

Title: Early onset hyponatremia in extremely preterm infants - are we underestimating the problem?

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Background: Serum sodium [Na] is a frequently ordered investigation in the NICU as premature infants are vulnerable to hyponatremia. However, there is a paucity of literature regarding the factors affecting Na in this setting. As recent research has described the association between hyponatremia and adverse neonatal outcome, we have chosen to further explore the epidemiology of hyponatremia in premature infants with an emphasis on fluid status.

Methods: The objectives were to investigate the 1) prevalence of hyponatremia in extremely preterm infants in the first 2 weeks of life; 2) investigations done and treatment course chosen for hyponatremia; 3) association between hyponatremia and fluid intake/sodium intake. This was a single center retrospective cohort study of extremely preterm infants (<28 weeks gestation) admitted between January 2018 and December 2019. Infants undergoing surgery and with hypoxic ischemic encephalopathy were excluded. Duration of data collection included day 1 to 14 after birth. Amount and type of fluid intake, total sodium intake from all sources, and Na values were recorded from chart review. The lowest value of Na for a day was collected. Investigations (repeat Na, serum creatinine, urine electrolytes/osmolality) and treatment [changes in total fluid intake (TFI) and sodium intake] following hyponatremia were explored. Mixed-effects logistic regression was used to investigate the relationship between TFI and the probability of hyponatremia. Hyponatremia was defined as at least one Na <135 mmol/L.

Results: There were 60 days of hyponatremia in the first 20 patients analyzed in the pilot study. After controlling for repeated measures, the prevalence for hyponatremia was 30.2%. Following an episode of hyponatremia, urine electrolytes/osmolality was ordered in 5% (n=3), serum sodium recheck in 71.6% (n=43) and serum creatinine in 36.6% (n=22) in the next 24 hours. Patients with hyponatremia were treated by increasing sodium intake in 33.3% (n=20) and by decreasing TFI in 1.6% (n=1). For every increase in 10ml of fluid/ kg/d, there was a 27% increase in the odds of hyponatremia, and for every increase in 1mmol of Na/kg/d, there was a 43% increase in the odds of hyponatremia.

Conclusion: Early onset hyponatremia is very common in extremely preterm neonates, but under investigated in terms of cause and associated conditions like acute kidney injury. Increase in fluid and Na intake are both associated with increased odds of hyponatremia. The interesting association between high sodium intake and hyponatremia may represent the usual response to supplement more sodium in hyponatremia without addressing etiological factors, as shown with the lack of investigations. Consequently, we suggest that TFI may need to be reduced more often (compared to increasing Na intake) to prevent severe hyponatremia. Further analysis is planned for a total sample size of 100.