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Occupational Lead Poisoning in Patients Attended at a University Hospital in Minas Gerais

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Abbreviations:

δ: Delta; ALLAH: δ -aminolevulinic acid; WING-D: δ-aminolevulinic acid dehydratase; ALA-U: Urinary δ -aminolevulinic acid; BAL: Dimercaprol; COPRO: Coproporphyrinogen; DNA: Deoxyribonucleic acid; EDTA: Ethylenediaminetetraacetic acid; PPE: Personal protective equipment; FUNED: Ezequiel Dias Foundation; GABA: Gamma-Aminobutyric Acid; GEP: Teaching and Research Management; HC: Clinical Hospital; IBPM: Maximum Allowed Biological Index; mcg/dL: Microgram per deciliter; mg/g: Milligram per gram; NR7: Regulatory Standard 7; Pb: Lead; Pb(s): Serum lead; PCMSO: Occupational Health Medical Control Program; SAME: Medical Archive and Statistics Service; SEST: Special Occupational Health Service; TCLE: Informed Consent Form; UFMG: Federal University of Minas Gerais

1. Summary

Lead is a heavy metal that has been used since ancient times, including in the production of wine with the aim of sweetening and reducing acidity. In the 1920s, this compound was added to gasoline, believing that it would result in better functioning of the automobile engine. These two applications were later interrupted due to knowledge about the risk of human and environmental toxicity. Even today, it is a material present in several areas, both in production and recycling, and worker contact with lead leads to the occurrence of poisoning (saturnism), which leads to symptoms resulting from its action on various systems and tissues of the human body. which is harmful. The main cause of the development of saturnism in adults is exposure during work activities, often favored by the precariousness of the workplace, which highlights the importance of using personal protective equipment. The objective of this work was to analyze medical records of patients treated at the UFMG University Hospital between 2003 and 2018 with a diagnosis of saturnism due to occupational exposure. The results found showed patients were all male and had incomplete primary education as the predominant level of education. Clinical management included regular measurements of serum lead and acid.-aminolevulinic acid and the symptoms presented corroborate those described in the literature. Of the eighteen cases analyzed, five had intervention with chelation therapy, of which two were discharged due to case resolution and normalization of serum lead as recommended by the Ministry of Health protocol, with serum levels <40 mcg/dL. Of the other three, one is still being monitored at the service, one has returned to work in activities without contact with lead and the last has returned to the same occupational activities before the saturnism was controlled.

2. Introduction

Lead (Pb) is a heavy metal widely used in the industrial area due to characteristics that facilitate its use, such as softness, malleability and low melting point (FLORA et al., 2012). The battery market is the largest consumer of the metal (WINCKEL and RICE, 1988), and the recycling process of these materials causes the release of

waste that contaminates the environment (FERNANDES et al., 2011). Workers' exposure to metal leads to an increased risk of developing poisoning, which is the main cause of saturnism in adult patients (JACOB et al., 2002). Poisoning is considered when serum metal values are above 40 µg/dL (BRASIL, 2006). In addition to being an exogenous compound and not essential to the human body, (CORDEIRO, 1995; XIE, 1998; JACOB, 2002), lead is not metabolized and can accumulate in different compartments in the body with a varied half-life. It can remain in the bone matrix for years, and is also found in serum levels for 36 days and in soft tissues for 40 days (PAPANIKOLAOU, 2005; GRACIA, R.C..; SNODGRASS, W.R.. 2007, MOREIRA and MOREIRA, 2004; CLARCK et al., 2010).

Some manifestations of acute poisoning include symptoms such as paresthesia, muscle weakness, encephalopathy, coma and general pain. In the case of the chronic form, it is possible to find the development of anemia, problems related to sleep, irritability, difficulty speaking and kidney failure. In common with both occurrences, there may be headache and convulsions (PEARCE, 2007). Furthermore, there may be damage to other systems such as the renal, hematopoietic, hepatic and central nervous systems (KALIA and FLORA, 2005; ASSUNCAO, ABREU & NUNES, 2020; SOUZA & SANTOS, 2019; ALMEIDA & SANTOS, 1986, VOLTARELLI et al., 2022).

