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BIOCHEMICAL SUFFOCANTS: CARBON MONOXIDE AND CYANIDE

ASFIXIANTES BIOQUÍMICOS: MONÓXIDO DE CARBONO Y CIANURO

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ABSTRACT

Objective: Gas poisoning, both voluntary and involuntary, has a high incidence and is often accompanied by high mortality. Occupational exposures and fires are the most common sources of inhalation injury. Chemical suffocants are substances that cause oxygen deficiency without interfering with respiratory mechanics, altering biological oxidative mechanisms. Among the main chemical suffocants are carbon monoxide and cyanide, which act by altering cellular respiration by blocking mitochondrial enzymes. When inadequately exposed to both gases, they can cause symptoms ranging from mild and nonspecific symptoms to alterations at the neurological and cardiovascular levels or even death within minutes. **Conclusion:** It is important to know the comprehensive management of patients poisoned by biochemical suffocants, in the case of carbon monoxide, the proper use of oxygen and support measures, and in the case of cyanide, the antidotes and their correct administration, to reduce mortality and sequelae.

Keywords: Poisoning; Carbon monoxide; Cyanide; Emergency medicine.(Source: MeSH NLM)

RESUMEN

Objetivo: La intoxicación por gases, tanto voluntaria como involuntaria, presenta una elevada incidencia y muchas veces se acompaña de una alta mortalidad. Las exposiciones ocupacionales y los incendios son las fuentes más comunes de lesiones por inhalación. Los asfixiantes químicos son sustancias que causan una deficiencia en oxígeno sin interferir con la mecánica respiratoria alterando los mecanismos oxidativos biológicos. Dentro de los principales asfixiantes químicos se encuentran el monóxido de carbono y el cianuro que actúan alterando la respiración celular a través de bloqueos de enzimas mitocondriales. Al exponerse de manera inadecuada a ambos gases, éstos pueden causar desde síntomas leves e inespecíficos hasta alteraciones a nivel neurológico y cardiovascular o incluso la muerte en minutos. **Conclusión:** Es importante conocer el manejo integral de los pacientes intoxicados por asfixiantes bioquímicos, en el caso del monóxido de carbono el uso adecuado de oxígeno y medidas de soporte y en el caso del cianuro los antídotos y su adecuada administración, para así disminuir la mortalidad y las secuelas.

Palabras clave: Intoxicación; Monóxido de Carbono; Cianuro; Medicina de Emergencia. (Fuente: DeCS BIREME)

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INTRODUCTION

A toxic substance is a substance of a chemical nature that, depending on the concentration it reaches in the organism, and the time in which this happens, acts on biological systems causing morphological, functional, or biochemical alterations [1]; Generally, brings with it harmful effects that can range from mild to fatal, which is why they have come to be considered by some as "multiple traumas of chemical origin" [2]. In a high percentage of poisoned patients, basic support accompanied by adequate fluid, electrolyte, and acid-base resuscitation is usually sufficient for stabilization [3,4]

Poisoning is considered a growing public health problem in most countries. Every year many people die as a result of poisoning, most of them being preventable and avoidable. In Mexico, they are the cause of around 13.600 hospital discharges that originate 34.900 days of hospital stay [5], As a consequence, 1.400 people die, 87% adults and 13% children6. 72% of cases are accidental and 28% correspond to suicide. In adults, mortality due to accidental poisoning occurred: in the first place due to the intake of medications (21.6%), inhalation of toxic gases (20.4%) ranked second, and exposure to pesticides (13.9%) third. In children, the first place was due to inhalation of toxic gases (41.8%), followed by the intake of medications (18.3%), and exposure to pesticides (13.1%) [7]. The repercussions that these phenomena have on the material losses and particularly on human lives are evident, conditioning sequels in the survivors.

Biochemical suffocants are substances that cause oxygen deficiency without interfering with the mechanics of respiration, either by displacing oxygen from the air (simple suffocants) or by altering biological oxidative mechanisms (chemical suffocants)[1].

