

Case Reports

An Unusual Complication of Cocaine Toxicity

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Abstract

A 25-year man presented to the Accident and Emergency Department complaining of dizziness and shortness of breath after taking 70 grams of cocaine over 10 hours. He said a friend had noticed that his skin had turned dark blue. On examination the patient was severely centrally and peripherally cyanosed. His pulse oximeter oxygen saturations were 88% on air. An arterial blood gas showed a methaemoglobin level of 45.6%. The patient was diagnosed with cocaine-induced methaemoglobinaemia and given methyl thioninium chloride (methylene blue). He made an uneventful recovery.

Keywords

Cocaine, methaemoglobulinaemia, methylene blue, amyl nitrite, recreational drugs.

Key Points

- Recreational drugs including amyl nitrite ('poppers') and cocaine adulterated with local anaesthetic can cause methaemoglobinaemia.
- Acute Physicians should be aware of the possibility of methaemoglobinaemia in recreational drug users who have unexplained cyanosis or low peripheral oxygen saturations, particularly in the presence of an apparently normal PaO₂ on arterial blood gases.
- Pulse oximetry is inaccurate in cases of significant methaemoglobinaemia with a tendency for SpO₂ to fall towards 85% with metHb levels >30%.
- Measurement of arterial PaO₂ may be misleading in this situation and does not reflect the oxygen carrying capacity of blood.
- The diagnosis of methaemoglobinaemia can be made using a blood gas analyser to measure percentage metHb. The blood generally appears dark chocolate or bluish-brown in colour.
- Oxygen and methylene blue are the treatment of choice for symptomatic methaemoglobinaemia.

Case History

A 25-year-old man presented to the Emergency Department complaining of shortness of breath and change in skin colour. He described how he had consumed in excess of 70 grams of cocaine over the past 10 hours. He had then begun to feel breathless and dizzy and vomited twice. His friend noticed that he had "turned blue".

He had a past medical history of depression and used recreational drugs including cocaine, cannabis and ecstasy regularly. He took no prescription medications and had no known allergies. He was a smoker, drank 15 units of alcohol per week, lived alone and was unemployed.

On examination the patient was markedly cyanosed. His respiratory rate was 18/minute and oxygen saturations were 88% on room air. On auscultation his chest was clear. His blood pressure was 115/75 mmHg and heart rate was 100/minute. Neurological examination was unremarkable. An ECG showed sinus tachycardia. A CXR was normal. An arterial blood gas (breathing air) showed: pH 7.36, PaO₂ 9.3, PaCO₂ 5.3, HCO₃ 22.6, BE 2.7, MetHb 45.6%. Blood results showed: Hb 14.4, WBC 27.6, Neutrophils 25.5, INR 1.2, Na 136, K 3.7, Urea 4.1, Creatinine 105. Troponin and liver function tests were normal.

The patient was diagnosed with methaemoglobinaemia due to adulterated cocaine ingestion. He was given high-flow oxygen, intravenous fluids and 10ml of 1% methyl-thioninium chloride (methylene blue) over 5 minutes. A subsequent arterial blood gas (with the patient breathing 15l/min of oxygen) showed: pH 7.40, PaO₂ 39.4, PaCO₂ 5.4, HCO₃ 24.8, BE 0.0 and MetHb 11%. An arterial blood gas the next morning was normal with a metHb level of 0.3%. The patient went home.

Discussion

Methaemoglobin (MetHb) is formed by oxidation of the haem molecule from the ferrous (Fe²⁺) to oxidised ferric (Fe³⁺) form. Normal physiological concentrations of MetHb are approximately 1–2%.¹ Higher levels (methaemoglobinaemia) cause tissue hypoxia by two mechanisms: MetHb cannot bind oxygen resulting in reduced oxygen transport and metHb increases the affinity of normal haem molecules for oxygen thereby impairing oxygen release in the tissues.²

The enzyme nicotinamide adenine dinucleotide phosphate (NADPH)–MetHb reductase is involved in maintaining physiological levels of MetHb. Patients with glucose-6-phosphate dehydrogenase deficiency (G6PD) (common in those of Asian,

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Mediterranean or African descent) have low levels of NADPH and are at increased risk of developing methaemoglobinaemia.