At the level of the hematopoietic system, lead is capable of acting with enzymatic inhibition of the acid-aminolevulinic dehydratase (ALA-D), causing acid accumulation-aminolevulinic (-ALA) which can be detected in both blood and urine (SOUZA, 2009). In this way, the dosage of acid. Urinary δ-aminolevulinic acid (ALA-U) is a method used for diagnosis and monitoring of the clinical picture together with the history of exposure, serum lead levels and the signs and symptoms presented. Detoxification treatment is normally carried out using chelating agents, the most common being dimercaprol (BAL), D-penicillamine and ethylenediaminetetraacetic acid (EDTA) (CAPITANI, 2009; SCHIFER et al, 2005; GUERRA and SILVEIRA, 2010), presented in the form of disodium calcium edetate or calcium versenate (BRASIL, 2006). Chelation can lead to a reduction in plasma concentration and metal reserves in bones (LIMA et al, 2012), forming acovalent bond with the metal (MONTEIRO et al., 2013), removing it from the environment in which it is found from the formation of a more stable complex (SÁ, 2018).

Lead (Pb) is a heavy metal widely used in the industrial area. Exposure in the workplace generates cases of poisoning known as saturnism and, therefore, the toxicological manifestations of the metal are being studied and well determined. Its use occurs mainly in the fields of automobiles, batteries, plastics, ceramics, solders and paints due to characteristics that facilitate its use, such as softness, malleability and low melting point (FLORA et al., 2012). In the 1920s, after studies of the automobile industry, tetraethyl lead was also added to gasoline with the aim of increasing the development of the automobile engine (ROSNER and MARKOWITZ, 1985). However, its incorporation into fuel was later stopped due to the perception of its negative impact on human health and the environment (LÖFGREN and HAMMAR, 2000). The battery market is the largest consumer of the metal (WINCKEL and RICE, 1988) and the recycling process of these materials causes the release of waste that contaminates the environment (FERNANDES et al., 2011). Furthermore, the exposure of workers to metal leads to an increased risk of developing poisoning, and corroborates the literature in which it is described that occupational exposure represents greater importance among cases of saturnism in adults (JACOB et al., 2002). Absorption occurs differently depending on the presentation of the compound. For the organic form, this process can occur through the skin due to the lipid solubility characteristic, which even favors its arrival to the central nervous system (TEIXEIRA et al., 2004). In the case of inorganic presentation, the main routes are gastrointestinal and inhalation, the latter being important for occupational cases (ATSDR, 2007; CAPITANI, 2009), as there may be inhalation of particles formed during activities involving handling lead-containing material. Therefore, to avoid or at least minimize the occurrence of poisoning, it is necessary for workers to use personal protective equipment (PPE) and the work environment to provide adequate ventilation and movement conditions, in addition to working hours that do not exceed the recommended in legislations. In addition to being an exogenous compound and not essential to the human body, (CORDEIRO, 1995; XIE, 1998; JACOB, 2002), lead is not metabolized and can accumulate in different compartments in the body with a varied half-life. It can remain in the bone matrix for years, and is also found in serum levels for 36 days and in soft tissues for 40 days (MOREIRA and MOREIRA, 2004; CLARCK et al., 2010). Some manifestations of acute poisoning include specific symptoms such as paresthesia, muscle weakness, encephalopathy, coma and general pain. In the case of the chronic form, anemia, problems related to sleep, irritability, difficulty speaking and kidney failure can be found. In common with both occurrences, there may be headache and convulsions (PEARCE, 2007). Furthermore, there may be damage to other systems such as the renal, hematopoietic, hepatic and central nervous systems (KALIA and FLORA, 2005). Some symptoms are illustrated in (Figure 1).

