Case report

Pseudohypernatremia secondary to trisodium citrate (Citra-Lock™)

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Abstract

Introduction: Hypernatremia is common among hospitalized patients especially in the intensive care units and presents an independent risk factor for mortality. Mild hypernatremia is often asymptomatic but severe hypernatremia causes central nervous system dysfunction with initial non-specific symptoms of encephalopathy that may progress to seizures, coma and death, if left untreated. Severe hypernatremia is a medical emergency and requires emergent medical attention.

Materials and methods: A haemodialysis patient who arrived for his scheduled haemodialysis treatment had monthly blood work drawn and was reported to have severe hypernatremia with serum sodium concentration of 183 mmol/L. The possibility of technique or laboratory error was considered and systematically evaluated.

Results: The serum sodium measurement using another analyser showed similar value of 182 mmolL. A repeat serum sodium level on a sample drawn 2 h later showed normal value of 139–140 mmol/L. A step-wise evaluation of the complete procedure from blood collection to analysis of the sample revealed this to be spuriously elevated serum sodium concentration secondary to contamination of the sample during sample collection with trisodium citrate, a catheter-lock solution, commonly used in dialysis units to maintain patency of dialysis catheters.

Conclusions: Spuriously elevated plasma sodium concentration (pseudohypernatremia) of mild degree is common but severe pseudohypernatremia is rare and the possibility of sample contaminations or laboratory error should be considered. Vigilance is required by both the medical and the laboratory staff to resolve such issues in a timely fashion to avoid unintended consequences.

Key words: assay interference; Citra-Lock; hypernatremia; pseudohypernatremia; dialysis catheter

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Introduction

Hypernatremia represents an abnormal ratio of total body sodium to water and is defined as serum sodium concentration of over 145 mmol/L (1). Hypernatremia is common among hospitalized patients, with a prevalence of approximately 0.5% to 2% (1-3) in general wards, but affecting 10 to 26% of patients in intensive care units (4,5) and is an independent risk factor for mortality among intensive care patients with mortality rates of 30% to 70% (1-3,5,6).

Many factors, alone or in combination, influence the ratio of sodium to water. Rarely excess sodium intake (7) can cause hypernatremia, but most cases are due to either insufficient water intake or hypotonic fluid losses, that could be renal or extrarenal (excessive sweating or diarrhea). Based on serum sodium level, hypernatremia may be mild (145 - 150 mmol/L), moderate (151 - 155 mmol/L) or severe (> 155 mmol/L). Mild hypernatremia is often asymptomatic, but severe hypernatremia, like severe hyponatremia, causes central nervous system dysfunction with initial non-specific symptoms of encephalopathy (lethargy, headache, nausea, confusion) that may progress to seizures, coma and death; if left untreated (6). Thus, severe hypernatremia, like severe hyponatremia, is a medical emergency and requires emergent medical attention. We report a case of severe pseudo-

hypernatremia in a haemodialysis patient secondary to trisodium citrate contamination during sample collection where due diligence and systematic assessment prevented unnecessary and possibly harmful intervention.

Materials and methods

Subject

A 61-year old man with chronic kidney disease had been receiving maintenance haemodialysis three times a week for past 2-years. He came for his scheduled haemodialysis treatment. He receives haemodialysis through a right internal jugular permanent catheter (Perm-Cath). He had monthly blood work done and the laboratory called an alert, as the serum sodium was 183 mmol/L (Table 1) and required immediate attention. Patient was assessed at this time and he denied symptoms of headache or nausea. He was alert and oriented. His medications were lisinopril 10 mg a day; sevelamer hydrochloride 800 mg three times a day and erythropoietin. Physical examination was unremarkable. Patient was undergoing the dialysis therapy, without any issues. A repeat sample for serum sodium was normal with serum sodium of 140 mmol/L. He completed the dialysis treatment uneventfully.

Methods

All haemodialysis patients undergo monthly blood work to assess dialysis adequacy, haemoglobin levels, nutritional and metabolic parameters. Blood sample for chemistry, including electrolytes were drawn, as *per* standard protocol (Table 2) by the nursing staff of the dialysis unit, using standard plasma tubes with gel separator and lithium heparin (BD PST™ II, Becton, Dickinson and Company, Franklin, New Jersey, USA) and sent to the laboratory situated within the hospital.

Trisodium citrate 4% (140 mmol/L citrate and 420 mmol sodium/L) solution (Citra-Lock™, Dirinco, Rosamalen, Netherlands) is used at our centre to lock the central venous catheters (both temporary and permanent catheters) to maintain their patency. We use pre-filled syringes that contain 3.0 mL of 4% trisodium citrate (CitraFlow™, Emergo-Europe, Hague, Netherlands). A volume of 1.7 to 1.9 mL of this solution is instilled in each lumen of the catheter at the end of each dialysis treatment to maintain patency of the catheter during the interdialytic period.

The laboratory uses the Siemens Advia 1200 analyser for serum electrolytes that uses Ion Selective Electrode (ISE) principle to measure serum sodium level. Lithium levels were also measured using the same machine. The same analyser (Siemens Advia 1200 A, Erlangen, Germany) was used to measure serum sodium in all samples. Whenever there is a discrepancy or discordant results, the laboratory staff runs the samples on a different analyser (Siemens Advia 1200 B, Erlangen, Germany) to assure accuracy and to rule out a technical issue.

