CHAPTER 128. CYANIDE POISONING

HIGH-YIELD FACTS

- Cyanide poisoning causes profound tissue hypoxia.
- Poisoning causes rapid onset of central nervous system and cardiovascular toxicity.
- Helpful laboratory clues include lactic acidosis and a diminished arterial–venous $O_2$ difference.
- Antidotal therapy with nitrites and sodium thiosulfate or with hydroxocobalamin needs to be considered early.

CYANIDE POISONING: INTRODUCTION

Cyanide poisoning is unusual in the United States and very rare among children, although its contribution to toxicity and death may be underestimated in victims of smoke inhalation from building fires. Hydrogen cyanide gas is formed as a combustion product of wool, silk, synthetic fabrics, and building materials in fires and is now recognized as a major cause of toxicity among fire victims previously thought to be poisoned by carbon monoxide. Acetonitrile, or methyl cyanide, is found in agents used to remove sculpted nails and has caused cyanide poisoning in children. Pediatric cyanide poisoning has also occurred from ingestion of cyanide-containing metal cleaning solutions imported from Asia and cyanogenic glycosides, like amygdalin, found in the seeds and pits of certain plants such as apples, apricots, and peaches.

TOXICOKINETICS

Hydrogen cyanide gas is rapidly absorbed in the lungs and may cause profound toxicity within seconds. Ingested cyanide salts, such as sodium cyanide and potassium cyanide, are also rapidly absorbed across the gastric mucosa and may result in toxicity within minutes. Acetonitrile appears to release cyanide through oxidative metabolism by the hepatic cytochrome P450 system, thus delaying clinical manifestations of toxicity for 2 to 6 hours from the time of ingestion. Ingestion of amygdalin and other cyanogenic glycosides requires hydrolysis to release cyanide, so toxicity may also be delayed up to several hours after ingestion.

The endogenous enzyme rhodanase (sulfurtransferase) converts cyanide to nontoxic thiocyanate: this mechanism is augmented in the presence of thiosulfate. In the presence of hydroxocobalamin (vitamin B$_{12a}$), cyanide is converted to cyanocobalamin (vitamin B$_{12}$), which is also nontoxic.

PATHOPHYSIOLOGY

Cyanide primarily causes tissue hypoxia by binding with ferric iron (Fe$^{3+}$) in cytochrome a-a$_3$ of
the mitochondrial cytochrome oxidase. Inhibition of cytochrome oxidase prevents efficient cellular oxygen use and disrupts ATP production, which results in anaerobic metabolism and severe lactic acidosis (Fig. 128–1). Cyanide also shifts the oxygen-hemoglobin dissociation curve to the left, further impairing oxygen delivery to the tissues. Cyanide inhibits a wide variety of other iron- and copper-containing enzymes, although their contribution to clinical toxicity is uncertain. The critical targets of cyanide are those organs most dependent on oxidative phosphorylation, namely, the brain and the heart.

Figure 128-1.

CLINICAL PRESENTATION

The clinical presentation depends on the route and dose of exposure. Inhalation of cyanide gas causes loss of consciousness within seconds, whereas symptoms from an oral exposure develop anywhere from 30 minutes to several hours. Initial symptoms in victims not experiencing rapid loss of consciousness include headache, anxiety, confusion, blurred vision, palpitations, nausea, and vomiting. With progression of toxicity, patients may experience a feeling of neck constriction, suffocation, and unsteadiness. Early clinical signs of cyanide poisoning are CNS stimulation or depression, tachycardia or bradycardia, hypertension, dilated pupils, bright red retinal veins on funduscopy, and declining mental status. Late signs of poisoning are seizures, coma, apnea, cardiac arrhythmias, and complete cardiovascular collapse. The characteristic smell of bitter almonds may be detected in some cases, but the ability to detect this is a genetically determined trait not possessed by every examiner. Although cyanide poisoning causes tissue hypoxia, the presence of cyanosis is a relatively late finding. Since cyanide poisoning typically causes a leftward shift of the oxygen dissociation curve, the absence of cyanosis in a patient with clinical evidence of severe hypoxia should prompt the examiner to consider the diagnosis of cyanide poisoning.
LABORATORY EVALUATION

Whole blood cyanide levels may be ordered from the ED, but these results are not available emergently and will therefore be of little value in guiding therapy. However, blood gas analysis and serum chemistries may be helpful in the acute setting. Arterial blood gases will typically show a marked metabolic acidosis. Obtaining a simultaneous venous blood gas analysis for comparison may demonstrate a diminished arterial–venous $O_2$ difference ($A_O_2 - V_O_2$ approaching zero) since the tissues' ability to extract oxygen from the blood is severely impaired. Serum chemistries may demonstrate an elevated anion gap due to the presence of a lactic acidosis from anaerobic metabolism.

