Sodium Bicarbonate Is Knocking at the Door of Neurocritical Care Unit: Should We Allow Its Entry?

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Mannitol has been traditionally the first-line osmotherapy for elevated intracranial pressure (ICP). However, it has concerns of hypotension secondary to osmotic diuresis. This has led some authors to advocate the use of 3% hypertonic saline (HTS), which does not cause diuresis and can be monitored easily by plasma sodium level and without the need for serum osmolarity measurement. Ideal dose of HTS is unclear, and it varies substantially among different studies. Typically, sequential boluses are titrated to achieve the desired effect. However, HTS may not be readily available all the times in every emergency department. Moreover, it does not offer any advantage over mannitol in traumatic brain-injured (TBI) patients.[1] Furthermore, repeated administration of HTS results in hyperchloremic metabolic acidosis (HMA) due to reduction in strong ion difference.[2]

Though there are contradictory reports on effects of hyperchloremia and HMA on sick patients, it may have subtle but potentially significant physiologic and clinical effects. HMA was associated with reduced gastric mucosal perfusion on gastric tonometry. Hyperchloremia was found to have profound effects on eicosanoid release in renal tissues leading to vasoconstriction and reduction in glomerular filtration rate.[3] Safety of HMA has not been established in prospective studies and, in particular, patients with critical illnesses. Moreover, clinical studies have not revealed effects of HMA on outcome. Of course, such studies have either been observational in nature, small in size, or both, though it is generally agreed that effects of hyperchloremia, especially when modest, are unlikely to influence outcome for most patients. However, given the HMA is often iatrogenic and associated with morbidity, it should be avoided when possible.[4]

Recent literature has highlighted the role of aquaporin (AQP) channels in water homeostasis across blood-brain barrier (BBB). AQPs are intimately associated with the production of cerebrospinal fluid (CSF) and control of water movement across BBB. Their levels are upregulated in animal models of trauma, stroke, and water intoxication, as well as around human malignant tumors. In particular, AQP-4 has been referred to as the "work horse" water channel at the BBB, being primarily expressed on astrocytic foot process.[5] It is also postulated that cortex acidosis that results following brain insult leads to dysfunction of AQP-4, and therefore it may play a significant role in edema development in a variety of pathological states, including TBI.[6–8]

Another ion channel called *acid sensing ion channel* (ASIC) also gets activated following neurologic insult that leads to cortical acidosis, and its activation enhances the severity of TBI.[9–11] Neuronal injury from acidosis is in part mediated by ASIC. Inhibiting ASICs also attenuated neuronal injury following reperfusion after ischemic insult in rats.[12] ASCI-1a (a subunit of ASIC) knockout mice or administration of sodium bicarbonate attenuated the severity of TBI.[13] Previous studies have shown that brain pH falls after TBI, and reduction in pH is more in patients with more severe injury.[14]

The above studies call for treatment of acidosis with an alkalinizing agent. One such agent that is quite familiar to clinicians, safe to administer, and readily available is sodium bicarbonate. Sodium bicarbonate has been shown to decrease brain water contents of neonatal dogs.[15] Various above studies make a strong case for treatment of brain acidosis to prevent aggravation of brain injury. It is suggested that 80 to 100 mL of 8.4% sodium bicarbonate may be a reasonable dose for the management of elevated ICP. The osmolarity of 8.4% sodium bicarbonate is 2,000 mOsm/L, which would be equivalent to the 5.8% saline. Thus 8.4% bicarbonate for osmotherapy and correction of cortical acidosis may be conceptualized as 6% saline. This makes it twice as powerful as the traditional 3% HTS. Therefore, instead of bolusing with 100 mL of 3% saline, clinician can bolus 50 mL of sodium bicarbonate (one ampoule/vial).[1] Administration of 1 mL/kg of bicarbonate raises plasma sodium by 1 mM/L. It should be given in a central vein, but in emergency it can be given via a peripheral vein. Approximately 3% HTS can be obtained by mixing 300 mL of normal saline with 200 mEq of sodium bicarbonate.

Two promising clinical studies have shown that when adults with TBI and increased ICP were given 85 mEq of 8.4% bicarbonate, they produced results superior to 3% HTS. Another benefit of this is that HMA is not caused by this compound,

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which is common with 3% HTS administration.[16,17] However, some concerns have been raised through animal models of either no effect[18] or even an elevation in ICP effect.[19] This partial pressure of carbon dioxide–mediated theory stems from old literature on the elevation of partial pressure of carbon dioxide with bicarbonate administered during resuscitation attempts.[20] The carbon dioxide produced so can be eliminated by increasing the ventilation.

Despite encouraging results, according to Zeiler et al,[21] the main limitation to use of sodium bicarbonate in reducing elevated ICP is availability of fewer quality studies with small number of patients. As of now, this compound should be considered as experimental in the management of high ICP in severe TBI patients. Future large-scale studies are required before it can replace existing osmotic agents in neurocritical care for reduction of elevated ICP.

Another situation in which sodium bicarbonate may be useful in neurointensive care unit is acute hyponatremia. Hyponatremia is a common occurrence in neurosurgical patients.[22] Acute onset of hyponatremia is particularly frequent in patients who have undergone any type of brain insult, including TBI, subarachnoid hemorrhage, and brain tumors. Unless corrected promptly, cerebral edema, impaired sensorium, and seizures result. Traditionally, symptomatic hyponatremia is managed with HTS, which consumes considerable time to raise plasma sodium to safe levels. Errors may result while calculating the required amount of sodium chloride in an emergent situation. Moreover, if the patient is seizing or showing signs of brain herniation, hypertonic therapy is often needed urgently. Sodium bicarbonate may come very handy in such circumstances. For a patient with symptomatic hyponatremia (seizures/coma), an increase in sodium by 4 to 6 mmol/L should be sufficient to relieve symptoms in most seriously ill patients.[23] On an average, approximately 2 mL/kg of 8.4% sodium bicarbonate administration raises plasma sodium by 2 mmol/L.[24] However, more large studies are needed before this agent is adopted as standard of therapy to correct symptomatic hyponatremia in neurointensive care.

The potential for future research surrounding the use of this compound in neurocritical care is exciting.

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