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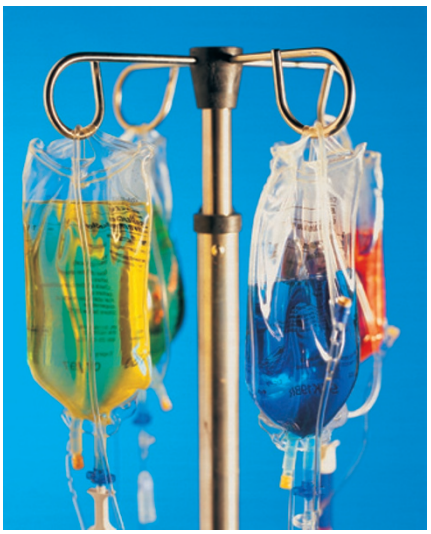
ACUTE KIDNEY INJURY

Restriction of intravenous chloride intake may reduce the incidence of AKI in critically ill patients

Some intravenous fluids contain supraphysiological levels of chloride, despite experimental evidence indicating a link between chloride administration and decreased renal function. A new study, published in *The Journal of the American Medical Association*, now reports associations between use of chloride-restrictive intravenous solutions and reduced incidence of acute kidney injury (AKI) and need for renal replacement therapy in critically ill patients.

Intravenous fluid therapy is widely used in critical care medicine and many types of fluid exist. Previous studies have demonstrated that excessive chloride administration can lead to adverse effects, including metabolic acidosis, renal vasoconstriction and decreased glomerular filtration rate. Moreover, critically ill patients are known to be at high risk of developing AKI. These findings led Nor'azim Mohd Yunos and colleagues to investigate whether a chloride-restrictive intravenous fluid strategy in critically ill patients might be associated with a decreased incidence and severity of AKI compared with a chloride-liberal approach. "Saline is ubiquitously used and yet physiologically irrational", explains corresponding author, Rinaldo Bellomo. "I wanted to see if removing the chloride was feasible, safe, and maybe beneficial."

The researchers performed a nonrandomized, controlled before-and-after study in a single centre in Australia. During the initial 6-month control period, patients admitted to the centre's intensive care unit (ICU) were given intravenous fluids as usual, with free use of chloride-rich fluids. The following 6 months were used to educate staff and prepare for the upcoming change in intravenous fluid practice. The next 6 months comprised an intervention period, during which chloride-rich solutions were made available only to individuals with specific



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conditions, such as hyponatraemia, traumatic brain injury, and cerebral oedema. Importantly, the intervention period coincided with the same season of the year as the control period, to control for the confounding effects of seasonal variation.

760 and 773 patients were admitted to the centre's ICU during the control and intervention periods, respectively. As expected, the researchers observed a substantial decrease in chloride administration, from 694 mmol per patient during the control period to 496 mmol per patient during the intervention period. Use of the chloride-rich solutions, including 0.9% saline (chloride concentration 150 mmol/l), a 4% succinylated gelatin solution (chloride concentration 120 mmol/l) and 4% albumin in sodium chloride (chloride concentration 128 mmol/l) were completely or partially replaced by Hartmann solution (chloride concentration 109 mmol/l), Plasma-Lyte® (Baxter, Deerfield, IL, USA; chloride concentration 98 mmol/l), and a 20% albumin solution (chloride concentration 19 mmol/l).

Yunos and co-workers found that patients treated during the intervention period experienced a significantly smaller rise in their serum creatinine level from baseline during ICU stay than did patients in the control phase (14.8 μmol/l versus 22.6 μmol/l, respectively; $P = 0.03$). The chloride-restrictive strategy was also associated with a decrease in the incidence of combined classes of renal injury and failure, defined by the RIFLE criteria for AKI (8% of patients in the intervention period versus 14% of patients in the control period; $P < 0.001$). A post-hoc analysis revealed a significant decrease in the secondary outcome—use of renal replacement therapy—in patients receiving chloride-restrictive solutions (6.3% during the intervention period versus 10% during the control period; $P = 0.005$). Adjusting for potential confounders did not alter the associations between use of chloride-restrictive solutions and the incidence of injury or failure classes of AKI or use of renal replacement therapy. No differences in hospital mortality, length of ICU stay, or long-term dialysis requirements after discharge were observed.

An accompanying editorial notes that these findings justify a more definitive study to examine the composition of intravenous fluids and test for adverse effects. The researchers plan to continue studying the effects of chloride-restrictive fluids on renal outcomes in critically ill patients. "I want to first confirm these findings in at least one other large teaching hospital. If confirmed, I plan to conduct a phase II randomized controlled trial", states Bellomo.

Susan J. Allison

Original article Yunos, N. M. *et al*. Association between a chloride-liberal vs chloride-restrictive intravenous fluid administration strategy and kidney injury in critically ill adults. *JAMA* **308**, 1566–1572 (2012)

Further reading Waikar, S. S. & Winkelmayer, W. C. Saving the kidneys by sparing intravenous chloride? *JAMA* **308**, 1583–1585 (2012)