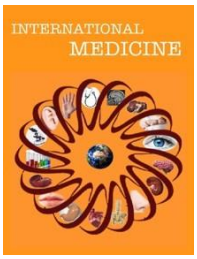

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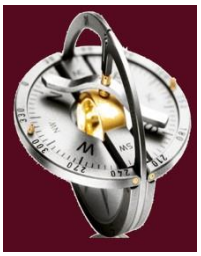

Original Research

Severe Recreational-Drug-Induced Methemoglobinemia Successfully Treated with Methylene Blue in the Emergency Department

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Abstract

Acquired methemoglobinemia is a rare but potentially life-threatening cause of hypoxia, often triggered by oxidising recreational substances. A 44-year-old man presented with acute chest pain, shortness of breath and general malaise after taking two sildenafil tablets, inhaling poppers and consuming approximately 1 litre of vodka. He appeared centrally and peripherally cyanosed and required high-flow oxygen. Arterial blood gas (ABG) analysis revealed a PO_2 of 32 kPa and methemoglobin of 28.9%. A diagnosis of methemoglobinemia was made, and intravenous methylene blue was administered promptly. Repeat ABG 10 minutes later demonstrated a PO_2 of 15.1 kPa on 3 L/min oxygen and a reduction in methemoglobin to 1.2%, with complete resolution of cyanosis. The patient was admitted for monitoring and discharged in good condition after a short inpatient stay. This case highlights the importance of considering methemoglobinemia in patients with unexplained hypoxia unresponsive to oxygen therapy, particularly in the context of recreational drug use.

Introduction

Methemoglobinemia is an uncommon cause of impaired oxygen delivery due to oxidation of haemoglobin to methaemoglobin, which is unable to bind oxygen effectively. Acquired forms are more common and may be triggered by medications, industrial chemicals or recreational agents such as alkyl nitrites (“poppers”). Early identification is essential, as hypoxia may persist despite high inspired oxygen concentrations, potentially leading to serious morbidity.

The mechanism of methemoglobinemia is the oxidation of iron in the hemoglobin molecule from the ferrous (Fe^{2+}) state to the ferric (Fe^{3+}) state, resulting in the formation of methemoglobin, which cannot effectively bind or deliver oxygen to tissues. This process can occur due to exposure to oxidant stressors such as nitrates, nitrites, and various pharmaceuticals (e.g., benzocaine, dapsone, phenazopyridine).[1,2,3] In the ferric state, hemoglobin loses its oxygen- carrying capacity, leading to tissue hypoxia despite normal partial pressures of oxygen.

The American Heart Association states that acquired methemoglobinemia is most commonly triggered by exogenous oxidizing agents, while hereditary forms result from mutations in hemoglobin subunits that favor iron oxidation.[1,2,4] Nitric oxide and nitrite ions are notable endogenous and exogenous contributors, respectively, as they directly oxidize hemoglobin.[5,6] Normally, methemoglobin is reduced back to hemoglobin by NADH-dependent cytochrome b5 reductase, but when the rate of oxidation exceeds the capacity of these enzymatic pathways, methemoglobinemia develops.[7,8,9]

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Clinically, this manifests as cyanosis, a saturation gap between pulse oximetry and arterial blood gas, and chocolate-brown blood, with severity proportional to the methemoglobin level.[1,2,10]

