critical care canada FORUM

Anticholinergic Toxidrome as a Possible Explanation for Methylene Blue Toxicity

McGill University Health Centre

INTRODUCTION

- Methylene blue treats refractory vasoplegia by inhibiting endothelial nitric oxide and guanylate cyclase.
- In combination with serotonin reuptake inhibitors, methylene blue may induce serotonin syndrome.
- No case exists of serotonin syndrome in the presence of methylene blue alone.
- Anticholinergic adverse events have been associated to the use of methylene blue.

OBJECTIVES

- Present a case report regarding a suspected adverse drug event potentially caused by methylene blue
- Dicuss the pharmacology of methylene blue explaining it's role in causing anticholinergic toxidrome

METHOD

CASE REPORT

- 50 year old male underwent elective mitral valve replacement with mechanical mitral valve.
- Upon arrival to the intensive care unit (ICU), pateint had an intra-aortic balloon pump, was hypotensive and tachycardic requiring high doses of vasopressors and inotropes.
- Transesophageal echocardiography showed diffuse left ventricular hypokinesis (LV) (ejection fraction of 25%) and moderate right ventricular (RV) failure with normally functioning mitral valve prosthesis. At which point the patient received crystalloids and colloids to augment preload and inhaled nitric oxide to decrease RV afterload and improve oxygenation.
- 2h after admission to the ICU: vasopressin 0.06 units/min, epinephrin 0.05 mcg/min, norepinephrin 0.3 mcg/kg/min. At this point, methylene blue 1.5 mg/kg was administered followed by 1 mg/kg/h continuous infusion and blood pressure initially improved. Methylene blue was then decreased to 0.6 mg/kg/h.
- 10h after admission to the ICU: hypotension worsened and patient became oliguric; methylene blue dose was increased to 0.8 mg/kg/h.
- 20h after admission to the ICU: another bolus of methylene blue 1 mg/kg was given, the patient became anuric, hyperthermic at 42 degrees Celsius with bilateral mydriasis and lactic acidosis. Internal cooling was initiated and patient's body temperature normalized within 5h. Continuous renal replacement was initiated.
- 32h after admission to ICU: doses of vasopressors had been reduced and methylene blue was stopped.
- The patient was discharged 4 months later and returned to his pre-operative functional status.

RESULTS

DISCUSSION

Differential diagnosis:

- Infectious causes were less likely as fever started with 24h post-operatively and microbiology was negative.
- Endocrine and neurological causes were excluded by CT and laboratory testing.
- Malignant hyperthermia and neuroleptic malignant syndrome were ruled out as patient did not present muscle rigidity.
- The patient did not meet Hunter Serotonin Toxicity Criteria.

What do other cases says?

- Patients typically presented with agitation, confusion, nystagmus, aphasia, hyperpyrexia and seizures.
- It was not possible to assess neurological status for our patient as he was obtunded due to profound shock and multiorgan failure.

Methylene blue pharmacology

- Methylene blue contains a phenothiazine pharmacophore which interacts with the muscarinic system.
- Methylene blue inhibits cytochrome P450 3A4 which interacts with sedation, including fentanyl.

Lessons learned

- Methylene blue toxicity is enhanced by multi-organ failure and may present as anticholinergic toxidrome.
- Assess patients for early discontinuation of methylene blue infusion or prioritize methylene blue intermittent bolus regimen.

CONCLUSION

- Methylene blue at high doses may cause anticholinergic toxidrome.
- Risk of anticholinergic toxidrome increases when methylene blue is combined with other anticholinergic drugs and drug elimination is altered.
- Early recognition of anticholinergic toxidrome and elimination of causal agents is warranted.

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ACKNOWLEDGEMENTS

We would like to thank Editage (www.editage.com) for English language editing.

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