TOXICOLOGY OBSERVATION

# Hemodialysis Complications of Hydroxocobalamin: A Case Report

**Mark Sutter · Nadia Tereshchenko · Rokhsara Rafii · G. Patrick Daubert**

**Abstract** Hydroxocobalamin is a new antidote approved by the FDA for the treatment of cyanide poisoning. Our report describes a patient with cyanide poisoning who survived after treatment with hydroxocobalamin and complications we encountered with hemodialysis. A 34-year-old female presented to the emergency department after a syncopal event and seizures. Her systolic blood pressure was 75 mmHg, her QRS complex progressively widened, and pulses were lost. She was intubated and resuscitated with fluids, sodium bicarbonate for her QRS widening and vasopressors. Venous blood gas demonstrated a pH of 6.36 with an $O_2$ saturation of 99%. Due to the acidemia with a normal pulse oximetry, simultaneous venous and arterial blood gases were obtained. Venous gas demonstrated a pH of 6.80 with a $PO_2$ of 222 mmHg, an $O_2$ saturation of 99%. The arterial blood gas showed a pH of 6.82, a $PO_2$ 518 mmHg, an $O_2$ saturation of 100%. Cyanide was suspected and hydroxocobalamin and sodium thiosulfate were given. Within 40 min of hydroxocobalamin administration, vasopressors were discontinued. Initially, nephrology attempted dialysis for metabolic acidosis; however, the dialysis machine repeatedly shut down due to a "blood leak". This was an unforeseen effect attributed to hydroxocobalamin. Cyanide level, drawn 20 min after the antidote was completed, was elevated at 22 mcg/dL. Her urinary thiocyanate level could not be analyzed due to an "interfering substance". Hydroxocobalamin is an effective antidote. However, clinicians must be aware of its effects on hemodialysis machines which could delay the initiation of this important treatment modality in the severely acidemic patient.

**Keywords** Hydroxocobalamin · Hemodialysis · Cyanide

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## Introduction

The lethal effects of cyanide poisoning have been well described [1]. Cyanide is a potent cellular toxin that interferes with aerobic metabolism by blocking cytochrome a-a3 of the electron transport system. This blockade eventually leads to a significant increase in anaerobic metabolism and a profound lactic acidosis. Death from cyanide toxicity is the result of multi-system organ failure that stems from the body's inability to utilize oxygen [2].

On December 15, 2006, a new antidote for the treatment of cyanide poisoning, hydroxocobalamin, (Cyanokit™, Dey Laboratories, Napa, CA, USA) was approved by the FDA [3]. In contrast to previously utilized antidotes, hydroxocobalamin binds cyanide without decreasing the oxygen carrying capacity of hemoglobin. Hydroxocobalamin binds to cyanide to form cyanocobalamin which can then be excreted in the urine. Additionally, sodium thiosulfate can also be administered to provide another mechanism to enhance cyanide excretion [4].

The side effects of hydroxocobalamin are minimal making it advantageous to previous antidotes. Hydroxocobalamin is known to cause an orange/red discoloration of the blood, urine, and secretions. This discoloration of the bodily fluids has been shown to interfere with several chemistry methodologies. This interference has been established to cause statically significant alterations in aspartate aminotransferase, bilirubin, creatinine, magnesium, and iron [5–7]. Other colorimetric tests have also been influenced by both hydroxocobalamin and the resulting cyanocobalamin. This

can lead to interferences and calculation errors by co-oximeter measurements of carboxyhemoglobin, methemoglobin, oxyhemoglobin, and hemoglobin [8, 9]. An additional side effect of hydroxocobalamin is hypertension; however, this is often a desired effect in the critically ill patient [5].

