Case Report

Successful Treatment of Lethal Cyanide Ingestion by Sodium Thiosulfate Alone: Case Report

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Background: Ingestion of cyanide may not manifest immediately in acute life-threatening symptoms. This delay presents an opportunity for recognition and appropriate management.

Case Report: A 23-year-old male purchased sodium cyanide through an internet order for suicidal gesture. He mixed sodium cyanide (5 grams) with cola soft drink (350 mL) to produce hydrogen cyanide. The patient inhaled cyanide gas for 30 minutes, however, he did not lose consciousness. He then drank the entire solution, causing him to vomit. The patient presented to the emergency medicine department about two hours after ingestion. He was conscious, and his vital signs were normal. Blood chemistries revealed wide anion gap metabolic acidosis (anion gap 16 mmol/L). Arterial blood gas and venous blood gas on arrival demonstrated no acidosis but narrow arterial and venous oxygen saturation gap (3%). He was treated with 12.5 grams of sodium thiosulfate intravenously, 50 grams of activated charcoal administered orally, and other supportive care. The patient condition improved clinically and laboratory. The narrow arterial-venous oxygen saturation gap was resolved (52%) at four hours post treatment. Hydrogen cyanide levels in patient's plasma and urine samples were confirmed by Gas Chromatography Mass Spectrometry methods.

Conclusion: The patient was a confirmed case of acute cyanide poisoning, exhibiting the early signs of cyanide poisoning, and was successfully treated with sodium thiosulfate alone.

Keywords: Cyanide, Hydrogen Cyanide, Sodium thiosulfate, Cyanide levels

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Cyanide exposure is associated with smoke inhalation, industrial processes, laboratory incidents, suicidal gestures, homicide attempts, terrorism, and nitroprusside toxicity. Some plant products contain cyanogenic glycosides and can cause cyanide poisoning after ingestion. These include apple seeds, bitter almond, apricot seeds, cassava roots, and bamboo shoots[1-3]. Common cyanide salts include sodium cyanide [NaCN] and potassium cyanide [KCN], and in form of hydrogen cyanide [HCN] reacts with water or acid. Most victims of cyanide poisoning die within minutes of exposure, typically through inhalation[4,5]. Ingestion of cyanide may cause delayed symptoms due to the latency period requiring for gastrointestinal absorption, as well as the time required to reduce tissue and circulatory oxygen content. Hence, this presents an opportunity for recognition, appropriate management, and medical treatment.

Incidents of cyanide exposure and fatalities have been underreported, due to victims not presenting to health care facilities. Diagnosis of cyanide exposure is considered primarily based on history of exposure, clinical judgement, and surrogate investigations. Confirmation of cyanide presence in plasma and urine is rarely performed, as the laboratory facilities capable of running the tests are not widely available[4-6]. Specific treatment for cyanide poisoning available in Thailand is to administer intravenous sodium nitrite and sodium thiosulfate or only sodium thiosulfate.

The authors demonstrated a case of cyanide poisoning by means of inhalation and ingestion that was successfully treated by sodium thiosulfate alone. Early diagnosis and prompt treatment based on history and surrogate investigations is emphasized.

Case Report

A 23-year-old Thai male attempted to produce hydrogen cyanide gas by mixing 5 gram (g) of sodium cyanide with 350 mL of cola soft drink for suicidal purpose. He learned how to produce the gas through an animated production popular amongst Asian teenagers, and through researching the subject via the Internet.

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Table 1. Blood gas analyses and anion gap taken before and after treatment with 12.5 g of sodium thiosulfate

Timeline	Arterial blood gas		Venous blood gas		Arterial-venous O_2 saturation gap (%)	Anion gap (mmol/L)
	pH	O_2 saturation (%)	pH	O_2 saturation (%)		
Before treatment	7.39	95	7.43	92	3	16
After treatment (4 hours)	7.34	96	7.23	44	52	13

Cyanide salt is a controlled substance under the Thai Hazardous Substance Act B.E.2535[7]. Special license is strictly required to supply, sell, and purchase cyanide. Most vendors set a minimum amount for any order as a factory portion hence it is less likely that a random person can obtain cyanide salt. However, this patient managed to purchase sodium cyanide without the requisite license by finding a vendor willing to sell the product based on the patient's verbal submission that he intended to use it for cleaning jewelry.

