ISMP Canada

Hospital-acquired acute hyponatremia and reports of pediatric deaths

By Christine Koczmara, RN, BSc, Andrew W. Wade, MD, PhD, FRCPC, Peter Skippen, MD, MBBS, FRCPC, FJFICM, MHA, Mary Jane Campigotto, RN, BScN, LLB, Kim Streitenberger, RN, Roxane Carr, PharmD, BCPS, Elaine Wong, BScPhm, and Karen Robertson, RN

Abstract

Information from four voluntary reports of hospital-acquired acute hyponatremia leading to the death of otherwise healthy children is highlighted. In this column, we present two cases and information from a recent ISMP Canada Safety Bulletin, as well as two cases reported to ISMP United States. Information is shared to enhance health care practitioners' awareness of the potential for acute hyponatremia and to provide an overview of some of the potential underlying factors.

Hospital-acquired acute hyponatremia and reports of pediatric deaths

Four pediatric deaths due to acute hyponatremia associated with intravenous (IV) administration of hypotonic solutions, three in a postsurgical setting and the other in a medical setting were voluntarily reported (two to the Institute for Safe Medication Practices Canada [ISMP Canada] and two to the Institute for Safe Medication Practices [ISMP] in the United States). Acute hyponatremia is defined as a decline in serum sodium to less than 130 mmol/L within a 48-hour period. This abrupt change can lead to cerebral edema as a result of electrolyte-free water moving into the brain cells. Acute hyponatremia can be fatal for both children and adults. However, children are more vulnerable to the effects of fluid and electrolyte imbalance. The early signs of acute hyponatremia and rising intracranial pressure are often nonspecific and include nausea, vomiting, headache, and decreasing level of consciousness. Information from the voluntary incident reports is shared here to enhance health care practitioners' awareness of the potential for acute hyponatremia and to provide an overview of some of the potential underlying factors.

Incident reports received by ISMP Canada

Case 1

A four-year-old child who weighed about 15 kg underwent a tonsillectomy as day surgery. No abnormalities were noted during a pre-admission assessment the day before the surgery. The tonsillectomy was performed under general anesthesia; the child was intubated and mechanically ventilated during the procedure. According to the records from the operating room, the child received a total of 250 mL of IV fluid (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. 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 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 (Institute for Safe Medication Practices Canada, 2009).

Case 2

A previously healthy three-year-old child was brought to an emergency department with a one-day history of vomiting and diarrhea. The child's pulse was more than 125 beats per minute, and the 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 two boluses of (0.9% sodium chloride) *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 more than 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 (3% or 5% sodium chloride) *was ordered, but none was available, so mannitol was administered IV, followed by a bolus of* 0.9% sodium chloride. *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 with brain herniation due to acute hyponatremia* (ISMP Canada, 2009).

Incident reports highlighted by ISMP (U.S.)

Case 1

A six-year-old child "underwent an outpatient tonsillectomy and adenoidectomy. Postoperative orders included IV fluids of '1000 cc D5W [dextrose 5% in water]*—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)… 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 eight hours) divided by three (the number of 600 mL 'doses' he thought would be needed for 24 hours) and arrived at 200 mL/hour infusion rate.

The nurse who started the infusion did not detect the pharmacist's error… she felt rushed by the hectic pace of the unit and was distracted during the verification process… 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, 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-like activity appeared to be more than dystonic reaction to promethazine, although none of the nurses had ever witnessed such a reaction. Unfortunately, during this time, the nurses failed to notice the infusion rate error or recognize that an infusion of plain D5W alone or an infusion rate of 200 mL/hour was unsafe for a six-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… The child had nonreactive pupils and exhibited decerebrate posturing. Stat lab studies showed a critically low concentration of sodium of 107 mEq/L. A CT scan of the brain revealed cerebral edema and, despite treatment, the child subsequently died (Institute for Safe Medication Practices [ISMP U.S.], 2009).

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 school physical. The child's postoperative course seemed to be progressing well, but later on the post-op day one, his physician prescribed a furosemide infusion (1 mg/hour) because the child's urinary output was less than expected despite several doses of EDECRINE (ethacrynic acid). By post-op day two, 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 two, 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 due to the pain medication—HYDROmorphone—that the child was receiving. Despite ongoing, repeated concerns expressed by the parents, the nurses failed to recognize that the child was exhibiting signs of severe, 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… the physician was not kept informed regarding the child's change in cognition, continued oliguria, vomiting, and seizure-like activity. When the 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 the hyponatremia and cerebral edema, the child died the following day (ISMP U.S., 2009).