Numerous electrocardiographic changes may occur in cyanide toxicity. Sinus bradycardia may be noted early, and later sinus tachycardia may be seen, as well as atrial fibrillation, atrioventricular block, ventricular ectopy, and ventricular dysrhythmias. A shortened QT segment or T waves originating high on the R wave may be seen.

TREATMENT

The management of cyanide poisoning requires immediate supportive care as well as specific antidotal therapy. Airway management with 100% oxygen should be initiated and an intravenous line established in all patients. Fluid resuscitation should be administered to patients with hypotension, and sodium bicarbonate should be considered in profound acidosis. Mouth-to-mouth resuscitation by primary rescuers should be avoided because of the theoretical risk of secondary cyanide exposure.

Cyanide Antidotes

Although some victims of cyanide poisoning have survived with supportive care alone, early antidotal therapy clearly improves survival and shortens the recovery period. Two options now exist in the United States for cyanide treatment: the Taylor Antidote Kit, which contains amyl nitrite perles, sodium nitrite solution, and sodium thiosulfate, or intravenous hydroxocobalamin.

TAYLOR KIT

Methemoglobin produced by the nitrite components of the Taylor Kit binds cyanide to form the relatively nontoxic cyanomethemoglobin. Several experimental and clinical findings suggest that methemoglobin formation is not the sole mechanism of benefit from nitrites, especially since clinical benefit is often seen before peak methemoglobin levels. Some authors suggest that the vasodilatory effect of nitrates allows for greater endothelial enzymatic degradation of cyanide.

Amyl nitrite perles held near the nose are used first while establishing an intravenous line and preparing the sodium nitrite solution. After an IV is established, sodium nitrite (9 mg/kg, or 0.3 mL/kg of a 3% solution, not to exceed 10 mL) is administered at a rate of 2.5 mL/min. In an unstable or hypotensive patient, or when there is concomitant CO poisoning, the dose may be given more slowly. Methemoglobin levels should be monitored periodically after the infusion and should not exceed 12% to 15%. Side effects of nitrite administration include headache, blurred vision, nausea, vomiting, and hypotension.
Sodium thiosulfate provides a sulfur donor for the rhodanase-mediated conversion of cyanomethemoglobin to methemoglobin and thiocyanate. Thiocyanate is minimally toxic and is excreted by the kidneys.

Sodium thiosulfate may be administered following nitrite therapy or concurrently at a separate site. The pediatric dose is 1.65 mL/kg of a 25% solution up to 50 mL (12.5 g). Thiosulfate itself is relatively safe, but accumulation of thiocyanate, especially in patients with impaired renal excretion, may be associated with nausea, vomiting, arthralgias, and psychosis.

HYDROXOCOBALMIN

Hydroxocobalamin, a precursor to vitamin B₁₂, detoxifies cyanide by binding it to form cyanocobalamin, a nontoxic compound excreted in the urine. Hydroxocobalamin was first approved for use in France in 1996 and approved in the United States in 2007. Although it has been studied primarily in adults, a case series of pediatric patients with smoke inhalation in France demonstrated a significant reduction in mortality when hydroxocobalamin was used at a dose of 70 mg/kg. Hydroxocobalamin is not associated with the complications of hypotension or excessive methemoglobinemia as has been seen with nitrite therapy. Red discoloration of the skin seems to be the primary adverse effect. Future studies may show a benefit to combining hydroxocobalamin with sodium thiosulfate.

SMOKE INHALATION

Several studies suggest a correlation between elevated carboxyhemoglobin levels and cyanide levels in smoke inhalation victims. Thus, when an elevated carboxyhemoglobin level is found in a severely ill fire victim, cyanide poisoning is possible, needs to be considered early, and treated appropriately. This is particularly true in a fire victim who requires intubation or has a persistent metabolic acidosis, abnormal mental status, or cardiovascular instability not resolving with conventional high-dose oxygen therapy for carbon monoxide poisoning.

DISPOSITION

Patients who are asymptomatic and whose exposure has apparently been minimal are observed for 4 to 6 hours. Those who have ingested cyanogenic glycosides are observed for at least 6 hours for evidence of the onset of toxicity. Those ingesting acetonitrile-containing compounds are observed for 12 to 24 hours. Patients requiring antidotal treatment are cared for in an intensive care unit where vital signs, mental status, arterial blood gases, methemoglobin, and carboxyhemoglobin levels can be checked frequently. Following recovery, patients are observed for 24 to 48 hours. Rarely, late neurologic syndromes have been reported following cyanide toxicity, and periodic outpatient follow-up is advised.

REFERENCES


