Revista Mexicana de Anestesiología

Clinical case

July-September 2024
Vol. 47. No. 3. p. 202-204

doi: 10.35366/116174

Received: 12-11-2023
Accepted: 04-03-2024

Cyanide poisoning treated with high doses of hydroxocobalamin. Case report and review of this complication

Intoxicación por cianuro tratada con dosis altas de hidroxocobalamina. Reporte de caso y reseña de esta complicación

Daniel Pérez-Ajami, M.D.,*,¶ Elisa Viscasillas-Navarro, M.D.,‡ Alejandro Gallego-Goyanes, M.D.,* Celia Enguídanos-Sánchez, M.D.,§ Joan Egea-Belda, M.D.,* Abel Guiu-Pérez, M.D.*

How to cite: Pérez-Ajami D, Viscasillas-Navarro E, Gallego-Goyanes A, Enguídanos-Sánchez C, Egea-Belda J, Guiu-Pérez A. Cyanide poisoning treated with high doses of hydroxocobalamin. Case report and review of this complication. Rev Mex Anestesiol. 2024; 47 (3): 202-204. https://dx.doi.org/10.35366/116174

Keywords:
cyanide poisoning, inhalation syndrome, hydroxocobalamin, kydney failure, major burn patient.

Palabras clave:
intoxicación por cianuro, síndrome de inhalación, hidroxocobalamina, insuficiencia renal, paciente quemado grave.

ABSTRACT. Cyanide poisoning frequently complicates major burn injuries with inhalation syndrome. The established treatment protocol recommends a standard dose of 70 mg/kg of hydroxocobalamin for adults, with the option to administer a second dose, not exceeding a maximum of 140 mg/kg. Our objective is to chronicle the case of a patient for whom an escalated dosage, exceeding the approved limit, was imperative to reverse the intoxication. The unconventional decision to administer such high doses proved life-saving, albeit not conforming to the medication's technical specifications. Notably, side effects observed were not markedly worse than those associated with the standard dose, except for the occurrence of moderate kidney failure. It is worth noting that this renal complication is also documented with standard doses and did not necessitate renal replacement therapy.

RESUMEN. *La intoxicación por cianuro frecuentemente complica las lesiones por quemaduras graves con síndrome de inhalación. El protocolo de tratamiento establecido recomienda una dosis estándar de 70 mg/kg de hidroxocobalamina para adultos, con la opción de administrar una segunda dosis, que no exceda un máximo de 140 mg/kg. Nuestro objetivo es relatar el caso de un paciente para quien una dosis escalonada, que excedía el límite aprobado, era imperativa para revertir la intoxicación. La decisión no convencional de administrar dosis tan altas resultó en salvarle la vida, aunque no se ajustara a las especificaciones técnicas del medicamento. Cabe destacar que los efectos secundarios observados no fueron notablemente peores que los asociados con la dosis estándar, excepto por la aparición de una insuficiencia renal moderada. Vale la pena mencionar que esta complicación renal también está documentada con dosis estándar y no requirió terapia de reemplazo renal.*

* MD, Anesthesiology and critical care in Hospital La Fe, Valencia, Spain.
‡ MD, Anesthesiology and critical care in Hospital La Ribera, Alzira, Spain.
§ MD, Orthopedic Trauma physician in Hospital La Fe, Valencia, Spain.
¶ ORCID: 0000-0003-0136-0246

Correspondence:
Daniel Pérez-Ajami
E-mail: daniajami1995@gmail.com

INTRODUCTION

Cyanide poisoning frequently complicates major burn injuries accompanied by inhalation syndrome. Recognizing cyanide toxicity as a component of inhalational injury is crucial for effective management. Early administration of treatment with accurate doses increases the likelihood of successfully overcoming intoxication. However, the evidence supporting the use of hydroxocobalamin as a cyanide antidote is limited, primarily due to a lack of randomized controlled trials in humans. The standard validated dose for hydroxocobalamin treatment in adults is 70 mg/kg, with the possibility of repeating a second dose up to a maximum of 140 mg/kg.

CASE REPORT

A 44-year-old male admitted to the burn unit following a house fire presented confusion and mild deterioration of consciousness. Pre-hospital care included orotracheal intubation

and the administration of 5 g of hydroxocobalamin. The in-hospital assessment revealed 4% body surface burns, mainly on the face, with second-degree burns. Inhalation syndrome was suspected, leading to the prescription of 100% FiO_2, fibrobronchoscopy, and monitoring with serial arterial blood gases and portable X-Ray *(Figure 1)*.

