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# TREAT BLUE WITH BLUE

**Aravind R** MD (internal medicine) final year post graduate

**Dr.Madhavan.K*** MD(internal medicine),Professor*Corresponding Author

**ABSTRACT**

Methemoglobinemia can result from either congenital or acquired processes. Acquired methemoglobinemia may be due to exposure to direct oxidizing agents. We present a 31 years old male who was brought unconscious and breathless to emergency room with ABG revealing high methemoglobin level. He was treated with methylene blue. Once the patient regained consciousness, he revealed that he consumed turpentine oil with alcohol with an intension to suicide, which resulted in significant methemoglobinemia

## INTRODUCTION:

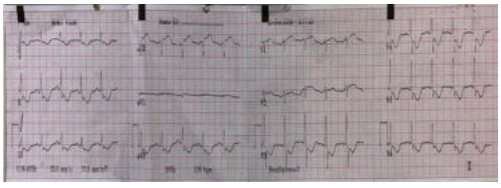
Methemoglobinemia is a condition with life-threatening potential in which diminution of the oxygen-carrying capacity of circulating hemoglobin occurs due to conversion of some or all of the four iron species from the reduced ferrous [Fe2+] state to the oxidized ferric [Fe3+] state. Ferric iron does not transport oxygen. Increased levels of methemoglobin results in functional anemia.

## CASE REPORT:

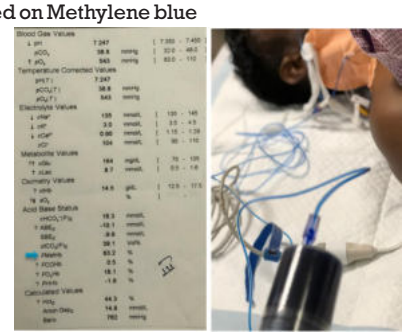
31yr old male with no known comorbid conditions brought to ER in unresponsive state. The informant said that the patient had complained of breathing difficulty for 2 hours following consumption of alcohol 3 hours ago followed by gradual deterioration in consciousness over the past 1 hour. There was no history of chest pain, palpitations, giddiness, vomiting, fever, cough, abdominal pain, diarrhea, dysuria, rash. There was no history of headache, altered mental status, seizures,or limb weakness.

On examination the patient was unconscious(GCS- 4/15) with severe peripheral Cyanosis. There was no pallor Clubbing, wheals,rashes, cyanosis or pedal edema. His Pulse rate was 104/min and BP was 80/50 mmHg. There was bilateral basal crepts. There was no wheeze. Both the pupils were 3mm reacting to light. Pulse oximeter revealed a room air saturation of 60%.

Patient was intubated and initiated on invasive mechanical ventilation in view of Low GCS. Gastric lavage was done. ECG revealed global ST depression. Cardiac markers were within normal limits. Complete blood count, Liver and Renal function tests were normal

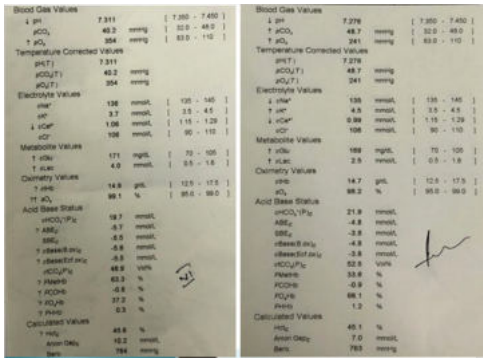


ABG revealed severe Methemoglobinemia (83.2%). Patient was started on Methylene blue



In view of Methemoglobinemia, Inj.Methylene blue 1mg/kg Stat was given and Tab.Vitamin C 500mg BD

Subsequent ABG analyses revealed gradual reduction in Methemoglobin level in blood



Patient regained consciousness and patient was extubated. He was requiring oxygen support for 5 days

## DISCUSSION:

Treatment of methemoglobinemia includes removal of the inciting agent and consideration of treatment with the antidote, methylene blue (tetramethylthionine chloride). High flow oxygen delivered by non-rebreather mask increases oxygen delivery to tissues and enhances the natural degradation of methemoglobin.

