

Intoxication by Methemoglobinizing, Propanil type

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Abstract

Intoxications by propanil herbicides are common in different agricultural areas, especially in rice fields. We present the case of a farmer patient, with no risk factors, who suffered moderate propanil intoxication. Despite the diagnostic limitations in each hospital center, the doubts, and the clinical data at the time of admission may be sufficient for the diagnosis and its respective management.

Key Words: Propanil, poisoning, Methemoglobinemia

Resumen: Las intoxicaciones por herbicidas propanil son frecuentes en las diferentes áreas agrícolas, sobre todo en los campos de cultivos de arroz. Se presenta el caso de un paciente agricultor, sin factores de riesgo, quien sufrió una intoxicación moderada por propanil. Pese a las limitaciones diagnósticas en cada centro hospitalario, la sospecha y los datos clínicos al ingreso pueden ser suficientes para la elaboración diagnóstica y su respectivo manejo.

Palabras clave: Propanil, intoxicación, metahemoglobinemia

Introduction

Intoxications have been a public health problem for mankind, this is due to the diversity of natural or chemical substances that can be toxic. Chemical substances include different components such as pesticides, herbicides, among others. According to WHO data, during the 1980s there were more than one million cases of pesticide poisoning, of which 7.3% resulted in death (1). Colombia is one of the countries with the highest intoxication rates due to its large agricultural area and its own production of these substances. According to reports, for the year 2020 about 17,270 cases of poisoning were reported, with the department of Caldas and its capital, Manizales, being the most affected (2). Although herbicide poisonings usually represent a small number of consultations in the emergency department in urban areas, in hospitals near rural areas the number of cases is higher, given the diversity of agricultural activities. Propanil is one of the most frequently used herbicides for rice cultivation and, according to the Colombian Ministry of Social Protection, this herbicide is classified as slightly hazardous to human health (toxicological category III) (3). Although mortality is usually low, this may vary depending on the chemical compound, the level, and the route of exposure. Therefore, a rapid recognition of the substance of concern is helpful in initiating management. This article presents the case of a patient in the city of Yopal, Casanare with herbicide intoxication (propanil).

Clinical case

A 45-year-old male patient with no previous history of relevance, agricultural profession, who was referred to a primary care center due to clinical symptoms of 12 hours of evolution consisting of hyporexia, headache, vertiginous symptoms, dyspnea, polypnea, cyanosis at the level of the fingertips of both hands and tongue (Figure 1).

The patient reported having finished spraying herbicide (Propanil) and subsequently presented symptoms. Vital signs on admission: HR 114 bpm, RR 45 rpm, BP 155/90mmhg, T 36C, SaO₂: 88%. Therefore, the patient was considered to be with suspected poisoning by methemoglobinizing agent "propanil" and medical management with methylene blue 1 mg/kg was started.

Figure 1. (A): Evidence of slate-gray skin color associated with cyanotic at lingual level, which does not respond with oxygen therapy. (B): Cytophilic with evidence of urine with blue-greenish coloration after administration of methylene blue.



Table 1 and 2 below show the admission and control paraclinics:

Table 1. Arterial gases on admission

Arterial gases	
pH	7,46
PCO2	41
PO2	86
FIO2	28
BE	5,2
HCO3-	29,2
PaO2/FiO2	307

«The patient reported having finished spraying herbicide (Propanil) and subsequently presented symptoms.» ➤

Table 2. Admission paraclinical tests (A) and control paraclinical tests at 48 hours (B).

Paraclinics	A	B
Leukocytes	9990	7820
Neutrophils	89%	48.5%
Lymphocytes	8%	36.8%
Hemoglobin	15	12.8
Hematocrit	44%	39,2
Blood platelets	272.000	232.000
Sodium	137	140
Potassium	3,9	4.1
Creatinine	1,07	0.9
Bun	11.6	16.1
Glucose	207	XX
AST	49	29
ALT	27	20
SARS COV -2	Negative	
Serum Cholinesterase	6722	XX

Figure 2 below shows the ECG performed on the patient:

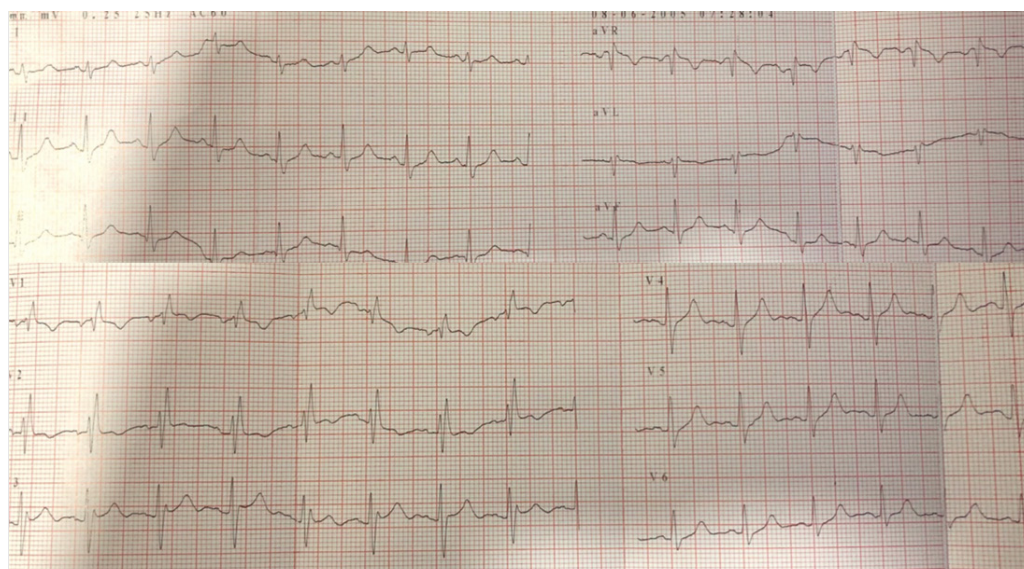


Figure 2. 12-lead ECG, evidence of sinus axis normal rhythm, no alterations at the P wave or PR segment level, QRS with block pattern. Incomplete right bundle branch block, no alteration of the ST segment or T wave.