The patient inhaled the mixture repeatedly for 30 minutes, however, it had no or negligible effect. He subsequently decided to ingest the solution. He suffered from nausea and vomited several times, 20 minutes after ingestion. Upon arrival to the hospital, two hours after ingestion, he was conscious. His vital signs were as follow, body temperature of 37.4°C, blood pressure 124/72 mmHg, pulse rate 74 per minute and respiratory rate 14 per minute. Physical examination findings were normal except mild tenderness over the epigastric region. Blood chemistries revealed wide anion gap metabolic acidosis (BUN 14 mg/dL, Cr 0.99 mg/dL, Na 143 mmol/L, K 3.6 mmol/L, CL 106 mmol/L, HCO_3 21 mmol/L, anion gap 16 mmol/L). Arterial blood gas on room air resulted in pH 7.39, $PaCO_2$ 33 mmHg, PaO_2 78 mmHg, O_2 saturation 95%. Venous blood gas on room air revealed pH 7.42, $PaCO_2$ 38 mmHg, PaO_2 63 mmHg, O_2 saturation 92%, evidencing a narrow arterial-venous oxygen saturation gap of 3% (normal values ≥10%). Complete blood counts were normal as followed, Hb 15 g/dL, Hct 47.8%, white blood cell 7,410 cell/mm^3 (N 64%, L 28%), platelet 310,000/mm^3.

The decision made by the medical toxicologist was to administer 12.5 g of sodium thiosulfate intravenously, in addition to 50 g of activated charcoal orally, and provide supportive care. The narrow arterial-venous oxygen saturation gap and the wide anion gap were resolved following four hours of sodium thiosulfate administration. Comparison of key arterial and venous blood gas analysis as well as anion gap results are demonstrated in Table 1. Hydrogen cyanide levels were confirmed by gas chromatography mass spectrometry [GC/MS] methods on the patient's plasma and urine samples as shown in Table 2. The patient subsequently improved and was discharged to psychiatric facility for major depression treatment on hospital day 3 in good condition.

Table 2. Hydrogen cyanide levels in plasma and urine at 4, 11, 35, and 44 hours after ingestion

Hours after ingestion	4	11	35	44
HCN level in plasma (mcg/mL)	0.77	0.13	0.02	<0.02
HCN level in urine (mcg/mL)	-	2.47	0.33	0.19

HCN = hydrogen cyanide

Discussion

Suicide, or attempted suicide by poisoning from cyanide salt are not commonly reported, as cyanide is a controlled substance under the regulations of most countries[8]. However, a fatal cyanide poisoning case from an individual who illegally purchased a suicide kit from the Internet was reported[9]. The present patient obtained sodium cyanide through the Internet and mixed it with an acidic solution to produce hydrogen cyanide. This is not a common scenario reported in medical literature.

Cyanide is an inhibitor of multiple enzymes in humans. It binds to and inactivates cytochrome a3, essential for oxidative phosphorylation hence resulting in cellular hypoxia and lactic acidosis. Cyanide also decreases oxygen utilization at tissue level. This is evidenced by high venous oxygen saturation, which results in a narrowing of the arterial-venous oxygen saturation gap and produces classic cherry red skin in some cases. However, it is important to note that high venous oxygen saturation is not specific to cyanide exposure. It may represent cellular hypoxia from multiple agents including carbon monoxide, hydrogen sulfide, and sodium azide, or other non-toxicological condition such as sepsis[4,5].

Victims who develop severe cyanide poisoning suffer from central nervous system and cardiovascular dysfunctions, which may result in death. Those who ingest cyanide may develop gastrointestinal symptoms such as nausea, vomiting, and abdominal pain. However, such symptoms can be non-specific, making it difficult to diagnose initial manifestations. Blood concentration levels of cyanide should be confirmed, but often take time to obtain. Therefore, treatments should be judged based on clinical manifestations as

well as surrogate investigations for cyanide poisoning such as metabolic acidosis due to lactic acid, and narrow arterial-venous oxygen saturation gap[4,10]. The present patient was treated based on the known history of cyanide ingestion, wide anion gap metabolic acidosis, and the observed narrow arterial-venous oxygen saturation gap. The diagnosis was subsequently confirmed by the presence of hydrogen cyanide in blood and urine samples.

Common antidotes used for cyanide poisoning include sodium nitrite, sodium thiosulfate, and hydroxocobalamin. Sodium nitrite is an oxidizing agent. It changes ferrous (Fe^{2+}) to ferric (Fe^{3+}) hence hemoglobin to methemoglobin, which has high affinity to cyanide and forms cyanomethemoglobin. As a result, cytochrome oxidase is free from cyanide. However, sodium nitrite may cause hypotension. Sodium thiosulfate provides a sulfur precursor that detoxifies cyanide into thiocyanate via a rhodonase enzyme. Thiocyanate has a low toxicity and is subsequently excreted by the kidneys. This antidote causes minimal side effects but may take some minutes for onset of action. Hence, in cases of severe cyanide poisoning, a combination therapy with sodium nitrite is recommended. Hydroxocobalamin has gained popularity as a cyanide antidote given its effectiveness and safety profile but is not currently available in Thailand, and is expensive[4,5]. The present patient was empirically treated by 12.5 g of sodium thiosulfate, as he did not exhibit severe toxicity symptoms and its safety profile[5].

