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Cyanide And Their Effect on The Body Clinical Management of Cyanide Exposure

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ABSTRACT

Cyanide blocks mitochondrial oxygen use and kills quickly. Natural, industrial, and home sources abound. Smoke inhalation causes most cyanide poisoning. Intravenous and inhalation cyanide exposures cause symptoms faster than oral or transdermal ingestions. The clinical manifestation depends on the physicochemical form of cyanide, dosage, route of entry, co-toxicants, and exposure latency. The central nervous system and cardiovascular system are most affected, along with nonspecific symptoms such nausea, vomiting, headache, dizziness, disorientation, coma, seizures, dilated pupils, and abnormal vital signs. Cyanide poisoning is likely to cause cherry-red skin and bitter almond breath. Patients with cyanide poisoning have high blood lactate. Cyanide poisoning may be diagnosed at 8 mmol/L lactate. Cyanide poisoning is confirmed by blood cyanide levels, but most hospitals do not do these and they may not correspond with toxicity, so they cannot guide therapy. Patients poisoned by cyanide get supportive care and antidotes. Cyanide poisoning kills quickly, thus medics must maintain the airway, breathing, and circulation. Cyanide poisoning is treated using cyanide binding, methemoglobinemia induction, and sulfur donors. Hydroxocobalamin and dicobalt edetate bind cyanide. Acute cyanide poisoning is treated safely and effectively with hydroxocobalamin. Methemoglobinemia antidotes include family, salt, and 4dimethylaminophenol. Fire victims and individuals with inadequate cardiopulmonary reserve should avoid nitrites. Sodium thiosulfate neutralizes sulfur donors. Available antidotes and diagnostic accuracy determine cyanide poisoning therapy recommendations.

Key words: Cyanide, poisoning, antidotes, hydrocobalamin, nitrites

INTRODUCTION

Cyanides are a diverse family of compounds that contain the highly reactive cyanide anion (CN-). Cyanides may be produced by things that take place in nature as well as by substances that are manufactured by humans. There are many different types of cyanide that may be found in nature, the most common of which is gaseous hydrogen cyanide. However, sodium cyanide and potassium cyanide are also found in nature. When this section makes use of the term "cyanide," it indicates that the material in question includes either the cyanide ion or the cyanogen radical (CN). It is possible for cyanides to be released into the environment via smoke and automobile exhaust, which include the incomplete combustion products of nitrogen-containing organic polymers. Cyanides may also be released through industrial usage. Hydrogen cyanide may be released by cyanogen glycosides, which are present in a wide variety of plant species, when they are ingested or biodegraded. Common fruit pits and seeds, such as those found in peaches, apples, and apricots, have far higher concentrations of cyanogen glycosides than the edible sections of the majority of plant species that are consumed in the diets of Americans. Because the cassava root, also known as tapioca, has a considerable quantity of cyanogen glycosides, which are a staple food in tropical regions, it is necessary to undergo certain processing in order to reduce the potential for toxicity via consumption.

The most common ways for members of the general public to be exposed to cyanides are via the intake of food and water, and to a lesser degree, by it being inhaled. There is an average concentration of cyanide in clean air that ranges from 0.160 to 0.166 parts per million (ppm) (0.180 to 0.187 mg/m3). For mainstream (inhaled) smoke, the amounts of cyanide in smoke from commercial cigarettes in the United States range from 10 to 400

μg per cigarette, whereas for sidestream smoke, the levels range from 0.006 to 0.27 μg per cigarette. Ninety-nine point eight percent of public water systems in the United States that depended on groundwater had cyanide contents that were lower than the legal limit of 0.2 mg/L during the years 1993 and 1998. The following food items have been discovered to have average levels of cyanide: cereal grains (ranging from 0.002 to 0.45 μg/g), soy protein products (ranging from 0.07 to 0.3 μg/g), canned unpitted fruits (ranging from 0 to 4 μg/g), commercial fruit juices (ranging from 1,900 to 4,600 μg/L), and lima beans from the United States (ranging from 100 to 170 μg/g). Because we do not have comprehensive data on the cyanide level of whole meal samples, we are unable to make an educated approximation as to how much cyanide individuals in the United States consume on a daily basis.