At the level of the hematopoietic system, lead is capable of acting with enzymatic inhibition of the acid-aminolevulinic dehydratase (ALA-D), causing acid accumulation-aminolevulinic (-ALA) which can be detected in both blood and urine (SOUZA, 2009). In this way, the dosage of acid. Urinary δ-aminolevulinic acid (ALA-U) is a method used for diagnosis together with the history of exposure, serum lead (Pb(s)) levels and the signs and symptoms presented. The route for the synthesis of the HEME group

and the possible points of inhibition by lead are shown in (Figure 2). Along with these enzymes, COPRO oxidase can also be interfered with by lead. The final consequence of the reduction in heme production is the appearance of anemia and fatigue, since there is a decrease in the production of the group for hemoglobin and cellular respiration (PATRICK, 2006). Furthermore, the increase in ALA, which is also an agonist of synaptic GABA receptors, causes selective competition with the acid-aminobutyric acid leading to a reduction in the release of the neurotransmitter by pre-synaptic inhibition (NEEDLEMAN, 2004). Intoxication is considered when Pb(s) values are above 40 mcg/dL and ALA-U is greater than 4.5 mg/g of creatinine. OMaximum Allowed Biological Index (IBPM) is 60 mcg/dL and 10 mg/g of creatinine respectively, according to Regulatory Standard 7 (NR7) referring to the Occupational Health Medical Control Program (PCMSO) of Ordinance No. 24, of December 29 1994(BRAZIL, 1994). The pharmacological management for saturnism is the performance of chelation cycles, with the most commonly used in Brazil beingethylenediaminetetraacetic acid (EDTA) in the form of calcium versenate (EDTACaNa2), dimercaprol (BAL) andD-penicillamine (CAPITANI, 2009). The chemical structures of these agents are illustrated in (Figure 3). The resulting reaction is a covalent bond with the metal (MONTEIRO et al., 2013), removing it from the environment in which it is found through the formation of a more stable complex (SÁ, 2018).

The desirable characteristics for a chelating agent include being highly hydrophilic, having high affinity for the compound to be chelated, low toxicity since the adverse effects (Table 1) become a limitation for the use in therapeutics, ability to reach metal storage sites and compete with natural chelating agents (SÁ, 2018). The indication for this type of intervention occurs when the patient is symptomatic and has serum lead above 60 mcg/dL (BRAZIL, 2006). In Brazil, there is no record regarding the number of individuals who were exposed to metal, whether occupationally or environmentally (BRAZIL, 2006). Carrying out studies means that cases are reported through the development of research, which ends up highlighting the incidence of poisoning. However, as there is no reliable statistics or a database with records of the occurrence of saturnism, this type of poisoning may end up not receiving attention at the level at which it is needed and the incidents may be underreported. The objective of this work includes analyzing the clinical, occupational and socioeconomic profile, as well as the management of the clinical conditions of patients treated at the Special Occupational Health Service due to lead poisoning according to occupational exposure. Cases that were being monitored between 2003 and 2018 were included, regardless of the year of diagnosis and entry into the SEST/HC/UFMG service. The data collected pointed out the most common forms of contact that trigger saturnism, the frequency of referral to care services at the University Hospital as a result of this poisoning, which tests were carried out for diagnosis and the procedures adopted, observing the main treatment used. In addition, information was recorded regarding the previous socioeconomic and clinical profile, as well as the conditions of the work environment and exposure time. Gathering this data allows inference of the way in which work activities are carried out. Due to the fact that contact and the occurrence of poisoning by heavy metals is a health problem present throughout the world, the objective of this study was to analyze medical records of patients treated at a University Hospital in Minas Gerais between 2003 and 2018 with a diagnosis of saturnism due to occupational exposure with a view to supporting decision-making on changes and improvements to be implemented.

