

## Commentary

# Sodium and brain injury: do we know what we are doing?

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See related research by Maggiore *et al.*, <http://ccforum.com/content/13/4/R110>

### Abstract

There is mounting evidence, including the recent report by Maggiore and colleagues, of an association between hypernatremia and mortality in patients with traumatic brain injury. This mandates a re-evaluation of routine administration of agents such as hypertonic saline for the management of intracranial hypertension in those with traumatic brain injury.

In the previous issue of *Critical Care*, Maggiore and colleagues [1] contributed significantly to our understanding of the incidence and associated consequences of hypernatremia in neurocritical care. This retrospective cohort study was performed in 130 consecutive patients with severe traumatic brain injury admitted to a tertiary academic referral institution. Hypernatremia was common, occurring in 51.5% of patients for 31% of the duration of their intensive care unit (ICU) stay. Hypernatremia was associated with a threefold increase in hazard of ICU death, even after adjustment for baseline risk. These results are consistent with the previous work of Aiyagari and colleagues [2], who found that hypernatremia was independently associated with increased mortality but only when severe (serum sodium >160 mEq/L) in a mixed neurocritical care sample that included patients with traumatic brain injury.

It is important to note that these non-interventional studies employed rigorous analytic techniques to account for the etiology of sodium disturbance. Such complex analytic techniques are required as sodium concentration abnormalities may be due to consequences of the injury (for example, central diabetes insipidus or hyperglycemia induced osmotic diuresis) or may be related to treatment (for example, hypertonic saline or mannitol). Maggiore and colleagues [1] admirably performed a detailed analysis that included many relevant potential confounders in an attempt to describe the independent association of hypernatremia and mortality.

Arguably, potentially important covariates have been excluded. Although adjusted for baseline risk using the impact prognostic model, the analysis did not include relevant ICU prognostic factors such as the development and degree of intracranial hypertension or systemic hypotension. This is significant when considering the indications for hypertonic saline and mannitol in neurotrauma. Both therapies are used as treatment of intracranial hypertension, but mannitol may potentiate systemic hypotension via osmotic diuresis. Hypertonic saline may have also been used in response to hyponatremia. Admittedly, one can never be certain that all relevant covariates are included in the correct manner in such models, and each additional covariate increases the complexity of the analysis and decreases power. Thus, it remains possible that hypernatremia is merely a marker of severity of illness.

In the meantime, where does this leave the clinician caring for the brain-injured patient? Should the results of Maggiore and colleagues be disregarded? Should therapies associated with hypernatremia, such as hypertonic saline or mannitol, be abandoned? Clearly, a mortality signal is not something clinicians can ignore, especially when studies are consistent. However, the treatment of intracranial hypertension is a generally adopted standard of care in neurotrauma. Multiple studies have shown hypertonic saline and mannitol to be physiologically beneficial with respect to the treatment of intracranial hypertension [3-5]. Indeed, sudden decreases in sodium concentrations may be detrimental in those with reduced intracranial compliance, and the maintenance of hypernatremia may be required [6]. There are limited human efficacy data for hypertonic saline use in neurocritical care. In a retrospective study, Qureshi and colleagues [7] found that hypertonic saline infusions were associated with higher in-hospital mortality (odds ratio 3.1, 95% confidence interval 1.1 to 10.2) after adjusting for differences between groups.

ICU = intensive care unit.

However, the small sample size and non-randomized methodology limit the generalizability of these results. Importantly, alternatives to hypertonic saline for the treatment of intracranial hypertension such as mannitol may also be detrimental [8]. Although these limited data are insufficient to mandate changes to standards of care, they provide ethical justification for the examination of these standards in randomized controlled trials.

Ultimately, the results of the study by Maggiore and colleagues emphasize the need for prospective randomized controlled studies in the neurotrauma population. It is clear that our interventions have potential both for benefit and for harm. The academic critical care community now has a mandate to move beyond retrospective associative evidence and examine interventions associated with sodium concentration variability. A thorough examination of hypertonic saline and mannitol for the management of intracranial hypertension is a logical starting point given the frequency of this indication.

## Competing interests

The author declares that they have no competing interests.

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