Sodium floracetate’s poisoning, a case report

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Abstract: Sodium floracetate, known as compound 1080, was discovered in Germany during the Second World War. Used as a rodenticide, however, as it is an odorless and tasteless substance, with a lethal dose in humans of 2 mg / kg, it was withdrawn from the market in some countries, including Colombia, however, it is obtained illegally. This substance has biochemical and physiological effects at the cellular level that alter the transport of citrate at the mitochondrial level, generating accumulation of lactic acid and alteration in the use of glucose. The clinical manifestations are nonspecific, there is no cardinal symptom. Therefore, its diagnosis is made due to high clinical suspicion, associated with establishment of exposure to the compound, since paraclinical confirmation is difficult to perform in a timely manner. We present a case report of intentional ingestion in an adolescent, associated added infection to the bloodstream by methicillin- sensitive Staphylococcus aureus (MSSA), who developed multiple complications and the need for support in the Intensive Care Unit (ICU) with satisfactory outcome. Not having a specific antidote, she was treated with ethanol to increase the level of acetate, thus offering an alternative substrate to the Krebs cycle and may offer benefits in the acute treatment of these patients.

Patient with sodium floracetate poisoning and kidney failure, receiving renal replacement therapy with a favorable evolution and survival at discharge from the intensive care unit of a third-level hospital in the city of Pereira, Risaralda, Colombia.

Sodium floracetate poisoning is relatively rare and can cause acute kidney injury and multi-organ failure with a high rate of complications and death. A case of self-inflicted poisoning that received early continuous renal replacement therapy with a favorable outcome in terms of survival and discharge from the intensive care unit of a third-level hospital in the city of Pereira, Risaralda, Colombia was presented.

Key words: Poisons, Poisoning, Toxicological Symptoms, Toxic Substances, Toxicity, Colombia (DeCS).

MeSH Keywords: Poisons, Blood Poisoning, Toxicology, Sodium Fluoroacetate, acute renal failure.

Introducción

Sodium Floracetate (FAS) poisoning poses a diagnostic challenge for healthcare personnel caring for patients with signs and symptoms secondary to toxicity from this compound. Despite being a prohibited substance in Colombia, it is widely used for rodenticidal purposes in the country. There are few reviews on the subject, so it is important to know basic aspects of the substance, mechanism of action, determination methods in the clinical laboratory and management of these patients).

The lethal dose for humans is between 2 and 10 mg / kg. Due to its illegality, the concentrations in commercial products are irregular and therefore it is very difficult to determine the exact dose that the intoxicated people ingested. It is a fat-soluble substance with good oral absorption and with rapid distribution to the tissues after ingestion. The highest concentrations are found in plasma followed by kidney and muscle and the lowest in liver. After the intake of the sodium floracetate, it requires the metabolic conversion of floracetate to fluorocitrate, obtaining increased levels thirty minutes after the intake of floracetate, and with a maximum peak at 4-6 hours, and returning to basal concentrations at 40 hours. Its excretion is renal and takes between one and four days. The main effect of the sodium floracetate was described by Sir John Peters in 1963 consisting of ATP depletion, by inhibition of the tricarboxylic acid cycle or Krebs (KC) cycle. Sodium floracetate reacts with the enzyme citrate synthesize to form monofluorocitrate instead of citrate, a substance that is not a useful substrate for the enzyme aconitate in the Krebs cycle and therefore blocks it. The reduction in oxidative metabolism contributes to lactic acidosis, which, added to the accumulation of ketone bodies, due to the non-oxidation of fatty acids, brings with it an increase in acidosis. Frequently affecting the brain, heart, kidney, spleen, and liver, despite its high metabolism, it accumulates less citrate.

The accumulation of citrate generates an electrolyte and acid-base imbalance, which leads to metabolic acidosis. The accumulation of lactate and cerebral citrate has been considered a cause of coma and seizure in the patient poisoned by floracetate. Hypocalcemia is related to the chelating effect of fluorine, citrate, and fluoracetate ions on calcium.

