Life-Threatening Hypoglycemia due to False Measurement of Glucose in a Peritoneal Dialysis Patient

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Continuous ambulatory peritoneal dialysis is used as an alternative to hemodialysis in diabetic patients with end-stage renal disease [1]. Extraneal® (Baxter Healthcare SA, Castlebar, Ireland) is an iso-osmotic peritoneal dialysis solution containing icodextrin, a polymer of glucose, as the primary osmotic agent. We report a case of overestimation of capillary blood glucose readings in a patient using icodextrin-containing solutions, which led to undetected life-threatening hypoglycemia.

PATIENT DESCRIPTION

A 60 year old man undergoing peritoneal dialysis was admitted because of 2 days of diffuse abdominal pain and vomiting. He had suffered from diabetes mellitus type I for many years, and had a history of ischemic heart disease and a slow-growing adenoid cystic carcinoma of the lung. For 9 months prior to admission, he was treated with CAPD, using an icodextrin solution.

On physical examination, he was afebrile, with oxygen saturation of 74% on room air, blood pressure of 145/80 and heart rate of 93 beats/min. Air entry was diminished in the right lung. On palpation, the abdomen was diffusely tender without signs of peritoneal irritation.

CAPD = continuous ambulatory peritoneal dialysis

The laboratory workup on admission included: white blood cell count 27,000 cells/μl, polymorphonuclear cells 91%, hemoglobin 12.1 g/dl, platelets 386,000 cells/μl and serum albumin 2.5 mg/dl. The peritoneal dialysis fluid was clear, and showed 23 white blood cells upon microscopic examination.

A finger stick glucose reading, using the Accu Chek® glucometer (Roche Diagnostics, Germany), showed a glucose level of 492 mg/dl, and a venous blood sample taken at the same time showed a serum glucose level of 320 mg/dl. Serum glucose levels were analyzed with Vitros5.1 analyzer (Ortho Clinical Diagnostics, USA) with dry chemistry slides.

Chest computed tomography revealed a 6.8 x 10 cm mass in the right lung and many lymph nodes at the mediastinum, with bilateral pleural effusions. Upper abdominal tomography was unremarkable. The patient refused to eat and received insulin injections using a sliding scale, guided by the values of the finger stick glucose readings.

The following morning he was unresponsive to verbal and pain stimuli. His temperature was 38°C and heart rate was 100 bpm. Bacterial cultures were drawn from blood, urine and dialysis solution. An endotracheal intubation was performed to protect the airways. Brain computed tomography was normal. Antibiotic treatment with ceftriaxone and vancomycin was started.

Finger-stick glucose testing using Accu Chek showed a glucose level of 170 mg/dl, while a venous blood specimen drawn at the same time showed a glucose level of 26 mg/dl. A repeat venous blood specimen confirmed the same result. After a bolus of intravenous glucose, the patient became alert and responsive to external stimuli and he was rapidly weaned from mechanical ventilation.

After 2 days the patient developed a new febrile episode. Again, bacterial cultures were drawn from blood, urine and dialysis solution, and the peritoneal showed 13 white blood cells. Antibiotics were switched to to piperacillin-tazobactam to cover hospital-acquired infection. The fever decreased, his hemodynamic condition was stabilized, and he regained consciousness and recovered gradually. One month following admission, the patient was discharged to an outpatient rehabilitation institution.

Table 1 shows the results of finger-stick glucose levels measured by the Accu Chek glucometer as compared to venous blood specimens drawn at the same time during the patient's hospitalization, compared to finger-stick levels measured by the Ascensia® glucometer (Bayer HealthCare, Switzerland). In addition, results for all three methods were compared in a non-CAPD patient.

As can be seen, the Accu Chek glucometer greatly overestimated the glucose level, while the Ascensia glucometer gave results very similar to those of the venous blood specimens in both the CAPD and non-CAPD patients.

