Serotonin Syndrome Precipitated by Methylene Blue Administration for Treatment of Methemoglobinemia

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Background
• Methylene blue is a phenothiazine derivative used clinically as an antidote for methemoglobinemia, as a surgical dye, and as a vasopressor in refractory vasodilatory shock
• Both methylene blue and its primary metabolite, azure B, are inhibitors of monoamine oxidase A

Hypothesis
• Low-dose methylene blue may precipitate serotonin syndrome

Case Report
• A 38 year-old female with a past medical history of depression, carcinoid syndrome, and dermatographia presented with palpitations and fatigue
• She reported a recent history of lethargy, anxiety, and lightheadedness
• She was taking dapsone for 12 months and had started paroxetine a few weeks prior
• Initial vital signs were T 98.6, HR 146, BP 169/104, RR 22, SpO₂ 90%

Case Report (continued)
• SpO₂ did not improve with 100% oxygen
• Laboratory workup was unremarkable (Hgb 13 mg/dL) except for a methemoglobin (MetHgb) level of 20.8%
• She was given a dose of methylene blue 1 mg/kg which was repeated after she failed to improve
• During transfer, she became diaphoretic, myoclonic, agitated, and intermittently confused
• Vital signs on arrival were T 98.6, HR 133, RR 16, BP 153/83, SatO₂ 95%
• She was awake, alert, anxious, and profusely diaphoretic
• Neurological exam was significant for mild trismus, repetitive flexion and extension of her left lower extremity, rigid lower extremities, and sustained clonus at the knees and ankles
• The diagnosis of serotonin syndrome was made by a medical toxicologist
• Intravenous lorazepam was used for symptomatic treatment
• Symptoms resolved and vital signs normalized within 24 hours
• Urine gas chromatography/mass spectrometry demonstrated paroxetine, dapsone, and methylene blue

Conclusion
• Concurrent use of methylene blue with serotonergic xenobiotics at doses as low as 2 mg/kg may precipitate serotonin syndrome