Serotonergic Toxidrome Following Methylene Blue Administration for Vasoplegia in A Patient on Multiple Serotonergic Medications: The Role of the Proactive Consult-Liaison Psychiatrist in Prevention

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INTRODUCTION

- Methylene blue (MB) is a monoamine oxidase inhibitor (MAOI) that is traditionally used as a procedural dye and for methemoglobinemia. It's unique structure is a precursor for TCA's, anti-malarials, and anti-psychotics.
- More recently its use has grown for patients who develop shock after cardiac procedures, such as coronary artery bypass graft (CABG).
- Here we present a case of methylene blue use to treat vasoplegic shock in a 60-year-old male with a past psychiatric history of Major Depressive Disorder and Alcohol Use Disorder, severe (in sustained remission) who presented to the hospital for scheduled three-vessel CABG.

CASE PRESENTATION

- TE is a 60 year-old-male with MDD and alcohol use disorder (in sustained remission)
- Past Medical History: Chronic low back pain, COPD, PVD, HTN, HLD, A-fib s/p ablation, CAD s/p 8 stents complicated by complete heart block and ICM (EF 30%) s/p ICD
- Psychiatric Medications: Duloxetine 120 mg daily, Fluoxetine 80 mg daily, Mirtazapine 7.5 mg daily, and Gabapentin 400 mg TID; no changes within the past three months prior to procedure
- Day 0 – CABG: TE required high doses of pressors in the OR due to severe vasoplegia (*widespread vasodilation and loss of systemic vascular resistance*).
- He was transferred to the ICU and started on epinephrine, precedex, norepinephrine, and vasopressin drips. He was also treated with ondansetron and two stress doses of hydrocortisone.
- Methylene blue (1 mg/kg loading dose) + 3 mg/kg maintenance dose administered for 6 hours.
- He was found to have pericardial fluid surrounding his Right Ventricle, requiring emergent re-sternotomy. He received Fentanyl 250 mcg for this intervention.
- His pressor requirement decreased for 3 hours and he began to become febrile to 40 °C.
- Day 1 - Toxicology Consult: Exam notable for 9 mm, poorly reactive, pupils, clonus in lower extremities, hyperreflexia, and "full body rigors." Scheduled Cyproheptadine started due to concern for Serotonin Syndrome.
- Day 5 - Psychiatry Consult - Requested assistance with agitation and medication management in the setting of serotonin syndrome. *Olanzapine 5 mg PO BID was started for four days, then decreased to 2.5 mg PO once.*
- Day 21 – Discharged after resolution of Serotonin Syndrome and Delirium

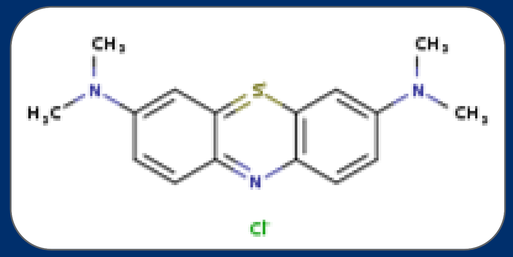

Fig. 1. Methylene Blue Structure

Vasoplegic Shock Treated With Methylene Blue Complicated by Severe Serotonin Syndrome, *Journal of Medical Toxicology, 2018*	Serotonin Syndrome Following Methylene Blue Administration for Vasoplegic Syndrome, *Journal of Cardiac Surgery, 2016*
. 15 y/o male developed severe vasoplegic shock 1.5 hours after OD on quetiapine XR, quetiapine IR, desvenlafaxine, venlafaxine, amlodipine, ramipril, fluoxetine, promethazine and lithium. Vasoplegia was resistant to high doses of vasopressin and NE. . A bolus of MB 1.5 mg/kg was given at 6.5-h post overdose, followed by an infusion of 1.5 mg/kg/h for 12 h and then 1 mg/kg/h for a further 12 h. MAP improved from 48 to 70 mmHg . 12 hrs post ingestion, pt developed severe SS that lasted 5 days . SS was due to MAO inhibition from MB and interaction with SSRI (fluoxetine) & SNRI (venlafaxine and desvenlafaxine) agents. . MB should be considered as a 2nd or 3rd tx'ment for severe vasodilatory shock, with lower doses or shorter infusions of MB should be considered in patients who are at risk .	. 50-year-old female with NYHA Class IV, Stage D nonischemic cardiomyopathy presented with acute HF, and was admitted for a right heart catheterization and LVAD evaluation. . She underwent implantation of a HeartWare LVAD and aortic valve replacement for her severe aortic insufficiency. . The postoperative course was complicated by coagulopathy and hypotension despite being on epinephrine, norepinephrine, phenylephrine, and milrinone. . Due to severe vasoplegia, MB 2 mg/kg IV bolus was administered over 30 minutes followed by continuous infusion of 0.5 mg/kg/hr. . Within an hour, the patient had fixed pupils, constant and uncontrollable shivering, spontaneous constant side-to-side eye movement, and fasciculations.

DISCUSSION

- Two other case reports have implicated MB as a significant contributor to the development of serotonin syndrome when it was used as treatment for vasoplegia.
- The current mortality rate of vasoplegia is as high as 25% compared to ~12% for serotonin syndrome.
- MB should be used as a 3rd-line agent for vasoplegia and delivered in small, frequent doses rather than a continuous infusion to minimize serotonergic activity.
- Preoperative proactive interdisciplinary serotonergic medications with Cardiology, Cardiac Surgery, Pharmacy and Psychiatry, particularly for patients at increased risk of complications. Such a model would also decrease hospital length of stay, of particular importance in today's ICU and general hospital bed strain.
- This discussion should also weigh the risks and benefits of holding medications as well as how far in advance medications should be held prior to surgery.
- Electronic health record to consider current as well as home medications when no ns.

CONCLUSION

- Patients and healthcare providers should be educated about the risk of serotonin syndrome if on three or more serotonergic medications.
- Psychiatry should be consulted proactively in patients with significant comorbidities for a planned procedure.

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