



ToxTalks:

A Bulletin for Healthcare Professionals Who Manage Poisoned Patients

In Partnership with the UVA Division of Medical Toxicology – Department of Emergency Medicine

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Oral Methylene Blue

What is methylene blue?

Methylene blue (MB), or tetramethylthionine chloride, is a blue-colored liquid that was historically used as a textile dye since as early as the 1870s. Since then, it has been used for a variety of purposes in the medical field, including tissue staining during surgical procedures, for refractory vasoplegia, and as an antidote for methemoglobinemia. More recently, MB has garnered popularity on social media as an oral supplement with multiple claims about its health benefits. These claims have ranged from general statements about antioxidant properties to improving mitochondrial function, anti-aging properties, and nootropic effects. *Recently, there has been an increase in calls to the Blue Ridge Poison Center (BRPC) regarding exposure to oral MB.*



Therapeutic uses and mechanisms of action

In humans, MB has a number of mechanisms that make it useful for therapeutic purposes. There has been increasing interest in its efficacy as an adjunctive therapy in refractory vasoplegia in critical care medicine because it inhibits both nitric oxide synthase and guanylyl cyclase in vascular smooth muscle, leading to direct vasoconstrictive effects and increasing cardiac output. Additionally, it inhibits production of free radicals and increases sensitivity to adrenergic vasopressors (i.e. norepinephrine and epinephrine). In toxicology, it is used as an antidote for methemoglobinemia. MB gets reduced to leukomethylene blue, which then reduces methemoglobin to hemoglobin. This restores the normal function of hemoglobin and improves signs and symptoms of methemoglobinemia (i.e. cyanosis, hypoxemia, dyspnea, and cardiovascular compromise).³ Dosing for MB varies based on indication, but generally starts at 1 mg/kg intravenously (IV). MB for pharmaceutical use is supplied as a 0.5% or 1% solution containing 50 or 100 mg per 10 mL vial, respectively. MB is not typically used orally in the medical setting, but is known to have an oral bioavailability of about 80%.³

Adverse effects and potential toxicity

While data on the adverse effects from oral MB are sparse, several studies report primarily mild and self-limited



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side effects, including dysuria, urine discoloration, gastrointestinal upset (nausea, vomiting, and diarrhea), and headache. , More data exist on adverse effects from IV dosing, which may allow for some extrapolation to oral ingestion. At doses of 2 mg/kg, the most common reactions included pain at the injection site, chromaturia, dysgeusia, feeling hot, sweating, dizziness, nausea, skin discoloration, and headache.4 MB is a potent inhibitor of monoamine oxidase (MAO) and can cause serotonin neurotoxicity at doses as low as 2 mg/kg in patients taking serotonergic agents. , Doses over 7 mg/kg have been associated with paradoxical methemoglobinemia and hemolytic anemia. , Additionally, in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency, MB must be used with caution due to higher risk of oxidative stress leading to clinically significant hemolysis. ,

Guidance for healthcare professionals

If asked about use of oral MB by patients, it is prudent to inquire about the source, dose, and concentration of the product. MB products available from online sellers typically report concentrations of 1 to 2% and recommend from 1 mg to 20 mg (2 to 10 drops) daily, depending on formulation. While these doses are very unlikely to cause more severe adverse reactions (i.e. methemoglobinemia), they may cause patients discomfort due to milder side effects. Additionally, because these products are sold as dietary supplements, they are not subject to U.S. Food and Drug Administration (FDA) standards or testing, meaning concentration and purity may vary greatly between products. Obtaining information about personal or family history of G6PD deficiency is also important, as non-therapeutic use of MB should be avoided in these patients. Due to its MAO inhibition, patients on serotonergic drugs should be discouraged from taking MB. For patients taking MB products, mild symptoms will likely be alleviated with discontinuation of the product. More significant symptoms or large ingestions may warrant laboratory evaluation, which could include a complete blood count to evaluate for hemolytic anemia, comprehensive metabolic panel for electrolyte or acid-base disturbances and hepatic enzyme abnormalities, or co-oximetry to assess methemoglobin concentrations.

If questions or concerns arise, please contact the Blue Ridge Poison Center (1-800-222-1222) for more in-depth guidance.

References available upon request.