

Preoperative Hyponatremia and Cardiopulmonary Bypass: Yet Another Factor for Cerebral Dysfunction?

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Presented at the 47th International Conference of the American Society of Extracorporeal Technology, San Antonio, Texas, March 12, 2009.

Abstract: Hyponatremia is common in patients prior to cardiopulmonary bypass (CPB), usually secondary to diuretic therapy. Rapid correction of chronic hyponatremia, which potentially occurs on commencing CPB, may in susceptible patients result in central pontine myelomatosis. There are three parts to this study. Part 1: Patients ($n = 170$) undergoing CPB with preoperative hyponatremia were analyzed by degree of hyponatremia, additive EuroSCORE, length of stay – intensive care and total hospital, and mortality. Part 2: Sodium concentrations of different prime constituents used clinically were collated from the literature. Part 3: Mathematical modeling of the effects of patient size, sex, preoperative hemoglobin, prime solution, and prime volume with regard to the effect on serum sodium during cardiopulmonary bypass was analyzed, assuming a preoperative serum sodium

of 125 mmol/L. Part 1: Patients with preoperative hyponatremia, even after matching by additive EuroSCORE, have longer length of stay – intensive care and total hospital, but not significantly different mortality rates. Part 2: Sodium concentrations of different primes used clinically varied from 0 mmol/L to 160 mmol/L. Part 3: Mathematical modeling revealed that patient size, sex, preoperative hemoglobin, prime solution, and prime volume all can exert a significant effect on serum sodium on initiation of cardiopulmonary bypass. Further work is needed to evaluate the roles of sudden changes in serum sodium, with regard to a rapid correction of chronic hyponatremia, or the rapid creation of acute hyponatremia, and cerebral outcomes in patients undergoing CPB. **Keywords:** cardiopulmonary bypass, hyponatremia, cerebral complications. *JECT. 2010;42:52–56*

Hyponatremia is common in patients prior to cardiopulmonary bypass (CPB), usually secondary to diuretic therapy (1). However, rapid correction of hyponatremia, which potentially occurs on commencing of CPB, in patients with chronic hyponatremia may have disastrous consequences (2).

Once the brain has adapted to hyponatremia, it is not well protected from the osmotic stress that accompanies correction (3,4). During rapid correction of chronic hyponatremia, which potentially occurs on CPB, the blood becomes hypertonic relative to the brain which will result in the movement of intracellular water causing cerebral dehydration, intramyelinic edema, a breakdown of the blood-brain barrier, and oligodendrocyte degeneration.

Increasing osmotic pressure while correcting hyponatremia, as is the case when adding mannitol to CPB, may not decrease the risk of inducing myelinolysis (5).

How rapid an increase in serum sodium concentration the brain can tolerate has been difficult to define. A figure of 12 mmol/L in 24 hours has been described (6,7). Correction while commencing CPB occurs instantly. To date, the potentially deleterious effects of acute hyponatremia and its rapid correction is well documented in urology and general medicine, where it is known as post transurethral resection of the prostate (TURP) syndrome and central pontine myelomatosis respectively, however it has not been described or investigated in cardiac surgery.

Received for publication March 3, 2009; accepted January 16, 2010.
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The senior author has stated that authors have reported no material, financial, or other relationship with any healthcare-related business or other entity whose products or services are discussed in this paper.

METHODS

Patients with Preoperative Hyponatremia

A prospective validated cardiac surgery database of 4944 patients containing preoperative serum sodium levels

was analyzed. Of these, 170 had a serum sodium less than 130 mmol/L. These 170 cases were matched by additive EuroSCORE to the contemporaneous 4774 patients, resulting in a control group of 1367. Their intensive care, hospital length of stay, and mortality was compared. Our database contains no cognitive impairment data. The use of length of stay as a surrogate marker of “cerebral injury” has previously been justified by Murkin et al. (8), who used the term “the brain as an index organ.”

Sodium Concentrations of Various CPB Prime Constituents

The sodium concentration of different primes used clinically was compiled from the literature. A high sodium prime constituent was classified as one with a sodium concentration of 150 mmol/L or higher, and a low sodium prime was classified as one with no sodium, i.e., 0 mmol/L, for purposes of mathematical modeling in subsequent sections. It was assumed that the preoperative serum sodium was 125 mmol/L for all calculations. A hematocrit of 30% was also assumed for all calculations unless specified.