CARBON MONOXIDE POISONING

The world has experienced some very important changes in the epidemiology of carbon monoxide (CO) poisoning, but it remains one of the world's leading toxicological causes of morbidity and mortality[6].

CO is a colorless, odorless, and tasteless gas that is produced during the incomplete combustion of various organic materials containing carbon[8].

SOURCES

The human body continually produces small amounts of CO, as one of the end products of the catabolism of hemoglobin and other heme groups. In physiological amounts endogenous carbon monoxide functions as a neurotransmitter. At low concentrations, CO could favorably modulate inflammation, apoptosis, and cell proliferation, in addition to regulating mitochondrial biogenesis. Thus, it is normal for a healthy individual to have a carboxyhemoglobin (COHb) saturation of one to 2% of total hemoglobin[8].

Exogenously, CO is produced by the combustion of carbon-containing materials in oxygen-poor environments. The eight-hour average upper exposure limit for carbon monoxide concentration should not exceed 50 ppm[9]. The industry constitutes 20% of the total production of CO, the most exposed workers are metal workers, miners, mechanics, and warehousemen. At the domestic level, the production of carbon monoxide originates from water heaters, stoves, fireplaces, and radiators that use butane, propane, or natural gas as fuel[8].

The fire remains the most common cause of death from carbon monoxide poisoning. In a fire, a carbon monoxide concentration of 100,000 ppm can be reached[10]. With Tobacco use, the smoke of which contains approximately 400 ppm, A person who smokes approximately one pack a day can reach COHb levels of five to 6%[11].

Household and industrial sprays and stain removers that contain dichloromethane, a solvent substance that metabolizes, after being inhaled, slowly into carbon monoxide is another source of exposure[10].

Exposure to CO from methyl chloride contained in paints and aerosols has also been reported. The risk of CO poisoning as a result of hookah smoking has become a frequent etiology in recent years [12,13]. Fatality depends on the time of exposure to carbon monoxide and its concentrations, which is crucially affected by the toxicity of other gases involved[14].

EPIDEMIOLOGY

The most recent available estimates of the incidence of CO poisoning in the United States, based on emergency department admissions, are 20,000 to 50,000 cases per year. Recent studies show a decreasing number of carbon monoxide deaths, however, in Germany they have increased [15]. Although the statistics are imprecise in Mexico, it is inferred that in fire situations up to 50% of the victims die from poisoning by suffocating gases and vapors, among which is CO, that emanate from the type of material in combustion. The vast majority are of accidental origin, motivated among other things by the lack of a prevention culture[16].

TOXICITY MECHANISMS

Once carbon monoxide is inhaled, it diffuses rapidly through the alveolar membranes to combine with hemoglobin (Hb) and cytochrome C oxidase, among other hemoproteins, affecting oxygen transport and impairing mitochondrial function. Pulmonary absorption is directly proportional to the concentration of CO in the environment, the exposure time, and the respiratory rate (RR) [17].

Once in the blood, CO binds stably to Hb, with an affinity 200 to 230 times greater than that of oxygen, giving rise to COHb. The carbon monoxide bound to Hb causes a shift to the left of the dissociation curve concerning the oxygen that remains bound to this molecule[18].

CO is also capable of binding to other hemoproteins located at the tissue level, such as myoglobin, cytochrome oxidase, cytochrome P450, and hydroperoxidase. Between 15-20% of the CO binds to these proteins, thus interrupting cellular respiration and causing the production of reactive oxygen species, which lead to neuronal necrosis and apoptosis[17].

Exposure to CO also causes inflammation, through multiple pathways independent of those of hypoxia, resulting in further neurological and cardiac damage.
In pregnancy, CO also produces fetal hypoxia, due to the property of this gas to easily cross the placental barrier and bind to fetal hemoglobin.

Elimination of CO is respiratory and only 1% is metabolized in the liver to carbon dioxide. The half-life of CO in healthy people who breathe ambient air ranges between three and four hours [19]. There is a correlation between the levels of COHb and the clinic, however, this correlation is not as exact, since it depends on factors such as the magnitude and time of exposure, the frequency and depth of respiration, and the minute cardiac volume and the metabolic activity [19].

