PSNet
PATIENT SAFETY NETWORK

Incomplete Orders for Hypertonic Saline to Treat Hyponatremia

January 29, 2020
Wiegley N, Morfín JA. Incomplete Orders for Hypertonic Saline to Treat Hyponatremia. PSNet [internet]. 2020.
https://psnet.ahrq.gov/web-mm/incomplete-orders-hypertonic-saline-treat-hyponatremia

The Case

A 54-year-old man was brought to the emergency department by his family members who stated that they had found him unconscious at home with multiple empty bottles of alcoholic beverages nearby. The patient was found to be confused and severely hyponatremic with a blood sodium level of 109 mEq/L (the lower limit of the normal range in adults is 135 mEq/l). This level placed the patient at risk for life-threatening seizures, so he was admitted to the intensive care unit (ICU) and a nephrology consultant was urgently called.

The nephrologist briefly reviewed the laboratory results and asked the intensivist to administer hypertonic saline immediately to increase the sodium level, and to recheck the sodium level in one hour. ("Hypertonic" saline contains 3% sodium, compared to normal saline solutions which are composed of 0.9% sodium.) He did not specify how much hypertonic saline should be administered. When the nephrologist came to the ICU about two hours later, the patient's confusion had not improved. The repeat laboratory results showed that the sodium had risen to 130 mEq/dL, a rapid increase that put the patient at risk of severe neurologic complications.

Given this rapid correction, the nephrologist asked what medications had been administered and noticed that a 500 mL bag of hypertonic saline had nearly finished infusing. The infusion was stopped immediately, and the patient was administered dextrose, free water, and desmopressin to mitigate the effect of the rapid sodium correction. Fortunately, the patient's sodium stabilized and his mental status gradually improved. The next day, he was conscious, oriented, and answering questions appropriately. He was eventually discharged to an inpatient alcohol use disorder treatment center.

An incident report was filed due to the medication error. Investigation revealed that the intensivist had intended to order administration of 50 mL of 3% saline. However, the default intravenous fluid order in the hospital's computerized order entry system was for a 500 mL infusion. A separate, customizable order was

available but not easily accessible. In a rush, the intensivist ordered the 500 mL infusion and added a free-text comment to "infuse 50 cc then recheck sodium." Unfortunately, the free-text comment was missed both by the pharmacist and the ICU nurse, resulting in the patient receiving a much larger infusion at a faster rate than intended.

The Commentary

By Nasim Wiegley, M.D. and José A. Morfín, M.D.

Severe hyponatremia (sodium <120 mEq/l) is associated with increased risk of morbidity and mortality and prompt treatment is important to avoid neurologic complications related to cerebral edema. However, rapid correction of severe hyponatremia can also lead to catastrophic neurologic injury, namely osmotic demyelination syndrome (ODS) (previously known as central pontine and extrapontine myelinolysis). ODS can lead to varying neurologic manifestations including seizures, encephalopathy, movement disorder with parkinsonian-like features, and locked-in syndrome.[1, 2] The most common risk factors associated with rapid correction of hyponatremia include younger age, female sex, lower initial serum sodium, and schizophrenia (primary polydipsia). The factors known to be associated with increased risk of incident ODS include alcoholism, malnutrition, hypovolemia, hypokalemia, hepatic failure and liver transplantation.[2, 3]

This case demonstrates the complex nature of hyponatremia management in patients with these high-risk factors. This patient presented with severe hyponatremia (serum sodium level of 109 mEq/l) in the setting of excessive alcohol use, suggestive of a unique syndrome of hyponatremia called “beer potomania”. Beer potomania, which was originally described in 1972, describes a state of chronic low solute intake, malnutrition and high alcohol use. This state of low solute and high free water intake leads to hypotonic hyponatremia resulting in suppression of anti-diuretic hormone (ADH). Low solute intake also causes low renal medullary concentration, leading to inability of the kidneys to produce concentrated urine. In patients in this state, administering solute via either isotonic or hypertonic saline leads to rapid water diuresis and thereby to unpredictably rapid serum sodium correction.[4] For this reason, patients with alcohol-related symptomatic hyponatremia require close monitoring of serum sodium, urine osmolarity and urine output in an intensive care unit; early detection of an increase in urine output and lower urine osmolarity should prompt timely adjustment of the management plan to avoid treatment complications.