A classical presentation of cyanide often includes the sudden onset of syncope, seizures, and eventual cardiovascular collapse [1]. We present a case consistent with cyanide poisoning who survived neurologically intact, after treatment with hydroxocobalamin and sodium thiosulfate. We also describe some challenges encountered after hydroxocobalamin administration.
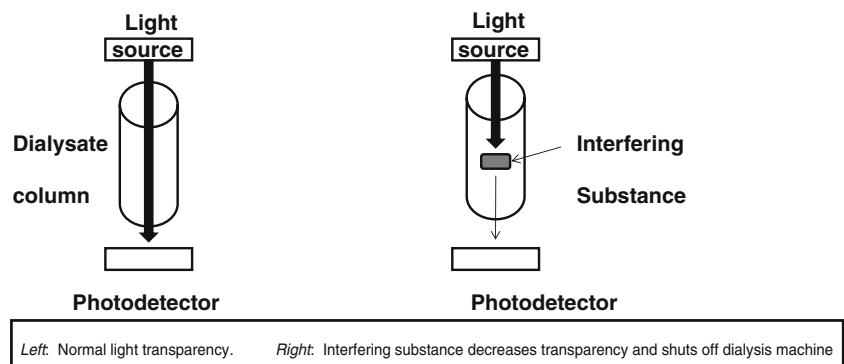
## Case Report

A 34-year-old female with bipolar disorder presented after her roommate witnessed a syncopal event followed by tonic-clonic seizure activity. She arrived in the emergency department 11 min after her roommate called 911. Her initial systolic blood pressure was 75 mmHg, and the cardiac monitor showed a narrow complex rhythm that began to widen just before carotid pulses were lost. The patient was intubated, intravenous fluids started and two ampoules of sodium bicarbonate were rapidly administered due to the QRS widening on the monitor. Cardiopulmonary resuscitation was begun and pulses returned following the administration of epinephrine and atropine. A critical lab value demonstrated a venous blood pH of 6.36. Two additional ampoules of sodium bicarbonate were pushed, and repeat venous blood gas exhibited a pH of 6.41. Norepinephrine was initiated and simultaneous placement of both an internal jugular venous line and a radial arterial line occurred with both returning bright red blood. Because of the findings of bright red venous blood in this severely acidemic patient with a pulse oximetry of 99–100%, we obtained simultaneous arterial and venous blood gases. The internal jugular venous gas demonstrated a pH of 6.80 with a $PO_2$ of 222 mmHg, an $O_2$ saturation of 99%, a $PCO_2$ of 57 mmHg and bicarcarbonate of 9 mEq/L. The radial artery

blood gas showed a pH of 6.82, a $PO_2$ 518 mmHg, an $O_2$ saturation of 100%, a $PCO_2$ of 55 mmHg, and bicarbonate of 9 mEq/L. Additionally, a carboxyhemoglobin level was 0.4% and methemoglobin was 0.6%. Cyanide toxicity was suspected given the profound metabolic acidosis and limited systemic oxygen extraction. The oxygen extraction from arterial to venous side was markedly decreased as the calculated oxygen extraction was only 6%. The patient received 5 g of hydroxocobalamin over 15 min followed by 12.5 g of sodium thiosulfate infused over 30 min.

Within 15 min of the start of the hydroxocobalamin infusion, blood pressure had increased, and norepinephrine was weaned. Forty minutes after the start of the hydroxocobalamin infusion, norepinephrine was discontinued and the patient's systolic blood pressure was 115 mmHg. Twenty minutes later, a repeat arterial blood gas demonstrated a pH of 7.32, a $PO_2$ of 445 mmHg, an $O_2$ saturation of 100%, a $PCO_2$ of 41 mmHg, and a bicarbonate of 23 mEq/L. Initial laboratories subsequently returned with a potassium of 4.1 mEq/L and a dramatically elevated lactic acid level of 32.4 mEq/L (normal 0.2–2.2 mEq/L).

During the initial resuscitation, the nephrology service attempted to dialyze the patient for overwhelming metabolic acidosis. However, the hemodialysis machine (Fresenius 2008 K) repeatedly alarmed and shut down due to a "blood leak". It took several hours to turn off the internal alarms to allow for hemodialysis to begin. Fortunately, by this time the acidosis had corrected and hemodialysis was no longer needed. Ethylene glycol and methanol levels returned as undetectable. The patient was extubated the next day and was neurologically intact. On hospital day 4, whole blood cyanide levels, which were drawn 20 min after the antidote was completely infused in the emergency department, returned elevated at 22 μg/dL (normal 0–20 μg/dL, ARUP Laboratories, Salt Lake City, UT, USA). Repeat cyanide levels from hospital day 3 were undetectable. Unfortunately, blood samples obtained prior to antidote administration were utilized for immediate testing and a sample was not available for send-out analysis. Urinary thiocyanate levels were unable to be analyzed due to an "interfering substance".



