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Out with the saline?

Reduced use linked to better outcomes

Two companion studies have shown that use of saline as intravenous fluid therapy, compared to crystalloids, was associated with poor survival and increased risk of kidney complications.

Matthew Semler, MD, MSc, assistant professor of Medicine at Vanderbilt University School of Medicine, told *ICU Management & Practice* in an email: "Because saline and balanced fluids are similar in cost and use of saline is based on historical practice and not scientific evidence, the results of these two large, randomised trials both showing the same benefit in patient outcomes with balanced crystalloids rather than saline may be sufficient evidence to change practice for many clinicians".

The research examined over 15,000 intensive care patients and over 13,000 emergency department patients, in pragmatic cluster randomised multiple crossover trials. Patients were assigned to receive saline (0.9% sodium chloride) or balanced fluids (lactated Ringer's solution or Plasma-Lyte A) if they required intravenous fluid. The primary outcome was a major adverse kidney event within 30 days.

Semler said the pragmatic trial aimed to answer the research question while keeping patient care during the trial as similar as possible to patient care outside of a study setting. "This improves the ease with which the study findings are applied to clinical practice. By comparing balanced fluids to saline without blinding clinicians, the trials provide an estimate of the effect of the fluids on outcomes that translates easily into clinical care", he said.

In the critically ill patient group, of 7942 patients in the balanced fluids group, 1139 (14.3%) had a major adverse kidney event. In the saline group 1211 of 7860 patients (15.4%) had an adverse kidney event. The incidence of new renal replacement therapy was 2.5% and 2.9% respectively, and the incidence of persistent renal dysfunction as 6.4% and 6.6% respectively. In septic patients, 30-day in-hospital mortality was 25.2% with balanced crystalloids and 29.4% with saline. In the study comparing fluids in non-critically ill patients, balanced crystalloids did not result in shorter time to hospital discharge than saline, but did result in lower incidence of the composite of death, new renal replacement therapy and persistent renal dysfunction. ■

References

Self WH, Semler MW, Wanderer JP et al; SALT-ED Investigators (2018) Balanced crystalloids versus saline in noncritically ill adults. N Engl J Med, 378(9): 819-28.

Semler MW, Self WH, Wanderer JP et al.; SMART Investigators and the Pragmatic Critical Care Research Group (2018) Balanced crystalloids versus saline in critically ill adults. N Engl J Med, 378(9): 829-39.

ICU delirium a distinct indicator of acute brain injury

More than half of ICU patients in a new study experienced delirium for long periods during their stay. Sedative-associated delirium was most common, while longer periods of hypoxic delirium and unclassified delirium were associated with worse cognitive function at follow-up one year after hospital discharge.

Patients were assessed for delirium while in the ICU twice a day using the Confusion-Assessment Method-ICU (CAM-ICU) and the Richmond Agitation-Sedation Scale (RASS) and once a day outside the ICU. The delirium phenotypes were classified according to the presence of hypoxia, sepsis, sedative exposure, or metabolic (eg, renal or hepatic) dysfunction, which were not mutually exclusive.

A total of 1040 patients with respiratory failure or septic or cardiogenic shock were included. Seventy-one percent of participants experienced delirium at least once during their stay, and delirium occurred on 31% of all 13434 participant days. In the 4187 days of delirium, one delirium phenotype was present during 1355 days (32%), two phenotypes present during 1213 days (29%), three during 1231 days (29%), and four were present during 388 days (9%). More than half of participants who experienced delirium had hypoxic, septic, or sedative-associated delirium at some time during the study; metabolic and unclassified delirium occurred less often.

Researchers assessed 564 (80%) patients at 3-month follow-up, and 471 (75%) at 1-year follow-up, to assess executive function. Longer periods of multiple delirium subcategories predicted worse cognitive decline after one year following hospital discharge. Metabolic delirium was the only phenotype that didn't affect long-term cognitive decline, after adjusting for age, severity of illness, doses of sedating medications and other factors.

Lead author Timothy Girard, MD, MSCI, associate professor of critical care medicine, Pitt School of Medicine, said in an email to *ICU Management & Practice*: "Based on this study, intensivists should monitor ICU patients for delirium and view delirium in the setting of sedation, hypoxia, and/or sepsis as red flags indicating high risk for long-term cognitive impairment. When treating a patient with sedative-associated, hypoxic, or septic delirium, they should work to identify and reduce potential risk factors, especially those that are iatrogenic and modifiable, e.g., sedation." He advised that when patients are discharged after a critical illness, those who experienced prolonged periods of sedative-associated, hypoxic, or septic delirium should be scheduled for follow-up in an ICU follow-up clinic or other setting that will facilitate assessment for cognitive impairment. ■

Reference

Girard TD, Thompson JL, Pandharipande PP et al. (2018) Clinical phenotypes of delirium during critical illness and severity of subsequent long-term cognitive impairment: a prospective cohort study. Lancet Respir Med, 6(3): 213-22.

Gut microbes protect against sepsis

New research published in *Cell Host & Microbe* suggests that gut bacteria may help in the fight against sepsis. In the study, mice were given particular microbes, which increased blood levels of immunoglobulin A (IgA) antibodies, protecting the mice against polymicrobial sepsis.

There is evidence showing that people with IgA deficiencies are more likely to succumb to sepsis. Also, previous research indicates that immunoglobulin M (IgM) antibodies quickly respond to blood-borne bacteria in sepsis and that gut microbes trigger immunoglobulin G (IgG) antibody responses that can block bacterial infection.

The current study aimed to determine whether gut microbes could trigger IgA responses that protect against sepsis. "We propose that serum IgA and IgG antibodies may play roles similar to the protective role proposed for natural IgM antibodies, with the IgA component providing a non-inflammatory mechanism for keeping invading bacteria in check," said first author Joel Wilmore of the Perelman School of Medicine at the University of Pennsylvania.

Wilmore and colleagues looked at IgA antibodies, which are readily detected in mice and humans but whose role in host protection against sepsis was unknown. The researchers found that exposing mice to a unique but natural microflora that included several members of the Proteobacteria phylum led to increases in IgA levels in the blood. Moreover, shifting the mouse gut to a Proteobacteria-rich microbiota led to IgA-mediated resistance to sepsis in mice.

When the researchers transferred blood lacking IgA into mice with sepsis, all but one animal died within two days. By contrast, mice that received blood enriched in IgA survived much longer. Taken together, the findings suggest that commensal microbes can have a substantial impact on IgA levels in the blood, resulting in protection against bacterial sepsis.

More studies are needed to further dissect the mechanism by which IgA confers protection against sepsis and explore ways to harness the specific properties of these antibodies to develop a treatment that may be applied to human disease. In the meantime, the researchers urge caution against over-interpreting the new findings.

"The study is limited by the fact that the microbiome in every person or animal is unique to some degree, and our study is in the context of the animal facility at the Perelman School of Medicine at the University of Pennsylvania," explains senior author David Allman, also at UPenn's Perelman School of Medicine. "While IgA protected mice in our study, it should not be assumed that IgA could replace standard treatments provided to patients in a clinical setting."

Reference

Wilmore JR, Gaudette BT, Allman D et al. (2018) Commensal microbes induce serum IgA responses that protect against polymicrobial sepsis. Published online in Cell Host & Microbe, February 22, 2018. DOI: 10.1016/j.chom.2018.01.005