CLINICAL PRESENTATION

In mild or moderate intoxications, the symptomatology is diverse and nonspecific, so the clinical suspicion or the context in which the patient was found is what will help us to make the diagnosis [20]. The most affected population in terms of symptoms are women in the gestational stage, children and older adults, also people with anemia, heart and lung diseases, and smokers. Currently, several studies have established that people who live at heights are also more likely to suffer from CO poisoning[20]. The signs and symptoms that occur in carbon monoxide poisoning can be grouped and divided as shown in Table 1 [21].

Table 1. Classification of carbon monoxide poisoning by symptoms.

SEVERITY	SIGNS AND SYMPTOMS
MILD	Asthenia, weakness, malaise, headache, dizziness, confusion, disorientation, blurred vision, nausea, and vomiting.
MODERATE	Ataxia, syncope, tachypnea, dyspnea, palpitations, chest pain.
SEVERE	Hypotension, arrhythmias, myocardial ischemia, coma, respiratory depression, acute noncardiogenic pulmonary edema, seizures, and respiratory arrest.

Adapted from Guzman JA. Carbon Monoxide Poisoning. Crit Care Clin. 2012; 28:537–548.

NEUROLOGICAL EFFECTS

The first observable manifestations in the case of CO poisoning consist of neurological symptoms: headache, bradypsychia, drowsiness, abnormal movements, and dizziness. Compensatory vasodilation as a result of hypoxia, added to the existing hypoperfusion, causes the passage of fluid into the interstitium, giving rise to the formation of edema at the local level, and causing an intracranial hypertension syndrome. In severe poisoning, there is demyelination and signs of focal necrosis[22].

Survivors of severe CO poisoning suffer long-term neurocognitive sequelae related to brain injury. Symptoms include memory problems, cognitive dysfunction, depression, anxiety, and vestibular and motor deficits. New biomarkers such as neuron-specific enolase and S100B show considerable potential to decrease these complications [23,24]. It has been shown that patients persist with a neurological deficit in 37% and a cognitive deficit in 19%[25].

CARDIOVASCULAR EFFECTS

CO produces endothelial dysfunction, since it increases the production of free radicals, generating coronary vasoconstriction, in addition to increasing thrombosis because CO bound to the heme group binds to fibrinogen, favoring platelet aggregation. CO intoxication increases the risk of developing arrhythmia, since the inhibition of oxidative phosphorylation and the lower availability of adenosine triphosphate (ATP), alters calcium gradients, finding ST segment depression, tachycardia, pathological T waves, and ventricular fibrillation [26,27].

Characteristics associated with high mortality are fire as a source of intoxication, loss of alertness, high levels of COHb, pH values below 7.20, and the need for mechanical ventilatory support [28].

DIAGNOSIS

Since the clinical presentation of CO poisoning is nonspecific, the diagnosis will depend on suspicion. The quantitative analytical determination of COHb in blood shows high levels, which is confirmatory for the diagnosis of intoxication, > 3% in non-smokers and > seven to 10% in smokers. However, initial symptoms begin at COHb levels of 10%, while the brain and heart can be severely affected at COHb levels above 20%. Said determination is also useful to evaluate the efficacy of the established treatment. Venous COHb measurement is adequate for diagnosis, predicting arterial levels with a high degree of accuracy [29].

Arterial blood gases show a pO2 (partial pressure of oxygen) within normal limits, even with elevated COHb levels. Metabolic acidosis with an elevated anion gap is considered a poor prognostic finding[30]. Myocardial damage generates elevation of cardiac markers such as creatinine phosphokinase (CPK) and troponin I, which has been proposed as an indicator marker for the start of hyperbaric oxygen[31]. Leukocytosis with left shift, myoglobinuria, hypokalemia, hyperglycemia, elevated amylase, and liver enzymes may occur [30].

