



Nurse Advise-ERR®

Educating the healthcare community about safe medication practices

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Plain D5W or hypotonic saline solutions post-op could result in acute hyponatremia and death in healthy children

ISMP recently learned about the tragic deaths of two 6-year-old children stemming from severe postoperative hyponatremia. (Two additional deaths were just reported by ISMP Canada. www.ismp-canada.org/ISMPCSafetyBulletins.htm) The fatal events occurred at two different hospitals. In at least one of these cases, it is clear that the rapid administration of plain D5W (dextrose 5% in water) postoperatively resulted in acute hyponatremia secondary to free water retention (also called *water intoxication*, which is described below). Postoperative children are at high risk for developing hyponatremia, and many fatalities from this disorder have been reported in the literature.¹⁻¹⁴ When the serum sodium concentration rapidly falls below 120 mEq/L over 24 to 48 hours—as in the two events described below—the body’s compensatory mechanism is often overwhelmed and severe cerebral edema ensues, resulting in brainstem herniation, mechanical compression of vital midbrain structures, and death.¹⁵

Case 1

In the first case, the child underwent an outpatient tonsillectomy and adenoidectomy. Postoperative orders included IV fluids of “1000 cc D5W–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 (eMAR). 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 a 200 mL/hour infusion rate.

The nurse who started the infusion did not detect the pharmacist’s error. She had quickly looked at the surgeon’s postoperative orders and obtained a bag of D5W to hang. But 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 verification of the pharmacist’s entry on the eMAR. This was not her usual practice; however, like other nurses on the unit, she had come to rely on the accuracy of their pharmacists who “never made mistakes.” When the first 1,000 mL bag of D5W 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, so he administered a dose of IV diphenhydramine and admitted the child to a medical-surgical unit.

During the next few hours, the child’s vomiting worsened, she became more unresponsive, and the seizure-like activity became much more pronounced and frequent. The nurses called the child’s surgeon multiple times to report the seizure-like activity, during which additional doses of IV diphenhydramine were prescribed and subsequently administered. Several nurses also told the surgeon that the seizure-

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safetywires

⚡ False belief regarding influenza vaccines.

We were surprised to learn from a hospital medication safety officer that some of their hospital staff held the false belief that the 2009-2010 seasonal influenza vaccines provide protection against influenza caused by the pandemic H1N1 2009 virus (swine flu). The staff thought immunization against the H1N1 2009 virus was unnecessary if the seasonal flu vaccine was given. This misconception stemmed from the fact that the seasonal influenza vaccine includes the **A/Brisbane/59/2007 (H1N1)** strain (see Figure 1). However, this is not the virus strain responsible for the H1N1 2009 pandemic. FDA has approved four Influenza A (H1N1) 2009 monovalent vaccines for the immunization of individuals against influenza disease caused by the pandemic H1N1 2009 virus. The strain used for these new monovalent H1N1 vaccines is **A/California/7/2009 (H1N1)**, which is not part of the seasonal influenza vaccine. It is critical to let practitioners and consumers know that the seasonal influenza vaccine does **not** provide protection against the H1N1 2009 influenza virus strain. For more information, visit: www.fda.gov/downloads/ForHealthProfessionals/UCM185724.pdf and www.cdc.gov/h1n1flu.

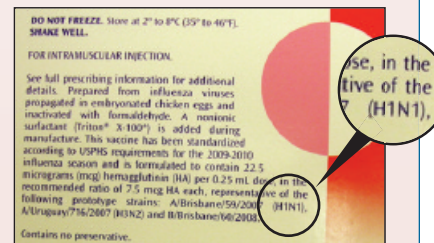


Figure 1. Label from **FLUZONE (sanofi-pasteur)** pediatric seasonal influenza vaccine may cause confusion—it does **NOT** protect against the pandemic H1N1 2009 virus!

⚡ Influenza vaccines mixed-up.

We recently learned of a series of mix-ups that possibly reached 13 child-

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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 failed to recognize that an infusion of plain D5W 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 D5W was hung after the second bag had infused.

After the child developed significant bradycardia that necessitated calling a code, the surgeon came into the hospital, observed the child 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 due to the erroneous infusion rate of 200 mL/hour during the previous 12 hours and the lack of sodium chloride in the infusate. The child had nonreactive pupils and exhibited decerebrate posturing. Stat lab studies showed a critically low concentration of sodium at 107 mEq/L. A brain CT scan revealed cerebral edema. But despite treatment, the child died.

Case 2

In the second case, the child underwent surgery for coarctation of the aorta, a condition that had been identified in this otherwise asymptomatic, healthy child during a school physical. The child's postoperative course seemed to be progressing well, but later on post-op 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 **EDECIN** (ethacrynic acid). By post-op day 2, the child's serum sodium level had dropped, so his physician prescribed an infusion of sodium chloride. It is uncertain whether the sodium chloride was ever administered, as 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 of post-op day 2, and his parents were concerned

when they could not awaken their son. The nurses assured the parents deep sleep was expected due to the pain medication—**HYDROMORPHONE**—the child was receiving. Despite repeated concerns expressed by the parents, nurses failed to recognize the child was not sleeping soundly but exhibiting signs of life-threatening hyponatremia.