To a certain extent, the toxicity of any cyanide compound is related to the rate at which it releases cyanide anion (CN-). On the other hand, basic cyanide salts, such as sodium or potassium cyanide, are poisonous due to the fact that cyanide radicals have a low affinity for alkali metals and a high affinity for ferric iron (Fe3+) and other metals. As a result, certain iron-containing cyanide compounds do not readily release CN- and are almost completely nontoxic. The principal toxicological action of cyanide is to inhibit the functioning of enzymes and cells by binding to the metallic cofactor in metalloenzymes. Cytochrome c oxidase, an enzyme that is part of the mitochondrial respiratory chain, is the most significant target of cyanide exposure. The inability of tissues to make utilization of oxygen is caused by the inhibition of this enzyme. Histotoxic hypoxia is a condition in which there is a decrease in oxygen levels throughout the body, which has the potential to cause damage to tissues. The tissues that are most susceptible to damage are those that are very sensitive, such as those that have a high oxygen need or a deficiency in detoxifying enzymes like rhodanese. The suppression of cellular oxygen utilization, which results in a reduction of the oxyhemoglobin unloading gradient, causes an increase in oxygen tensions in peripheral tissues. Oxyhemoglobin, which is a biomarker of cyanide exposure, is carried via the veins of the lower bloodstream. The binding of cyanide to cytochrome c oxidase and the inhibition of enzymes such as catalase, peroxidase, hydroxocobalamin, phosphatase, tyrosinase, ascorbic acid oxidase, xanthine oxidase, and succinic dehydrogenase may both contribute to the toxic effects of cyanide.

Cyanide exposure has an impact on the whole body, but the effects on the central nervous system, which is responsible for controlling respiratory function and has a high metabolic need for oxygen, are the most significant. The first stimulation of the carotid and aortic bodies, in addition to the effects on the central nervous system, might have a negative influence on the operation of the respiratory system. This, in turn, contributes to the prevalence of histiotoxic hypoxia around the globe, which finally results in death. As a consequence of this, the harmful effects that cyanide has on respiration extend to the physiological level as well as the cellular level. At high levels of exposure, whether inhaled, taken orally, or applied topically, the inactivation of the centers that regulate breathing causes convulsions, unconsciousness, and death. This occurs regardless of the route of administration. Even at lesser exposures, headaches and vertigo are possible side effects.

OBJECTIVE

1. Describe the basic pathophysiology and toxicokinetic of cyanide toxicity.
2. Outline the examination and evaluation procedures for diagnosing cyanide toxicity, including any applicable laboratory testing.

Mechanism of poisoning

A reduction in the effectiveness of oxidative phosphorylation is one of the most significant consequences that

can result from cyanide poisoning. In order to produce ATP, also known as adenosine triphosphate, this process requires oxygen, which is why it is so important for cells. The Kreb's Cycle is responsible for the production of nicotinamide adenine dinucleotide (NADH), and in order to transfer electrons from NADH to oxygen, a considerable number of electron carriers are necessary. The mitochondrial cytochrome oxidase enzyme system is responsible for carrying out the activity, and the issue arises from the fact that cyanide inhibits cytochrome oxidase a3, which is the substrate for the enzyme. This occurs as a consequence of the fact that cyanide has a strong attraction to the ferric ion that is present in the haem component of the oxidized enzyme form. The structural integrity of the enzyme is compromised as a result of the subsequent chemical reaction, which also results in the enzyme's decreased efficiency.

As a direct result of this, the use of oxygen by tissues is impeded, which accelerates the breakdown of essential functions. The condition known as metabolic acidosis takes place when other metabolic processes continue to take place and the rate of glycolysis substantially rises. However, the pyruvate that is produced as a result of this cannot be used by the impaired Kreb's Cycle and is instead transformed to lactate. It has been shown that cyanide causes an increase in lactate levels and a significant decrease in ATP levels in the brain.

It is believed that additional pathways play a significant role in instances of severe poisoning, and the cytochrome oxidase aa3 complex is not the sole enzyme that is affected by extreme poisoning. Because of this, it is predicted that vasoconstriction of the coronary arteries and/or the pulmonary arteries might occur, which would result in a decrease in cardiac output and, in extreme cases, would lead to cardiac shock. It is also possible that the secretion of biogenic amines plays a role in this development. There has also been a presence of pulmonary edema that has been seen. It is hypothesized that this is connected with left ventricular failure, and this is more so than damage to the capillary endothelium or neurogenic causes. However, the precise manner in which the blood vessels adjust is still a matter of controversy.

Signs and symptoms

A headache, nausea, a taste similar to metal, lethargy, vertigo, anxiety, irritation of the mucous membranes, and hyperpnea are some of the symptoms that are associated with mild acute poisoning. Dyspnea, bradycardia, hypotension, arrhythmias, cyanosis, and bouts of unconsciousness are among symptoms that reveal themselves in succeeding stages of the disease. Convulsions, circulatory collapse, shock, and pulmonary edema are some of the symptoms that might result in a fatal outcome in those who have severe cases.