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 (Arieff, Ayus, & Fraser, 1992; Hoorn, Geary, Robb, Halperin, & Bohn, 2004; Moritz & Ayus, 2003). 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 six years old, but the skull does not reach adult size until a person is 16 years of age) (Arieff et al., 1992).

Since the early signs and symptoms of acute hyponatremia are often nonspecific, health care professionals may attribute them to other causes, such as the postoperative effects of anesthetics, medications administered such as opioids for pain, or the presenting illness. A rapid decline in serum levels of sodium leading to 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.

The kidney is the main regulator of water through the activity of antidiuretic hormone (ADH), also known as vasopressin. ADH acts directly on the kidneys, causing them to reabsorb

water, which helps to maintain the serum sodium concentration and, thus, the osmolality of the blood, within normal limits. A reduction in serum osmolality (as occurs with a reduction in serum sodium concentration) typically inhibits the release of ADH, whereas an increase in serum osmolality causes the release of ADH. This "osmotic" feedback system in the body allows for variability in electrolyte-free water intake and excretion so that serum osmolality and serum sodium remain within normal range. (One need only consider how much free water can be lost through the extreme volumes of dilute urine output that are produced in patients who have diabetes insipidus and the absence of ADH.) The normal adult kidney can excrete up to 10 L of water per day provided there is a normal solute intake. As such, an extraordinary amount of free water would have to be provided to cause hyponatremia in an individual with a ***normal*** ADH response.

ADH is also released in response to numerous "nonosmotic" stimuli, even when serum sodium falls to below-normal values. Two of the most potent stimuli for ADH release are nausea and vomiting. Other nonosmotic stimuli for the release of ADH include pain, stress, gastroenteritis, hypoxia, positive pressure ventilation, trauma, and commonly used medications such as opioids (Hoorn et al., 2004; Moritz et al., 2003; Neville, Verge, O'Meara, & Walker, 2005). Numerous disease states such as pneumonia are also known to cause the release of ADH. The release of ADH after surgery in response to nonosmotic stimuli typically resolves by the third postoperative day, but can last up to the fifth postoperative day (Moritz et al., 2003). Children appear to be at particular risk after surgical procedures, and deaths have been reported after even minor surgery (Arieff et al., 2003; Auroy, Benhamou, Péquignot, Jougla, & Lienhart, 2008; McRae, Weissburg, & Chang, 1994).

Importantly, *in the presence of ADH, the kidneys cannot eliminate excess electrolyte-free water* (Hoorn et al., 2004; Moritz & Ayus, 2003). In addition to the administration of hypotonic parenteral solutions, such as D5W or 2/3 and 1/3, oral and enteral intake may be a source of electrolyte-free water that contributes to the development of acute hyponatremia (e.g., hypotonic feeds, water, ice chips) (Shafiee et al., 2005). Experts have noted that hyponatremia is the most common electrolyte disturbance among children being treated in hospital because such patients are commonly exposed to nonosmotic stimuli for ADH, and also because the administration of hypotonic solutions is routine practice in many hospitals (Hoorn et al., 2004; Moritz & Ayus, 2003).

Parenteral solutions

IV solutions are often required in hospitalized children to rehydrate or maintain hydration, to treat electrolyte abnormalities and for acid-base balance. It is important to understand how fluids can act within the body in order to monitor and assess ongoing response to fluids, particularly when the control of the fluid intake is no longer dependent on an individual's normal thirst mechanism, but rather in the control of the practitioner.

The IV solution 2/3 and 1/3 contains only 51 mmol/L of sodium. Outside of the body, the osmolarity of the solution is 269 mOsmol/L (sodium and dextrose combined), which is similar to blood. However, once the solution is infused, it is extremely hypotonic, as the dextrose is rapidly metabolized resulting in two-thirds of the solution (e.g., two-thirds of 1 litre, 667 mL) being electrolyte-free water. In the case of D5W, it contains no electrolytes. Although outside of the body the osmolarity of D5W is 250 mOsmol/L and similar to blood, once a litre of D5W solution is infused and the dextrose is metabolized, the entire litre (1, 000 mL) of solution is free water.