Initially, most patients are asymptomatic, but in a few hours they will present nausea, vomiting, sialorrhea, mydriasis, and electrolyte imbalances (especially hypocalcemia due to the chelating properties of calcium in sodium floracetate), as occurred in the clinical case described. Central nervous system compromise occurs frequently as a diverse manifestation from drowsiness, vertigo, fasciculations, tremor, seizures and respiratory failure of central origin as occurred in this case. However, the cause of respiratory failure due to community-acquired pneumonia or initial shock is not ruled out. At the cardiovascular level, it manifests with arrhythmias, prolongation of the QTc segment and less frequently myocarditis, 5,6 hypotension that could be due to the blockage of the tricarboxylic acid cycle and acidosis in the vascular epithelium. Death is generally due to cardiopulmonary abnormalities. The diagnosis is made based on a clinical history that confirms the ingestion of substances containing sodium floracetate and the presence of symptoms and signs described by various authors for this toxicosis2,7,8. (Table 1)

Case report:

A 14-year-old patient, with no significant personal or family history, who was admitted to the emergency department referred from the local unit, due to a clinical condition of 7 hours of evolution consisting of voluntary intake of a sodium floracetate for suicidal purposes, in the first level of attention, gastric lavage and oral doses of activated carbon are administered. It evolves inadequately with increased dyspnea and desaturation, which is why it is transferred to the 3rd level of care.

Patient entered the 3rd level of attention in very poor general conditions, desaturated, sialorrheic and with a Glasgow coma scale of 8, fasciculations and hypotension. It was decided to secure the airway due to the risk of bronchoaspiration and the alteration of the state of consciousness. Treatment with ethanol, calcium gluconate is started and transferred to the ICU.

Upon admission to the intensive care unit, patient in poor general conditions, Blood Pressure: 69/40 mmHg, Average Blood Pressure: 50 mmHg, Heart Rate: 116 per minute, Temperature: 36 °C, diaphoretic,
vasopressor support with Norepinephrine was started without achieving blood pressure goals requiring vasopressin to reach the goal during the first 24 hours of evolution. Mechanical ventilation assisted mode volume control, PEEP (Positive end-expiratory pressure) 6 FIO2 100%, glaucometry: 137 mg/dL. Physical examination shows hypochromic conjunctiva, normoreactive isocoric pupils, dry oral mucosa, mobile neck, thorax: rhythmic heart sounds without murmurs, tachycardia, decreased vesicular murmurs in both fields with bibal crepitus, depressible soft pain without peritoneal irritation, extremities without edema, capillary refill 4 seconds neurological RASS -5 (Richmond Agitation Sedation Scale).

Patient who behaves anuricly during the first 12 hours of their stay in the ICU, with levels of nitrogen containing compounds within normal limits, with persistent hyperlactatemic metabolic acidosis, multifactorial, secondary to intoxication per se, use of ethanol as established medical management and kidney injury rapidly progressing to KDIGO III (Kidney Disease: Improving Global Outcomes) acute kidney injury, which is why it was decided to start renal replacement therapy with continuous venovenous hemodialfiltration. And a management protocol was established with ethanol at a dose of 0.1 gr / kg, / hour, calcium infusion at 3 mg / k / h, hydric resuscitation, an antibiotic therapy with continuous venovenous hemodialfiltration. And a management protocol was established with ethanol at a dose of 0.1 gr / kg, / hour, calcium infusion at 3 mg / k / h, hydric resuscitation, and vasoactive support for a target of mean arterial pressure greater than 65 mmHg. And a mechanical ventilation assisted mode volume control, PEEP (Positive end-expiratory pressure) 6 FIO2 100%.

The patient was admitted to an ICU with a diagnosis of sodium fluoracetate poisoning, also known as fluoroacetate poisoning or fluoroacetate intoxication, is a type of toxicological poisoning that results from exposure to the toxic compound fluoroacetate. It is a metabolic poison that was first described in 1940 by the German scientist in the journal Archiv für Toxicologie. The symptoms of sodium fluoracetate poisoning include headache, dizziness, confusion, agitation, and convulsions. These symptoms are caused by the compound's ability to inhibit a key enzyme in the Krebs cycle, which is a process that is responsible for the production of energy in the body.

The table below shows the laboratory results of the patient over the course of the hospital stay:

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td><strong>BLOOD COUNT</strong></td>
<td>White blood count 23130 N 87% Hb 15 HCTO 44 Platelets 329.000</td>
<td>White blood count 11650 N 86% Hb 13 HCTO 38 Platelets 388.000</td>
<td>White blood count 14500 N 75% Hb 11 HCTO 33 Platelets 268.000</td>
<td>White blood count 11350 N 81% Hb 9.2 HCTO 26 Platelets 156.000</td>
<td>White blood count 9700 N 79% Hb 8.1 HCTO 23 Platelets 138.000</td>
</tr>
<tr>
<td><strong>UREA NITROGEN IN BLOOD</strong></td>
<td>15 mg/dl</td>
<td>11 mg/dl</td>
<td>5 mg/dl</td>
<td>5 mg/dl</td>
<td>5 mg/dl</td>
</tr>
<tr>
<td><strong>CREATININ</strong></td>
<td>0.5 mg/dl</td>
<td>1.0 mg/dl</td>
<td>0.4 mg/dl</td>
<td>0.4 mg/dl</td>
<td>0.4 mg/dl</td>
</tr>
<tr>
<td><strong>SODIUM POTASSIUM</strong></td>
<td>144 mmol/L 3.1 mmol/L</td>
<td>137 mmol/L 3.50 mmol/L</td>
<td>131 mmol/L 3.20 mmol/L</td>
<td>131 mmol/L 3.20 mmol/L</td>
<td>135 mmol/L 3.1 mmol/L</td>
</tr>
<tr>
<td><strong>CHLORINE PHOSPHORUS MAGNESIUM CALCIUM</strong></td>
<td>104 mmol/L 6.1 mg/dl 1.9 mg/dl 1.22 Ionic 7.2 mmol/L</td>
<td>105.0 mmol/L 1.6 mg/dl</td>
<td></td>
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</tr>
<tr>
<td><strong>PREGNANCY TEST</strong></td>
<td>NEGATIVE 2.39 mUI/ml</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PCR</strong></td>
<td>18mg/dl</td>
<td>14.9 mg/dl</td>
<td>27mg/dl</td>
<td>24.0 mg/dl</td>
<td></td>
</tr>
<tr>
<td><strong>COAGULATION TIMES</strong></td>
<td>PT 11 Seg. PTT 28 Seg. INR 0.91</td>
<td>PT 19 PTT &gt;240 INR 1.3</td>
<td>PT 25.3 PTT &gt;240 INR 1.68</td>
<td></td>
<td>TOTAL BILIRRUBIN 1.4 TGP 54 U/L TGO 58 U/L</td>
</tr>
<tr>
<td><strong>LIVER PROFILE</strong></td>
<td>AST 56 ALAT 67 U/L Total Bilirubin 0.4 mg/dl</td>
<td>TOTAL BILIRRUBIN 1.0 ALKALINE PHOSPHATASE 115 TGP 62 TGO 99 U/L</td>
<td>TOTAL BILIRRUBIN 0.9 AMYLASE 391 U/L ALKALINE PHOSPHATASE 146 U/L TGP 71 U/L TGO 107 U/L</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ALBUMIN</strong></td>
<td>5.1 gr/dl</td>
<td></td>
<td></td>
<td></td>
<td>2.2</td>
</tr>
<tr>
<td><strong>ARTERIAL GASES</strong></td>
<td>pH 6.98 pCO2 50 pO2 277 HCO3 1 be -19.85 Lactate 7.4 PAFI 277</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ARTERIAL GASES</strong> PH 7.50 PCO2 35 PO2 96 HCO3 27 LACTATE 0.7 PAFI 336 VENOUS SATURATION 67%</td>
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</tbody>
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which was not successful, concomitantly finding febrile episodes and microbiological reports of growth of staphylococcus aureus, therefore which was attributed to a pneumonic process that is covered with an antibiotic scheme. After 10 days of management, the patient is discharged from the intensive care unit with a satisfactory evolution.

**Discussion**

The sodium fluoroacetate known in our environment as liquid “Guayaquil” (Figure 1) and compound 1080 in the United States, was developed in 1940 by Marais when observing the effects produced in the goats, the paralysis of the animal’s posterior train, for which it was called the "rear bankruptcy", it was later used as a rodenticide, considered one of the most toxic substances in the world. It is also a substance that despite its distribution and use is prohibited in Colombia, it is widely used for rodenticidal purposes in the country and in some cases also as a way of committing suicide. In its 100% pure form it is a white powder that, when dissolved in water, forms an odorless, colorless and tasteless solution, it is generally found on the market mixed with a blue dye to differentiate it from other substances. In self-inflicted poisonings and for which patients arrive consciously at the emergency department, the approach is a little easier than those who arrive unconscious, since there is a basic approximation of the substance that was ingested and thus there is a prudent time to calculate when and how the substance will have an effect on the body, in addition to the actions that must be necessary for the management of the patient. This does not mean that patients do not need intensive therapy measures, but in these cases, the minutes become the probability of survival.