Mathematical Modeling of the Effects of Patient Size, Sex, Preoperative Hemoglobin, Prime Solution, and Prime Volume on Serum Sodium during CPB

The estimated blood volume of an individual (EBV) can be calculated from:

$$EBV (mL) = \text{weight (kg)} \times \text{average blood volume (mL/kg)}$$

Average blood volume in an adult male is 75 mL/kg, and in an adult female 65 mL/kg.

Assuming minimal cell transmembrane flux of sodium, the serum sodium is distributed in the plasma volume (PV), which can be calculated from

$$PV (mL) = EBV * (1 - Hematocrit \% / 100)$$

The estimated resultant sodium concentration, $[Na^+_{CPB}]$ mmol/L, after the mixing of prime volume (PrV) (L), and estimated blood volume:

$$[Na^+_{CPB}] \text{ mmol/L} = \frac{([Na^+ \text{ prime}] * PrV) + ([Na^+ \text{ blood}] * PV / 1,000)}{[PV + PrV]}$$

The effect of patient size: The effects of patient size, range 50–120 Kg, is shown in Figure 1 with a high sodium prime and Figure 2 with a low sodium prime, for male patients.

The effect of being male or female: The effects of being male or female is shown in Figure 3 with a high sodium prime and Figure 4 with a low sodium prime. A 1 L prime was assumed for all calculations.

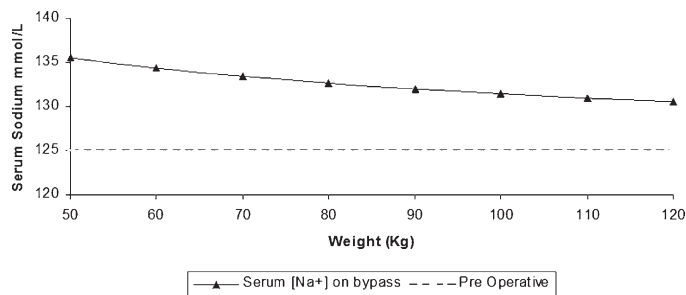


Figure 1. Effect of patient size on serum sodium on commencing bypass with a high sodium prime in a hyponatremic male patient.

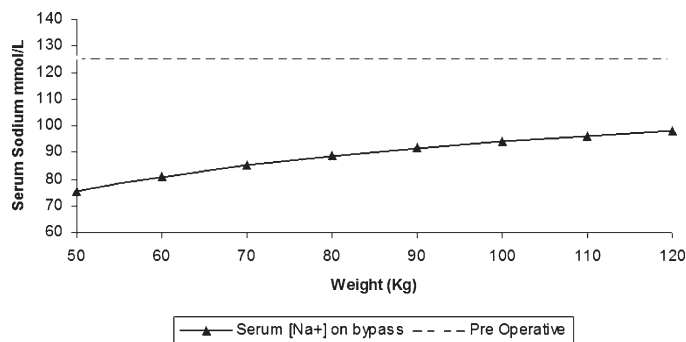


Figure 2. Effect of patient size on serum sodium on commencing bypass with a low sodium prime in a hyponatremic male patient.

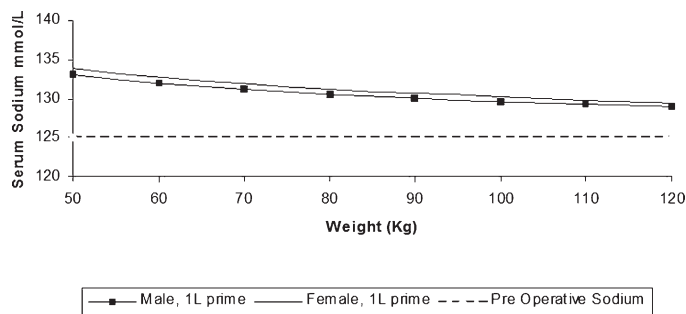


Figure 3. Effect of sex on serum sodium on commencing bypass with a high sodium prime.

