Maryland Poison Center
UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY

ToxTidbits: Antidote Facts

1-800-222-1222

Methylene Blue for Methemoglobinemia

Methemoglobinemia occurs when iron atoms in hemoglobin become oxidized. During oxidation, the iron atom loses an electron to an oxidant and is converted from the ferrous state (Fe^{2+}) to the ferric state (Fe^{3+}). Normal methemoglobin levels are 1-3%. A variety of medications and other xenobiotics (Table 1) can cause elevated methemoglobin level, leading to decreased oxygen-carrying capacity and oxygen delivery. This can result in cyanosis, dizziness, fatigue, headache, dyspnea on exertion, and tachycardia; at levels above 50% seizures, dysrhythmias, hypotension, acidosis, coma, and death can occur. Methylene blue is an oxidizing agent that is the treatment of choice for acquired methemoglobinemia.

Table 1. Common Causes of Methemoglobinemia

Benzocaine, lidocaine, and prilocaine
Dapsone
Organic nitrites/nitrates: amyl nitrate, nitroglycerin, nitroprusside
Inorganic nitrates: fertilizers, contaminated well water, preservatives
Chlorates
Phenazopyridine
Quinones: chloroquine, primaquine
Sulfonamides

Mechanism/Indications: Methylene blue is reduced to leukomethylene blue by erythrocyte methemoglobin reductase in the presence of nicotinamide adenine dinucleotide phosphate (NADPH). Leukomethylene blue then reduces methemoglobin to oxyhemoglobin. Methylene blue is indicated in patients with methemoglobin levels >20-25%, or who have lower levels but are symptomatic.

Dosing: Adults and children: 1-2 mg/kg (0.1-0.2 ml/kg of 1% solution) intravenously infused over 5 minutes. Methylene blue has a rapid onset of action; maximal effects are normally seen within 30 minutes. The dose may be repeated in 1 hour if cyanosis persists.

Adverse Effects/Contraindications: Nausea, vomiting, headache and dizziness have been reported. At doses of $\geq$7 mg/kg, confusion, chest pain, fever, profuse sweating, bluish discoloration of the skin and mucous membranes, methemoglobinemia, and hypotension may occur. Hemolysis can occur, especially in neonates. Patients with G6PD deficiency are more likely to develop hemolysis and methemoglobin production; therefore, judicious use is warranted. Extravasation results in local pain and tissue necrosis. Methylene blue has MAOI activity; therefore, concomitant use of methylene blue with serotonergic drugs (e.g. selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, tricyclic antidepressants, norepinephrine-dopamine reuptake inhibitors, triptans, ergot alkaloids) may increase the risk of serotonin syndrome. Methylene blue is contraindicated in patients with severe renal impairment.

For more on methylene blue:

- *El-Husseini A, Azarov N. Is threshold for treatment of methemoglobinemia the same for all? A case report and literature review. Am J Em Med. 2010;28:748.e5-748.e10.*
- *Price DP. Methemoglobin inducers. In: Hoffman RS, et al, editors. Goldfrank's Toxicologic Emergencies. 10th ed. New York: McGraw Hill; 2015;1622-1630.*

May 2011 (revised February 2013, July 2018)