The initial symptomatic presentation of this patient with encephalopathy, in the setting of severe hyponatremia, resulted in appropriate escalation of care and admission to a medical intensive care unit. The severity of this patient’s hyponatremia and his significant alcohol intake made rapid correction of serum sodium a high-risk undertaking for him; use of hypertonic saline without close patient monitoring resulted in excessive correction of sodium and put him at high risk for developing ODS.

Use of Hypertonic Saline

Data regarding treatment strategies for management of severe hyponatremia are sparse and primarily driven by physiological principles, observational studies and case reports. In 2013, an American panel of experts in hyponatremia developed additional guidance on hyponatremia treatment. The updated guidance recommended a daily correction goal of 4-6 mEq/L for patients at high risk of overcorrection and ODS, with

an upper limit of 8 mEq/L in a 24-hour period, and a slightly higher goal and limit of daily correction for patients at lower risk of ODS. In cases with severe neurologic symptoms, such as seizures or coma, the panel recommended use of a 10-minute infusion of 100 ml 3% saline, repeated up to two additional times until symptoms resolve, regardless of known chronicity.[5] Alternatively, European guidelines recommend use of a 150 ml bolus of 3% saline for severely symptomatic hyponatremic patients, followed by one additional bolus 20 minutes later if symptoms persist.[6] Patients with milder symptoms can be managed by administering 0.5-2.0 ml/kg/hr of 3% saline, which should correct serum sodium levels by approximately 5 mEq/L.[5]

For symptomatic hyponatremic patients, such as the patient in this case, the goal of therapy should be to raise serum sodium by 4-6 mEq/L over the first few hours, as this rate of rise in serum sodium is usually sufficient to alleviate symptoms by reducing cerebral edema and preventing herniation.[7] However, this patient inadvertently received nearly 500 ml of hypertonic saline instead of a “one-time” 50 ml bolus, resulting in dramatic overcorrection of serum sodium (>20 mEq/L) in the initial two-hour interval. This medical error was primarily related to a breakdown in communication among the nephrologist, intensivist, bedside nurse and pharmacist. Lack of a standardized order set for hypertonic saline management also contributed to the medication error in this case. Specifically, the prescriber was obligated to enter a personalized order with free-text instructions, but these instructions were missed by the pharmacist and the bedside nurse, resulting in an incorrect dose of this high-risk medication being administered.

Administered appropriately, hypertonic saline is an effective medication for management of symptomatic hyponatremia regardless of the underlying etiology and can be used, for example, to increase serum sodium in cases of syndrome of inappropriate antidiuretic hormone (SIADH), and as a volume expander in hypovolemic hyponatremia.[8] However, the effect of hypertonic saline on serum sodium can be unpredictable; therefore, characterizing it as a high-risk medication is appropriate since it requires careful monitoring of serum sodium levels and urine output with urine osmolarity measurements in order to avoid catastrophic neurologic complications. In addition, both European and American expert panels recommend therapeutic lowering of serum sodium by administering free water (mostly in the form of D5W), with or without desmopressin (DDAVP), to treat inadvertent overcorrection. The combined administration of hypertonic saline and DDAVP has been shown to raise serum sodium in a more controlled fashion, and this strategy should be considered when treating patients with high risk of developing ODS.[9]

Approaches to Improving Safety

The safety of high-risk medications, such as hypertonic saline, can be increased by developing and using a carefully designed, standardized order set that includes appropriate directions for administration (concentration, dose, pre-specified duration for continuous weight-based infusions) and orders for monitoring patients closely. For symptomatic hyponatremia, this order set would include laboratory assessment of serum sodium at frequent intervals, as well as nursing orders for strict hourly urine output assessment. Such order sets decrease variation and unintended inaccuracies, reduce the potential for medication errors through integrated safety alerts and reminders, and ultimately improve patient outcomes.[10] Of course, standardized order sets do not obviate the need for close communication among all the medical professionals involved in the care of medically complex patients. In this case, the nephrologist should have communicated clear and specific recommendations regarding proper dose, duration of

treatment, and frequency of laboratory and urine output monitoring. The intensivist should have also closed the loop by clarifying the recommendation with the nephrologist and, subsequently, with the bedside nurse. Lastly, orders for high-risk medications, such as the hypertonic saline in this case, should be reviewed by a pharmacist prior to their release to ensure the recommended dose, and explicit start and end time points, are verified.