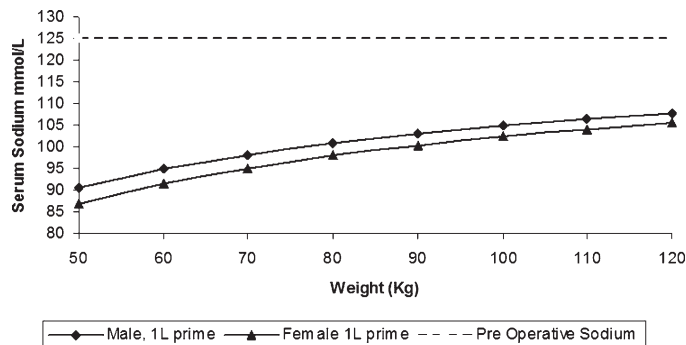


Figure 4. Effect of sex on serum sodium on commencing bypass with a low sodium prime.

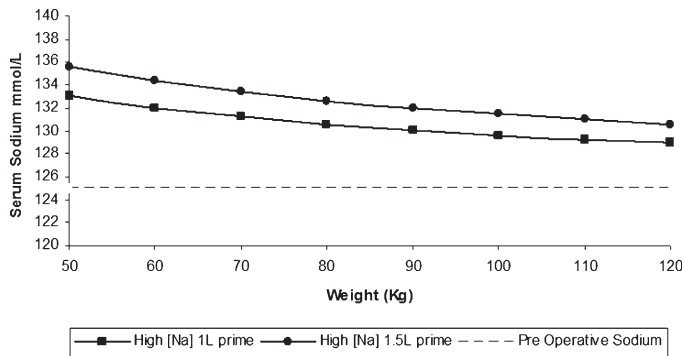


Figure 5. Effect of prime volume on serum sodium on commencing bypass with a high sodium prime.

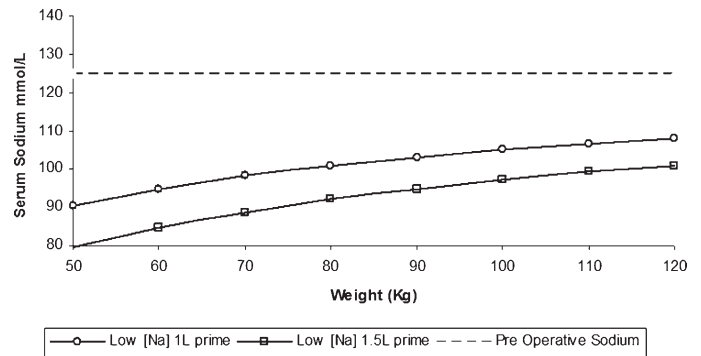


Figure 6. Effect of prime volume on serum sodium on commencing bypass with a low sodium prime.

The effect of different primes solutions and volumes: The effects of different prime solutions and volumes, 1 L or 1.5 L, used clinically is shown in Figure 5 with a high sodium prime and Figure 6 with a low sodium prime.

The effect of preoperative hemoglobin: The effects of preoperative hemoglobin, range 7–13.5 g/dL, is shown in Figure 7 with a high sodium prime and Figure 8 with a low sodium prime.

Statistics

A level of $p < .05$ was taken as statistical significance. Data analysis was carried out using Microsoft Excel with pivot table analysis and the statistics package.

RESULTS

Patients with Preoperative Hyponatremia

Table 1 demonstrates that mortality was statistically not significantly different for hyponatremia patients compared with normonatremic patients. However the intensive care and total hospital length of stay was significantly longer in the hyponatremic group, $p < .05$.

Sodium Concentrations of Various CPB Prime Constituents

The sodium concentration of different prime constituents used clinically varied widely from 0 mmol/L to 160 mmol/L (Table 2). Published surveys reveal a high sodium prime is used by the majority of units (9,10).

Mathematical Modeling of the Effects of Patient Size, Sex, Preoperative Hemoglobin, Prime Solution, and Prime Volume on Serum Sodium during CPB

The effect of patient size on serum sodium in hyponatremic patients: The effects of patient size, range 50–120 Kg, is shown in Figure 1, for a high sodium prime and Figure 2 for a low sodium prime. Large patients have smaller changes in serum sodium on initiation of bypass as they have larger plasma volumes so the volume of the prime is relatively less.

