[ID-P#073] Recurrent Acute Intravascular Hemolysis after Treatment with Methylene Blue for Severe Naphthalene-Induced Methemoglobinemia: A Case Series

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Background and Objective: Methylene blue (MB) is indicated in patients with symptomatic methemoglobinemia (metHGB) at levels 20% and beyond; moreover, in patients with anemia such as naphthalene-induced hemolytic anemia. The current IV dose of 1-2mg/kg MB has been safe and effective in reversing metHGB produced by sulfanilamide, aniline dyes, silver nitrate, benzocaine, nitrites, and phenazopyridine; however, it is unknown in naphthalene ingestion. Furthermore, in high doses, MB induces acute hemolytic anemia independent of the presence of methemoglobinemia and is related to glucose-6-phosphate dehydrogenase (G6PD) deficiency, which is prevalent among Asian population. This aims to discuss two cases of acute intravascular hemolysis after treatment with MB in a patient with severe naphthalene-induced methemoglobinemia without G6PD.

Case Series: The first case is a 23-year-old male without G6PD who intentionally ingested four mothballs containing 99.1% naphthalene presented at the Emergency Department (ED) after 3 days with generalized weakness, hemolytic anemia, and metHGB (15-20% estimated based on colorimetric chart with filter paper test4). Activated charcoal with cathartics, oral N-acetylcysteine (NAC), and MB (2 doses of 1mg/kg, 1 hour apart) were given, and the patient was advised for therapeutic plasma exchange; however, the latter was not available. After giving MB which improved the metHGB, the patient's hemoglobin dropped from 8.9mg/dL to 4.5mg/dL with changes in the sensorium and a recurrence of tea-colored urine on the 2nd hospital day. The patient was transfused a total of six bags of packed red blood cells (pRBC), which improved her overall health, and was discharged with improved health. The G6PD assay revealed normal results two weeks post-ingestion and after 3 months. The second case is a 19-year old female without G6PD who intentionally ingested four mothballs presented at the Emergency Department (ED) after 54 hours with generalized weakness, abdominal pain, jaundice, hemolytic anemia, and metHGB (30-40% estimated based on colorimetric chart). Transfusion of 2 units leukoreduced pRBC and MB (2 doses of 1 mg/kg, 3 hour apart) were given. Patient's metHGB improved but hemoglobin dropped from 8.4mg/dL to 5.1mg/dL, hence further blood transfusions were performed. Workup revealed normal chest and abdominal CT scan and normal G6PD assay.

Discussion: Although the patients did not have congenital or acquired G6PD deficiency, the RBCs previously vulnerable to oxidative stress from alpha-naphthol – a metabolite from naphthalene metabolism5 – were again subjected to another oxidative stress brought about by methylene blue exposure by unknown mechanisms. We postulate that it may be more pronounced after the second dose. Most case reports for naphthalene toxicity use Vitamin C and NAC as method for alleviating both methemoglobinemia and oxidative stress5-8. In our cases, RBC transfusion was effective in correcting hemolytic anemia and reversing effects of MB. Similar observations were reported by Kapoor et al. in a 14-year-old male with autism spectrum disorder who accidentally ingested unknown amounts of naphthalene9. This case highlights exercising caution in giving methylene blue in naphthalene toxicity as MB may further induce hemolytic anemia.