COMMENT

We have described a case of induced hypoglycemia in a CAPD patient who was on an icodextrin-containing peritoneal dialysis solution. The use of this solution caused false hyperglycemia and resulted in the administration of fast-

Table. Glucose measurement during hospital stay

		Capillary blood glucose level (mg/dl)		
	Day of measurement	Accu Chek® Glucose dehydrogenase enzyme system	Ascensia® Glucose oxidase enzyme system	Venous blood glucose level (mg/dl)
Patients	Day 1	492		320
	Day 2	170		26
	Day 4	172		53
	Day 5	353		169
	Day 6	>500		501
	Day 9	308	113	115
	Day 11	594	355	314
Controls	Day 5	187	185	189
	Day 6	114	113	118

acting insulin, and consequent clinically significant hypoglycemia.

Icodextrin is a colloid osmotic agent, starch-derived, water-soluble glucose polymer linked by alpha (from 1 to 4) and less than 10% alpha (1 to 6) glucosidic bonds. Icodextrin induces ultrafiltration by oncotic rather than osmotic pressure, and the solution is actually isosmotic relative to normal plasma. Since the icodextrin molecule is too large to diffuse across the peritoneal membrane, systemic absorption can occur only through lymphatic flow. This does occur but not to a degree that impairs the ability of icodextrin to induce ultrafiltration in a sustained manner during long dwells. The main theoretical concern about icodextrin is that it leads to unphysiologically high levels of maltose and other oligosacccharides in serum.

Each saccharide chain generated by the metabolism of icodextrin in systemic circulation has a free reducing group of glucose located at its end. This can react with glucose dehydrogenase glucometers based on the coenzyme pyrroloquinolinequinone system (GDH-PQQ), as used in our hospital, leading to falsely increased readings of glucose levels [1,2]. Although our patient used the Freestyle® (Abbott Diabetes Care,USA) glucometer that employs the GDH-PQQ system, there was no report of false glucose readings from the patient before he came to the hospital. His compliance during the period before his admission was poor, and it is likely that his glucose levels were too high for clinical hypoglycemia to develop.

Wens et al. [3] investigated discrepancies in measurements of hyperglycemia in CAPD patients. They compared glucose levels as measured by capillary blood samples, using the Accu Chek glucometer, and the Glucocard glucometer (Menarini Diagnostics, Italy), which is based on the glucose oxidase system. All the values were compared to glucose levels obtained from a venous blood sample drawn at the same time. They observed overestimation of hyperglycemia in the Accu Chek glucometer of 65 ± 26 mg/dl ($P < 0.01$), compared to venous blood, and of 69 ± 25 mg/dl ($P < 0.001$), compared to measurements obtained with the Glucocard glucometer in CAPD patients who were using icodextrin solution in their dialysis fluid [3].

Intravenous immunoglobulin preparations containing maltose (e.g., intragam P) can also interfere with the readings of blood glucose monitors that use test strips with glucose dehydrogenase. This enzyme reacts with the disaccharide isomer maltose present in intragam P at concentrations of 10 g/100 ml, resulting in falsely elevated blood glucose level results [4].

In 2003, Roche Diagnostics issued a warning about the potential risk of using the Accu Chek sensor and other glucose-measuring machines using the GDH-PQQ system in CAPD patients [5]. There are other glucose-specific measuring instruments that "ignore" the maltose in the icodextrin solution, such as the Optium-Xceed® glucometer (Abbott Diabetes Care, USA)and the Ascensia Contour glucometer (Bayer HealthCare, Switzerland) based on glucose dehydrogenase nicotinamide adenine dinucleotide (GDH-NAD) and glucose dehydrogenase flavin-adenine dinucleotide (GDH-FAD) systems, respectively, which are safe to use in these patients.

Since the effect of icodextrin on glucose testing has been reported before and warnings from the Israeli Society of Nephrology and Hypertension were issued in 2005 and 2008, medical providers should increase their awareness of falsely elevated glucose readings in peritoneal dialysis patients. This could minimize the risk of undiagnosed hypoglycemia with potential life-threatening consequences.

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