EDITORIAL

Normal Anion Gap Metabolic Acidosis in Pediatric Acute Diarrhea: A Menace or an Innocent Bystander?

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The under-5 mortality rate (U5MR) remained a significant health concern globally as well as in India. Among various causes of U5M, acute diarrheal illness or acute gastroenteritis (AGE) remained one of the leading preventable contributing factors to death. Severe dehydration due to an imbalance between fluid intake and output through stool, electrolyte disturbances, hypoglycemia, sepsis, hypovolemic shock, acute kidney injury (AKI), and underlying malnutrition are various predictors of mortality among hospitalized children with diarrhea.[1,2] Despite improving healthcare facilities and modernization of therapeutic aspects in India, malnutrition, and hypoalbuminemia still contributed as significant threats to patients with diarrhea.[3]

Metabolic acidosis is commonly seen in pediatric patients with AGE, especially if improperly treated with oral or intravenous (IV) rehydration therapy.[4,5] Loss of bicarbonate through the intestinal route, associated sepsis, and septic shock with or without AKI are risk factors for metabolic acidosis among patients with AGE.[6] Acute metabolic acidosis is harmful in critically ill patients as it suppresses immunity, worsens inflammation, causes vasodilation, and predisposes them to myocardial depression.[7] Several studies found metabolic acidosis as an independent predictor of mortality and prolonged hospital stay among patients in various age-groups.[8–10] Though the significant impact of metabolic acidosis is due to the high-anion-gap metabolic acidemia (HAGMA) component, the effects of non-anion-gap metabolic acidemia [Normal anion gap metabolic acidosis (NAGMA)] and the measures to correct it are still an area of interest among researchers.[11,12]

Acute NAGMA, also known as hyperchloremic acidemia, is frequently found in seriously ill AGE patients. Passage of large quantities of the base through diarrheal stool and therapy with high chloride-containing IV fluids to correct shock or hypovolemic states are the most common factors leading to acute NAGMA in children. Hyperchloremic acidosis may decrease renal cortical blood flow, worsen AKI, and augment pro-inflammatory response by altering interleukin pathways.[13,14] The detection of NAGMA and therapeutic aspects to prevent or treat this became essential topics for research.

In the current issue of the journal, Takia et al. have reported that severe NAGMA (sNAGMA) is associated with electrolyte imbalance, organ dysfunctions, prolonged hospital stay, and adverse outcomes in patients with diahhrea.[15] They found 13% of patients, out of 929 admissions due to severe AGE, had severe dehydration and sNAGMA. Their study also indicated prolonged resolution time of acidemia in patients with sNAGMA due to severe dehydration. The authors must be commended for conducting this study, especially for highlighting the importance of NAGMA in critically ill patients. Because of the large sample size and heterogeneous study population, the results of this study may add to the future prognostication model and therapeutic plan for severely ill pediatric diarrheal patients. However, a few limitations of this study must be considered while interpreting the results. Firstly, as NAGMA corroborates with the amount of bicarbonate loss in diarrhea, it is primarily a marker of illness severity and is expected to be associated with severe dehydration in these patients. To mention sNAGMA as the causative factor of poor outcomes, we require further prospective studies, as highlighted by the authors. Secondly, because of the retrospective nature of the study, the time taken for resolution of acidemia may not represent the real pathophysiology of sNAGMA as in many patients; the time of discharge from the emergency area was considered the endpoint even in the absence of measured serum pH or bicarbonate level.

The therapeutic role of bicarbonate in correcting acidosis has been debated over the years, mainly in critical care settings. Except in patients with AKI, the beneficial effects of bicarbonate therapy were not well established, even in patients with severe metabolic acidosis.[16] Moreover, IV sodium bicarbonate may precipitate volume overload, hypokalemia, ionized hypocalcemia, hypernatremia, and paradoxical intracellular acidosis. Hence, it is recommended to focus on treating the causes of metabolic acidosis rather than sodium bicarbonate infusion.[17] In their study, Takia et al., emphasized the need for a properly conducted trial to determine the role of IV soda bicarbonate therapy in treating severe acidosis, especially the NAGMA component, during the management of patients suffering

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from acute diarrhea and severe dehydration. Evidence-based guidelines on correcting metabolic acidosis and the indications of bicarbonate therapy may help critically ill pediatric patients.

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