Letter

Causes and effects of hyperchloremic acidosis

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Gunnerson and colleagues [1] found in their retrospective study that critically ill patients with lactate acidosis had a higher mortality compared to patients with hyperchloremic acidosis, whose mortality was not significantly different from patients with no acidosis. Because of its iatrogenic etiology the authors commented that it is reassuring that hyperchloremic acidosis is not associated with an increased mortality. Previous randomized controlled trials have, however, generated concerns regarding the adverse effects of hyperchloremic acidosis associated with rapid isotonic saline administration. Rapid isotonic saline infusion predictably results in hyperchloremic acidosis [2]. The acidosis is due to a reduction in the strong anion gap by an excessive rise in plasma chloride as well as excessive renal bicarbonate elimination. In a randomized controlled trial with a mixed group of patients undergoing major surgery, isotonic saline infusion was compared to Hartmann's solution with 6% hetastarch with a balanced electrolyte and glucose solution. Two-thirds of patients in the isotonic saline group but none in the balanced fluid group developed hyperchloremic metabolic acidosis [3]. The hyperchloremic acidosis was associated with reduced gastric mucosal perfusion on gastric tonometry. Another randomized double blind trial of isotonic saline versus lactated Ringer's in patients undergoing aortic reconstructive surgery confirmed this result and the acidosis required interventions like bicarbonate infusion and was associated with the application of more blood products [4].

Hyperchloremia was found to have profound effects on eicosanoid release in renal tissue, leading to vasoconstriction and a reduction of the glomerular filtration rate [5].

The increased eicosanoid release may also explain the findings of reduced gastric perfusion in the hyperchloremia mentioned above [3]. The main adverse effect of saline induced hyperchloremic acidosis, however, may be the action that is taken to correct the abnormality. Acidosis is often seen as a reflection of poor organ perfusion or poor myocardial function and a negative base excess may prompt the application of boluses of more saline containing fluids exacerbating the acidosis, the use of blood products, escalation of inotrope support and initiation of ventilatory support [6,7].

The safety of hyperchloremic acidosis has not been established in prospective studies and in patients with different types of critical illness. Particularly in critically ill patients with other co-morbidities like renal disease, more physiological electrolyte solutions (e.g., Ringers lactate solution) may be preferable to isotonic saline and a slow fluid replacement protocol safer than rapid infusions.

Authors' response

John A Kellum and Kyle J Gunnerson

We would like to thank Dr Eisenhut for his insightful comments regarding our article [1]. Historically, hyperchloremic metabolic acidosis has been viewed as a 'necessary evil' of volume resuscitation in critically ill patients. Dr Eisenhut has appropriately included several studies published in the past 10 years highlighting some of the adverse effects of this iatrogenic hyperchloremia [2-7]. We agree with his current comments and have editorialized on this in the past as well [8].

Not only has hyperchloremia been associated with a variety of clinical effects cited by Dr Eisenhut, we have also found various cellular and hemodynamic responses attributed to the 'type' of metabolic acidosis rather than the 'degree' of

acidosis *per se*. Lipopolysaccharide-stimulated macrophage-like cells in culture exhibited an augmented inflammatory response when subjected to hyperchloremic acidosis whereas hyperlactemia attenuated this response [9]. Hyperchloremia also caused hypotension in a cecal ligation and puncture model of sepsis in the rat; an effect partially mediated by nitric oxide [10]. Furthermore, in an endotoxin model of sepsis, decreased survival was noted when normal saline was used as a resuscitative fluid compared to Hextend (synthetic colloid dissolved in a balanced salt solution) [11].

However, clinical studies have not revealed effects of hyperchloremic acidosis on outcome. Of course, such studies have either been observational in nature, small in sample size or both. Our large, observational study did reveal a trend showing hyperchloremic metabolic acidosis was worse than the no metabolic acidosis group; however, it did not reach statistical significance. Thus, we suspect that the effects of hyperchloremia, especially when modest, are unlikely to influence outcome for most patients. However, given that hyperchloremic acidosis is often iatrogenic, and associated with morbidity, it should be avoided whenever possible.

Competing interests

The authors declare that they have no competing interests.

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