Survival after severe methemoglobinemia secondary to sodium nitrate ingestion

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CASE REPORT

Sodium nitrate is used as a food preservative and color fixative. Sodium nitrate poisoning has occurred in the setting of well water contamination with nitrogenous waste runoff. Most clinically significant exposures result from improper labeling or unintentional use. We describe a case of severe methemoglobinemia associated with intentional sodium nitrate ingestion. A 23-year-old female presented to the emergency department (ED) for an intentional ingestion of sodium nitrate obtained from an online distributor. Upon arrival, blood pressure was 89/42 mmHg and oxygen saturation was 74% on pulse oximetry. Due to clinical decline, the patient underwent endotracheal intubation in the ED. Co-oximetry demonstrated a methemoglobin (MetHb) level of 92.7%, which is among the highest recorded MetHb levels. The patient received two doses of 1 mg/kg methylene blue, and experienced dramatic clinical improvement and subsequent successful extubation. We present a case of severe methemoglobinemia after intentional ingestion of sodium nitrate in a suicidal patient.

Introduction

Sodium nitrate is commonly used as a food preservative and color fixative [1,2]. In an expert committee report of Joint Food and Agriculture, the United Nations and World Health Organization established an acceptable daily intake of 0–3.7 mg/kg body weight in individuals greater than three months old [2]. Sodium nitrate occurs naturally and may appear in well water contaminated with nitrogenous waste [3–5]. Most clinically significant sodium nitrate exposures are accidental, as a result of improper labeling [6–8]. We present a case of severe methemoglobinemia after intentional ingestion of sodium nitrate in a suicidal patient.

Case report

A 23-year-old female presented to the emergency department (ED) after intentionally ingesting an unspecified amount of sodium nitrate purchased from an online distributor. As per emergency medical services (EMS), the patient sent a text message on her phone detailing the ingestion roughly 30 minutes prior to EMS arrival at the scene. She presented by ambulance to the hospital profoundly cyanotic and unresponsive. The patient had a blood pressure of 82/42 mmHg, pulse of 130 beats per minute (bpm), and oxygen saturation of 74% on 100% oxygen with active respiratory support by bag-valve-mask. Due to a depressed level of consciousness and apnea, the patient underwent intubation on arrival in the ED. Upon placement of peripheral intravenous lines, her blood was chocolate-brown in color. The clinical picture of cyanosis and abnormal appearance of blood supported the diagnosis of methemoglobinemia.

Medical toxicology was consulted with the recommendation to administer one dose of 1 mg/kg methylene blue over five minutes [1,7]. The patient’s initial methemoglobin (MetHb) level on venous blood gas (VBG) analysis was 92.7% (reference less than 1.5%), with an initial pH of 7.15 (reference range 7.35–7.45) and a lactate of 17 mmol/L (reference range 0.5–1.0 mmol/L). Hemoglobin (Hb) level returned at 13.6 g/dL (reference range 12.0–15.5 g/dL) and hematocrit 40.6% (reference range 37%–48%). The patient received an initial 60 mg dose of methylene blue. A repeat VBG analysis revealed a pH of 6.9 and MetHb level of 77%. The patient then received an additional 60 mg dose of methylene blue along with two doses of 50 mEq sodium bicarbonate and subsequent bicarbonate infusion at 22.5 mEq/hr. The patient’s clinical status improved dramatically, with

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resolution of her cyanosis as well as improvement in hemodynamic status with a blood pressure of 146/81 mmHg and heart rate of 89 bpm. Following the administration of the second dose of methylene blue, about 20 minutes later, the patient’s MetHb level was 41.2%. Further testing for hemolysis such as peripheral smear, haptoglobin, and lactate dehydrogenase was not performed.