The intracellular compartment comprises approximately two-thirds of the total body water and the extracellular compartment approximately one-third. Therefore, two-thirds of infused free water will move into cells and only one-third will remain in the extracellular compartment. Thus, for every 1 litre of 2/3 and 1/3 infused, 444 mL (two thirds of the 667 mL of electrolyte-free water) will move into cells; for every 1 litre of D5W infused, 667 mL (two-thirds of the entire litre) will move into the body cells—including brain cells. (Refer to

Table One: Select IV solutions, their osmolarity, sodium content, total electrolyte-free water content and its disposition in the body[i]

IV Fluid	Osmolarity (mOsmol/L)	Sodium (mmol/L)	Electrolyte-Free Water			
			Total Volume** (mL)	Extracellular		Intracellular
				Intravascular	Interstitial	
1 L of D5W[ii]	252	0	1000 mL	83 mL	250 mL	**667 mL**
1 L of D5W and 0.2% NaCl[iii]	321	34	778 mL	65 mL	194 mL	**519 mL**
1 L of 2/3 and 1/3[iv]	269	51	667 mL	56 mL	167 mL	**444 mL**
1 L of D5W and 0.45% NaCl	406	77	500 mL	42 mL	125 mL	**333 mL**
1 L of 0.9% NaCl	308	154	0 mL	0 mL	0 mL	**0 mL**
1 L of D5W and 0.9% NaCl	560	154	0 mL	0 mL	0 mL	**0 mL**

[i] Thirty-three per cent of the electrolyte-free water disperses into the extracellular compartment and 67% disperses into the intracellular compartment. Within the extracellular compartment, ¼ remains intravascular and ¾ moves into the interstitial space. (Information adapted from Cook, 2003; Baxter Canada, Inc., 2009.); [ii] D5W refers to dextrose 5% in water; [iii] NaCl refers to sodium chloride; [iv] 2/3 and 1/3 refers to 3.3% dextrose and 0.3% sodium chloride.

Table One for these and other examples of fluid distribution.) Free water combined with nonosmotic secretion of ADH will reduce the ability of the kidneys to excrete the excess water and dilutional hyponatremia can ensue. This can also occur or be compounded further with enteral feeds because they are hypotonic, and when oral fluids are given in the form of ice chips and water, which are also very hypotonic.

Electrolyte solutions, such as 0.9% sodium chloride and lactated ringer's, once infused, do not lead to changes in tonicity among the fluid compartments. Approximately 25% of the solution will remain in the intravascular compartment and 75% in the interstitial space. Another example is D5W combined with 0.9% sodium chloride. Although outside of the body, it has an osmolarity greater than blood (osmolarity is about 560 mOsm/L), once infused, however, the dextrose is rapidly metabolized and what remains is an isotonic fluid. In the absence of cellular dehydration, the fluid will remain in the extracellular compartment and there will be no movement of the fluid into body cells.

Although hypotonic fluids have been identified to be most frequently associated with hospital-acquired hyponatremia, the infusion of 0.9% sodium chloride has also been reported to be associated with hyponatremia—a process called desalination. This has been reported, for example, in patients postoperatively. Patients can experience a reduced vascular tone from anesthetics and other medications administered intraoperatively, which results in decreased blood pressure. Infusing 0.9% sodium chloride intraoperatively can compensate to maintain a normal blood pressure. Postoperatively, once the vascular tone returns to normal, receptors in vasculature are activated, natriuretic peptides are released, and the kidney responds by excreting a disproportionate amount of sodium to free water to rid itself of excess fluid.

