Hyponatremia and Death in Healthy Children From Plain Dextrose and Hypotonic Saline Solutions After Surgery

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INTRODUCTION

Two 6-year-old children died at two different hospitals as a result of severe postoperative hyponatremia. In at least one case, the rapid administration of plain dextrose 5% in water (D_5W) after surgery resulted in acute hyponatremia secondary to free water retention (water intoxication). Children are at high risk for hyponatremia postoperatively, and many fatalities from this disorder have been reported in the literature.[1–14] When serum sodium concentrations rapidly fall below 120 mEq/L over a period of 24 to 48 hours, as they did in these two children, the body's compensatory mechanism is often overwhelmed. Severe cerebral edema ensues, resulting in brainstem herniation, mechanical compression of vital midbrain structures, and death.[15]

Case 1

A child underwent an outpatient tonsillectomy and adenoidectomy. Postoperative orders included intravenous (IV) fluids of *1,000 cc D_5W–600 cc q8h*.

An experienced pharmacist accidentally calculated the infusion rate incorrectly and entered *200 mL/hour* instead of *75 mL/hour* on the child's electronic medication administration record (MAR). He used a calculator and performed the calculation twice but had set up the mathematical problem incorrectly. Thinking in terms of how many 600-mL "doses" would be needed, he set up the calculation as follows: 600 mL (the volume to infuse over 8 hours), divided by 3 (the number of 600 mL "doses" he thought would be needed for 24 hours), and arrived at an infusion rate of 200 mL/hour.

The nurse who started the infusion did not detect the pharmacist's error. She had quickly looked at the surgeon's postoperative orders and had obtained a bag of D_5W to hang. However, she felt rushed by the hectic pace of the unit and was distracted during the verification process because she had to find an infusion pump to administer the IV solution.

The nurse thought her memory of the written order was sufficient for verifying the pharmacist's entry on the MAR. This was not her usual practice; however, like other nurses on the unit, she had come to rely on the accuracy of pharmacists who "never made mistakes." When the first 1,000-mL bag of D_5W was empty, the nurse hung a second bag to infuse at 200 mL/hour.

Several times throughout the day, the child vomited small amounts of dark, bloody secretions, as expected from the surgery. Near the anticipated time of discharge that afternoon, the child's mother asked a nurse to administer an antiemetic before she took her daughter home.

About 40 minutes after receiving promethazine 12.5 mg IV, the child became lethargic and began experiencing jerking movements, rigid extremities, and rolled-back eyes. The surgeon attributed this to a dystonic reaction from promethazine. A dose of IV **diphenhydrAMINE** was administered, and the child was admitted to a medical–surgical unit.

During the next few hours, the child's vomiting worsened and she became less responsive. The seizure-like activity became even more pronounced and frequent. The nurses called the child's surgeon multiple times to report the seizure-like activity, during which time additional doses of IV diphenhydrAMINE were prescribed and subsequently administered. Several nurses also told the surgeon that the seizure-like activity appeared to be more than a dystonic reaction to promethazine, although none of the nurses had ever witnessed such a reaction.

Unfortunately, during this time, the nurses did not notice the error involving the infusion rate or recognize that an infusion of plain D_5W alone or an infusion rate of 200 mL/hour was unsafe for a 6-year-old child. Subsequently, a third 1,000-mL bag of D_5W was hung after the second bag had been infused.

Because of significant bradycardia, it was necessary to call a code. The surgeon came to the hospital, observed that the child was having a grand mal seizure, and consulted a pediatrician to help manage the seizures. The consulting pediatrician finally recognized that the child was experiencing hyponatremia and water intoxication from the erroneous infusion rate of 200 mL/hour during the previous 12 hours and from the lack of sodium chloride in the infusate.

Laboratory studies showed a critically low concentration of sodium of 107 mEq/L. Computed tomography of the brain revealed cerebral edema. Despite treatment, the child died.

Case 2

A child underwent surgery for coarctation of the aorta, a condition that had been identified in this otherwise asymptomatic, healthy child during a physical examination. The child seemed to be progressing well, but later on postoperative day 1, his physician prescribed a furosemide infusion (1 mg/ hour) because the child's urinary output was less than expected despite several doses of IV ethacrynate sodium (Sodium Edecrin, Aton/Valeant).

By postoperative day 2, the child's serum sodium level had dropped. His physician prescribed an infusion of sodium chloride. It is uncertain whether the sodium chloride was ever administered, because the child's sodium level continued to drop and administration of the prescribed infusion was never documented on the MAR.

The child became less responsive throughout the morning, and his parents expressed concern to several nurses when they could not awaken their son. The nurses assured the parents that deep sleep was expected because of the pain medication (**HYDROmorphone)** that the child

was receiving. Despite repeated concerns expressed by the parents, the nurses failed to recognize that the child was not simply sleeping soundly but was exhibiting signs of severe, life-threatening hyponatremia.

When the child began experiencing seizure-like activity in the early afternoon, the nurses attributed the movements to the child being "fidgety" from pain. The child also began vomiting. Unfortunately, the physician was not kept informed about the child's change in cognition, ongoing oliguria, vomiting, and seizure-like activity.

When the critical-care intensivist visited the child in the early evening for a routine assessment, he quickly recognized the problem. By then the child exhibited no reflexes or responses to painful stimuli.

Despite intubation and ventilation support, as well as aggressive treatment of hyponatremia and cerebral edema, the child died the following day.

Although many of the contributing factors and deeply seated root causes of these events differ, two common causes are clear: (1) the staff's lack of knowledge about the causes and signs of hyponatremia, and (2) the failure of the staff to respond to concerns expressed by nurses in Case 1 and by parents in Case 2 regarding the rapidly deteriorating condition of these children.

