Novel treatment (new drug/intervention; established drug/procedure in new situation)

Hydroxocobalamin treatment of acute cyanide poisoning from apricot kernels

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Summary

Clinical experience with hydroxocobalamin in acute cyanide poisoning via ingestion remains limited. This case concerns a 35-year-old mentally ill woman who consumed more than 20 apricot kernels. Published literature suggests each kernel would have contained cyanide concentrations ranging from 0.122 to 4.09 mg/g (average 2.92 mg/g). On arrival, the woman appeared asymptomatic with a raised pulse rate and slight metabolic acidosis. Forty minutes after admission (approximately 70 min postingestion), the patient experienced headache, nausea and dyspnoea, and was hypotensive, hypoxic and tachypnoeic. Following treatment with amyl nitrite and sodium thiosulphate, her methaemoglobin level was 10%. This prompted the administration of oxygen, which evoked a slight improvement in her vital signs. Hydroxocobalamin was then administered. After 24 h, she was completely asymptomatic with normalised blood pressure and other haemodynamic parameters. This case reinforces the safety and effectiveness of hydroxocobalamin in acute cyanide poisoning by ingestion.

BACKGROUND

Cyanide, a mitochondrial toxin is one among the most rapidly acting lethal poisons known to man. If untreated, exposure to cyanide can kill within minutes. Current treatment of cyanide poisoning includes the intravenous administration of hydroxocobalamin. This case report describes unusual cyanide poisoning due to ingestion of large quantities of apricot kernels containing amygdalin, a compound which forms hydrogen cyanide when metabolised in the intestine and thus induces typical symptoms observed with cyanide poisoning.

CASE PRESENTATION

A 35-year-old mentally ill woman was admitted while conscious to our emergency department and clinical toxicology unit. The patient's parents reported that they found their daughter in the living room, surrounded by apricots from which she had extracted and eaten the cores. Further investigation revealed that the woman had swallowed 20–30 apricot kernels, with extrapolation from the remaining uneaten kernels suggesting that this equated to a total kernel consumption of 10–15 g. The approximate time of consumption was 30 min prior to admission, and on arrival, the patient was uncooperative and appeared asymptomatic.

INVESTIGATIONS

The following measurements were taken: blood pressure 120/70 mm Hg, pulse rate 120 beats/min, respiratory rate 26 breaths/min, temperature 37.5°C and SpO₂ on room air 98%. Arterial blood gas analysis also revealed slight metabolic acidosis (pH 7.33, pO₂ 90 mm Hg, pCO₂ 35.5 mm Hg, and HCO₃⁻ 20 mmol/l). The anion gap at admission was

19 mEq/l. Lactate and cyanide levels were not measured and no significant ECG changes were noted.

TREATMENT

After consultation with the clinical toxicology unit, she was subjected to a gastric lavage. One hundred grams of activated charcoal and 30 g of magnesium sulphate were administered, followed by hydration therapy (1000 ml of normal saline) and ECG monitoring. Approximately 70 min postingestion, the patient experienced headache, nausea and dyspnoea. Her vital signs were: blood pressure 75/50 mm Hg, pulse rate 145 beats/min, respiratory rate 30 breaths/min and SpO₂ 93% (with supplementary oxygen mask: 3l/min). Arterial blood gas analysis revealed metabolic acidosis (pH 7.20, pO₂ 75 mm Hg, pCO₂ 34.2 mm Hg and HCO₃⁻ 16 mmol/l). The anion gap was now 23 mEq/l.

Two 1 ml phials of 5% amyl nitrite via inhalation, and intravenous infusion of 50 ml of 25% sodium thiosulphate in 1000 ml of 5% glucose solution (infusion rate 5 ml/min) were subsequently administered as recommended by the toxicologist. Following this therapy, the patient's methaemoglobin level was 10%, prompting the administration of oxygen via a facemask. Electrolytic solution (1000 ml) was then administered. This slightly improved her vital signs and her blood pressure rose to 80/60 mm Hg. A 30-min intravenous infusion of 5 g hydroxocobalamin (Cyanokit; Merck Sante, Semoy, France) in 200 ml saline solution was then administered. This evoked rapid clinical improvement, including blood pressure normalisation at 40 min postadministration. A slight (and transient) discolouration of the patient's urine was observed. No significant ECG changes were observed.

After 24 h in the emergency department and clinical toxicology unit, the patient was transferred to the Psychiatry department for further observation and treatment.

OUTCOME AND FOLLOW-UP

At the time of discharge from the emergency department and clinical toxicology unit, the patient was totally asymptomatic: blood pressure 110/60 mm Hg, pulse rate 80 beats/min, respiratory rate 20 breaths/min and SpO₂ in room air 98%. Arterial blood gas concentrations were now within normal parameters.

DISCUSSION

Many foods have toxic components. In small quantities these foods may not cause any adverse effects, but if they are ingested in large quantities (due to ignorance or with the intention of suicide), they can be lethal.