The patient was admitted to the medical intensive care unit and arterial blood gas (ABG) then demonstrated a MetHb level of 6.3%. Ultimately, laboratory studies revealed a negative immunoassay urine drug screen, as well as undetectable plasma salicylate, acetaminophen, and alcohol levels. Approximately 6 hrs after admission, the patient tolerated extubation with an oxygen saturation of 95% on 3-L nasal cannula. Her repeat ABG showed a pH of 7.38 and lactate of 1.7 mmol/L. The following morning, which was 12 hrs post-ingestion, the patient’s final MetHb level returned as less than 1%.

Additional information obtained from the patient’s parents revealed a reported history of depression, with prior use of aripiprazole and fluoxetine. She had no known history of glucose-6-phosphate dehydrogenase (G6PD) deficiency and had no subsequent formal testing for G6PD deficiency performed. Her parents also stated that there was no known family history of enzymatic deficiencies.

Discussion

As a white powder with the appearance and taste of table salt, sodium nitrate is used in curing meat, fish, and cheese [1,2]. It is also commercially available to protect pipes and prevent corrosion [1,2]. There have been historical outbreaks of methemoglobinemia in association with wells containing drinking water contaminated with sodium nitrate [3–5]. Sodium nitrate can directly oxidize Hb from the ferrous (Fe2+) to the ferric (Fe3+) state, known as MetHb [7]. Methemoglobinemia occurs when MetHb levels in the circulation are greater than 1.5%. Notably, sodium nitrite is a very similar substance to sodium nitrate, and may also cause methemoglobinemia; such toxicity is treated in a similar fashion [9–13].

In healthy humans, erythrocytes are continually exposed to oxidative stress from natural metabolism [1,7]. The spontaneous formation of MetHb from ferrous Hb is reversed by the protective enzyme systems cytochrome-b5 reductase and nicotinamide adenine dinucleotide phosphate (NADPH) MetHb reductase. These pathways maintain a MetHb level less than 1.5% in normal individuals. The inundation of stress on biological mechanisms that normally defend against oxidation leads to an increase in MetHb levels [1,7].

Levels of MetHb as low as 10%–20% can produce cyanosis, and MetHb levels greater than 30% can result in tachycardia, muscle weakness, nausea, and vomiting [7]. Clinically, MetHb levels greater than 55% can lead to coma, and at levels greater than 70%, there is a high risk of death. Previously reported cases of methemoglobinemia secondary to sodium nitrate ingestion include individuals inadvertently using sodium nitrate in place of table salt due to inappropriate or non-existent labeling [6–8]. Our patient survived after a MetHb level of 92.7% on co-oximetry, which is among the highest recorded MetHb levels [9,10]. Katabami et al. describe a case of methemoglobinemia after intentional ingestion of sodium nitrite with a MetHb level of 92.5%[9]. Edwards and Ujma [10] present a patient who developed a MetHb level of 94% after recreationally inhaling amyl nitrite.

Treatment of methemoglobinemia includes methylene blue, which acts as a cofactor for NADPH MetHb reductase, hastening enzymatic activity and increasing the rate of conversion of MetHb to ferrous Hb. Functional G6PD enzymes are needed to generate NADPH, which is required by NADPH MetHb reductase to reduce MetHb back to ferrous Hb. Methylene blue is not typically used in patients with G6PD deficiency due the possibility of hemolysis [1,6]. Exchange transfusion and hyperbaric oxygen therapy are alternative treatments to methylene blue in the setting of allergy, hypersensitivity, history of adverse reactions to methylene blue, or G6PD deficiency with hemolysis [1,6,8,14].

Conclusion

We describe a case of severe methemoglobinemia associated with intentional sodium nitrate ingestion. The patient presented in this case obtained sodium nitrate from an online supplier and used the substance in a suicide attempt. Management included methylene blue as well as supportive measures of endotracheal intubation, mechanical ventilation, sodium bicarbonate, and intravenous fluids. Though this poisoning is rare [6–8], it is important to be aware of the possible clinical effects of methemoglobinemia associated with sodium nitrate use.

Disclosure statement

No potential conflict of interest was reported by the authors.

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