While cyanide is highly toxic, the present patient survived despite inhaling and ingesting a potentially lethal 5 g dose. By comparison, small doses of potassium cyanide (200 mg) can cause death[8]. Hydrogen cyanide level measured in this patient's plasma was 0.77 mcg/mL exceeding lethal hydrogen cyanide level in plasma of 0.25 mcg/mL reported in a previous study[11]. Several factors contributed to the survival of the present patient. Firstly, he mixed cyanide salt with a weak acid, which produced none or only a minimal level of hydrogen cyanide. Secondly, the gas he potentially created quickly dissipated, as he was in an outdoor public area known as "Sanam Luang" (or Royal Plaza). Thirdly, he vomited intensively before arrival to the hospital so less amount of ingested cyanide was absorbed. Finally, early treatment with 12.5 g sodium thiosulfate detoxified the cyanide that had entered his body.

Cyanide poisoning through ingestion often results in death[9,12]. Wananukul and Kaojarern[13] reported a case of accidental ingestion unknown amount of potassium cyanide. The patient exhibited severe toxicity and was successfully treated by sodium nitrite and sodium thiosulfate[13]. In some cases, the life-threatening effects of the poison is delayed, giving opportunity to halt the toxic process, and minimize the risk of morbidity and mortality. Hence, the authors encourage early treatments for any symptomatic conditions of cyanide poisoning, notwithstanding the pending confirmation of the condition through test results, or development of more serious symptoms such as metabolic acidosis. In less severe cases, treatment with sodium thiosulfate alone is considered sufficient[5].

Conclusion

The present patient was a confirmed case of acute cyanide ingestion who exhibited early signs of cyanide poisoning after intentionally inhaling and ingesting a mixture of cyanide salt and cola soft drink. He was successfully treated with sodium thiosulfate alone, and recovered fully. While cyanide salt is a controlled substance under Thai regulations, the patient was able to purchase the product without the required license. It is recommended that the supply of such chemicals be regulated more effectively, for the protection of the public.

What is already known in this topic?

Cyanide poisoning is life-threatening and can result in death within minutes. Effective antidotes commonly used for cyanide poisoning include sodium nitrite, sodium thiosulfate, and hydroxocobalamin. A combination of sodium nitrite and sodium thiosulfate or hydroxocobalamin administration is recommended in cases of severe cyanide poisoning.

What this study adds?

Sodium thiosulfate alone is an effective antidote for patients who ingest potentially lethal doses of cyanide salt but do not exhibit severe manifestations. In all cases, gastric decontamination, supportive care, and close monitoring should be provided as indicated.

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Potential conflicts of interest

The authors declare no conflict of interest.

Reference

1. Sang AG, Guharat S, Wananukul W. A mass cyanide poisoning from pickling bamboo shoots. Clin Toxicol (Phila) 2011;49:834-9.
2. Coentrão L, Neves A, Moura D. Hydroxocobalamin treatment of acute cyanide poisoning with a jewellery-cleaning solution. BMJ Case Rep 2010; 2010.
3. Garlich FM, Alsop JA, Anderson DL, Geller RJ, Kalugdan TT, Roberts DJ, et al. Poisoning and suicide by cyanide jewelry cleaner in the US Hmong community: a case series. Clin Toxicol (Phila) 2012;50:136-40.
4. Reade MC, Davies SR, Morley PT, Dennett J, Jacobs IC. Review article: management of cyanide poisoning. Emerg Med Australas 2012;24:225-38.
5. Hall AH, Dart R, Bogdan G. Sodium thiosulfate or hydroxocobalamin for the empiric treatment of cyanide poisoning? Ann Emerg Med 2007;49: 806-13.
6. Mowry JB, Spyker DA, Brooks DE, Zimmerman A, Schauben JL. 2015 Annual report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 33rd Annual report. Clin Toxicol (Phila) 2016;54: 924-1109.
7. Thai Hazardous Substance Control Bureau. Hazardous Substance Act B.E. 2535. Bangkok: The Government Gazette; 1992.
8. Zakharov S, Vaneckova M, Seidl Z, Diblik P, Kuthan P, Urban P, et al. Successful use of hydroxocobalamin and sodium thiosulfate in acute cyanide poisoning: A case report with follow-up. Basic Clin Pharmacol Toxicol 2015;117:209-12.
9. Le Garff E, Delannoy Y, Mesli V, Allorge D, Hedouin V, Tournel G. Cyanide suicide after deep web shopping: A case report. Am J Forensic Med Pathol 2016;37:194-7.
10. Musshoff F, Schmidt P, Daldrup T, Madea B. Cyanide fatalities: case studies of four suicides and one homicide. Am J Forensic Med Pathol 2002;23:315-20.
11. Chaturvedi AK, Smith DR, Canfield DV. Blood carbon monoxide and hydrogen cyanide concentrations in the fatalities of fire and non-fire associated civil aviation accidents, 1991-1998. Forensic Sci Int 2001;121:183-8.
12. Musshoff F, Kirschbaum KM, Madea B. An uncommon case of a suicide with inhalation of hydrogen cyanide. Forensic Sci Int 2011;204: e4-e7.
13. Wananukul W, Kaojarern S. Acute cyanide poisoning: a case report with toxicokinetic study. J Med Assoc Thai 1992;75:304-9.