In the case of severe intoxications that lead to a coma in the first six hours, a decrease in the density of the white matter and globus pallidum, in addition to edema, can be seen in the computerized axial tomography (CAT) of the skull. Low-density areas in the globus pallidus are a poor prognostic sign. Magnetic resonance imaging (MRI) is more effective in detecting brain lesions, hemorrhages and brain atrophy [32].

TREATMENT

The treatment of the patient intoxicated by CO begins with the removal of the patient from the place of exposure, immediate administration of supplemental oxygen, and transfer to a hospital unit where support measures should be initiated and, if necessary, respiratory and cardiovascular support. The half-life of CO is four to five hours in ambient air, which is reduced to one hour with 100% oxygen therapy and 20 minutes in a hyperbaric oxygen chamber that accelerates the dissociation of CO from Hb and extravascular proteins (myoglobin, cardiac myoglobin, cytochromes, guanylate cyclase, nitric oxide synthetase). Likewise, it accelerates the dissociation of CO from mitochondrial cytochrome c oxidase, normalizing oxidative phosphorylation and reducing the production of free radicals [33]. The limitations of this therapy are the presence of chronic lung disease, pulmonary bullae, optic neuritis, or infection [34]. Therefore, hyperbaric oxygen therapy should be considered for those patients who present severe poisoning, in the following circumstances and within six to 12 hours of exposure/ acute intoxication [35,36]:

- Decreased alertness.
- Seizures.
- Persistence of neurological symptoms despite the application of high-flow oxygen for at least four hours.
- Cardiac disorders (arrhythmias, angina, heart attack, patient after cardiac arrest).
- Severe metabolic acidosis.
- Patients older than 36 years with COHb value ≥ 20%.
- Pregnant women with COHb value ≥ 15%.

Pharmacological treatments that reduce reperfusion injury and apoptosis, such as erythropoietin, hydrogen-rich saline, granulocyte colony-stimulating factor, nimodipine, fructose diphosphate, hyperoxygenated solution, and edaravone, require further investigation [37]. Treatment will depend on the symptoms of poisoning as shown in Table 2. Figure 1 shows the comprehensive approach to the poisoned patient.

Table 2. Treatment of carbon monoxide poisoning

MILD POISONING	MODERATE POISONING	SEVERE POISONING
Administer supplemental oxygen at 100% FIO2, using a non-recirculating mask with a high-flow reservoir (ten to 12 L/min).	Administer supplemental oxygen at 100% FIO2, using a non-recirculating mask with a high-flow reservoir (ten to 12 L/min), and then continue with 35-50% FIO2.	Admit to a resuscitation room, apply ALS measures, and, if necessary, CPR or endotracheal intubation. Administer oxygen with 100% FIO2. Evaluate hyperbaric oxygen.
If there is no determination of COHb, the supply of O2 must be maintained for a minimum of six hours.	Cardiac monitoring and control of vital signs. Give symptomatic treatment of headache and vomiting.	Continuous cardiac monitoring and hourly vital signs check.
Paraclinical: carboxyhemoglobin levels, ECG, and CPK levels.	Paraclinical: COHb levels, ECG, arterial blood gases, blood count, blood glucose, CPK, troponin I, ionogram, creatine, urea, complete urine, hepatic transaminases, and chest X-ray.	Paraclinical: COHb levels, arterial blood gases, co-oximetry, blood glucose, CPK, ionogram, liver transaminases, blood count, platelets, fibrinogen, kidney function, ECG, chest X-ray, and brain CT or MRI.

Hospitalization for 24 hours, despite the mild clinical picture, to patients who meet the following criteria: -Pregnant with any evidence of CO exposure. -History of ischemic heart disease. -suicide attempt. -Determination of COHb >15%, within the first hour post-exposure.	Given the finding of abnormal ECG, with or without precordial pain, or pre-existing coronary disease, serial determination of cardiac enzymes and specific treatment should be performed. Hospitalize for clinical observation for a minimum period of 24 hours.	Seizures – IV diazepam. Cerebral edema - keep the head elevated 30 degrees, mannitol, control, and monitoring of ICP and BP. Metabolic acidosis – should be corrected only with a pH less than 7.15 and in a non-aggressive way, since it is usually corrected with the administration of oxygen alone.
Assess discharge until the COHb level is less than 5% and/or the patient is asymptomatic.	Evaluate discharge when the patient is asymptomatic; COHb < 5%; normal ECG; CPK. Indicate rest.	Assess discharge when the patient has COHb < 5%; ECG and CPK normal. Rehabilitation: indicate reduced physical activity for two to four weeks.

