Case report

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Use of levocarnitine as an alternative treatment for non-anticoagulant rodenticide poisoning

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Abstract

The objective of this text is to inform and motivate further investigation about the use of levocarnitine as an alternative antidote in patients poisoned by non-anticoagulant rodenticides in a kind of retrospective study through the report of 3 serial cases presented in the Intensive Care Unit (ICU) of the General Hospital Zacatecas 'Luz González Cosío', in Zacatecas, Mexico. Two of them were intoxicated with zinc phosphide and one with sodium fluoracetate, all with similar signs and symptoms. In addition to having received vital support measures in the ICU, levocarnitine was administered intravenously, with remission of symptoms in the short term and hospital discharge without apparent sequelae. Therefore, it is appropriate to consider future research on the use of levocarnitine in this kind of patients, in addition to vital support measures.

Key words: Levocarnitine, antidote, zinc phosphide, sodium fluoracetate, poisoning.

Introduction

Poisoning by rodenticides in humans is currently a health and social impact problem, generally in developing countries, due to its easy access to the public and its high rate of lethality despite measures of life support in Intensive Care Units. Rodenticides can be divided in a practical way into anticoagulants and non-anticoagulants, this article focuses on non-anticoagulants, specifically zinc phosphide and sodium fluor-acetate (generally known as 1080).

Zinc phosphide

At present there is no known antidote and its mortality ranges from 37 to 100%, lethal doses of 80 mg/kg have been proposed. After ingestion the zinc phosphide is metabolized to phosphine gas, which is absorbed into the blood stream through the gastrointestinal mucosa, and then captured by the liver and lungs, (1) producing various toxic effects. The main symptoms are circulatory collapse, hypotension, shock, myocarditis, acute liver failure, acute pulmonary edema and congestive heart failure. Among other manifestations is hyperglycemia, worsening prognosis. The mechanism of action is not entirely clear; it is believed that phosphine gas inhibits mitochondrial respiration. (2) Previous liver transplants have been performed in this type of patients, comparing the results with non-transplanted patients, showing a clear decrease in mortality in patients receiving liver transplantation. (3)

Sodium fluoracetate

The literature deals with a lethal dose of 2-10 mg/kg. When it is ingested, it becomes its active metabolite, the fluorocitrate, which is the cause of inhibition of the Krebs cycle, thereby blocking energy production, causing bio-chemical and physiological manifestations, such as accumulation of citrate and lactic acid, alteration in glucose regulation, hydroelectrolytic imbalance with main affection to calcium, (4) elevation of hepatic transami-

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nases, among others. Patients usually present with a clinical onset with nausea, vomiting and hypotension, with hypotension being one of the markers of worse prognosis in this kind of poisoning, it has been documented that the patients remain in a state of hypovolemic shock despite the fluids administration and inotropic support. Previous studies have shown that the state of shock in intoxication by sodium fluoroacetate is due to the decrease in peripheral vascular resistance and an increase in cardiac output. (5)

Levocarnitine as energetic substrate

Levocarnitine facilitates the transport of the long chain fatty acids from the cytosol to the mitochondria, facilitating the substrates for the oxidation reactions that take place in these corpuscles, with the consequent production of energy for the cell and favoring the cellular respiration. (6) Therefore, levocarnitine plays an essential role as an energetic substrate; its presence in tissues suggests a selective uptake system especially in skeletal muscle, myocardium, liver and kidney. Levocarnitine deficiency causes alterations in lipid metabolism, manifesting a deficient energy production.