3. Methods

This was a retrospective and descriptive study in which medical records of patients who were treated at a University Hospital in Minas Gerais from 2003 to 2018 were analyzed, regardless of the year of diagnosis, including the first consultation and return visits, seeking those who had poisoning due to occupational exposure. The project was submitted and approved by the Research Ethics Committee (CAAE 91160618.8.0000.5149), with exemption from presenting the Informed Consent Form (TCLE). The medical records who had an electronic record of care, initially 26 cases were identified, of which 18 met the inclusion criteria, determined as being over 18 years of age and whose exposure was only through occupational means. The collection of socioeconomic, occupational and clinical information was recommended, such as the patient's age, sex, alcohol consumption and smoking, education, income, mode and time of exposure to the metal, use or not of personal protective equipment (PPE), requested exams, main symptoms, previous existing comorbidities, therapy used and general evolution of the case.

Figure 1: Symptoms that may occur as a result of lead poisoning

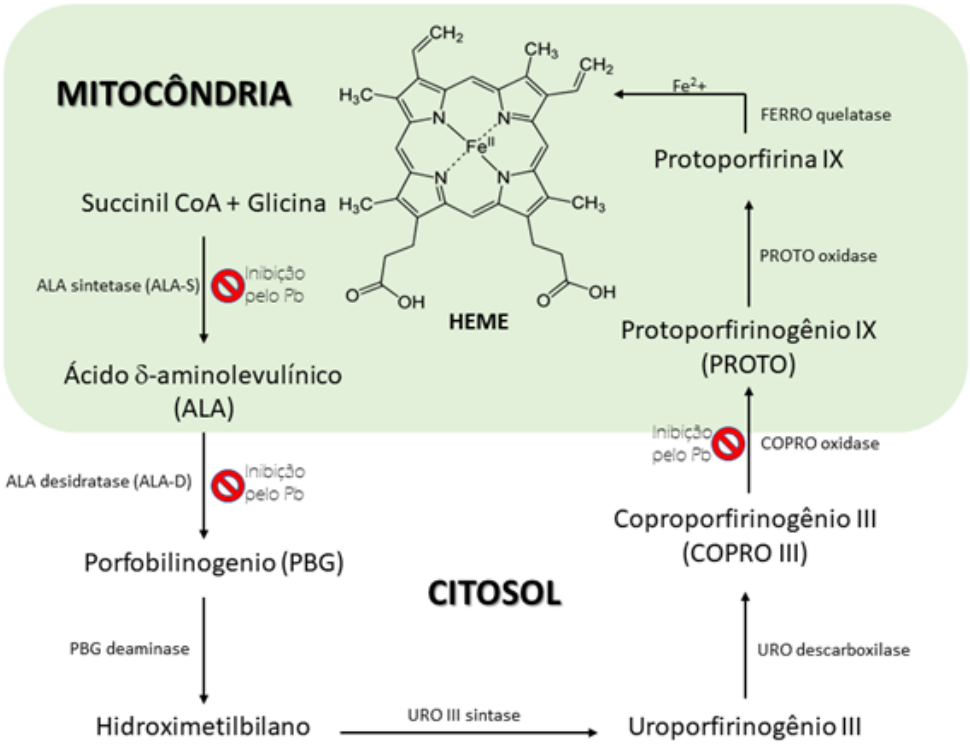
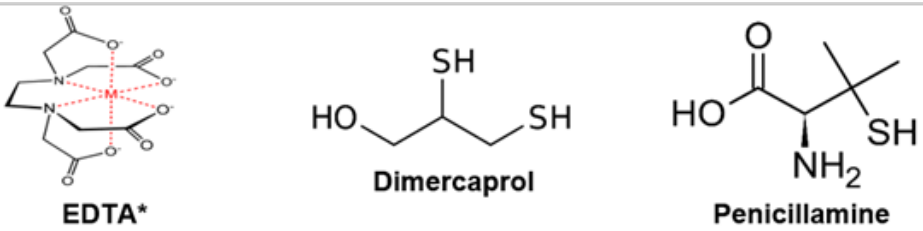


Figure 2: Own preparation - Schematic of the synthesis of the HEME group with the possible inhibition pathways by lead *Pb – Lead; †Fe2+ - Bivalent iron.