![Figure 1: Sodium fluoroacetate “Guayaquil”](image)

**Treatment**

In the case of sodium fluoroacetate poisoning, the initial approach should be carried out as in all intoxicated patients; It is essential to take into account the initial ABCD, determining the need to obtain a definitive airway, correcting hemodynamic instability, and determining the oxygen and glucose supply of these patients. Management of support and correction of hypokalemia is essential. Different antidotes have been studied, however progress in humans is limited. The management of seizures should be done with benzodiazepines, of which diazepam is the most recommended, in the event that the crisis does not stop, barbiturates such as thiopental should be used, which would additionally act as a brain protector, reducing the risk of cerebral edema and local ischemia. In the initial decontamination, the removal of contaminated clothing and external washing with soap and water is essential, as well as gastric lavage should be considered if the patient is admitted with less than 1 hour of oral exposure. Activated carbon has been shown to adsorb fluoroacetate, however, there is no data on the impact on the clinical outcome of these patients. Hemodynamic management should be performed with intravenous fluids, followed by vasopressors (norepinephrine) in cases where hypotension is not corrected. The presence of hypotension, acidemia and creatinine elevation is correlated with high mortality, so these disorders must be managed promptly. The most important electrolyte disorder is hypocalcaemia, which must be properly determined and corrected in these patients: improvement in survival has been found in animals when calcium chloride supplements are administered, although the results are not conclusive. Calcium has been reported to be useful in improving muscular activity (tetanic convulsive movements) and in cardiac arrhythmias.

**Antidotes**

The use of antidotes in sodium fluoroacetate poisoning is based on the need to prevent the production of fluorocitrate and inhibition of aconitase, in addition to achieving mitochondrial citrate output. In this order of ideas, acetate donors such as ethanol and glycerol monoacetate are the most widely used antidotes in the management of this poisoning. Ethanol has shown the best results and is the most used, its oxidation produces elevation of acetate levels, which competes in the formation of fluorocitrate. Several protocols have been proposed for the management with ethanol, it has been described that after the acute administration of fluoroacetate, 40 - 60 cc of 96% ethanol should be administered, followed by 1.0 - 1.5 g / kg of ethanol 5-10% intravenously in the first hour and subsequently 0.1 g / kg every hour for 6 - 8 hours. The exact dose of ethanol has not been determined, the most logical possibility is to achieve a serum ethanol concentration of 100 mg / dl, administering the same doses used in ethylene glycol and methanol poisoning. Ethanol, outside of blocking the production of fluorocitrate, produces a decrease in hyperglycemia and increases GABA levels in the central nervous system. In animal studies, the best results in methanol management are obtained after 10 min of fluoroacetate poisoning. Glycerol monoacetate and acetamide have been proposed as antidotes, animal studies have been developed that demonstrate the effectiveness in decreasing ketone body levels, decreasing citrate in the brain, kidney and heart, improving neurological and cardiac effects. However, in humans an increase in hyperglycemia, worsening of metabolic acidosis, damage to capillaries and erythrocyte hemolysis are noted. Therefore, some reviews do not recommend the use of glycerol monoacetate or acetamide in the management of fluoroacetate poisoning in humans. Other antidotes have been tried to develop, to produce energy by supplying intermediates of the tricarboxylic acid cycle, in addition to blocking the production of fluorocitrate. The use of calcium salts (calcium gluconate), sodium succinate and α-ketoglutarate have been evaluated, which have shown benefit as long as calcium is administered concomitantly, which shows the importance of correction of hypocalcaemia in these patients. The most effective regimen appears to be administering 240 mg / kg sodium succinate and 130 mg / kg calcium gluconate fifteen minutes after administration of fluoroacetate.

**Renal replacement therapy**

There are 3 techniques for eliminating toxins: hemodialysis, hemofiltration, and hemoperfusion. However, hemodialysis is the most adequate to eliminate low molecular weight and water-soluble toxins, being the elimination in this patient. Given the persistence of symptoms, anuria for 12 hours, severe metabolic acidosis, associated with the ingestion of the poison, early initiation of renal replacement therapy was decided. The decision to start this therapy in the case was made due to acute kidney injury and the presence of intoxication with severe clinical manifestations of the toxin, due to the unavailability of a specific antidote and its specification of the renal route, plus the patient was anuric, and it would be perpetuated the symptoms of poisoning.

**Conclusions**

Sodium fluoroacetate poisoning is relatively rare and can cause acute kidney injury and multi-organ failure with a high rate of complications and death. A case of self-inflicted poisoning that received early continuous renal replacement therapy with a favorable outcome in terms
Sodium fluoracetate’s poisoning, a case report

of ICU survival was presented. The favorable outcome of the patient is due to a possible low dose of the toxin, to the implementation of initial decontamination measures, and to early management in the intensive care unit with renal replacement therapy. Long-term clinical outcomes are unknown due to non-follow-up to this case.

Bibliography