CO carbon monoxide; FIO2 fraction of inspired oxygen; COHb carboxyhemoglobin; O2 oxygen; ECG electrocardiogram; CPK creatine phosphokinase; LDH lactic dehydrogenase; ALS advanced life support; CPR cardiopulmonary resuscitation; IV intravenous; ICP intracranial pressure; BP blood pressure; CT computerized axial tomography; MRI magnetic resonance. Own creation.

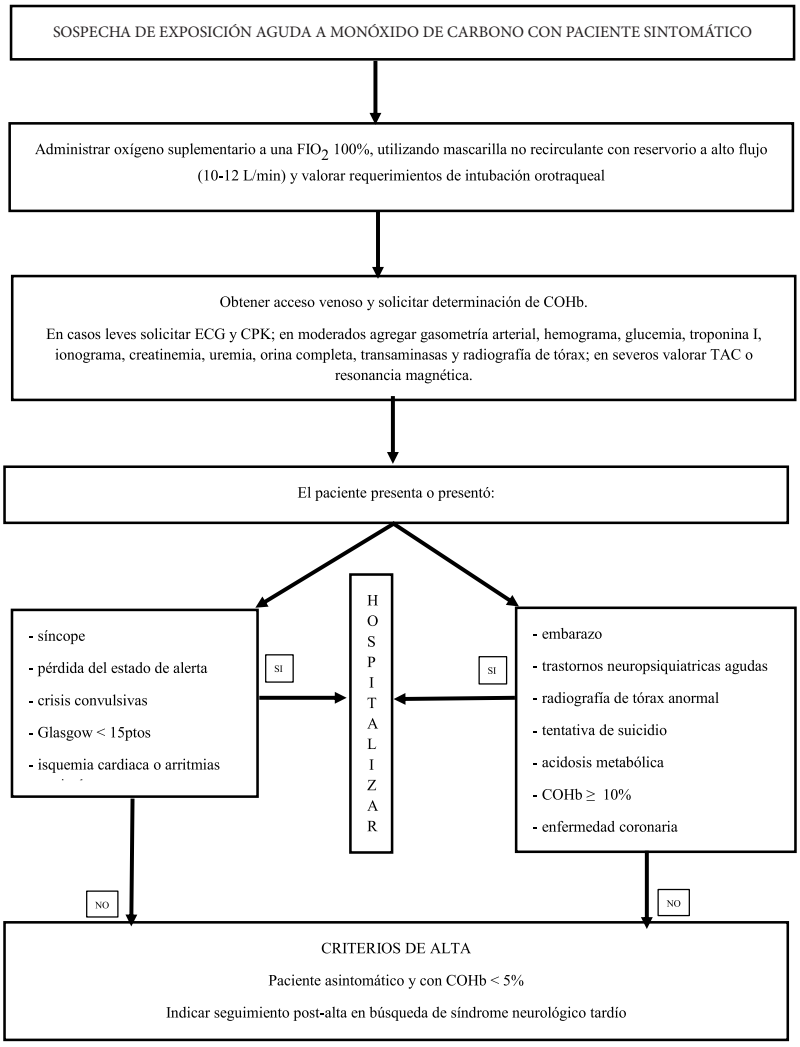

Figure 1. Comprehensive approach to the patient with carbon monoxide poisoning

PREVENTION

The prevention of CO poisoning is very important, CO detectors can be used for closed spaces, reduce exposure to tobacco smoke and avoid wandering through roads with a lot of vehicular traffic, as well as to give annual maintenance to appliances that work with gas, oil, or coal, in the same way, keeping vents free of debris or obstructions [37].

