Hospital-Acquired Acute Hyponatremia and Parenteral Fluid Administration in Children

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INTRODUCTION

Parenteral fluids administered for the purpose of hydration have not traditionally been viewed with the same rigour as medications. These fluids are usually distributed through the materials management division of hospital operations. In addition, fluids are often not reviewed by pharmacists as part of pharmaceutical care activities. Fluid and electrolyte management is a crucial aspect of overall patient management, and there is an opportunity for pharmacists to offer greater support in this area.

This article highlights the issue of hospital-acquired acute hyponatremia in children.[1] Acute hyponatremia is defined as a decline in serum sodium within a 48-hour period to less than 130 mmol/L, an abrupt change that can lead to cerebral edema as a result of electrolyte-free water moving into the brain cells.

Various literature reports,[2-7] pediatric inquests,[8] and a recent newsletter from the US Institute for Safe Medication Practices[9] have highlighted cases of acute hyponatremia leading to the in-hospital deaths of children. The National Patient Safety Agency in the United Kingdom has identified hospital-acquired hyponatremia in children as a major patient safety issue. Several safety alerts and guidelines for the administration of fluids to children have been published internationally.[10-13] The Canadian Medical Protective Association recently highlighted a case of hospital-acquired hyponatremia in a child.[14] A provincial coroner identified 6 pediatric deaths related to acute hyponatremia in hospital settings over a 10-year period and provided a guideline for practitioners administering parenteral fluids to children.[15]

Two pediatric deaths due to acute hyponatremia associated with IV administration of hypotonic solutions have been voluntarily reported to ISMP Canada.[1] Information from these reports is shared to enhance understanding of the potential for fatal hyponatremia in children.

INCIDENT REPORTS

Case 1

A 4-year-old child who weighed about 15 kg underwent tonsillectomy as day surgery. No abnormalities were noted during a preadmission assessment the day before the surgery. The tonsillectomy was performed under general anesthesia, and the child was mechanically ventilated during the procedure. The child received a total of 250 mL of normal saline IV (0.9% sodium chloride). After the procedure, an infusion of 3.3% dextrose and 0.3% sodium chloride solution (referred to herein as "2/3 and 1/3")* was ordered for IV administration at 55 mL per hour. Oral intake of fluids was also encouraged. The child was transferred to a patient care area with orders to be discharged home when drinking well.

*The combination of 3.3% dextrose and 0.3% sodium chloride (known as 2/3 and 1/3) contains only 51 mmol/L of sodium. Outside the body, the osmolarity of the solution is 269 mOsmol/L (sodium and dextrose combined). Once the solution is infused, however, the dextrose is rapidly metabolized, which leaves two-thirds of the solution (667 mL) as electrolyte-free water and renders the solution extremely hypotonic.

Shortly after arriving in the patient care area, the child experienced several episodes of vomiting. Oral intake of clear fluids over the next several hours was about 200 mL. The child was kept in hospital, and the IV administration of "2/3 and 1/3" was continued as originally ordered over the rest of the day and night. The child voided several times, but the amount was unknown. Overnight, the child became incontinent and was noted to be drowsy. Toward the next morning, the child had several seizures, which were treated initially with lorazepam and later with phenobarbital. Blood testing indicated a sodium level below 120 mmol/L. The IV solution was changed to sodium chloride 3%, and the child was transferred to a regional pediatric centre. The child died shortly thereafter. The cause of death was severe cerebral edema with brain herniation due to acute hyponatremia.

Case 2

A previously healthy 3-year-old child was brought to an emergency department with a 1-day history of vomiting and diarrhea. The child's pulse was more than 125 beats per minute; blood pressure was 85/60 mm Hg. The child's mucosal membranes were dry and the eyes sunken. Laboratory testing indicated normal serum electrolytes, elevated blood urea nitrogen (BUN), and normal creatinine; a urine test was positive for ketones. In the emergency department, the child received 2 boluses of normal saline by IV administration, totalling about 450 mL. Follow-up blood work revealed that the sodium level was 138 mmol/L and BUN had decreased to within normal limits. The child was admitted, and "2/3 and 1/3" was administered at 130 mL per hour IV. Over the course of the next 12 hours (through the evening and overnight), the child voided about 110 mL urine in total and received over 1.5 litres of "2/3 and 1/3". The child's nausea continued.