MECHANISMS OF TREATMENT

Direct combination, sulphur detoxification, and methaemoglobin production are the three primary categories that may be used to classify cyanide antidotes. These categories are based on the primary mechanism of action that they possess.

Sulphur detoxification

The most important naturally occurring cyanide detoxification mechanism is the addition of a sulfur atom, which results in the production of the thiocyanate ion, which is far less toxic. B-mercaptopyruvate sulfur transferase and mitochondrial rhodanese, also known as thiosulfate-cyanide sulfur transferase, are the two enzymes that play the most significant roles in in this process.8. A great number of synthetic compounds have been used as sources of additional sulphur in order to facilitate this natural process. In spite of the fact that it is theoretically not ideal since it does not readily pass through the mitochondrial membrane, which is where the rhodanese system operates, sodium thiosulfate has been the most often used. The administration of exogenous

rhodanese in conjunction with a sulphur-donating chemical has been a novel antidotal approach that has been used in animal trials. This has enabled the whole reaction to take place without any difficulty inside the bloodstream, hence reducing the need for thiosulfate to enter the mitochondria. Nevertheless, this is still in the examination stage at this point. Furthermore, there has been little progress made in the direction of therapeutic use of B-mercaptopyruvates or other sulfur donors that interact with non-mitochondrial sulfur transferase enzyme systems.

Methaemoglobin formation

As a result of the discovery that cyanide interacts with met-Hb, many methaemoglobin formers have been studied as possible antidotes. The process of converting oxy-Hb to met-Hb includes oxidizing the iron atoms in the haem groups from the ferrous (2 +) state to the ferric (3 +) state. This is necessary because of the high affinity that exists between cyanide and iron in the trivalent ferric state. The production of methaemoglobin results in a significant amount of ferric ion being circulated throughout the body. This is done in order to maintain a balance between the binding of necessary cyanide to the ferric ion of cytochrome oxidase a3. Due to the lower binding affinity of cyanide to metHb in comparison to cytochrome oxidase, a significant portion of the cyanide may combine to produce cyanmethaemoglobin. This can compensate to some degree for the lower binding affinity of cyanide to metHb. Therefore, cyanide is released into the circulation at a consistent pace, diffusing out of red cells and into plasma at a rate that the rhodanese and other sulfur detoxifying enzyme systems in the liver are able to handle with more ease. In the typical regimen, which is supported by Chen and Rose9 '10 and other individuals, intravenous sodium nitrite and sodium thiosulfate are based on the traditional practice of delivering exogenous sources of sulfur to assist in the process.

It is possible to classify the substances that are responsible for the production of hemoglobin into three distinct categories: those that act directly, those that act indirectly (requiring metabolic activation), and those that need oxygen. It is important to note that sodium nitrite is a slower metHb forming than 4-dimethylaminophenol (DMAP), despite the fact that nitrites operate directly on hemoglobin.12 This is shown by the fact that DMAP, which is the third group, has basically taken its position in Germany and other countries. Despite this, the evidence shows that met-Hb is only tangentially connected to the effects of nitrite. Even after methylene blue had stopped a significant amount of metHb synthesis, sodium nitrite remained to give protection, which suggests that there was probably a therapeutic influence previous to this.13' 14 Furthermore, the influence that nitrites have on the processes of hemodynamics in the circulatory system could shed some light on the situation. A During the course of the experimental trials, the raised central venous pressure (CVP) was swiftly reversed following amyl nitrite treatment, and arterial pressure also improved. On the other hand, cyanide may produce systemic hypotension and a fast rise in CVP.16 The reason why this occurrence takes place is because it is believed that nitrites have a more significant influence on the veins than they do on the arteries, which are responsible for causing resistance to blood flow.

Factors in the choice of antidote

Prior to making a decision about whether or not to give an antidote for cyanide poisoning, the IPCS/CEC Committee emphasized the significance of taking into consideration a number of different criteria. There are a number of elements that need to be taken into consideration, including (1) the kind of cyanide material and the circumstances of exposure, (2) the severity of the poisoning, (3) the antidote toxicity risk factors, (4) the number of patients, and (5) the distance to medical facilities.

As a result of this, it is abundantly evident that there is no cure that is beneficial in every situation. Nitrites and other metHb formers are not recommended for people who have been affected by fires, young children, or people who have enzyme deficiencies (such as G6PD), since these individuals are more prone to the disease. On the other hand, kelocyanor should not be used to address situations that are mild or equivocal situations.

