney injury**Introduction**

In this issue we introduce 'Research News', a new section of the Netherlands Journal of Critical Care. In this section recent landmark papers relevant to critical care medicine will be reviewed. Furthermore, possible implications of the results of these studies will be discussed. We believe this section will increase the scope of the journal. In general, contributions to this section will be on invitation; however, inquiries can be sent to a.p.vlaar@amc.uva.nl.

**Article:** Effect of a buffered crystalloid solution vs saline on acute kidney injury among patients in the intensive care unit. The SPLIT randomised clinical trial. Published in JAMA October 2015.<sup>[1]</sup>

**Why was this research done?**

Intravenous fluid therapy is one of the most commonly applied interventions in the intensive care setting. Worldwide 0.9% sodium chloride (saline) is the most frequently used resuscitation fluid. Observational studies show an association between the high chloride content of saline and the onset of acute kidney injury (AKI) in critically ill patients. An alternative to saline is a 'buffered' or 'balanced' crystalloid solution, with an electrolyte composition that more closely resembles that of plasma. Observational studies suggest that the use of a buffered crystalloid solution results in a decreased risk of AKI and death compared with saline. So far no randomised trial has investigated the effect of buffered crystalloids on the onset of AKI compared with saline in the critically ill patient population.

**Research question**

To determine the effect of a buffered crystalloid compared with saline on renal complications in patients admitted to the intensive care unit (ICU)

**How was this investigated?**

The study design was a double-blind, cluster randomised, double-crossover trial. The study was performed in four ICUs in New Zealand from April 2014 to October 2014. All patients admitted to the ICU in need of crystalloid fluid therapy were eligible for inclusion. Patients with established AKI requiring renal replacement therapy were excluded. Participating ICUs were assigned a masked study fluid, which was either saline or a buffered crystalloid, for alternating seven-week treatment blocks. The treating clinician determined the rate and frequency of fluid administration. The primary outcome was the proportion of patients with AKI, defined as a rise in serum creatinine level of at least twofold or a serum creatinine level of  $\geq 3.96$  mg/dl with an increase of  $\geq 0.5$  mg/dl. Secondary outcomes were incidence of renal replacement therapy and in-hospital mortality. All outcome data were censored at day 90.

**Main conclusions**

The use of a buffered crystalloid compared with saline did not reduce the risk of AKI in critically ill patients receiving crystalloid fluid therapy.

**Consequences for daily practice**

This is a well-conducted randomised trial in patients admitted to the ICU comparing saline and buffered crystalloid solution with respect to the onset of AKI. In contrast to previous observational studies, this randomised study does not show an increased risk for the onset of AKI in patients admitted to the ICU receiving saline. An explanation for the difference in outcome could be the superior study design of the SPLIT study compared with the previous observational studies, as it is known that observational studies are sensitive for confounding. However, the SPLIT trial has some important shortcomings which need to be highlighted before discussing the consequences for daily practice. First, the patients included in this trial were mainly elective postoperative ICU admissions.

These are not the patients at high risk of developing AKI. It is unclear why the authors chose this population instead of at risk critically ill patients. Second, the patients included in this study received only a median of 2000 ml study fluids during their ICU admission. Of note, this amount was almost equal to the amount of fluid infused prior to admission to the ICU. One could argue that a study using an intervention in a low-risk population with a primary outcome with a low incidence needs high exposure to the intervention fluid to detect any signal. It is unclear whether the 2000 ml of study fluids was sufficient to induce the effect which is suggested to be causative for renal complications. Unfortunately the authors did not report chloride or pH values in the study (only a severe acidosis of pH <7.2). This would at least convince the reader that the intervention induced the hypothesised underlying mechanism responsible for the onset of AKI. Although these drawbacks limit extrapolation of results to the general ICU population, this study sets the stage for future randomised trials. These trials should be guided by both the success of the trial (its simple and feasible design) as

well as by its limitations. Hence, these trials should investigate the effect of saline compared with buffered crystalloids on the onset of AKI in at risk critically ill patients who are exposed for a longer period of time to a larger amount of the intervention fluids. At present, the SPLIT trial shows that for elective patient admissions to the ICU receiving only a limited amount of intravenous fluids, the safety of saline and buffered crystalloids is similar in respect to onset of AKI and mortality.

#### Disclosures

The author declares no conflict of interest. No funding or financial support was received.

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#### References

1. Young P, Bailey M, Beasley R, et al. Effect of a Buffered Crystalloid Solution vs Saline on Acute Kidney Injury Among Patients in the Intensive Care Unit: The SPLIT Randomized Clinical Trial. *JAMA*. 2015;314:1701-10. Article information: the section Research News represents the opinions of the authors and the NJCC and not those of the NVIC.