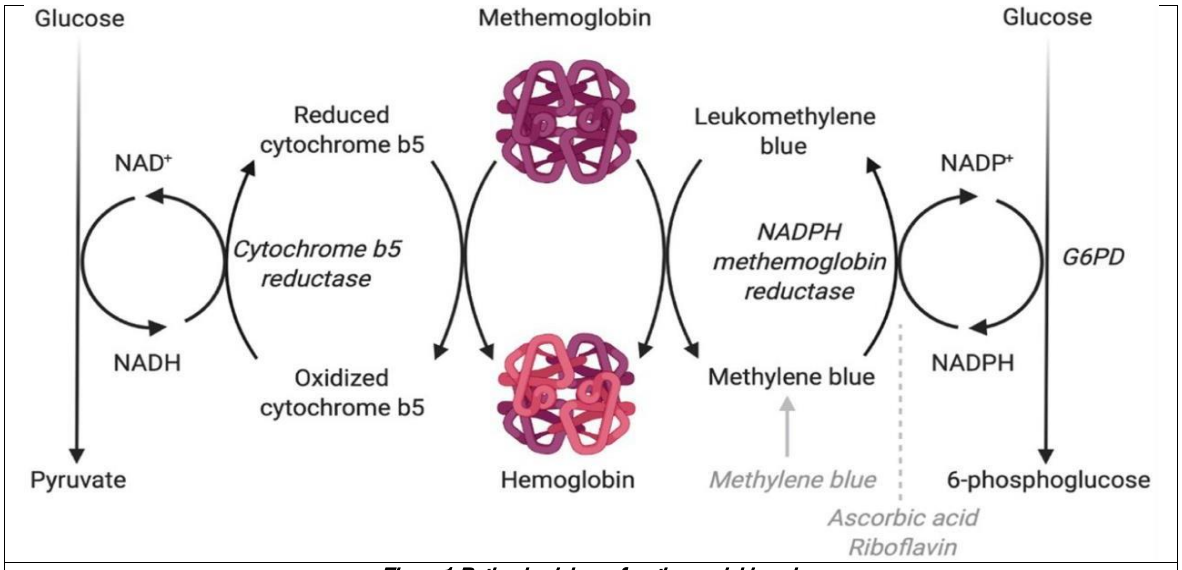

Figure 1: Pathophysiology of methemoglobinemia

Figure 2: Chocolate-brown blood in ABG on non rebreather mask

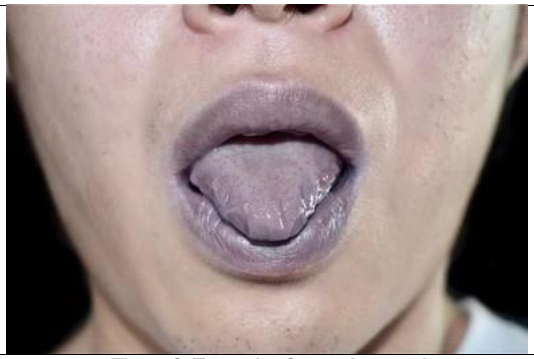

Figure 3: Example of central cyanosis

CASE PRESENTATION

A 44-year-old man attended the emergency department with chest pain, shortness of breath and general malaise. He reported ingesting two sildenafil tablets, inhaling poppers and drinking approximately 1 litre of vodka shortly before symptom onset. On arrival he was visibly cyanosed centrally and peripherally and required high-flow oxygen to maintain satisfactory saturations.

Investigations

Initial arterial blood gas analysis on high-flow oxygen showed a markedly elevated methemoglobin level of 28.9% ECG and chest radiograph demonstrated no acute abnormalities.

Differential Diagnosis

- Acute coronary syndrome
- Pulmonary embolism
- Pneumonia or sepsis
- Heart failure
- Carbon monoxide poisoning
- Recreational drug toxicity
- Methemoglobinemia (favoured)

Treatment

The patient received intravenous methylene blue (1 mg/kg) as per TOXBASE guidance. Rapid clinical improvement and Cyanosis resolved completely.

Repeat ABG 10 minutes post-treatment showed:

Parameter	Pretreatment on 15 L of Non rebreathing mask	Post treatment with Methylene blue on 3L of nasal cannula
PH	7.42	7.45
Po2	32.7 kpa	15.12 kpa
Pco2	4.88 kpa	4.5 kpa
Hco3	23.5 mmol/l	23.0 mmol/l
FMethb	28.9	1.9

Table 1

The Rest of the Blood gas parameters were unremarkable

Outcome and Follow-Up

The patient was admitted for observation, remained clinically stable and was discharged home in good condition after a short inpatient stay. He was advised to avoid further exposure to oxidising recreational substances.

Discussion

Alkyl nitrites ("poppers") are potent oxidising agents capable of inducing methemoglobinemia, especially when combined with other substances such as alcohol or phosphodiesterase inhibitors. The hallmark of methemoglobinemia is cyanosis and hypoxia unresponsive to oxygen therapy. Pulse oximetry is unreliable; therefore, co-oximetry is essential for diagnosis. Methylene blue is the first-line antidote and typically results in rapid resolution by restoring functional haemoglobin.

Learning Points

- Consider methemoglobinemia in patients with persistent cyanosis despite high-flow oxygen.
- Recreational substances, particularly alkyl nitrites, are important causes of acquired methemoglobinemia.
- Diagnosis relies on co-oximetry rather than pulse oximetry.
- Prompt administration of methylene blue leads to rapid clinical improvement.
- Early recognition in the emergency department prevents severe hypoxic injury.

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