*EDTA -ethylenediaminetetraacetic acid -for reaction with the metal, exemplified by the letter M.

Figure 3: Chemical structure of the three chelating agents

Table 1: Adverse effects and contraindications in the use of chelators

	EDTA*	DIMERCAPROL	PENICILLAMINE
POSSIBLE ADVERSE EFFECTS	Hypercalcemia, zinc deficiency, anorexia, nausea, vomiting, diarrhea, fatigue, nephrotoxicity, nasal congestion.	Hypertension, tachyarrhythmia, contact dermatitis, injection site pain, rash, skin finding, increased body temperature, abdominal pain, vomiting, hemolytic anemia, headache, paresthesia, tremor.	Alopecia, erythroderma, extravasation injury, nail damage, pemphigus, rash, toxic epidermal necrolysis, urticaria.
CONTRAINDICATIONS	Anuria, hepatitis, active kidney disease.	Liver failure (except postvenous jaundice)	Breastfeeding, during pregnancy, except for the treatment of Wilson's disease and certain cases of cystinuria, hypersensitivity to penicillamine products, penicillamine-related aplastic anemia/ agranulocytosis, rheumatoid arthritis patients with a history or evidence of renal failure.

Source: Own preparation with information from the Micromedex®28 database.
*EDTA -ethylenediaminetetraacetic acid.

4. Results

Of the 18 cases included in the study, the patients were all male (100%) with a mean age of 36 years. The results (Table 2) predominant ones showed education with the incomplete 1st degree (55.6%), income between 1 and 2 minimum wages (33.3%), presence of alcohol consumption (50.0%) and non-smoking (44.4%). According to the occupational characteristics of the patients, eight (44.5%) had exposure to the metal for a period between one and ten years, with 14 (77.8%) using some type of personal protective equipment. Furthermore, 13 (72.2%) had no previous health problems or they did not make chronic use of medication. The main lines of work included activities that required some type of handling of automotive batteries (61.1%), with one of the workers recycling this material independently in his own home. The average initial blood pressure found was 79.31 µg/dL, with the lowest value being 47.65 µg/dL and the highest being 99.90 µg/dL. Among the diagnostic procedures, laboratory tests were requested to measure serum lead andacid-urinary aminolevulinic acid, mostly carried out by the Minas Gerais Public Health Laboratory (Lacen/MG) of the Ezequiel Dias Foundation (FUNED). A complete blood count, urea, creatinine, creatinine clearance, uric acid and determination of renal function were also requested. Once the diagnosis of occupational poisoning was confirmed, the request to leave the workplace so that exposure could cease was the main non-pharmacological approach used. Among the cases, five required chelation cycles with calcium versenate (EDTACaNa2), and the initial blood pressure in these patients had an average of 77.86 mcg/dL. Of the eighteen patients, nine (50.0%) were discharged due to blood lead levels <40 µg/dL, two (11.1%) were still being monitored, six (33.3%) did not adhere to the treatment protocol and one (05.6%) was transferred for follow-up at a health service in another city.

Table 2: Results that characterize the sociodemographic, behavioral, occupational and clinical profile of patients

Sociodemographic Characteristics	**Total, n (%)**
Average age (in years)	36
Sex	
Masculine	18 (100%)
Feminine	0 (0%)
Education level	
Incomplete 1st degree	10 (55.6%)
1st degree complete	3 (16.7%)
Incomplete 2nd degree	3 (16.7%)
complete 2nd degree	2 (11.1%)
Income	
Between 1-2 minimum wages	6 (33.3%)
Between 2.5-3 minimum wages	4 (22.2%)
≥ 3 minimum wages	2 (11.1%)
Not declared	6 (33.3%)
Behavioral Characteristics	
Alcoholism	
alcoholic	9 (50.0%)
Non-alcoholic	6 (33.3%)
Former alcoholic	2 (11.1%)
Not declared	1 (05.6%)
Smoking	
Smoker	6 (33.3%)
Non-smoker	8 (44.4%)
Former smoker	3 (16.7%)
Not declared	1 (05.6%)
Occupational Characteristics	
Average initial blood pressure (in µg/dL)	79.31
Lead Exposure Time	
< 1 year	4 (22.2%)
Between 1-10 years	8 (44.5%)
≥ 10 years	6 (33.3%)
Use of Personal Protective Equipment	
Yes	14 (77.8%)
No	2 (11.1%)
Not declared	2 (11.1%)
Clinical Features	
Previous Health Problem	
Yes	5 (27.8%)
No	13 (72.2%)
Chronic Medication Use	
Yes	5 (27.8%)
No	13 (72.2%)