Discussion

Incidents of hospital-acquired acute hyponatremia in children leading to severe harm and death have been reported internationally associated with hypotonic solutions. Various literature reports (Arieff et al., 1992; Auroy, Benhamou, Péquignot, Jougla, & Lienhart, 2008; Duke, Kinney, & Waters, 2005; Hoorn, et al., 2004; McRae, Weissburg, & Chang, 1994; Moritz & Ayus, 2003), and pediatric inquests (Hyponatremia Progress Hearing, 2008) have highlighted cases of acute hyponatremia leading to the in-hospital deaths of children who were otherwise healthy. The National Patient Safety Agency in the United Kingdom has identified hospital-acquired hyponatremia in children as a major patient safety issue. Safety alerts and guidelines for the administration of fluids to children have been published as a result, including the requirement for sodium chloride 0.18% with glucose 4% intravenous solution to be removed from wards and general stock (Ellis, 2008; Government of Northern Ireland, Department of Health, Social Services and Public Safety, 2007; National Patient Safety Agency, 2007; National Patient Safety Agency, 2008). In Canada, the Canadian Medical Protective Association recently highlighted a case of hospital-acquired hyponatremia in a child (The Canadian Medical Protective Association, 2008). A provincial coroner identified six 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 (Office of the Chief Coroner Province of Ontario, 2007).

There appears to be general consensus that isotonic IV fluids such as 0.9% sodium chloride should be used for children during surgery and in the treatment of moderate to severe hypovolemia. However, there has been a debate as to which solution is the best choice for maintenance of hydration (Arieff et al., 1992; Auroy et al., 2008; Beck, 2007; Choong, Kho, Menon, & Bohn, 2006; Coulthard, 2008; Duke et al., 2005; Hatherill, 2004; Holliday, Friedman, Segar, Chesney, & Finberg, 2004; Holliday, Ray, & Friedman, 2007; Holliday & Segar, 2003; Hoorn et al., 2004; McRae et al., 1994; Moritz & Ayus, 2003; Moritz, & Ayus, 2006; Neville, Verge, O'Meara, & Walker, 2005; Neville, Verge, Rosenberg, O'Meara, & Walker, 2006; Shafiee, Bohn, Hoorn, & Halperin, 2003; Skippen et al., 2008; Taylor & Durward, 2004).

Pediatric experts are questioning the widespread use of hypotonic solutions for parenteral maintenance, a practice based on a formula that was developed more than 50 years ago (Holliday & Segar, 1957). 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 ADH released in response to nonosmotic stimuli, a process that was identified since the original development of the formula and that is commonly seen in hospitalized children. Although there is no single IV solution that is ideal for all children, a variety of studies, including randomized trials from pediatric ICUs, are answering questions regarding the use of maintenance fluids for children (Au et al., 2008; Montañana et al., 2008; Yung & Keeley, 2009). In one recent study, a key factor in the development of hospital-acquired hyponatremia was the use of hypotonic maintenance solutions (Montañana et al., 2008). Yung and Keeley identified that postoperative and very ill children were at risk for hyponatremia when given dextrose with hypotonic saline solutions at traditional rates.

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 a central supply and redistribution service or through hospital stores, as part of the materials management division of hospital operations.

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 (BC Children's Hospital, 2008a; BC Children's Hospital, 2008b; Hospital for Sick Children, 2007; Hurdowar et al., 2009).

Conclusion

Hospitalized children have multiple risk factors that predispose them to nonosmotic release of ADH that can lead to the retention of free water, particularly in the critical care setting. Monitoring of serum electrolyte values, including trends in serum sodium levels, assessing fluid status through physical assessments, keeping accurate records of intake and output and cumulative balances, daily weights, review and consideration of

the type of solutions infused (IV, enteral) and those taken orally, and informing the intensivist when fluid intake greatly exceeds output balance can facilitate recognition of fluid imbalance that requires further assessment and a change in the plan of care.

As critical care practitioners often respond to calls in other areas of a hospital, as part of rapid response teams, it is also important to be on the alert for, and consider the possibility of acute hyponatremia, and to take the opportunity to educate peers. Critical care practitioners can advocate for enhancements to how these fluids are stored and labelled within critical care areas, so that there is not only adequate access to the various solutions that may be needed, but also clarity for practitioners as to the type of fluid being selected (e.g., indication of tonicity upon infusion). Practitioners can provide valuable input regarding which types of fluids should be made readily accessible outside of critical care, and which may require additional safeguards. Practitioners who work in pediatric centres can take a lead role to ensure that guidelines within their own centre include use of optimal IV solutions and rates, as well as the application of minimum monitoring and assessment practices to prevent incidents similar to those described in this article. Furthermore, such guidelines can be shared with peripheral hospitals caring for children to inform them of changes in practice.