HYPONATREMIA AND WATER INTOXICATION

Hyponatremia is the most common electrolyte disorder,[15] particularly among hospitalized patients. Studies suggest that clinically significant hyponatremia develops in more than 4% of patients within 1 week of surgery and in 30% of patients treated in intensive-care units (ICUs).[15–18]

In general, the causes of hyponatremia are varied, including:

- some medications (e.g., diuretics, heparin, opiates, desmopressin, proton pump inhibitors).
- disease states (e.g., renal and liver impairment, hypothyroidism, cortisol deficiency).
- environmental conditions outside the hospital (e.g., prolonged exercise in a hot environment).
- self-imposed conditions (e.g., psychogenic polydipsia or feeding infants tap water or formula that is too diluted).

However, the causes of hospital-acquired hyponatremia most relevant to children's deaths are twofold: administration of plain D_5W or hypotonic saline parenteral solutions postoperatively, and failure to recognize the compromised ability of children to maintain water balance.[15]

A review of the literature suggests that administration of hypotonic saline or parenteral fluids without saline is physiologically unsound and potentially dangerous for hospitalized children.[1] In an analysis by Moritz et al.,[1] more than 50 cases of neurological morbidity and mortality were reported, including 26 deaths, during a 10-year period, resulting from hospital-acquired hyponatremia in children receiving hypotonic saline parenteral fluids.[1–14] More than half of these cases occurred in previously healthy children after minor surgery.

Children are particularly vulnerable to water intoxication because they are prone to experiencing a syndrome of inappropriate antidiuretic hormone (SIADH).[1] Common childhood conditions requiring IV fluids, such as pulmonary and central nervous system infections, dehydration, and the postoperative state, are associated with a non-osmotic—and therefore inappropriate—stimulus for antidiuretic hormone (ADH) production.[1,14] The postoperative non-osmotic stimulus for ADH release typically resolves by the third postoperative day, but it can last until the 5th postoperative day.[1,18] Pain, nausea, stress, opiates, inhaled anesthetics, and the administration of hypotonic saline or solutions without saline also stimulate the excessive release of ADH in children.[1,14]

Children are also more vulnerable to the effects of cerebral swelling caused by hyponatremia; they develop encephalopathy at less significant decreases in normal serum sodium levels compared with adults, and the prognosis is poor if timely therapy is not instituted. In children, there is little room for brain expansion because of their higher brain-to-skull size ratio.[1,17,19] Adult brain size is achieved by 6 years of age, but full skull size is not achieved until 16 years of age.

Hyponatremic encephalopathy can be difficult to recognize in children, because symptoms may be variable.[2,18] The most consistent symptoms include headache, nausea, vomiting, weakness, mental confusion, and lethargy. Advanced signs include cerebral herniation, seizures, respiratory arrest, noncardiogenic pulmonary edema, dilated pupils, and decorticate or decerebrate posturing.[1]

Irreparable harm can ensue when low serum sodium levels are corrected too quickly or too slowly. After the source of free water has been eliminated, the sodium level is typically increased by 4 to 6 mEq over the first 1 to 2 hours via an isotonic or near-isotonic sodium chloride infusate.[15] Patients with seizures, severe confusion, coma, or signs of brainstem herniation may need hypertonic (3%) saline to correct sodium levels, but only enough to arrest the progression of symptoms.

Formulas exist for determining the dose of hypertonic saline during replacement therapy.[14] Some clinicians believe that in serious cases, treatment of hyponatremia should be rapid because the risk of treating too slowly (i.e., cerebral herniation) is thought to be greater than the risk of treating too quickly (i.e., osmotic demyelination syndrome, associated with lesions in the white matter of the brainstem).[14] These lesions are more common in adults.

CONCLUSION

Standards of practice should be established for postoperative IV solutions that are used to hydrate patients, particularly children. The standards should acknowledge that the administration of solutions with saline in maintenance parenteral fluids is an important measure that can be taken to prevent hyponatremia in children, who tend to experience increased ADH production.[15] If appropriate, criteria should include a schedule of when laboratory studies are required to determine electrolyte levels in patients receiving IV fluids for hydration over an extended period of time.

Protocols should be established to identify, treat, and monitor patients with hyponatremia, water intoxication, and SIADH. Clinically significant hyponatremia may be nonspecific in its presentation; therefore, professional staff members must include this possibility in the differential diagnoses in patients presenting with early symptoms or an altered level of consciousness. All physicians, pharmacists, and nurses need to be knowledgeable about fluid and electrolyte balance and the pathophysiology of hyponatremia, water

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intoxication, and SIADH to increase their index of suspicion when symptoms appear so that they will be more responsive to voiced concerns regarding the patient's condition.

All hospitals should also consider establishing a rapid-response team (RRT). Implementing this policy allows all health care workers to summon an interdisciplinary team to a patient's bedside for a full evaluation when they fear something is seriously wrong and have expressed their concerns without an adequate response. The team provides an opportunity to step in before a fatality occurs. After the team has been formed and is functioning well, it would be prudent to consider inviting patients and families to call in the RRT to address unresolved concerns about the patient's safety and health. Subtle changes may be more easily identified as abnormal or uncharacteristic by family members than by health care professionals.

Note: The information in this column should not be used to guide the treatment of hyponatremia or used as an evidence-based standard of care. It is provided only to convey the message that expert opinions vary regarding prevention and treatment of hyponatremia and to encourage discussion among an interdisciplinary clinical team charged with developing electrolyte-replacement protocols.

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