Apricots kernels contain amygdalin (D-mandelonitrile-β-D-gentiobioside), which is metabolised via hydrolysis to form hydrogen cyanide and two molecules of glucose. The flavouring agent found in almond extract benzaldehyde is also produced.¹ Cyanide inhibits aerobic metabolism by binding to the ferric ion in the cytochrome oxidase a-a₃ complex.²⁻⁴ In humans, the lethal dose of cyanide is normally assumed to be 1.5 mg/kg, although a case has been reported involving fatal concentrations as low as 0.56 mg/kg.⁵ The literature suggests that the cyanide content of apricot kernels ranges from 0.122 to 4.09 mg/g.⁶ Very often, clinical signs of acute cyanide poisoning are non-specific and generalised, so an early diagnosis is very difficult.⁷ Initial symptoms can include: flushing, tachycardia, tachypnoea, headache, dizziness and agitation.³ The hampering of aerobic respiration leads to acidosis due to the production of lactic acid.² Moreover, rapid symptom escalation to severe hypotension, apnoea, convulsion and death can ensue.³ In half of all cases of cyanide poisoning, shock and cardiac arrest occur.⁸ Thus, to reduce mortality and chronic morbidity, the rapid administration of a cyanide antidote is now considered mandatory. For cases like this, we also recommend administration of activated charcoal, as it can bind to numerous poisons in the gastrointestinal system, thereby reducing their absorption.⁹ Implementing a subsequent gastric lavage may increase the possibility of seizure and inhalation of gastric contents; therefore, to protect the airways, it is recommended the patient is intubated prior to this procedure. Adjunctive administration of 100% oxygen is also recommended, regardless of a normal pO₂, due to its synergistic effect when administered alongside cyanide antidotes.^{1 3}

The antidotes for cyanide poisoning include hydroxocobalamin (5–10 g intravenously), amyl nitrite inhalant (15% in 1 ml phial repeated after 30 min) and sodium thiosulphate (10% in 10 ml phial).^{9 10} Hydroxocobalamin is administered to chelate cyanide forming cyanocobalamin and counters cyanide's hypotensive effects.¹⁰ Hydroxocobalamin has a favourable tolerability profile¹¹ and is also commonly used to treat vitamin B₁₂ deficiency, albeit in much smaller doses

(1 mg rather than 5–10 g). Amyl nitrite sequesters cyanide, thus competing with cytochrome oxidase for cyanide ions^{1 7} to form cyanomethaemoglobin. Effective amyl nitrite treatment results in 10–30% methaemoglobinaemia,^{1 7} although this effect can also prove toxic as the ability of the blood to transport oxygen to the cells is reduced.¹² Sodium thiosulphate is a sulphur donor that reduces the toxicity of cyanide via the thiosulphate sulphurtransferase-mediated conversion of cyanide to thiocyanate, which can then be safely excreted in the urine.⁹

Learning points

- ▶ Physicians should remember that ingestion of certain foods can lead to cyanide poisoning.
- ▶ Cyanide ingestion can cause the release of hydrogen cyanide from the stomach. This may poison hospital staff, particularly during intubation.
- ▶ Hydroxocobalamin is a safe and effective antidote for acute cyanide poisoning.
- ▶ Hydroxocobalamin's rapid administration in suspected cases of cyanide poisoning, together with appropriate decontamination and supportive measures, can significantly improve patient outcomes.

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REFERENCES

1. **Rubino MJ**, Davidoff F. Cyanide poisoning from apricot seeds. *JAMA* 1979;**241**:359.
2. **Beasley DM**, Glass WL. Cyanide poisoning: pathophysiology and treatment recommendations. *Occup Med (Lond)* 1998;**48**:427–31.
3. **Vogel SN**, Sultan TR, Ten Eyck RP. Cyanide poisoning. *Clin Toxicol* 1981;**18**:367–83.
4. **Holland MA**, Kozłowski LM. Clinical features and management of cyanide poisoning. *Clin Pharm* 1986;**5**:737–41.
5. **Suchard JR**, Wallace KL, Gerkin RD. Acute cyanide toxicity caused by apricot kernel ingestion. *Ann Emerg Med* 1998;**32**:742–4.
6. **Holzbecher MD**, Moss MA, Ellenberger HA. The cyanide content of laetrile preparations, apricot, peach and apple seeds. *J Toxicol Clin Toxicol* 1984;**22**:341–7.
7. **Gonzales J**, Sabatini S. Cyanide poisoning: pathophysiology and current approaches to therapy. *Int J Artif Organs* 1989;**12**:347–55.
8. **Fortin JL**, Giocanti JP, Ruttimann M, et al. Prehospital administration of hydroxocobalamin for smoke inhalation-associated cyanide poisoning: 8 years of experience in the Paris Fire Brigade. *Clin Toxicol (Phila)* 2006;**44**(Suppl 1):37–44.
9. **Kerns W**, Isom G, Kirk MK. Cyanide and hydrogen sulfide. In: Goldfrank LR, ed. *Goldfrank's Toxicologic Emergencies*. Seventh edition. New York, NY: McGraw-Hill 2002:1498–510.
10. **Kerns W**. Cyanide antidotes. In: Goldfrank LR, ed. *Goldfrank's Toxicologic Emergencies*. Seventh edition. New York, NY: McGraw-Hill 2002:1511–14.
11. **Borron SW**. Recognition and treatment of acute cyanide poisoning. *J Emerg Nurs* 2006;**32**(4 Suppl):S12–18.
12. **Hall AH**, Kulig KW, Rumack BH. Suspected cyanide poisoning in smoke inhalation: complications of sodium nitrite therapy. *J Toxicol Clin Exp* 1989;**9**:3–9.

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