Two days later, at the next scheduled dialysis session before initiating dialysis therapy, two separate blood samples were drawn from the dialysis catheter. One sample was drawn directly from the catheter without discarding 5 mL of blood from the catheter lumen (label "C" - *contaminated sample with catheter-lock solution*, CitraFlow™) and another blood sample was drawn after discarding initial 5 mL of blood from each catheter lumen (label "P" – *protocol based blood sample*). Both samples were sent to the laboratory with instructions to perform serum electrolytes.

Results

The serum sodium levels in all other samples performed at the same time were within normal range, except for this individual. After alerting the dialysis unit of a critical laboratory value, the laboratory staff ran this individuals blood specimen on a different analyser (Siemens Advia 1200 B), as *per* protocol of a discordant result, to assure accuracy and noted similar results (Table 1). Repeat serum sodium level, 2-hours later, using the same analysers showed a normal value. The serum albumin was normal at 38 g/L. The lithium level was not elevated.

The serum sodium concentration was 220 mmol/L in sample "C" compared to normal serum sodium concentration of 140 mmol/L in sample "P" (Table 1).

Table 1. Laboratory results at different times during assessment

Test	Analyser	Normal range	10 am Index sample		12:10 pm Repeat blood work		2 days later - before start of next haemodialysis treatment	
			Initial run	Second run	Initial run	Second run	Sample "C" drawn directly* from dialysis catheter	Sample "P" drawn from catheter as *per* protocol
Sodium (mmol/L)	Siemens Advia A	135-145	183	183	140	139	220	140
	Siemens Advia B		182 (mean of 20 repeated measurements)					
Potassium (mmol/L)	Advia A	3.5–5.0	4.8		4.6		2.8#	4.1
Chloride (mmol/L)	Advia A	99–109	87		88		65#	100
Lithium (mmol/L)	Advia A		0.77		0.94			

*Direct sample "C" was drawn from the dialysis catheter without discarding the initial 5mL of blood from the lumen of the catheter, and is contaminated with catheter lock solution, trisodium citrate.
#The low values of serum potassium and chloride in sample "C" are artifactual because about 1.5ml of 4.5 ml (or 1/3) of blood sample is the residual amount of trisodium citrate present in the lumen of the catheter and these values represent about 2/3 of normal values.

Table 2. Protocol for blood sample collection from haemodialysis catheter

Under aseptic condition:

- Using a 10 ml syringe, withdraw catheter-lock solution (heparin or sodium citrate) from the arterial port of the catheter, along with blood to a total of 5 mL. Discard the contents of the syringe in a bio-hazardous container.
- Connect a new syringe or collection vacutainer device and fill to desired level of blood volume.
- Proceed with treatment initiation according to protocol.

Discussion

Mild degree of spuriously elevated serum sodium (pseudohypernatremia) is common and is often due to decreased plasma proteins (8). However, severe pseduohypernatremia is rare. There are only a handful of case reports in the literature, and none has been reported secondary to contamination with trisodium citrate. Gaylord *et al.* in 1991 reported factitious hypernatremia and hyperkalemia secondary to the release of benzalkonium chloride (BZK) from heparin-bonded umbilical catheters (9). Either heparin or trisodium citrate is used as catheter lock solutions during the interdialytic period to maintain the patency of the central venous catheters. Sodium citrate, in addition to its anticoagulant activity also has antibacterial activity (10) and is the preferred catheter-lock solution (11) in many centres including our centre, so the likelihood of heparin-associated contamination was not likely. The laboratory staff had already excluded the technical issues with the analyser, as other samples ran at the time of index sample showed no aberrant or discordant results and when these samples were ran on the other analyser showed similar results. The contamination of blood samples from collection tubes (12,13) was considered as the soft gel separator in the BD Vacutainer

tubes contain lithium heparin, and the possibility of lithium leak from the soft gel separator contaminating the sample was excluded as there was no significant difference in the lithium levels in the index and the 2-hour sample. Then, the possibility of the sample being contaminated with the trisodium citrate, the catheter-lock solution was considered as a variable part of the catheter locking solution remains in the catheter (14) that has very high sodium concentration. There are established protocols when drawing blood samples from central lines or central venous catheters to prevent contamination of blood samples with catheter-lock solutions. This possibility was considered, and at his next scheduled dialysis, two blood samples (sample "C" and sample "P") were drawn simultaneously as described earlier. The markedly elevated serum sodium concentration in sample "C" highly supports that the initial sample at the time of index event was not drawn properly and led to the contamination of the sample with trisodium citrate.

This case report illustrates that when in doubt, a systematic approach to the issue often results in the resolution of the problem at hand.

In conclusion, severe pseudohypernatremia is rare and when it occurs, assay interference or technical issues in the specimen collection should be considered and evaluated systematically. Vigilance is required by both the medical and the laboratory staff to resolve such issues in a timely fashion to avoid unintended consequences.

Potential conflict of interest

None declared.

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