Methaemoglobinaemia can be congenital (due to inherited diminished enzymatic reduction of metHb), or acquired (usually due to the oxidative effects of certain drugs). Most cases of methaemoglobinaemia are acquired. Exposure to nitrate and nitrite compounds such as amyl nitrate and glycerine trinitrate are the commonest causes.³

Methaemoglobinaemia due to cocaine abuse is rare. Although cocaine itself does not cause methaemoglobinaemia, adulteration with local anaesthetics or phenacetin in order to enhance the numbing properties that users associate with good quality cocaine, is a recognised cause. In a recent review, Hunter *et al.*⁴ found four cases of methaemoglobinaemia due to cocaine adulterated with local anaesthetics, including benzocaine and lidocaine. Methaemoglobinaemia due to local anaesthetic administration is well recognised.⁵

Typical clinical effects of methaemoglobinaemia depend on the metHb level and are shown in table 1.⁶ Patients with significant methaemoglobinaemia are often profoundly cyanosed and typically have low peripheral oxygen saturations (SpO₂) for reasons that may not be immediately apparent on presentation. Oxygen saturation as measured by arterial blood gas (SaO₂) is usually markedly reduced (provided the ABG machine uses a co-oximeter) giving rise to an apparent 'saturation gap'. Acute physicians should be aware of the possibility of methaemoglobinaemia in recreational drug users who have unexplained cyanosis or low oxygen saturations - often in the presence of a relatively normal PaO₂ on arterial blood gas measurement.

Measurement of PaO₂ in cases of methaemoglobinaemia is therefore falsely reassuring as the PaO₂ merely reflects the concentration of unbound oxygen dissolved in plasma; provided there is no co-existing problem with gas exchange, PaO₂ can remain normal in the face of low total blood oxygen content and life-threatening tissue hypoxia due to the lack of oxygen binding to metHb.

Pulse oximetry is inaccurate in patients with methaemoglobinaemia and may also mask life threatening hypoxia.^{7,8} Standard oximetry uses light absorbance to calculate relative concentrations of oxy- and deoxy-haemoglobin. Methaemoglobin

Table 1. Clinical effects of methaemoglobinaemia.

MetHb level (%)	Clinical Effects
0-15	Clinical effects unlikely
15-30	Mild: Cyanosis of tongue, lips and earlobes, fatigue, dizziness, headache
30-50	Moderate: Weakness, tachycardia, tachypnoea, mild dyspnoea
50-70	Severe: Stupor, coma, convulsions, respiratory depression, cardiac dysrhythmia, metabolic acidosis
>70	Often Fatal

absorbs both of these wavelengths equally. At high levels of metHb (>30%), the pulse oximeter often reads saturations approximating 85%, which correspond with an absorbance ratio of 1:1.⁴

Mild methaemoglobinaemia can be treated by oxygen and removal of the precipitant. Normal metHb levels will be restored by physiological enzymatic reduction of the ferrous iron. The treatment of choice for severe (>30%) or symptomatic methaemoglobinaemia is methyl thioninium chloride (methylene blue) in addition to high-flow oxygen. The recommended dose is 1-2 mg/kg of 1% solution intravenously over 5 minutes.⁹ Methylene blue acts as a substrate for the enzyme NADPH-MetHb reductase. Reduced methylene blue then acts as an electron donor, converting metHb back to haemoglobin.⁵ Patients should be warned to expect blue-green discolouration of their urine following the administration of methylene blue.

Conclusion

Acute physicians should be aware of the possibility of methaemoglobinaemia in recreational drug users, particularly when there is a low SpO₂ or cyanosis in the presence of relatively normal arterial PaO₂. The diagnosis can usually be made from arterial blood gas sampling. When cocaine overdose is suspected, concomitant clinical effects from adulterants as well as those of the illicit drug itself should be considered.

Conflict of Interest

All authors have no conflict of interest to declare. No extraneous funding was obtained.

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