When the child began experiencing seizure-like activity in the early afternoon, nurses attributed the movements to the child being “fidgety” from pain. The child also began vomiting. Unfortunately, the physician was not kept informed regarding the child's change in cognition, continued 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 response to painful stimuli. Despite intubation and ventilation support, and 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 causes common to both are clear: 1) lack of professional staff knowledge regarding the causes and signs of hyponatremia, and 2) the failure of professional staff to respond to concerns expressed by several nurses in Case 1, and by the 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 more than 4% of post-op patients develop clinically significant hyponatremia within 1 week of surgery, as do 30% of patients treated in intensive care units (ICUs).¹⁵⁻¹⁸ In general, the causes of hyponatremia are varied, ranging from certain medications (e.g., diuretics, heparin, opiates, desmopressin, proton pump inhibitors) and disease states (e.g., renal and liver impairment, hypothy-

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ren at an immunization clinic. The children were scheduled to receive a dose of the injectable seasonal influenza vaccine (**FLUZONE**) as well as a dose of the new intranasal H1N1 2009 vaccine. However, the pre-filled, single-use intranasal sprayers of **FLUMIST** (influenza vaccine live) and the new intranasal Influenza A (H1N1) 2009 monovalent vaccine live, both manufactured by MedImmune, look similar (see Figure 1). The children received FluMist rather than the H1N1 2009 intranasal vaccine. As a result, as many as 13 children received two doses of the seasonal influenza vaccine (one Fluzone and one FluMist) but no H1N1 2009 vaccine. No adverse effects have been noted in the children. We have notified FDA and asked the manufacturer, MedImmune, to investigate strategies to differentiate these products more clearly. Meanwhile, consider the following strategies to reduce the risk of mix-ups:

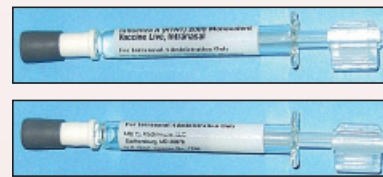


Figure 1. Look-alike pre-filled, single-use sprayers (**MedImmune**)—new intranasal H1N1 2009 vaccine (top) and FluMist (bottom).

- When these products arrive at your practice site, differentiate them with stickers or labels to highlight which one is the seasonal influenza product and which one is the H1N1 2009 vaccine.
- Store the intranasal seasonal influenza and H1N1 2009 vaccines on different shelves of the refrigerator or in separate refrigerators and label appropriately. The same should be done with the injectable formulations of seasonal influenza and H1N1 2009 vaccines.
- Have two practitioners check each other when vaccines are prepared for administration.
- Use separate immunization stations for administering the seasonal influenza vaccine and the H1N1 2009 vaccine. Do not pre-populate any vaccine administration forms with lot numbers prior to

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Hyponatremia continued from page 2 roidism or cortisol deficiency), to outpatient environmental conditions (e.g., prolonged exercise in a hot environment) and self-imposed conditions (e.g., psychogenic polydipsia, feeding infants tap water, or formula that is too dilute). However, the causes of hospital-acquired hyponatremia most relevant to the events described above are twofold: administration of plain D5W or hypotonic saline parenteral solutions post-op, and failure to recognize the compromised ability of children to maintain water balance.¹⁵

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 A 2003 analysis¹ found more than 50 reported cases of neurologic morbidity and mortality, including 26 deaths, during a 10-year period resulting from hospital-acquired hyponatremia in children who were receiving hypotonic saline parenteral fluids.¹⁻¹⁴ More than half of these cases occurred in the post-op setting in previously healthy children who underwent minor surgeries. Children are particularly vulnerable to water intoxication because they are prone to developing syndrome of inappropriate antidiuretic hormone (SIADH).¹ Common childhood conditions requiring IV fluids, such as pulmonary and central nervous system infections, dehydration, and the post-operative state, are associated with a nonosmotic—and therefore inappropriate—stimulus for antidiuretic hormone (ADH) production.^{1,14} The post-op nonosmotic stimulus for ADH release typically resolves by the third post-op day but can last until the fifth 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 more vulnerable to the effects of cerebral swelling due to hyponatremia because they develop encephalopathy at less significant decreases in

normal serum sodium levels than adults and have a poor prognosis if timely therapy is not instituted. In children, there is little room for brain expansion due to a higher brain-to-skull size ratio.^{1,17,19} Children achieve adult brain size by 6 years of age, whereas full skull size is not achieved until 16 years of age.

