

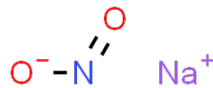


Clinical Pharmacology & Toxicology Pearl of the Week

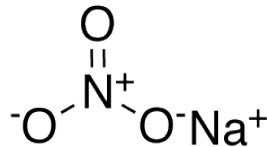
~Sodium Nitrite and Nitrate~

Background

- Sodium nitrite has long been used as a color enhancer in cured meats and fishes, a preservative, and an antimicrobial agent (by inhibiting *Clostridium botulinum*). It is also used therapeutically in the treatment of cyanide poisoning.



- Sodium nitrate is commonly used as a food preservative (“pink salt” for curing meat, fish, and cheese), color fixative, as a fertilizer, and to protect pipes and prevent corrosion. It also occurs naturally and may appear in well water contaminated with nitrogenous waste.



- Episodes of human toxicity have occurred when both nitrates and nitrites have been mistaken for table salt or granulated sugar and ingested. Nitrites are also sold online as a component of “suicide kits,” similar to sodium cyanide and sodium azide.



Pathophysiology

- In healthy humans, erythrocytes are continually exposed to oxidative stress from natural metabolism.
- The spontaneous formation of methemoglobin (MetHb) from ferrous Hb is reversed by cytochrome-b5 reductase and NADPH MetHb reductase. These pathways maintain a MetHb level less than 2% in normal individuals.

- Both sodium nitrate and nitrite can directly oxidize Hb from the ferrous (Fe²⁺) to the ferric (Fe³⁺) state, producing MetHb.
- Both sodium nitrate and nitrite are also potent vasodilators. They are converted to nitric oxide (NO) in tissues or blood with the lowest oxygen concentrations.

Clinical features of nitrate/nitrite toxicity

- MetHb:
 - Levels of 10%–20% generally cause cyanosis.
 - Levels of 20%–50% may cause symptoms such as respiratory distress, dizziness, headache, and fatigue.
 - Loss of consciousness and death can occur at levels of 50%–70%.
- Hypotension
- Headache, tachycardia, palpitations, dysrhythmias, blurred vision, nausea, vomiting.

Management

- MetHb
 - Methylene blue 1-2 mg/kg IV over 5 minutes
 - It acts as a cofactor for NADPH MetHb reductase, increasing the rate of conversion of MetHb to ferrous Hb.
 - Not typically used in patients with G6PD deficiency due the possibility of hemolysis.
- Hypotension
 - IV crystalloid boluses
 - Vasopressors (norepinephrine, epinephrine)
 - Methylene blue may also inhibit vasodilatory effects of nitric oxide and treat drug-induced distributive shock.

References:

1. Durao et al. Journal of Forensic and Legal Medicine 73 (2020).
2. Neth et al. Prehospital Emergency Care, DOI: 10.1080/10903127.2020.1838009
3. Katabami et al. Case Reports in Emerg Med. 2016
4. Cruz et al. Toxicology Communications. 2;1:21–23, 2018.
5. Nishiguchi et al., J Forensic Res 2015, 6:1. 2015.

The Clinical Pharmacology (CP) physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA on the AHS Insite page. CP consultations are also available through Netcare e-referral, Specialist Link and through RAAPID. You can also find us in the [Alberta Referral Directory](#) (ARD) by searching "Pharmacology" from the ARD home page. Click [HERE](#) for more details about the service.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414 (AB and NWT) or 1-866-454-1212 (SK). Information about our outpatient Medical Toxicology Clinic can be found in [Alberta Referral Directory](#) (ARD) by searching "Toxicology" from the ARD home page.

More CPT Pearls of the Week can be found [HERE](#).

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