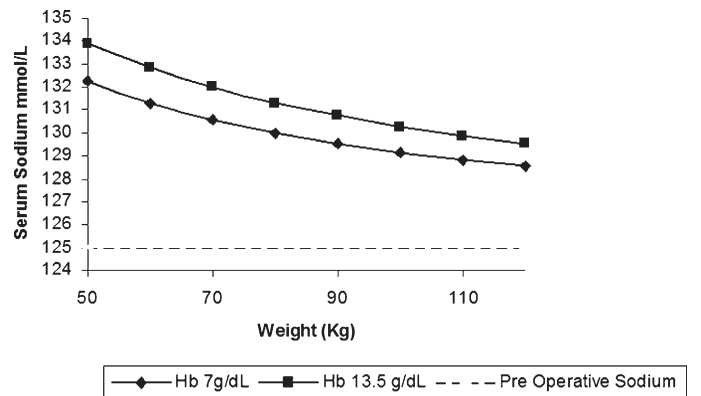


Figure 7. Effect of preoperative hemoglobin on serum sodium on commencing bypass with a high sodium prime.

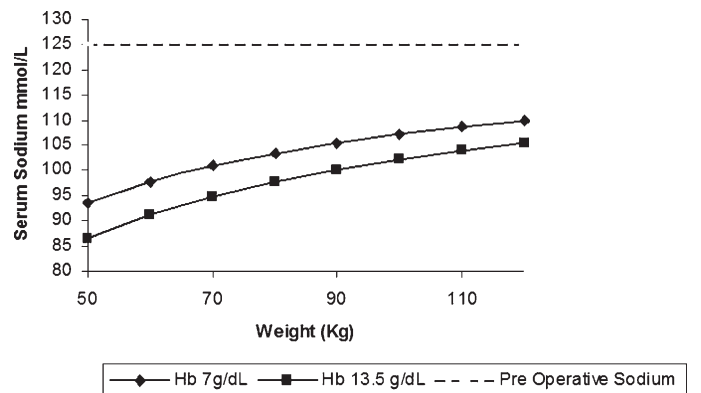


Figure 8. Effect of preoperative hemoglobin on serum sodium on commencing bypass with a low sodium prime.

The effect of being male or female on serum sodium in hyponatremic patients: The effects of being male or female is shown in Figures 3 and 4 for high and low sodium primes respectively. It can be seen that females have a higher change in serum sodium compared to males. This is because men have a larger plasma volume than women (75 mL/Kg versus 65 mL/Kg).

Table 1. Intensive care stay, hospital length of stay, and mortality for hyponatremia patients matched by additive EuroSCORE to Contemporaneous Control Group.

	Sodium < 130 mmol/L (n = 170)	Additive EuroSCORE Matched Control Group 135 < [sodium] < 145 (n = 1367)
Average additive EuroSCORE (%)	6.6	6.6
Intensive care stay (days)*	3.6	2.9
Hospital length of stay (days)*	13.2	7
Mortality (%)	5.3	5

*p < .05

Table 2. Sodium concentrations of frequently used prime constituents for cardiopulmonary bypass (9–16).

Prime Solution	Sodium Concentration mmol/L
5% Dextrose	0†
5% Dextrose saline (.45% NaCl)	77†
Saline (.9% NaCl)	154*
Hartmann's	131†
Lactated Ringers	130†
Balanced solution	140‡
Mannitol 10%	0†
Hydroxyethyl starch (HES) 6%	154*
Gelatin-S	154*
Albumin 4.5%	100–160
10% Dextran 40 in .9% NaCl	154*
6% Dextran 70 in .9% NaCl	154*

*High sodium content [Na+] > 145 mmol/L.

†Low sodium content [Na+] < 135 mmol/L.

‡Normal serum sodium range 135 mmol/L < [Na+] < 145 mmol/L.

The effect of different primes solutions and volumes:

The effects of different prime solutions and volumes used clinically with high and low sodium concentrations is shown in Figures 5 and 6. A large prime, 1.5 L, results in greater acute changes in serum sodium secondary to its relative volume to patient plasma volume.

The effect of preoperative hemoglobin on serum sodium in hyponatremic patients: The effects of preoperative hemoglobin, 7–13.5 g/dL, is shown in Figures 7 and 8 for a high sodium and low sodium prime, respectively. Lower hemoglobins were affected least as they are associated with a higher plasma volume secondary to their lower hematocrit (blood volumes are identical).

DISCUSSION

Patients with preoperative hyponatremia can potentially be exposed to dangerous acute sodium level changes secondary to initiation of CPB. The changes in serum sodium are greater in small female patients, who

have a large volume prime solution with a high sodium concentration.

