ToxTidbits

Maryland Poison Center
UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY

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The Maryland Poison Center's Monthly Update: News, Advances, Information

Methylene Blue

Methylene blue (tetramethylthionine chloride) is a blue dye that is used for the treatment of methemoglobinemia. Methemoglobinemia is defined as a blood methemoglobin level above 1% and can be caused by chemicals that oxidize Fe^{2+} to Fe^{3+} in hemoglobin. This oxidized form of hemoglobin is called methemoglobin and has poor oxygen carrying capacity. Causes include nitrites and nitrates (found in preserved meats and well water contaminated with fertilizer), local anesthetics (e.g. teething gels, benzocaine spray), aniline dyes, antimalarials, and dapsone. Inducers of methemoglobinemia are usually ingested rather than inhaled.

Methylene blue is an effective antidote for methemoglobinemia due to its own oxidizing properties. It oxidizes NADPH, forming the reduced product leukomethylene blue. Leukomethylene blue in turn acts as a reducing agent converting methemoglobin to hemoglobin and thus restoring oxygen carrying capacity. Methylene blue is indicated in patients with symptomatic methemoglobinemia (e.g. cyanosis, dyspnea, confusion, seizures, coma, metabolic acidosis, dark or brown blood), usually occurring at methemoglobin levels of >20-30%. Those with high risk comorbidities (anemia, CHF, pneumonia, angina) may require methylene blue at lower methemoglobin levels.

Dosing for methylene blue is 1-2 mg/kg (0.1 to 0.2 mL/kg) of a 1% solution administered intravenously over five minutes. The neonatal dose is 0.3-1 mg/kg. Administration is followed by a 15mL-30mL fluid flush to reduce local pain, as IV methylene blue is highly irritating to tissue. Onset is rapid with maximal effect in 30 minutes. If cyanosis persists or a repeat methemoglobin level is elevated, the dose can be repeated in 30-60 minutes. Further doses are usually not necessary unless ongoing absorption or slow elimination of the causative agent (e.g. dapsone) is suspected. In this case, a maximum total dose of 7mg/kg has been suggested. Continuous infusion at 0.10 mg/kg/hr or 3-7 mg/hr has also been used.

Methylene blue can worsen methemoglobinemia. Reduction by NADPH is needed for methylene blue to work. In excessive amounts, methylene blue may directly oxidize hemoglobin instead of NADPH, creating more methemoglobin. Methylene blue may be less effective in some patients with G6PD deficiency because of a reduced ability to generate NADPH. Other adverse effects of methylene blue include shortness of breath, chest pain, paresthesias, restlessness, nausea, and blue tinged urine, skin, and mucous membranes. Hemolysis has been induced at suprathera-peutic doses, requiring transfusions. The presence of methylene blue in the blood can interfere with pulse oximeter and co-oximeter readings. Finally, methylene blue inhibits the monoamine oxidase enzyme and can interact with serotonergic drugs (e.g. selective serotonin reuptake inhibitors), resulting in serotonin syndrome.

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Did you know?

Methylene blue has been used in the treatment of refractory shock?

There is evidence that methylene blue may be useful for the management of refractory hypotensive states due to sepsis, anaphylaxis, and toxin-related shock (e.g. calcium channel blockers). Methylene blue inhibits the nitric oxide-cyclic guanosine monophosphate pathway. By blocking this pathway, it prevents smooth muscle vasodilation and increases blood pressure.

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