It is also important that all practitioners engage family members whenever they express concerns about their child's behaviour—subtle changes may be more readily identified as abnormal by family members than by health care providers and, thus, can provide an invaluable source of assessment information. Prompt recognition and treatment of acute hyponatremia is vital to prevent brain herniation and death.

This article was written using materials from ISMP Canada, with permission (ISMP Canada Safety Bulletin. October 27, 2009, 9(7), 1–2. Available from: http://www.ismp-canada.org/download/safetyBulletins/ISMPCSB2009-7-HospitalAcquiredAcuteHyponatremia.pdf).

ISMP Canada gratefully acknowledges the valuable lessons learned and information reported by professionals in the Canadian healthcare community that can then be shared to enhance medication system safety. All ISMP Canada Safety bulletins are available from **http://www.ismp-canada.org/ISMPCSafetyBulletins.htm**.
ISMP Canada is an independent national not-for-profit organization committed to the advancement of medication safety in all healthcare settings. ISMP Canada maintains a national voluntary medication incident and 'near miss' reporting program founded for the purpose of sharing the learning experiences from medication errors. Our collaborative goal is implementation of preventive strategies and system safeguards to decrease the risk for error-induced.

ISMP Canada is a key partner in the Canadian Medication Incident Reporting and Prevention System (CMIRPS). Medication Incidents (including near misses) can be reported to ISMP Canada:
(i) through the website
http://www.ismp-canada.org/err_report.htm or
(ii) by phone: 416-733-3131 or toll free: 1-866-544-7672.
ISMP Canada guarantees confidentiality and security of information received, and respects the wishes of the reporter as to the level of detail to be included in publications.

About the authors

Christine Koczmara, RN, BSc, is a Senior Medication Safety Analyst with the Institute for Safe Medication Practices Canada (ISMP Canada). She also holds a casual position as a bedside nurse in an Intensive Care Unit (ICU). E-mail: ***ckoczmara@ismp-canada.org***

Andrew W. Wade, MD, PhD, FRCPC, Paediatric Nephrology, University of Calgary, Calgary, Alberta.

Peter Skippen, MD, MBBS, FRCPC, FJFICM, MHA, is the Medical Director and Division Head Clinical Professor, Division of Critical Care at BC Children's Hospital, Department of Pediatrics, University of British Columbia.

Mary Jane Campigotto, RN, BScN, LLB, is a Consultant to the ISMP Canada.

Kim Streitenberger, RN, is the Quality Manager in the Pediatric Intensive Care & Cardiac Critical Care Units at The Hospital for Sick Children, Toronto.

Roxane Carr, PharmD, BCPS, is a Clinical Leader, Pharmacy Critical Care Services, Department of Pharmacy, Children's & Women's Health Centre of BC and is a part-time Assistant Professor, Faculty of Pharmaceutical Sciences, University of British Columbia.

Elaine Wong, BScPhm, is a Pediatric Intensive Care Unit (PICU) Pharmacist and a Medication Safety Pharmacist at the Children's Hospital of Eastern Ontario (CHEO) in Ottawa, Ontario.

Karen Robertson, RN, Clinical Leader, PICU, Children's Hospital of Eastern Ontario, Ottawa, Ontario.

References

Arieff, A.I., Ayus, J.C., & Fraser C.L. (1992). Hyponatraemia and death or permanent brain damage in healthy children. **British Medical Journal, 304,** 1218–1222.

Au, A.K., Ray, P.E., McBryde, K.D., Newman, K.D., Weinstein, S.L., & Bell, M.J. (2008). Incidence of postoperative hyponatremia and complications in critically-ill children treated with hypotonic and normotonic solutions. **Journal of Pediatrics, 152**, 33–38.

Auroy, Y., Benhamou, D., Péquignot, F., Jougla, E., & Lienhart, A. (2008). Hyponatraemia-related death after paediatric surgery still exists in France. **British Journal of Anaesthesia, 101**, 741.