Myelinolysis is a neurological disorder that can occur after the rapid correction of hyponatremia. Initially named “central pontine myelinolysis,” this disease is now known to also affect extrapontine brain areas. The term “central pontine” (17) is used to indicate the location of the lesion and the term “myelinolysis” to indicate that myelin was affected out of proportion to the neuronal elements. The word “demyelination” is avoided to distinguish the pathology of myelinolysis from that of multiple sclerosis and related diseases in which inflammation accompanies myelin loss.

The patient's mental status classically fluctuates with initial improvement followed by neurological deterioration 48–72 hours later. Neurological examination is key as magnetic resonance imaging or computed tomography imaging of the brain stem may not reveal an obvious anatomic disturbance. Findings include confusion, horizontal gaze paralysis, dysarthria, dysphagia, and spastic quadriplegia. Brain magnetic resonance imaging reveals intense symmetric demyelination in the brain stem pons. The volume of demyelination within the pons is variable. The loss of myelin can occur in adjacent brainstem and supratentorial areas. Thus, a diverse spectrum of examination findings and long-term disabilities are found (7).

Various studies (18,19) have shown that the brain uses several mechanisms to avoid severe edema during hyponatremia. There is a decrease in the brain concentration of sodium and potassium which occurs within hours in the presence of hyponatremia, together with anion loss in the form of chloride and losses in organic osmolytes such as phosphocreatine and myo-inositol and amino acids glutamine, taurine, and glutamic acid. With these adaptive measures, the water content in the brain returns to normal within approximately 48 hours and remains stable there after (20).

Acute changes in a patient's serum sodium level, regardless of them being normonatremic or hyponatremic, may cause encephalopathy as seen in patients following transurethral resection of the prostate and is commonly referred to as “water intoxication” or “post-TURP syndrome” (21). This condition results from the movement of free water into brain cells leading to cerebral edema with its attendant increase in intracranial pressure and cerebral hypoxia. There is an array of non-specific signs and symptoms which are common. Some of these include nausea, vomiting, headache, and disorientation. This may progress to obtundation, seizures, coma, and respiratory arrest. The majority of patients who develop hyponatremic encephalopathy do so more than 24 hours postoperatively with serum sodium of 116–128 mmol/L. Our preliminary mathematical modeling predicts that patients may be subjected to acute hyponatremia or acute correction of hyponatremia,

depending on the prime used. It should be pointed out that our model does not factor in the effects of osmotic additives to the prime such as mannitol.

The normal concentration of sodium in the blood plasma is 136–145 mmol/L. Hyponatremia is defined as occurring when sodium levels fall below 136 mmol/L. We chose a serum sodium of 125 mmol/L as this was felt to be a realistic serum sodium level encountered in patients undergoing cardiopulmonary bypass.

The issue of choosing the right priming solution for adult CPB in a patient who is hyponatremic is an important consideration. It can be seen from the different sodium concentrations of the clinically used priming solutions, that when dealing with a hyponatremic patient to prevent the possibility of myelinolysis by the rapid over correction of sodium, the use of .9% sodium chloride, balanced electrolyte solution (neutral pH and concentrations of electrolyte ions similar to that of human plasma), and lactated ringers could be viewed as hazardous. The use of mannitol 10% may also be considered as harmful in view of the fact that it is a hypertonic solution, which will draw water from the body cells causing cerebral dehydration (5). Similarly, to prevent a “post TURP-syndrome” the use of 5% dextrose or dextrose saline as a priming solution should be avoided.

Concomitant hypokalemia, a frequent accompaniment in patients on chronic diuretic therapy and/or malnutrition (cardiac cachexia) can make myelinolysis worse (22,23). Hyponatremic patients may need the prime altered to fit them, as opposed to them “fitting” the prime. This could be achieved by the addition of water or 5% dextrose to lower the prime sodium concentration.

It is known that not all patients who are made acutely hyponatremic or have a rapid correction of their chronic hyponatremia become symptomatic. The reasons for this are currently unknown (6). The aim of this study was to highlight the possible importance of preoperative hyponatremia as a potential risk factor for patients undergoing cardiopulmonary bypass.

FUTURE WORK

A prospective analysis of hyponatremic patients undergoing CPB that is adequately powered with neuropsychological assessment is required. Stroke rate as a sole outcome measure is too crude to detect pontine myelomatosis.

LIMITATIONS

This study has a number of limitations: the clinical part of the study contained no neuropsychological assessment, mathematical modeling made a number of assumptions such as no intracellular extra cellular shift, fluid loss,

or effects of osmolarity, and serum sodium changes were mathematically calculated but not clinically confirmed.

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