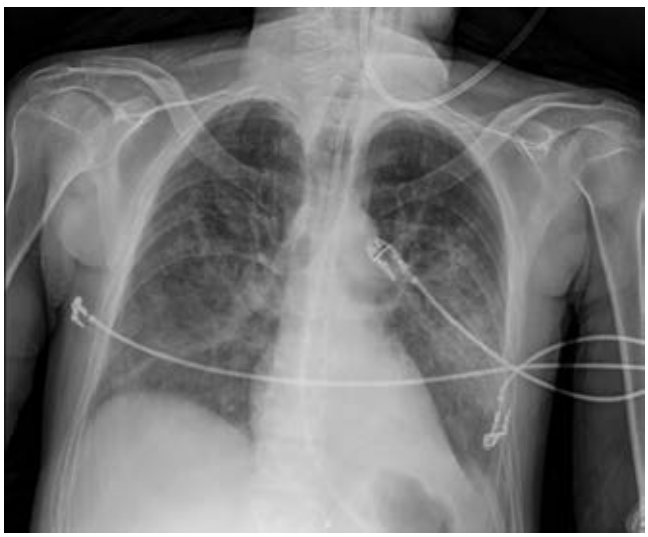

Figure 1: Chest X-Ray at 24 hours after admission compatible with adult respiratory distress due to inhalation syndrome.
Source: authors.

Table 1: Arterial blood gas test 12 hours after admission with the maximum elevation of lactate despite hydroxocobalamin.

$SatO_2$		96.8%
Total hemoglobin		13.7 g/dl
Calculated hematocrit		41%
Oxyhemoglobin		95.3%
Deoxyhemoglobin		3.1%
Carboxyhemoglobin		0.0%
Methemoglobin	↑	1.6%
PO_2 (A-a)		99.0 mmHg
PO_2(a)/FO_2(I)		355 mmHg
Shunt estimation (critical patients)	↑	25.5%
Bicarbonate (T^a)	↓	19.6 mmol/L
Standard bicarbonate	↓	20.0 mmol/L
Base excess	↓	-6.2 mmol/L
Excess liquid base extracel	↓	-6.7 mmol/L
Sodium		136 mmol/L
Chlorine		106 mmol/L
Potassium		4.8 mmol/L
Ionic calcium		4.4 mg/dL
Ionic calcium (SI)	↓	1.10 mmol/L
Calcium corrected to pH 7.4	↓	4.3 mg/dL
Glucose	↑	166 mg/dL
Lactate	↑	8.2 mmol/L

Source: authors.

Table 2: Arterial blood gas test 12 hours after the third dose (15 grams) of hydroxocobalamin.

Arterial Gasometry		
Fraction of inspired oxygen		100%
pH	↓	7.29
Corrected pH		7.30
PCO_2	↑	53.0 mmHg
Corrected PCO_2		51.00
PO_2	↑	430.0 mmHg
Corrected PO_2		424.00
$SatO_2$		98.0%
Total hemoglobin		13.6 g/dL
Calculated hematocrit		41%
Oxyhemoglobin		95.0%
Deoxyhemoglobin		1.9%
Carboxyhemoglobin		1.4%
Methemoglobin	↑	1.7%
PO_2 (A-a)		225.0 mmHg
PO_2 (a)/FO_2 (I)	↑	430 mmHg
Shunt estimation (critical patients)	↑	28.6%
Bicarbonate (T^a)		25.5 mmol/L
Standard bicarbonate		23.4 mmol/L
Base excess		-1.9 mmol/L
Excess liquid base extracel		-1.1 mmol/L
Sodium		134 mmol/L
Chlorine	↑	109 mmol/L
Potassium	↑	5.2 mmol/L
Ionic calcium	↓	4.2 mg/dL
Ionic calcium (SI)	↓	1.05 mmol/L
Calcium corrected to pH 7.4	↓	4.0 mg/dL
Glucose	↑	137 mg/dL
Lactate	↑	3.0 mmol/L

Source: authors.

Initial blood gases indicated lactic acidosis (pH 7.29, lactate 1.5 mmol/L). Over the next six hours, it increased to 5.3, prompting a second dose of 5 grams of hydroxocobalamin. Continuous monitoring showed rising lactate levels until 8.2 mmol/L after 12 hours *(Table 1)*, leading to the administration of a third dose (15 grams total in the first 24 hours). Lactic acid levels progressively decreased to 3 mmol/L after the third dose *(Table 2)*. The patient developed acute renal failure with a creatinine increase from 0.85 mg/dL to 1.12 mg/dL, which resolved without the need for pharmacological or replacement therapy. The patient was discharged ten days later with excellent renal and respiratory function and partial recovery of normal lung anatomy *(Figure 2)*.