Case reports

1. Zinc phosphide poisoning

A 4-year-old male patient was brought to the emergency room for having accidentally ingested zinc phosphide, started with neurological deterioration with a Glasgow of 9, vomiting, tachypnea, tachycardia, hypoglycemia up to 15 mg/dl, added a metabolic acidosis with pH of 6.7 and bicarbonate of 7.7 mmol/L. Also hepatic failure: AST 3279, ALT 3023, DHL 5676. In addition to prolonged coagulation times: TP 30.3, INR 2.44, and TPT 47.7. The patient was admitted to the Pediatric Intensive Care Unit to provide vital support, without clinical improvement. The patient continued with multiple organ failure and a situation of metabolic stress. Intravenous administration of levocarnitine, with improvement of health status, improvement of neurological status, AST 66, ALT 415, with correction of the acid-base balance, and without respiratory difficulty, all of the above within a few hours after administration of levocarnitine 1 g intravenously every 8 hours. The patient was discharged after seven days, for improvement and without apparent sequelae.

2. Zinc phosphide poisoning

A 40-year-old female patient with previously diagnosed major depressive disorder was admitted to the emergency department after ingesting zinc phosphide with suicidal intentions. At the time of admission, there was loss of alertness, Glasgow of 5, sialorrhea, acute pulmonary disease, metabolic acidosis with a pH of 7.0 and bicarbonate of 14 mmol/L, lactate 7.2 mmol/L. She was admitted to the Intensive Care Unit. Endotracheal intubation was performed for mechanical ventilation, fluid resuscitation, and administration of levocarnitine 1 g intravenously every 8 hours, with a considerable improvement in the neurological, pulmonary, and acid-base balance with a pH of 7.42, bicarbonate of 19 mmol/L, lactate 1.4 mmol/L. After 48 hours she was withdrawn for improvement, and was transferred to a psychiatric hospital.

3. Sodium fluoracetate poisoning

A 16-year-old female with a history of body dysmorphic disorder, swallowed sodium fluoracetate for suicidal purposes. She had seizures and was admitted to the emergency room in the postictal period. She was performed arterial gasometry, and presented metabolic acidosis with pH of 7.19, bicarbonate of 13.6 mmol/L, and lactate of 5 mmol/L. In a moment after admission she fell into cardiorespiratory arrest, and was assisted with advanced resuscitation maneuvers for 15 minutes. After achieving a return to sinus rhythm she was intubated for airway protection. Then she was moved to the ICU, where we treated her metabolic acidosis and bradycardia (heart rate 40 beats per minute). Levocarnitine intravenously 1 g every 8 hours was given, which resulting in clinical improvement, pH was 7.36, bicarbonate 18.9 mmol/L, lactate 3.9 mmol/L, and heart rate was improved to 60 beats per minute. She was extubated, and after 72 hours was discharged and transfered to a psychiatric hospital.

Discussion

In the literature we could not find any case reports or studies where levocarnitine was used as an adjuvant treatment in poisoning by non-anticoagulant rodenticides. Phosphine gas can block cytochrome C oxidase, inhibiting oxidative phosphorylation at the mitochondrial level. On the other hand, fluoroacetate enters the tricarboxylic acid cycle, and when combines with co-enzyme A forming fluoroacetyl CoA, which is enzymatically condensed with oxaloacetate by citrate synthase, producing fluorocitrate (instead of citrate) that blocks aconitase because it is more related than citrate to the active site of aconitase, thereby blocking energy production that leading to cell death. It is believed that levocarnitine intervenes or modifies the pathophysiological mechanisms of the agents in ques-

tion, providing the substrates of which the Krebs cycle has been deprived in one of its points. The 3 cases reported seem to support the above, the 3 patients shared severity data and a poor prognosis due to the etiology of their condition, they were provided vital support in ICU without obtaining favorable clinical evolution, until the administration of levocarnitine.

Conclussion

What is exposed through article motivates us and must motivates more colleagues in the medical profession and professionals involved in the health area to do more in-depth research on the mechanisms of action of harmful substances such as non-warfarin rodenticides and their potential antidotes, especially levocarnitine. If this research is carried out with sufficient human and financial resources, we could be faced with a new treatment option for this type of patient, with enough scientific support to be considered as one of the first line treatments.

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