Discussion

Poisoning by chemical substances has been a subject analyzed for thousands of years. Hippocrates described it for the first time when he found a bluish coloration in patients who consumed meats cured with root extracts(4). At that time, it was not known that cured meats had nitrites among their components, substances capable of causing intoxication and generating methemoglobinemia, which reduces the capacity to transport oxygen by various associated chemical mechanisms (5).

On the other hand, in 1952 the use of herbicides for the control of diverse weeds was introduced for the first time, since then reports of cases of intoxication began. These chemical compounds are categorized as pre-emergent and post-emergent, with propanil being part of the latter group (6). According to the Colombian Ministry of Social Protection, this herbicide is classified as slightly hazardous to human health. Its intoxication depends on exposure in time and quantity.

Hemoglobin is a tetrameric compound consisting of two heme groups and two globin chains. The iron of the heme group, under normal conditions, is in the ferrous state (Fe^{+2}), however, upon exposure to propanil, the active metabolite 3,4-dichloroanilide makes it susceptible to oxidation by changing its valence to the ferric state (Fe^{+3}), which leads to the formation of methemoglobin and therefore a reduction in tissue oxygen transport capacity (4)(7).

Under normal conditions methemoglobin levels oscillate in the range of 1 to 2% (8)(9), this is due to multiple enzymatic processes at cellular level (erythrocyte) such as methemoglobin reductase and the nicotinamide adenine dinucleotide NADH system, which help in reduction and electron transport processes. Thus conditioning a reduction of methemoglobin levels, all in order to maintain these values within the limits described above (10).

The symptoms depend on the degree of exposure and the level of methemoglobin in the blood (11). Several authors categorize severity according to the percentage of this compound in the bloodstream (See Table 3).

«According to the Colombian Ministry of Social Protection, this herbicide is classified as slightly hazardous to human health.»



Table 3. Severity levels according to percentage of methemoglobin in the bloodstream.

Methemoglobin <30%	MILD	Headache, fatigue, weakness, dizziness, cyanosis, slate-gray skin. 18% may be asymptomatic.
Methemoglobin 30 - 50%	MODERATE	Vomiting, abdominal pain, syncope, increased respiratory distress.
Methemoglobin 50 - 70%	SEVERE	Bradycardia, seizures, cardiac arrhythmias, metabolic acidosis, coma and cardiorespiratory arrest
Methemoglobin >70%	DEATH	Asystole

In the case presented, dermal and inhalation exposure was the mechanism of intoxication of the patient, presenting moderate symptomatology, as described in the literature. Most of the diagnosis of herbicide intoxication is made by the history of exposure and the clinical presentation of the patient, as shown in the case described.

The measurement of methemoglobin levels in blood is a very useful tool for the confirmation of the diagnosis; however, few health centers have the necessary technological equipment for its processing. For this reason, other methods are used which, although they do not confirm the diagnosis, help to evaluate the patient's functional status. A clear example is arterial blood gas analysis, which can be seen in some cases without alterations or show slight changes.

In the clinical case described, there is evidence of mild metabolic alkalosis, without oxygenation disorder, which compared to the clinical picture presents no correlation since the patient persisted cyanizing despite the use of oxygen therapy. On the other hand, SaO₂% values do not allow an adequate correlation due to the wavelength censored by the transducer on methemoglobin, since it is similar, which could give us a false impression of these values to direct therapy (6)(12).

On the other hand, if propanil intoxication is suspected, treatment should be initiated as soon as possible, which is based on the use of methylene blue as an antidote at doses of 1-2 mg/kg and a second dose can be repeated (13). However, given the scarce bibliographic material, the use of this drug is recommended in cases of intoxication with methemoglobin values below 20% and the presence of symptoms or in the absence of symptoms with levels >30%. In spite of the fact that methemoglobin levels were not

taken in our institution, the clinical history, the symptoms presented and the absence of response to oxygen therapy were characteristic of methemoglobinizing intoxication, for which the use of this drug was indicated, showing adequate clinical response (9)(12).

There are other techniques such as stomach cleansing or the use of activated carbon that have not been shown to reduce the absorption of these compounds, lacking effectiveness in the clinical setting (6). On the other hand, the use of vitamin C has not established a significant reduction in methemoglobin levels, therefore, its use requires further studies (4) as well as the use of exsanguinotransfusion (14)(15).

Conclusion

In propanil intoxication, the patient's symptoms and history are key to initiate treatment. Likewise, the mechanism and time of exposure to the agent will intervene in the clinical presentation of the patient. Finally, there are several treatments, such as activated carbon, gastric lavage, ascorbic acid, among others. However, methylene blue has more studies and greater verification of its usefulness in these cases.

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