Methylene blue usually works rapidly and effectively through its interaction with the aforementioned secondary pathway of methemoglobin reduction, where NADPH-MetHb reductase reduces methylene blue to leukomethylene blue using NADPH from the G6PD-dependent hexose monophosphate shunt. Leukomethylene blue then acts as an electron donor to reduce methemoglobin to hemoglobin. In cases of acquired methemoglobinemia, treatment with methylene blue should occur when methemoglobin exceeds 20-30%, or at lower levels, if the patient is symptomatic. Treatment decision should be made on clinical presentation and not withheld for confirmational laboratory values. The methylene blue dose is 1-2 mg/kg (0.1-0.2 mL/kg of 1% solution) intravenously over 5 minutes. (*Methemoglobinemia: Pathogenesis, Diagnosis, and Management - PubMed*, n.d.) The dose can be repeated in 30-60 minutes if significant symptoms or levels remain above the treatment threshold.

Practitioners should be aware of the side effect profile of methylene blue. Benign side effects include green or blue discoloration of urine and patients should be forewarned. Significant side effects are based on methylene blue, itself, being an oxidizing agent and an inhibitor of monoamine oxidase A (MAO-A). As an oxidizing agent, methylene blue

can actually precipitate methemoglobinemia or hemolysis in high doses or when ineffectively reduced. Methylene blue administration in a patient taking a serotonergic agents may predispose to serotonin syndrome.(*Methylene Blue and Serotonin Toxicity: Inhibition of Monoamine Oxidase A (MAO A) Confirms a Theoretical Prediction - PubMed*, n.d.) Caution should also be practiced with treating neonates as they are also very sensitive to oxidizing agents. Also, methylene blue is a United States Food and Drug Administration (FDA) pregnancy category X drug, indicating that studies have shown concrete evidence of human fetal risk.

Although methylene blue administration is controversial in the setting of G6PD-deficiency due to reduced levels of NADPH, it is not contraindicated and should be administered cautiously and judiciously. Many G6PD deficient patients may have some level of G6PD that can still provoke an adequate response, and therefore, treatment should not be withheld. Doses of methylene blue observed to produce hemolysis in patients with G6PD deficiency has been observed to be over 5 mg/kg, which is more than twice the recommended dose.(*Hemolytic Effect of Therapeutic Drugs. Clinical Considerations of the Primaquine-Type Hemolysis - PubMed,* n.d.)

If methylene blue administration is ineffective after the second dose, underlying conditions including, but not limited to, G6PD and NADPH-MetHb reductase deficiency should be considered as reasons for refractoriness to treatment. However, methemoglobinemia alone is not an indication to screen for these disease processes.

When treatment with methylene blue is ineffective or not recommended, additional options may include ascorbic acid, exchange transfusion, hyperbaric oxygen therapy.(Cho et al., 2017; Grauman Neander et al., 2018) High-dose ascorbic acid (vitamin C), up to 10 g/dose intravenously, can be considered to treat methemoglobin. However, it is generally ineffective and not considered standard of care. High dose ascorbic acid administration is associated with increased urinary excretion of oxalate. In the presence of renal insufficiency, high dose ascorbic acid may be predisposed to renal failure due to hyperoxaluria.(Lee & Park, 2014)

## CONCLUSION:

All cases of methemoglobinemia should be managed in consultation a medical toxicologist. Critical care may be necessary in cases where prolonged treatment or observation are warranted, or if there have been significant adverse outcomes as a result of the elevated methemoglobin. For acquired methemoglobinemia, patients should receive education on how exposure to the offending agent led to the development of methemoglobinemia. The patient should be counselled to avoid future exposure.

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