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Case Report

Activation of Blood Leak Alarm during Hemodialysis Secondary to Hydroxocobalamin Therapy of Nitroprusside Induced Cyanide Toxicity

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Abstract

For safety of the patient, dialysis machines come with various kinds of sensors that when activated can set off an alarm stopping dialysis. A blood leak alarm is one such example, which works by detecting the loss of transparency of the dialysate effluent typically due to damaged dialyzer. Hydroxocobalamine, used in cyanide toxicity characteristically causes reddish discoloration of the dialysate leading to 'pseudo-activation of the blood leak alarm' causing the dialysis to stop. We report a case of 61 years old end stage renal disease patient who received continuous infusion of sodium nitroprusside for 9 days for uncontrolled blood pressure in the setting of impending abdominal aortic aneurysm rupture. She developed cyanide toxicity secondary to that and was placed on hydroxocobalamine, which led to a unique complication discontinuing dialysis.

Keywords: Blood leak alarm; Cyanide toxicity; Dialysis machines; Dialysate discoloration; Hydroxocobalamine therapy

Introduction

Sodium nitroprusside (SNP) is a parenteral agent that has been used for nearly five decades as an agent causing rapid onset of arterial and venous vasodilation. Metabolism of SNP leads to release of nitric oxide leading to rapid lowering of blood pressure. Due to concerns over serious side effects, SNP is used only in select circumstances, including treatment of hypertensive emergencies. The most life-threatening side effect of SNP is development of cyanide toxicity. Nitroprusside metabolism generates cyanide, which can lead to development of cyanide (or, rarely, thiocyanate) toxicity, that can be fatal. Cyanide toxicity has been reported to occur as little as four hours of nitroprusside infusion. Typical presentation includes development of altered mental status and lactic acidosis. Major risk factors for nitroprusside induced cyanide toxicity include high-dose infusion, prolonged infusion, and the presence of impaired kidney function [1,2].¬¬

Hydroxocobalamin has been approved by the FDA for use in cyanide toxicity and is currently utilized for empiric therapy for cyanide toxicity [3,4]. Hydroxocobalamine in the blood forms cyanocobalamine when combining with cyanide and is then excreted via urine. Cyanocobalamin produces reddish discoloration of the urine which may persist up to 35 days (3). Finally, a small amount of unmetabolized cyanide is eliminated through sweat and expiration [1,2].

Hydroxocobalamin, with a molecular mass is 1,346.37 g/mol, is dialyzable and leads to reddish discoloration of dialysate which can activate hemodialysis blood leak detector alarms, thereby preventing continuation of the dialysis procedure [5]. This has been termed pseudo-activation of the blood leak alarms and is machine dependent, depending on the type of sensor utilized in the dialysis machine blood leak alarm system. The following case highlights this machine dependency during the treatment of nitroprusside induced cyanide toxicity that was treated with hydroxocobalamin.

Case

A 61-year-old female with a past medical history of dialysis dependent end stage renal disease secondary to poorly controlled hypertension presented with severe blood pressure elevation of 247/125 mmHg and a pulse of 87/min with imaging studies demonstrating a 5.6 cm abdominal aortic aneurysm with concerns for impending rupture. Patient was immediately treated with a continuous infusion of sodium nitroprusside to achieve rapid lowering of blood pressure in the intensive care setting. She subsequently received intermittent dialysis with Fresenius

FMC 2208k dialysis machine and was continued on continuous infusion of SNP at the lowest titratable dosage for 9 days. Urine output varied between 500ml-700ml/day. On the 9th day, patient abruptly developed an increased anion gap metabolic acidosis: Na 145 mEq/L, K 4.5 mEq/L, Cl 96 mEq/L, HCO3 level 18 mEq/L, BUN 24 mg/dl, Cr 2.52 mg/dl, and with a plasma anion gap of 31. Due to continued sodium nitroprusside use, cyanide toxicity was suspected. Unfortunately, thiocyanate level was unable to be measured. At this point SNP was discontinued and hydroxocobalamin 5g was administered intravenously and was repeated twice. The patient's plasma and urine were noted to be severely discolored following hydroxocobalamin administration. Intermittent hemodialysis with the Fresenius 22o8k dialysis machine were complicated by repeated activation of the blood leak detector, preventing continued hemodialysis. The patient was then started on CVVHDF (continuous venovenous hemodiafiltration) utilizing the Prismaflex machine and continued for 3 days. Lactic acid level was noted on the day of initiation of CRRT to be 2.5 mg/dl. The reddish discoloration of the urine, plasma, and CRRT effluent output gradually resolved. Patient was successfully converted back to intermittent dialysis using the Fresenius FMC dialysis 2008k machine, with no further activation of the blood leak detector. She improved overall and was able to be transitioned to long term acute care facility where she stayed for several months before ultimately advancing to hospice care.