The next day, the child voided once, but the amount was not determined or recorded. Shortly thereafter, the child experienced incontinence of urine and seemed to be sleepy. A few hours later, the child appeared lethargic and rigid. The infusion was stopped, and blood tests revealed a sodium level below 120 mmol/L and lower-than-normal levels of potassium, BUN, and creatinine. The child experienced a seizure and was treated with lorazepam. Hypertonic saline was ordered, but none was available, so mannitol was administered IV, followed by a bolus of normal saline. Because of continued seizure activity and oxygen desaturation, the child was intubated and ventilated. Shortly thereafter, the child experienced cardiac arrest and could not be resuscitated. The cause of death was cerebral edema due to acute hyponatremia.

BACKGROUND INFORMATION ABOUT ACUTE HYPONATREMIA

Hyponatremia can occur if there is a disproportionate loss of sodium such as occurs with primary kidney disease or conditions that affect the ability of the kidneys to conserve sodium. It can also occur because of a disproportionate gain of electrolyte-free water in the vascular compartment, also known as dilutional hyponatremia or water intoxication. The increased ratio of free water to sodium in the vascular space will cause the water to move from this extracellular compartment into the intracellular compartment until osmolality is equalized—free water will enter body cells (i.e., brain cells) and cellular edema will result.

In acute hyponatremia, the brain cells are unable to compensate for the rapid decrease in serum osmolality; as such, minor increases in electrolyte-free water can lead to disproportionately large increases in intracranial pressure due to swelling of the brain cells.[2-4] Acute hyponatremia can be fatal for both children and adults; however, children are more vulnerable to the effects of fluid and electrolyte imbalance. Children exhibit symptoms more quickly than adults in response to abnormal sodium levels because there is less room for the brain cells to swell (the brain reaches its adult size by the time the child is 6 years old, but the skull does not reach adult size until a person is 16 years of age).[4]

The early signs and symptoms of acute hyponatremia and rising intracranial pressure are often nonspecific (nausea, vomiting, headache, and decreasing level of consciousness) and thus may be attributed to other causes, such as the postoperative effects of anesthetics, medications administered for pain, or the presenting illness. A rapid decline in serum sodium levels combined with symptoms of increased intracranial pressure is a medical emergency, as further increases in brain-cell swelling can cause seizures, respiratory depression, coma, irreversible brain damage, or brain herniation and death.

DISCUSSION

There appears to be general consensus that isotonic fluids such as normal saline should be used for children during surgery and in the treatment of moderate to severe hypovolemia; however, there is debate as to which solution is the best choice for maintenance of hydration.[2,7,16-28] Pediatric experts are questioning the widespread use of hypotonic solutions for parenteral maintenance based on a formula that was developed more than 50 years ago.[29] The formula is derived from minimum free-water requirements based on caloric expenditure per kilogram of body weight. Experts argue that this formula overestimates maintenance requirements for a variety of reasons; most importantly, the formula presumes normal excretion of free water by the kidneys and thus does not take into account antidiuretic hormone released in response to nonosmotic stimuli, a process that was identified since the original development of the formula and that is commonly seen in children being cared for in hospital. In one recent study, a key factor in the development of hospital-acquired hyponatremia was the use of hypotonic maintenance solutions.[30] A variety of studies, including randomized trials, are answering

questions about the use of maintenance fluids for children.[30-32] Experts do agree, however, that there is no single IV solution that is ideal for all children.

Recommendations and Considerations for Pharmacists

Many Canadian pediatric centres have recognized hospital-acquired hyponatremia as an important issue that merits attention and have revised (or are in the process of revising) their practice guidelines and management of fluids and electrolytes accordingly.[33-35] Pharmacists are urged to advocate for and participate in reviewing and updating the guidelines for fluid and electrolyte therapy for children within their respective organizations to ensure that these guidelines correspond with those of the regional pediatric referral centre. Readers are encouraged to consult the *ISMP Canada Safety Bulletin*[1] for an overview of suggested considerations for such guidelines.

Monitoring of parenteral fluid and electrolyte administration, particularly in pediatric patients, is a logical extension of the pharmaceutical care role. It is hoped that this article will serve as an alert to all pharmacists and will result in increased attention to fluid-use processes.

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- by telephone at 416.733.3131 or toll-free at 1.866.544.7672 (1.866.54.ISMPC)