DISCUSSION

Hydroxocobalamin is a hydroxylated active form of vitamin B12, precursor of methylmalonyl CoA mutase cofactors and homocysteine remethylation[1]. It is essential for cell reproduction and growth, metabolism of some amino

acids, myelin synthesis and the integrity of the nervous system and maintenance of normal erythropoiesis. Its use in medicine is wide, being mainly used to treat malabsorptive or deficient syndromes such as occurs with resections of the digestive tract or in pernicious anemia, or in the pediatric population for patients with methylmalonic acidemia with or without homocystinuria[1]. However, it has acquired special relevance in burn patients due to its potential capacity for the treatment of cyanide poisoning, whose main origin is the combustion of materials such as wool, nylon, polyurethanes, polyacrylonitriles or resins. Cyanide, due to its high affinity for iron, causes the inhibition of enzymes such as cytochrome oxidase, blocking ATP production and inducing cellular hypoxia[2].

The mechanism of action of hydroxocobalamin consists of its ability to bind 1:1 to circulating cyanide in the blood to form cyanocobalamin, a stable and non-toxic compound that is eliminated in the urine[3]. The standard validated dose is 70 mg/kg, simplified as 5 grams for the adult population, and a second dose can be repeated up to a maximum of 140 mg/kg or 10 grams[3]. However, some cases have been reported of administration of higher doses up to 370 mg/kg[4] without relevant consequences in patients as in this case where the prescription of a third dose (15 grams in total or 250 mg/kg) was able to reverse the cyanide intoxication and save the patient's life. Renal alterations secondary to high doses should be highlighted due to their importance in burn patients. Cases of acute renal failure with acute tubular necrosis, renal failure and presence of calcium oxalate crystals have been reported[5]. Therefore, regular monitoring of renal function should be carried out up to seven days after initiation of treatment.

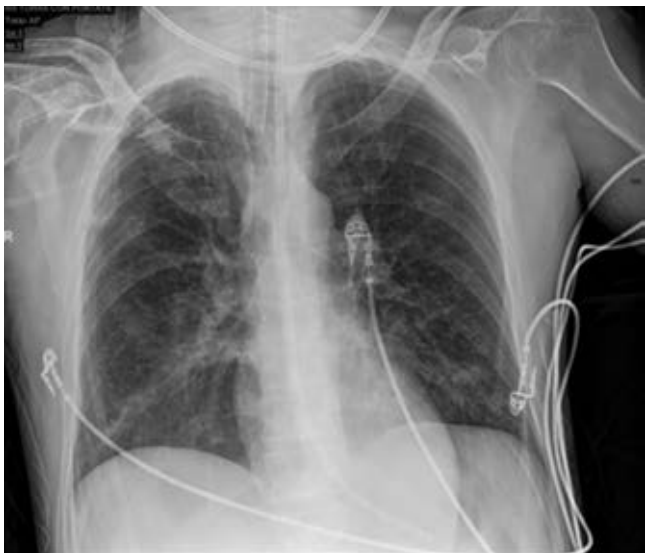

Figure 2: Chest X-Ray after seven days in the Intensive Care Unit. Significant improvement is observed with remains of inflammation in the right lower lobe.
Source: authors.

CONCLUSIONS

The comprehensive understanding and timely use of hydroxocobalamin is transcendental for any physician who deals with burn patients and, due to its excellent safety profile, its use should not be delayed whenever there is suspicion of a possible cyanide poisoning[5], taking into consideration the renal complications that are added to those already characteristic of severe burns. However, it cannot be asserted that it is safe to administer up to 250 mg/kg of hydroxocobalamin in a patient with cyanide poisoning because it is a single patient. On the other hand, thanks to this clinical case together with others reported in the literature, there are more and more indications of the safety of this compound and its scarce side effects, so it is essential to carry out studies with a larger sample size in order to prove this hypothesis.

REFERENCES

1. Sanchez RJJ. Stability of hydroxocobalamin in water for injection as an antidote against cyanides: elaborated from military pharmacy. Sanid Mil. 2012; 68: 87-96. doi: 10.4321/S1887-85712012000200005.
2. Gonzales J, Sabatini S. Cyanide poisoning: pathophysiology and current approaches to therapy. Int J Artif Organs. 1989; 12: 347-355. doi: 10.1177/039139888901200601.
3. Cummings TF. The treatment of cyanide poisoning. Occup Med (Lond). 2004; 54: 82-85. doi: 10.1093/occmed/kqh020.
4. Friedman BT, Chen BC, Latimer AJ, Valento MJ. Iatrogenic pediatric hydroxocobalamin overdose. Am J Emerg Med. 2019; 37: 1394.e1-1394.e2.
5. MacLennan L, Moiemen N. Management of cyanide toxicity in patients with burns. Burns. 2015; 41: 18-24. doi: 10.1016/j.burns.2014.06.001.