Take Home/Teaching Points

- Severe hyponatremia is associated with increased risk of morbidity and mortality. Early recognition of high-risk factors, and the use of evidence-based strategies for management of severe hyponatremia, are very important to avoid catastrophic complications such as osmotic demyelination syndrome.
- To prevent medication errors, clinicians should be vigilant about the potential complications of, and be familiar with evidence-based approaches and guidelines for, using hypertonic saline. Having knowledge of the best methods for reversing such errors is also important for preventing long-term patient harm.
- Effective communication among all members of a patient's care team is critical for understanding the timely start and discontinuation of therapy to achieve optimal clinical targets.
- For high-risk medications like hypertonic saline, standardized order sets specifying dose, route of administration, clearly defined start and end points, and specific laboratory tests for monitoring patients can reduce the potential for medication errors.

Nasim Wiegley, MD
Clinical Nephrology Fellow
Department of Internal Medicine, Division of Nephrology
University of California, Davis Medical Center

José A. Morfín, MD
Health Sciences Clinical Professor
Department of Internal Medicine, Division of Nephrology
University of California, Davis Medical Center

References

1. Martin RJ. Central pontine and extrapontine myelinolysis: the osmotic demyelination syndromes. J Neurol Neurosurg Psychiatry. 2004;75 Suppl 3:iii22-8.
2. George JC, Zafar W, Bucaloiu ID, Chang AR. Risk factors and outcomes of rapid correction of severe hyponatremia. Clin J Am Soc Nephrol. 2018;13(7):984-992.
3. Sterns RH, Hix JK, Silver S. Treatment of hyponatremia. Curr Opin Nephrol Hypertens. 2010;19(5):493-8.
4. Liamis GL, Milionis HJ, Rizos EC, Siamopoulos KC, Elisaf MS. Mechanisms of hyponatraemia in alcohol patients. Alcohol Alcohol. 2000;35(6):612-6.

5. Verbalis JG, Goldsmith SR, Greenberg A, Korzelius C, Schrier RW, Sterns RH, et al. Diagnosis, evaluation, and treatment of hyponatremia: expert panel recommendations. Am J Med. 2013;126(10 Suppl 1):S1-42.
6. Spasovski G, Vanholder R, Allolio B, Annane D, Ball S, Bichet D, et al. Clinical practice guideline on diagnosis and treatment of hyponatraemia. Nephrol Dial Transplant. 2014;29 Suppl 2:i1-i39.
7. Sterns RH, Nigwekar SU, Hix JK. The treatment of hyponatremia. Semin Nephrol. 2009;29(3):282-99.
8. Ayus JC, Moritz ML. Misconceptions and barriers to the use of hypertonic saline to treat hyponatremic encephalopathy. Front Med (Lausanne). 2019;6:47.
9. Sood L, Sterns RH, Hix JK, Silver SM, Chen L. Hypertonic saline and desmopressin: a simple strategy for safe correction of severe hyponatremia. Am J Kidney Dis. 2013;61(4):571-8.
10. Medication Safety Self-Assessment or High-Alert Medications. Institute for Safe Medication Practices 2017. Available at: https://www.ismp.org/sites/default/files/attachments/2018-01/EntireAssessmentWorkbook.pdf.

This project was funded under contract number 75Q80119C00004 from the Agency for Healthcare Research and Quality (AHRQ), U.S. Department of Health and Human Services. The authors are solely responsible for this report's contents, findings, and conclusions, which do not necessarily represent the views of AHRQ. Readers should not interpret any statement in this report as an official position of AHRQ or of the U.S. Department of Health and Human Services. None of the authors has any affiliation or financial involvement that conflicts with the material presented in this report. View AHRQ Disclaimers