Mild poisoning

In situations when the symptoms suggest that the poisoning is moderate, rest and oxygen treatment could be adequate relief. In the event that the condition worsens, it is necessary to provide amyl nitrite treatment (0.2-0.4 ml using an Ambu bag) and make preparations for transfer to the hospital. As a result of the fact that some compounds, such as acetonitrile, only release cyanide when they are metabolized, symptoms may not develop immediately. In situations like these, you will need to use the utmost caution in order to determine whether or not to transmit the medicine. Although it has been observed that amyl nitrite can produce metHb levels as low as 7% when it is inhaled or self-administered, there is growing evidence that the cardiovascular effects of nitrites are their primary mode of action. This is the case despite the fact that these levels are not high enough to bind a potentially lethal dose of cyanide.

Moderate poisoning

The use of intravenous antidotes is occasionally required for less severe instances of poisoning. In these circumstances, the symptoms may include cyanosis, convulsions, or a brief period of unconsciousness. It seems evident that the best location to deliver these is in a hospital, and more specifically in an intensive care unit, since there is where they will have the most influence on the overall health of patients. As a first line of defense, sodium thiosulfate could be administered in the event that the diagnosis is not entirely obvious.

Severe poisoning

A severe poisoning is characterized by symptoms such as deep coma, dilated pupils that do not respond, and a decrease in cardiorespiratory function. In order to treat these symptoms, an additional intravenous antidote must be administered. In the event that cyanide poisoning is misdiagnosed, methaemoglobin formers and kelocyanor both provide hazards; however, the former is more likely to occur more often. According to a straightforward risk-benefit analysis, hydroxocobalamin could be the best option to proceed with. There is a possibility that nitrites and kelocyanor may have a role in the future, particularly for medical professionals who are already familiar with them; nevertheless, the administration of these substances comes with a price tag and presents some logistical issues.

The proposed dose regimens for the different antidotes are listed in Table 1, which may be found here. If the first dosage does not provide the desired results, it is possible that it is time to try again. After thirty minutes, provide half of the first dose of sodium nitrite, or use the same quantity of thiosulfate or Kelocyanor. Both of these options are satisfactory. Before administering Kelocyanor or sodium nitrite once again, it is imperative that you monitor the patient's vital signs and always be on the lookout for any indications of toxicity.

Supportive treatment

There is now a clear understanding of the necessity of oxygen treatment, as well as the need for ongoing biochemical and clinical monitoring. More recent experimental study has shown that

Table 1. Recommended cyanide antidote dosage regimens*

Sodium thiosulphate	50 ml of 25% solution (12.5 g) IV over 10 min
Sodium nitrite	10 ml of 3% solution (300 mg) IV over 5-20 min
4-DMAP	5 ml of 5% solution (250 mg) IV over 1 min
Dicobalt edetate	20 ml of 1.5% solution (300 mg) IV over 1 min
Hydroxocobalamin	10 ml of 40% solution (4 g) IV over 20 min

* Recommended initial doses may be somewhat higher in children,7 e.g., sodium thiosulphate: 300-500 mg/kg; sodium nitrite: 4-10mg/kg.

The antidotal impact of oxygen is very apparent. It is possible that it will hasten the reactivation of cytochrome oxidase, in addition to perhaps having other mechanisms of action or mechanisms of action. It is essential that the use of 100% oxygen in artificial ventilation be carefully restricted to a time frame of 12 to 24 hours. Continuous monitoring of vascular pressure (CVP), monitoring of the patient's state of awareness, monitoring of hydration and electrolyte balance, monitoring of arterial blood gas, and active support of respiratory function are all extremely important. In addition to being a useful management tool, blood cyanide estimates are also worth considering. For this reason, it is possible that this test is not a reliable diagnostic of plasma free cyanide levels, which are more directly associated to symptoms. This is because the majority of cyanide in the circulation is stored in red cells, even in the absence of metHb production. However, according to the IPCS/CEC study, blood concentrations that are below 2 mg/1 are often associated with mild poisoning, while levels that are over 3 mg/1 are typically related with severe instances; these findings may be useful in monitoring the clinical course of the condition.

CONCLUSION

Cyanide poisoning in the workplace has usually resulted in an emotional first aid reaction being administered to medical personnel. The purpose of this article is to make it clear that a range of therapeutic treatments may be delivered with adequate judgment, taking into consideration the clinical state of the victim as well as the circumstances surrounding their exposure. Oxygen and amyl nitrite are the drugs that are advised for treatment when the symptoms are not severe. In situations that are classified as moderate to severe, patients who need immediate first aid resuscitative techniques, such as the injection of oxygen and amyl nitrite, should be sent to an intensive care unit without any delay. When cyanide is used in a controlled work environment, it is very required for medical personnel, such as physicians, nurses, or first-aiders, to have the appropriate training to provide intravenous treatments in accordance with the procedures that have been developed.

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