Discussion

Sodium nitroprusside is a parenteral medication most often used for treatment of hypertensive emergencies in intensive care settings. During normal cellular metabolism, ATP is generated from oxidative phosphorylation utilizing the mitochondrial cytochrome complex. Nitroprusside is metabolized with generation of cyanide. Cyanide binds to cytochrome oxidase a3 (specifically to ferric ion) leading to inhibition of the final enzyme in the mitochondrial cytochrome complex. This, in turn, inhibits oxidative phosphorylation. In this setting, cellular metabolism shifts to anaerobic metabolism for the generation of ATP leading to formation of lactic acid. Hydrogen ions generated from ATP hydrolysis no longer are taken up by aerobic ATP production, further contributing to the development of increased anion gap metabolic acidosis [1].

Symptoms and signs of toxicity appear at blood cyanide level of approx. 40 µmol/L. Cyanide is rapidly distributed in the body with an estimated volume of distribution of 1.5 L/kg, with approximately 60 percent of cyanide being protein bound. Inside the body, cyanide is neutralized byseveral mechanisms, the most important one being the detoxification of cyanide by rhodanese. Rhodanese is an enzyme found in many different type of organs, including muscle and liver [1-3]. Small amounts of unmetabolized cyanide is eliminated through urine, sweat, and expiration (1). Prior treatment modalities for cyanide poisoning include sodium nitrite, amyl nitrite, and sodium thiosulfate [6,7]. Thiosulfate donates sulphur to cyanide converting it to thiocyanate - a water-soluble molecule rapidly excreted in the urine, rhodanese being the catalyst of that reaction [1,2,8]. Hydroxocobalamin administration has become a standard treatment for cyanide toxicity, as hydroxocobalamin combines with cyanide to form cyanocobalamin, which is then excreted through the kidney [8].

Noted reversible risk factors for cyanide poisoning due to nitroprusside include prolonged treatment of >24 - 48 hours, preexisting renal impairment, and higher doses that will not allow the body to detoxify cyanide. Normally, this dose needs to be under 2mcg/kg per minute. When providing this medication, consideration should be noted to use the lowest achievable dose for desired effect, and to avoid prolonged use and under 2-3 days of use at most [1,8]. It should be noted as well to carefully monitor for unexplained acidemia and decreased serum bicarbonate concentrations. It is also to be noted that doses of 10 mcg/kg per minute should never be given for more than 10 minutes and that sodium thiosulfate infusion can be provided in patients for the provision of sulfur donor to detoxify cyanide into thiocyanate [1,2].

Blood detection alarms in dialysis machines have been designed to pause dialysis upon the detection of blood in the dialysate. When the alarm is activated, the blood and ultrafiltration pump is stopped, and the venous clamp is occluded [5,9]. Fresenius dialysis machines comes with a blood leak alarm which consists of a bicolored (Dual LED array) light source transmitter and sensor (one emits green and the other emits red) at the top and bottom of the dialysate column, respectively, monitoring the transparency of the dialysate which is altered by presence of RBCs and medications causing discoloration of plasma and subsequently the dialysate. Green light, having a wavelength of 562-575 nm, triggers the photodetector when it is absorbed by the blood. Usually, leak detector is placed in the outflow line of the dialysis solution and uses sensor in dialysate effluent path. Blood leakage into the dialysate most commonly occurs due to physically damaged dialyzers that have been not appropriately handled. Intravascular hemolysis usually cannot lead ultimately to activation of the blood detector system, since the size of hemoglobin molecule is too large in mass to pass across the dialysis membrane.

Previous reports of hydroxocobalamin induced 'pseudo-activation of the bloodleak alarm' during hemodialysis have described successful conversion to CRRT using either the NxStage or Prismaflex machines [10-13]. Pseudo-activation of the blood leak alarm due to the presence of hydroxocobalamin induced reddish discoloration of the dialysate does not occur while performing CRRT using the Gambro Prismaflex TM or NxStage. The blood leak detector of the Gambro Prismaflex TM and NxStage machine

consists of a single optical emitter infrared light (wavelength of 880-nm) programmed to detect light scatter [13,14]. This method is not dependent on light absorption and therefore does not 'misread' hydroxocobalamin as blood. Although successful intermittent hemodialysis using the standard Gambro Phoenix X36™ machine is still in question.

Conclusion

With increasing use of hydroxocobalamin administration for treatment of cyanide toxicity, it is important that critical care physicians and nephrologists are aware of the machine dependency of hydroxocobalamin induced false blood leak alarm so that arrangements for CRRT or alternative dialysis machines are made [15]. It is also best practice to avoid sodium nitroprusside infusions in patients with renal insufficiency.

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