CYANIDE POISONING

Cyanide poisoning is a rare condition; however, it leads to high mortality, especially when adequate treatment is not available[38].

Cyanide can be found in gas form, such as hydrocyanic acid, a colorless gas with a characteristic odor of bitter almonds, although this ability to perceive this specific odor is absent in 20-40% of the population[39].

SOURCES

It is found naturally as an organic component in some fruits that have a large seed, such as melon, medlar, apricot, and almonds. It can also be found in the gases produced by vehicle engines, in tobacco smoke, and in the smoke from the combustion of plastics that contain nitrogen[38].

Cyanide is currently used in metallurgy to obtain gold by chemical leaching; in the steel industry; in jewelry; in chemical and clinical laboratories; in the glue and plastics industry; in paintings; as solvent and glaze; as herbicide, pesticide, and fertilizer. Most of the consumption goes to methyl methacrylate and the manufacture of adiponitrile (a precursor to nylon). It is also used for the manufacture of methionine or other amino acids in the animal feed industry[39].

EPIDEMIOLOGY

World consumption of cyanide is close to 1.5 million tons per year. In 2016, the American Association of Poison Control Centers reported 268 cases of poisoning by the substance, most of them accidental[40].

Although in Mexico there are no recent estimates of the incidence of cyanide poisoning, we must remember that in fire situations up to 50% of the victims die from poisoning by suffocating gases and vapors, among which is cyanide[7].

TOXICITY MECHANISM

When inhaling its vapors, cyanide is absorbed instantly, if ingested in liquid form it is absorbed through the gastrointestinal and respiratory tracts, but it can also be absorbed directly through the skin[41]. After being absorbed, cyanides are distributed throughout the body by the blood. A concentration of 100 ppm can cause death within 30 minutes, concentrations of 270 ppm cause immediate cardiovascular collapse [42].

The natural pathway of cyanide metabolism is its conversion to thiocyanate, catalyzed by the enzymes rhodanese, thiosulfatesulfide-transferase, and/or three-mercaptopyruvatesulfide-transferase. The route of greatest elimination of cyanide as thiocyanate is the urinary route, but in small amounts, it is also eliminated through the respiratory and digestive tracts. A portion of free cyanide is excreted unchanged with the breath, saliva, sweat, and urine [41,42].

Cyanide inhibits the enzymatic systems that use iron for oxidation-reduction reactions, the main mechanism of toxicity is the blockage of the use of oxygen by the mitochondria, through inhibition of cytochrome oxidase. When inhibited, cellular hypoxia is produced, mainly in the cytochrome a3 portion of the electron transport chain. Another important factor related to the inhibition of cytochrome a3 is that in this intoxication NADH predominates over NAD, causing the metabolic pathway from lactate to pyruvate to be reversed, obtaining greater production of lactate, likewise, binding to the carbonic anhydrase enzymes occurs (leading to acid-base disturbances), glutamate decarboxylase (inducing seizures), superoxide dismutase, and succinic acid dehydrogenase. In addition, cyanide affects multiple neurotransmitters, including dopaminergic, GABAergic, and glutamatergic pathways [41].

Poisoning occurs when the rate of cyanide buildup in the blood is greater than the body's ability to detoxify it. Levels above 0.5 µg/ml are considered toxic and above 3 µg/ml lethal [43]. The maximum safe inhalation concentration for humans is accepted to be 11 mg/m3 and concentrations above 20 mg/m3 are expected to show at least slight effects. Concentrations between 70 mg/3 and 300 mg/3 are fatal in 30 minutes or less [41].

CLINICAL PRESENTATION

The clinical manifestations of this intoxication are broad and vary according to the route, dose, and exposure time. The most serious manifestations are secondary to the compromise of the systems most sensitive to hypoxia: the central nervous system and the cardiovascular system[44]. In mild poisoning: headache, abdominal pain, nausea, vomiting, dizziness, weakness, anxiety, and eye irritation may occur; in moderate: dyspnea, tachypnea, palpitations, and tachycardia; in severe: pulmonary edema, hypotension, shock, arrhythmias, seizures, and coma.