BC Children's Hospital. (2008a). **Fluid management in hospitalized children: Preventing iatrogenic hyponatremia**. Version 1. Retrieved from http://74.125.93.132/search?q=cache:rb_67KnrxNoJ:www.childhealthbc.ca/resources/category/11-fluid-management-in-hospitalised-children%3Fdownload%3D21%253Afluid-management-guileline+Fluid+management+in+hospitalized+children:+preventing+iatrogenic+hyponatremia&cd=1&hl=en&ct=clnk&gl=ca

BC Children's Hospital. (2008b). **Intravenous fluid management in hospitalized children: Preventing iatrogenic hyponatremia.** Retrieved from http://www.childhealthbc.ca/resources/category/11-fluid-management-in-hospitalised-children?download=22%3Aintravenous-fluid-management-algorithm

Beck, C.E. (2007). Hypotonic versus isotonic maintenance intravenous fluid therapy in hospitalized children: A systematic review. **Clinical Pediatrics, 46**, 764–770.

Baxter Canada, Inc. (2009). Medication delivery catalogue: Parenteral solutions. Retrieved from http://www.baxter.ca/en/products/sub/medication_delivery_catalogue.html#

Choong, K., Kho, M.E., Menon, K., & Bohn, D. (2006). Hypotonic versus isotonic saline in hospitalised children: A systematic review. **Archives of Disease in Childhood, 91**, 828–835.

Cook, L.S. (2003). IV fluid resuscitation. **Journal of Infusion Nursing, 26**, 296–303.

Coulthard, M.G. (2008). Will changing maintenance intravenous fluid from 0.18% to 045% saline do more harm than good? **Archives of Disease in Childhood, 93**, 335–340. Erratum in: Archives of Disease in Childhood, 93, 1079.

Duke, T., Kinney, S., & Waters, K. (2005). Hyponatraemia and seizures in oncology patients associated with hypotonic intravenous fluids. **Journal of Paediatrics and Child Health, 41**, 685–686.

Ellis, D. (2008, May). **Clinical guidelines: Medical paediatrics wide. Women & children's directorate—Management of symptomatic hyponatraemia.** Retrieved from http://www.clinicalguidelines.scot.nhs.uk/YOR-DIV-004%20Symptomatic%20Hyponatraemia%20approved%20pdf%20new.pdf

Government of Northern Ireland, Department of Health, Social Services and Public Safety, Belfast (IE). (2007, September). **Paediatric parenteral fluid therapy (1 month–16 yrs): Initial management guideline** [wall chart]. Retrieved from http://www.dhsspsni.gov.uk/hsc__sqsd__20-07_wallchart.pdf

Hatherill, M. (2004). Rubbing salt in the wound. The case against isotonic parenteral maintenance solution. **Archives of Disease in Childhood, 89**, 414–418.

Holliday, M.A., Friedman, A.L., Segar, W.E., Chesney, R., & Finberg, L. (2004). Acute hospital-induced hyponatremia in children: A physiological approach. **Journal of Pediatrics, 145**, 584–587.

Holliday, M.A., Ray, P.E., & Friedman, A.L. (2007). Fluid therapy for children: Facts, fashions and questions. **Archives of Disease in Childhood, 92**, 546–550.

Holliday, M.A., & Segar, W.E. (1957). The maintenance need for water in parenteral fluid therapy. **Pediatrics, 18**, 823–832.

Holliday, M.A., & Segar, W.E. (2003). Reducing errors in fluid therapy management. **Pediatrics, 111**, 424–425.

Hoorn, E.J., Geary, D., Robb, M., Halperin, M.L., & Bohn, D. (2004). Acute hyponatremia related to intravenous fluid administration in hospitalized children: An observational study. **Pediatrics, 113**, 1279–1284.

Hospital for Sick Children. (2007, December 4). **Hospital-wide patient care clinical practice guideline. Fluid and electrolyte administration in children**. Retrieved from http://www.cags-accg.ca/docs/Fluid_and_Electrolyte_Administration_-_CPG.pdf

Hurdowar, A., Urmson, L., Bohn, D., Geary, D., Laxer, R., & Stevens, P. (2009). Compliance with a pediatric clinical practice guideline for intravenous fluid and electrolyte administration. **Healthcare Quarterly, 12**, Special No. Patient, 129–134.