5. Discussion

Our findings made it possible to evaluate the follow-up of cases of saturnism due to occupational exposure. The main symptoms reported by patients included discomfort in the upper and/or lower limbs (72.2%), abdominal pain/colic (50.0%), headache (33.3), tiredness, weakness, sleep difficulties, weight loss and anorexia (22.2%). The others presented less frequently included chronic diarrhea, anemia, arthralgia, tremors, constipation, back pain, epigastric pain, excessive heat, flank pain, cramps, hyporexia, neck pain, sweating and joint pain, each of which was mentioned by only one of the patients appearing, therefore, in only 05.6% of cases. For those who used personal protective equipment, the most reported devices were face masks with filters (72.2%), which were exchanged at different intervals between companies, varying between three days and daily. Gloves (61.1%), boots (38.9%), aprons (22.2%), ear protectors (16.7%), uniform (11.1%) and glasses (05.6%). The use of this equipment is extremely necessary, especially when it comes to protecting the respiratory tract, since the main route of absorption in this environment is inhalation (CAPITANI, 2009). Follow-up periods varied depending on each case, with an average of 2.9 years among the fifteen patients in which the time could be calculated. Consultations were maintained until blood lead levels returned to normal. After discharge, return visits occurred at a six-month interval to check serum metal levels. The conduct of removal from the workplace is indicated to achieve two consecutive serum levels below 40 µg/dL. However, patients' non-adherence makes it impossible to carry out chelation therapy, as exposure would continue to be maintained. The practice of battery recycling being carried out autonomously and, in the home, allows exposure not only to the worker, but also to other residents, increasing the chances and the number of people susceptible to developing poisoning. Despite being compulsory to report, it is believed that some cases are not reported, sometimes because the patient does not seek help. Research with this focus also serves to highlight the clinical form of manifestation as well as the means by which it occurs and the interventions that can be carried out for saturnism. At work "Exposure to chemical agents at work in Brazil: results from the National Health Survey (Brazil,2013) reports the prevalence of self-reported exposure to chemical substances at work in a sample of Brazilian adults. This can be correlated with the findings of This one study, where patients reported symptoms of saturnism due to occupational exposure. The prevalence of exposure to chemical substances at work, as described in work, may be an indicator of the risk of developing saturnism. In the article "Saturnism after accident caused by a large-caliber firearm: case report" (SILVA, SANTOS & OLIVEIRA, 2019) describes a clinical-surgical case of saturnism due to a firearm accident in a male patient with exposure to multiple fragments and limit levels of blood lead. Although the context is different (firearm accident versus occupational exposure), the clinical manifestation of saturnism it is similar. Therefore, the symptoms reported in this case can be compared to the symptoms reported by patients of this study

6. Conclusion

Due to lead poisoning affecting the health status of the exposed individual, referral to specialized centers is of great importance for monitoring the general clinical condition. By analyzing the medical records, it was possible to observe that saturnism leads to the need for frequent consultations to monitor metal levels, as well as verify the resolution of the symptoms presented. Due to the fact that contact and the occurrence of poisoning by heavy metals is a health problem present throughout the world, studies are necessary to increasingly cover methods of avoiding or at least reducing these occurrences, as well as defining clinical and therapeutic management to minimize the impact of symptoms on the lives of intoxicated individuals.

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