NEUROLOGICAL EFFECTS

Headache, agitation, confusion, anxiety, lethargy, mydriasis, seizures, and coma are found. The most frequently involved areas are the basal ganglia, the cerebellum, and the sensorimotor cortex. The compound directly activates the N-methyl-D-aspartic acid receptors in the central nervous system, thus increasing the release of glutamate and inhibiting the blockade of these receptors by magnesium [44].

CARDIOVASCULAR EFFECTS

Cyanide has a negative chronotropic and inotropic depressant effect on the cardiac muscle, initially compensated by the sympathetic nervous system (tachycardia and hypertension). As intoxication progresses, arterial pressure falls and cardiac output is compensated by tachycardia, which later when the reserve is depleted, leads to profound shock with hypotension and bradycardia[44].

Other compromised systems are the respiratory system, especially in cases of inhalation, producing pulmonary edema and ventilatory failure, requiring mechanical ventilation in up to 66% of cases [45,46]. It also stimulates the chemoreceptors of the carotid and aortic bodies until hyperpnea occurs. Death occurs due to respiratory arrest of central origin, which occurs in seconds or minutes[47].

DIAGNOSIS

Measurement of cyanide concentrations in whole blood confirms the diagnosis, although it is initially performed on clinical suspicion [41]. Lactic acidosis correlates very well with blood cyanide concentration, so lactic acid concentrations equal to or greater than 10 mmol/l suggest blood cyanide concentrations equal to or greater than 0.2 mg/dl [48]. A wide variety of rhythm disturbances can be found on the electrocardiogram, including sinus tachycardia, atrial fibrillation, ventricular tachycardia, ventricular fibrillation, bradyarrhythmias, and nonspecific ST-segment and T-wave changes[49].

TREATMENT

The treatment focuses on the administration of the available antidote, according to the place of care and the general support measures as shown in Table 3. Always controlling the biosafety of the medical personnel and, in the event of starting prehospital care, ensuring the place[50]. Clothing should be removed and the skin washed with water and detergents. In addition, gastric lavage and activated charcoal can be administered within the first hour of exposure [45].

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Table 3. Treatment of cyanide poisoning.

Drug	Mechanism of action	Dose	Adverse effects
Methemoglobinemia-Inducing Agents			
Amyl nitrite	It converts a tolerable fraction of total circulating hemoglobin into methemoglobin, which has a greater affinity for cyanide than cytochrome oxidase, thereby promoting the dissociation of this enzyme.	Inhale the content of one pearl and repeat until sodium nitrite is administered. They should not be used simultaneously.	High concentrations of Met-Hb and cyanMet-Hb result in poor oxygen transport. Hypotension and reflex tachycardia.
Sodium nitrite	Produces methemoglobinemia 30 minutes after its administration, cyanide is more similar to it than cytochrome a3, restoring its function.	300 mg (ten ml of 3% solution) I.V. infused at 75 to 150 mg/min. May be repeated at half the original dose if there are still signs of toxic two y at two hours.	High concentrations of Met-Hb and cyanMet-Hb result in poor oxygen transport. Hypotension and reflex tachycardia.