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

Irreparable harm can happen when low serum sodium levels are corrected too quickly or too slowly. Once the source of free water has been eliminated, the sodium level is typically increased by 4-6 mEq over the first 1-2 hours using 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 since the risk of treating too slowly—cerebral herniation—is felt to be greater than the risk of treating too quickly—osmotic demyelination syndrome, which has been associated with lesions in the white matter of the brainstem.¹⁴ These lesions are more common in adults. (**Please note:** The preceding information is in no way sufficient to guide the treatment of hyponatremia or suggested as an evidence-based standard of care. It was provided only to convey that expert opinions vary regarding prevention and treatment of hyponatremia and to encourage discussion among an interdisciplinary clinical team

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All is not as it seems...

Dose not necessarily missing

A patient with a deep vein thrombosis and pulmonary embolism had been switched from heparin to warfarin. The patient's INR was elevated to 3.8, so the physician ordered an IV dose of vitamin K1 (phytonadione) (see Figure 1). Although injectable vitamin K1 was in an automated dispensing cabinet (ADC), it could not be removed until a pharmacist verified the order. When the drug wasn't available in the ADC within the usual time it took a

PT 7.11.09 R.M.
Vitamin K 20mg IV x 5
US Consultant Thrombotic in A

Figure 1. How much vitamin K1 was prescribed?

pharmacist to review the order, the nurse faxed a “missing medication” request to pharmacy for 20 mg of vitamin K1 (see Figure 2). The pharmacist recognized that 20 mg of vitamin K1 was a considerably high dose for an INR of 3.8. The pharmacist verified the dose with the physician and learned that he had prescribed 2 mg of vitamin K1, not 20 mg. The patient could have experienced an adverse outcome from receiving a 10-fold overdose, such as attenuating the effect of

Missing med
05/17/09 @ 1750
Vitamin K 20mg IV x 1

Figure 2. Nurse's interpretation of the vitamin K1 order (as pictured above).

warfarin for weeks¹ or experiencing a fatal allergic reaction.² Nurses who administer anticoagulants should be familiar with the typical doses of antagonists. This should be reviewed during orientation and their annual competency evaluations. Nurses should also have easy access to drug references or anticoagulation protocols to verify prescribed doses of antagonists before administration.

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Hyponatremia continued from page 3 charged with developing electrolyte replacement protocols.)

Conclusions

Standards of practice should be established for post-op IV solutions used to hydrate patients—particularly children. The standards should acknowledge that the administration of solutions with saline in maintenance parenteral fluids is an important prophylactic measure taken to prevent hyponatremia in children, who are prone to an increase in ADH production.¹⁵ Plain dextrose should not be used for post-op fluid maintenance in pediatrics. Criteria should include when lab studies need to be drawn 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/or SIADH. Clinically significant hyponatremia may be nonspecific in its presentation; thus, practitioners must include this in the differential diagnoses in patients with early symptoms or an altered level of consciousness. All healthcare providers need a thorough understanding of fluid and electrolyte balance and the pathophysiology of hyponatremia, water intoxication, and SIADH to increase their index of suspicion when symptoms appear, and to become more responsive to voiced concerns regarding the patient's condition.

All hospitals should also consider establishing a rapid-response team (RRT) that allows any healthcare worker to summon an interdisciplinary team to a patient's bedside for a full evaluation when they fear something is seriously wrong with the patient and have expressed their concerns without an adequate response. The RRT provides an opportunity to step in *before* a tragedy occurs. Once the RRT has been formed and is functioning well, consider inviting patients and families to call the RRT to address unresolved concerns about their safety and health; subtle changes may be more readily identified as abnormal by family members than by healthcare

providers. For more on RRTs, please see our June 1, 2006 newsletter (www.ismp.org/Newsletters/acutecare/articles/20060601.asp).

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immunizing the patients.

■ When administering vaccines to children, hand the parent or caregiver the vaccine information sheet so that they are aware of the name and purpose of the vaccine. Have nurses read the names of the vaccines aloud, with simultaneous confirmation by the parent or caregiver. Have both the nurse and the parent or caregiver sign and date the log.



Medication patch slips into wrong ADC pocket.

While withdrawing a patient's nicotine patch from an automated dispensing cabinet (ADC), a carousel pocket opened to reveal two nicotine patches and one fentaNYL 50 mcg/hour patch. The nurse immediately called the pharmacy to report the discrepancy. Pharmacy found it was not a dispensing error. Both patches (nicotine and fentaNYL) were stored in the same medication carousel, and the fentaNYL patch had slipped over the top of one pocket and into the other pocket. Generally, carousel pockets are reserved for controlled substances, but there had been a history of pilferage of the nicotine patches, so pharmacy began stocking them in secure carousel pockets with the tracking feature on to count the product. FentaNYL was in a nearby pocket, so when the carousel turned, patches sticking up from the pocket were dragged to another pocket. The hospital now keeps the nicotine patches in a lidded container and keeps the tracking feature on to deter diversion.

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