**Fig. 1** Hemodialysis blood leak alarm

**Light source**

**Light source**

**Dialysate column**

**Interfering Substance**

**Photodetector**

**Photodetector**

*Left*: Normal light transparency.  *Right*: Interfering substance decreases transparency and shuts off dialysis machine

The patient denied a suicidal ingestion of cyanide or potential exposure to any other cellular toxins, such as hydrogen sulfide, that would explain her clinical condition and rapid response to the therapy provided. However, there were several concerning factors in the patients social situation that prompted law enforcement involvement. An investigation for attempted homicide is on-going.

## Discussion

This case demonstrates the successful treatment of cyanide poisoning by combining supportive care with hydroxocobalamin and sodium thiosulfate. Our patient presented with syncope, seizures, and an overwhelming lactic acidosis. The finding of the arteriolization of the venous blood gas with minimal oxygen extraction immediately led us to suspect cyanide toxicity. The patient's rapid clinical response to our therapy including hydroxocobalamin and sodium thiosulfate, in combination with her elevated blood cyanide level convinced us that our diagnosis was correct. Additional etiologies were considered; however, urine toxicology screens were negative for drugs of abuse, adrenal and thyroid function testing was normal, blood cultures did not isolate any organisms, and other etiologies known to elevate cyanide levels such as cigarette smoking and nitroprusside were absent.

We did experience unexpected challenges following hydroxocobalamin administration. The major difficulty we encountered was the inability to perform hemodialysis. Internal alarms repeatedly shut down the hemodialysis machine due to detection of a "blood leak". Normally, in the circuit of a hemodialysis machine, blood passes on one side of a semi-permeable membrane, and red blood cells do not cross into the dialysate. As a safety precaution, all hemodialysis machines have built-in infrared or photodetector sensors that alarm and stop the machine if red blood cells penetrate into the dialysate. This photodetector is at the bottom of the dialysate column with the light source on the top shooting light towards the photodetector. Substances that deflect or scatter light will be detected because transparency at the base of the column is lost triggering the dialysis machine to stop (Fig. 1). Commonly, the substance that interferes by deflecting light is red blood cells; therefore, this alarm is called a "blood leak" [10]. With hydroxocobalamin administration, bodily fluids become discolored. The hemodialysis machine falsely interprets this discoloration as a "blood leak" and shuts down machine operation. It took several hours to disable the internal alarms to perform hemodialysis. Fortunately, hemodialysis was probably unnecessary for our patient because her metabolic acidosis resolved. However, if hydroxocobalamin were given empirically to a patient with an overwhelming acidosis of an unknown etiology (i.e., toxic alcohols, sepsis, or metformin-associated lactic acidosis), the ability to perform

hemodialysis might be delayed or prevented altogether. This delay in dialysis initiation would be unacceptable in most cases of overwhelming metabolic acidosis.

Another problem we encountered was the inability to assay for urinary thiocyanate which is often used to confirm cyanide exposure. Hydroxocobalamin is known to cause a reddish discoloration of the urine which typically resolves within 48 h [5]. Urinary thiocyanate levels were measured by spectroscopy and the reddish color of hydroxocobalamin likely interfered. This interference has been demonstrated with other chemistry testing [6]. To further support this assumption, repeat urinary thiocyanate levels sent 72 h after the antidote was infused was able to be completed with a level detected at 2 μg/ml (normal 0–20 μg/ml). The interfering substance was no longer present. It is important to give the antidote despite the possibility that confirmatory urinary levels will likely be rendered unobtainable. Pre-treatment blood and urine samples would avoid this minor limitation.

In summary, hydroxocobalamin is an effective antidote for cyanide poisoning. However, clinicians must also be aware of its effects on hemodialysis machines which could delay the initiation of this vitally important treatment modality in the severely acidemic patient. Recognizing and communicating this potential complication to the treating nephrologist can facilitate adjustment of the hemodialysis machine to enable dialysis to occur.

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