Dimethylaminophenol	It is a methemoglobin inducer, but it is considered more potent and faster acting than sodium nitrite.	3.25 mg/kg I.V.	Elevation of liver enzymes, hemolysis, and skin reactions. It has been associated with excess met-Hb formation (up to 70% after the recommended dose) and multi-organ failure in the absence of severe intoxication.
Sulfur donating agents			
Sodium thiosulfate	Contains a sulfide, that bonds with only one other sulfur that can be used by the enzyme rhodanese found in the liver and skeletal muscle, favoring the conversion from cyanide to thiocyanate, which is easily excreted in urine	12.5 g (50 ml of a 25% solution) I.V. May be repeated at half the initial dose if signs of intoxication reappear or for prophylaxis after 2 hours of initial administration.	Vomiting, agitation, blurred vision, hallucinations, mental changes, muscle cramps, joint pain, and tinnitus.
Direct bonding agents (cobalt)			
Hydroxocobalamin	It is a metalloprotein with a central cobalt atom, which, in the presence of cyanide, binds to it forming cyanocobalamin, which is excreted in the urine and slowly releases the cyanide, allowing rhodanese to detoxify it.	70 mg/kg, usually 5 g I.V. for 15 min. This can be repeated for a total of 10 g. The rate of infusion of the second dose can vary from 15 min to 2 hrs. depending on the patient's condition.	Orange-red discoloration of the skin and burgundy-red discoloration of the urine.
Dicobalt edetate	Acts as a cyanide chelator, forming a stable complex.	600 mg I.V., a dose of 300 mg can be repeated after 15 min if no favorable results have been obtained.	Facial edema, vomiting, chest pain, ventricular tachycardia, and hypotension. Skin rashes, laryngeal edema, and anaphylactoid reactions have been reported.

I.V. intravenous, Met-Hb methemoglobin, cyanMet-Hb cyanmethemoglobin. Own creation.

Administration of 100% oxygen through a reservoir mask is indicated. Hyperbaric oxygen would only be indicated in the case of coexisting intoxication with Co [51]. Fluids, bicarbonate in case of severe acidosis, and sympathomimetic vasopressors should be administered to correct hypotension. If the patient presents convulsive crises, its control is indicated through the administration of benzodiazepines [52].

The main cyanide antidote kits in use were developed in the United States (sodium amyl nitrite, sodium thiosulfate), France (dicobalt edetate and hydroxocobalamin), and Germany (dimethylaminophenol). Most of the Western Hemisphere and parts of Asia until the end of the century used "Kit Lilly" (amyl nitrite, sodium nitrite, and sodium thiosulfate). Britain and its allies have chosen dicobalt edetate. Much of Western Europe and Scandinavian countries have adopted hydroxocobalamin since it was marketed in France in 1996. This drug has been used in the United States since 2006 when it became the first cyanide antidote approved by the Food and Drug Administration (FDA) [3].

Met-Hb-forming agents impair oxygen delivery to tissues, and therefore should not be used in victims of smoke inhalation [54,55]. Sodium thiosulfate is efficient and safe, but has a slow onset of action, and, is generally unsuccessful on its own in cases of acute poisoning. Dicobalt edetate and hydroxocobalamin are efficient and act immediately, and although they have been used successfully for decades, they have numerous side effects that limit their use [56,57].

Research continues in search of new safer and more effective cyanide antidotes. The most studied are in animal tests, so they are not yet approved for human use. Some of those mentioned are: Cobinamide, Alpha-ketoglutarate, Hydroxylamine, Sodium sulfanogen, and Molybdenum sulfur compounds [31,36].

PREVENTION

Personnel rescuing victims must wear self-contained breathing apparatus, protective clothing, and nitrile gloves. When disposing of contaminated clothing and other items, rescuers should place them in a plastic bag and seal them [58].

CONCLUSION

In Mexico, poisonings represent a public health problem since they constitute a common cause of requesting emergency medical care and there is an underreporting of them due to little recognition by health personnel. Learning what carbon monoxide and cyanide poisoning consist of, its clinical picture, diagnostic approach, initial management, and specific therapy favor improvement in the effectiveness, safety, and quality of medical care, thus contributing to the well-being of people and communities, which is the central objective and reason for being of health services. A patient with a diagnosis of carbon monoxide poisoning needs to have a suspicion of the coexistence of cyanide poisoning and vice versa. In general, in the emergency care of an intoxicated patient, there should be no treatment limitations, if the specific toxic substance is not certain, since there are only diagnostic tests for 40 to 150 toxic substances, approximately one million potentially toxic substances. Timely treatment of these patients reduces mortality and serious neurological sequelae. Current research points toward new therapies and antidotes that could even be administered immediately on site.

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