Hyponatremia Progress Hearing. (2008, May). **Progress hearing in the matter of: Hyponatraemia-related deaths**. Hilton Hotel, Belfast (IE). Retrieved from http://www.ihrdni.org/hearing-30may08-transcript.pdf

Institute for Safe Medication Practices (ISMP U.S.). (2009, August 13). Plain D5W or hypotonic saline solutions post-op could result in acute hyponatremia and death in health children. **ISMP Medication Safety Alert!, 14**, 1–4. Retrieved from http://www.ismp.org/Newsletters/acutecare/articles/20090813.asp

Institute for Safe Medication Practices Canada. (2009, October 27). Hospital-acquired acute hyponatremia: Two reports of pediatric deaths. **ISMP Canada Safety Bulletin, 9**, 1–2. Retrieved from: http://www.ismp-canada.org/download/safetyBulletins/ISMPCSB2009-7-HospitalAcquiredAcuteHyponatremia.pdf

McRae, R.G., Weissburg, A.J., & Chang, K.W. (1994). Iatrogenic hyponatremia: A cause of death following pediatric tonsillectomy. **International Journal of Pediatric Otorhinolaryngology, 30**, 227–232.

Montañana, P.A., Modesto i Alapont, V., Ocón, A.P., López, P.O., López Prats, J.L., & Toledo Parreño, J.D. (2008). The use of isotonic fluid as maintenance therapy prevents iatrogenic hyponatremia in pediatrics: A randomized, controlled open study. **Pediatric Critical Care Medicine, 9**, 589–597.

Moritz, M.L., & Ayus, J.C. (2006). Preventing neurological complications from dysnatremias in children. **Pediatric Nephrology, 21**, 1048–1049.

Moritz, M.L., & Ayus, J.C. (2003). Prevention of hospital-acquired hyponatremia: A case for using isotonic saline. **Pediatrics, 111**, 227–230.

National Patient Safety Agency. (2007). **Patient safety alert 22: Reducing the risk of hyponatraemia when administering intravenous infusions to children**. Retrieved from http://www.nrls.npsa.nhs.uk/EasySiteWeb/getresource.axd?AssetID=60073&type=full&servicetype=Attachment

National Patient Safety Agency. (2008). **Background information: Patient safety alert 22: Reducing the risk of hyponatraemia when administering intravenous infusions to children.** Retrieved from http://www.nrls.npsa.nhs.uk/EasySiteWeb/getresource.axd?AssetID=60071&type=full&servicetype=Attachment

Neville, K.A., Verge, C.F., Rosenberg, A.R., O'Meara, M.W., & Walker, J.L. (2006). Isotonic is better than hypotonic saline for intravenous rehydration of children with gastroenteritis: A prospective randomised study. **Archives of Disease in Childhood, 91**, 225–232.

Neville, K.A., Verge, C.F., O'Meara, M.W., & Walker, J.L. (2005). High antidiuretic hormone levels and hyponatremia in children with gastroenteritis. **Pediatrics, 116**, 1401–1407.

Office of the Chief Coroner Province of Ontario, Toronto. (2007). **Report of the paediatric death review committee and deaths under five committee**. Retrieved from http://www.oacas.org/pubs/external/pdrcannualreportfinal07june04.pdf

Shafiee, M.A., Bohn, D., Hoorn, E.J., & Halperin, M.L. (2003). How to select optimal maintenance intravenous fluid therapy. **American Journal of Medicine, 96**, 601–610.

Shafiee, M.A., Charest, A.F., Cheema-Dhadli, S., Click, D.N., Napolova, O., Roozbeh, J., et al. (2005). Defining conditions that lead to the retention of water: The importance of the arterial sodium concentration. **Kidney International, 67**, 613–621.

Skippen, P., Adderley, R., Bennett, M., Cogswell, A., Froese, N., Seear, M., et al. (2008). Iatrogenic hyponatremia in hospitalized children: Can it be avoided? **Paediatrics & Child Health, 13**, 502–506.

Taylor, D., & Durward, A. (2004). Pouring salt on troubled waters. **Archives of Disease in Childhood, 89**, 411–414.

The Canadian Medical Protective Association. (2008). **Hyponatremia in children**. Retrieved from http://www.cmpa-acpm.ca/cmpapd04/docs/resource_files/infoletters/2008/pdf/com_il0840_1-e.pdf

Yung, M., & Keeley, S. (2009). Randomized controlled trial of intravenous maintenance fluids. **Journal of Paediatrics and Child Health, 45,** 9–14.