ToxTidbits

Maryland Poison Center
UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY
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The Maryland Poison Center's Monthly Update: News, Advances, Information

Sodium Nitrite Poisoning

The Maryland Poison Center received a call about a patient who reportedly ingested a lethal dose of sodium nitrite (NaNO2). Upon presentation to the emergency department, the patient's blood pressure rapidly deteriorated, prompting aggressive resuscitation. Sodium nitrite is a water-soluble, yellow-whitish crystalline powder. It is used in food preservation and pharmaceutical manufacturing. It is also a component of an older cyanide antidote sodium nitrite/sodium thiosulfate kit (Nithiodote®).

Nitrite toxicity involves the conversion of nitrite to nitric oxide, a potent vasodilator that causes smooth muscle relaxation, resulting in hypotension. Nitrite is also a potent oxidizing agent that can oxidize iron from the ferrous (Fe^{2+}) state to the ferric (Fe^{3+}) state on hemoglobin, forming methemoglobin. Severe methemoglobinemia in the 50-70% range may lead to acidosis, coma, and seizures; levels > 70% are associated with a high risk for death (*Ann Emerg Med 1999 Nov;34(5):646-56*). Methylene blue is the antidote for sodium nitrite (and other methemoglobin inducers). It primarily functions as a reducing agent for methemoglobin. Other mechanisms include decreased nitric oxide stimulation. Methylene blue has been used for ifosfamide encephalopathy and for refractory vasodilatory shock associated with cardiac surgery, sepsis, anaphylaxis, and refractory cases of metformin and amlodipine overdose.

Recent literature highlights an increase in sodium nitrite suicide attempts. Between 7/1/15-6/30/20, the United States National Poison Data System (NPDS) had 47 cases of sodium nitrite exposures (*Clin Toxicol (Phila). 2021 Dec;59(12):1264-1269*). There were no cases during the first 22 months of the study, until April 2017. Afterward, there was an annual uptrend from 2017 to the end of the study period by June 2020. The median patient age was 23 years (IQR 19-30) and 52% were female. The majority (44/47, 94%) were ingestion. Three cases were excluded due to unknown outcomes. Methylene blue was administered in 34/44 (77%) cases. Other supportive therapies included intubation (17/44), vasopressors (9/44), and blood transfusion (4/44). Thirteen of the 44 patients (30%) died, 10 of whom received methylene blue. In Southern Australia, data retrieved from the Toxicology Section at Forensic Science South Australia (FSSA) showed that from 2010-2019, there were 10 deaths attributed to sodium nitrite toxicity, all occurred from 2017 to 2019 with 1, 4, and 5 cases per year, respectively (*Forensic Sci Med Pathol. 2022 Sep;18(3):311-318*). Autopsy examination findings were consistent with post-mortem signs of methemoglobinemia. No post-mortem cases were identified between 2000-2016. Similar increases were observed in South Korea, Italy, and Ontario, Canada (*Forensic Sci Int. 2022 Jun;335:111279, Leg Med (Tokyo). 2022 Nov;59:102146,* and *Forensic Sci Int. 2021 Sep;326:110907*).

Given the potential rapid patient decline in severe sodium nitrite poisoning, prompt identification, close monitoring, and early therapy are crucial to patient care. Initial management includes oxygen supplementation with a non-rebreather mask, IV access, IV fluids, and vasopressors. Methylene blue is indicated if there is a high suspicion of exposure, patient is symptomatic, or when methemoglobin >20%. The usual dose of methylene blue for acquired methemoglobinemia is 1-2 mg/kg IV over 5 minutes. Because methylene blue is hypotonic, dilute in D5W (e.g., $\leq$ 1 mg/ml) followed by a flush of 15-30 ml to minimize local pain. Chloride may lower the solubility of methylene blue. Therapeutic effects can be seen in minutes, with maximal effects at 30 minutes. Side effects at 2 mg/kg include extremity pain, skin and urine discoloration, diaphoresis, and dysgeusia. Blood transfusion, exchange transfusion, or hyperbaric oxygen can also be considered in life-threatening methemoglobinemia. Contact your local poison center at 1-800-222-1222 for treatment recommendations for nitrite poisoning.

Sodium Nitrite

Did you know?

Methylene blue has some adverse effects.

Administration of methylene blue may temporarily alter monitor readings such as pulse oximetry and bispectral index. Doses may be repeated up to a max cumulative dose of 7 mg/kg. Higher doses may increase the risk of methylene blue-induced methemoglobinemia or hemolysis. Cases of serotonin syndrome have been reported with concurrent serotonergic medications (*Semin Cardiothorac Vasc Anesth. 2021 Mar;25(1):51-56*). Fetal harm was associated with intraamniotic injections for second trimester amniocentesis (*Prenat Diagn. 1996 Jan;16(1):39-47*).

Since methylene blue may not be routinely stocked in the Emergency Department, coordinate with your pharmacist and pharmacy team to prioritize methylene blue dispensing.

Angela Lam, PharmD, BCACP, BCCP, BCOP, BCPS

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