Case Report

Fatal Methaemoglobinaemia Due To Intentional Sodium Nitrite Poisoning

GR Huntington & JM Pennington

Abstract

We report a case of fatal methaemoglobinaema resulting from sodium nitrite poisoning. A 28 year old woman arrested in the emergency department following collapse. During resuscitation a venous blood gas revealed a methaemoglobin percentage of 81%. Following treatment with methylene blue, sodium bicarbonate and adrenaline, the methaemoglobin decreased. Prior to transfer to intensive care, a CT head revealed extensive hypoxic brain injury. Two days later brain death was confirmed on brainstem testing. Severe methaemoglobinaemia is rapidly fatal, with fast diagnosis and treatment associated with improved outcomes.

Keywords

toxicology, methaemoglobinaema, sodium nitrite, poisoning,

Key Points

- Sodium nitrate poisoning is an unusual though increasingly common cause of methaemoglobinaemia
- Clinicians should be suspicious of methaemoglobinaemia in cases of cyanotic hypoxia refractory to supplemental oxygen.

Introduction

Intentional sodium nitrite poisoning is an unusual acquired cause of methaemoglobinaemia though the number of reports are increasing due to its ease.[1,2] Methaemoglobinaemia is the presence of significant increased ratios of abnormal methaemoglobin to haemoglobin. The presence of methaemoglobin is detrimental to oxygen transport and exchange. With sufficient quantities it produces a cellular hypoxia. In this report we describe a fatal case of severe methaemoglobinaemia due to intentional ingestion of sodium nitrite and highlight teaching points pertaining to its reductive mechanism.

Case History

A 28 year old woman was brought into the emergency department cyanosed and in cardiac arrest. She was found collapsed in a park with a note detailing that she had ingested an unknown quantity of sodium nitrite (obtained from an online supplier) at up to six hours prior for the purposes of ending her life. With the ambulance service she was unconscious and cyanosed, with vital signs reflected peri-arrest (hypotension, sinus tachycardia, hypoxia and cool peripheries).

Upon arrival into the emergency department she went into PEA arrest (pulseless electrical activity) with slow narrow complexes on her ECG. Ambulance crew commenced cardiopulmonary resuscitation while the patient was intubated. Her skin and lips were noted to be blue-grey and extremely pale and upon venepuncture sampling her blood was a dark colour. Staff caring for the patient (including ambulance staff) used PPE precautions recommended to frontline professionals during the CoVID-19 pandemic. Although sodium nitrite may be absorbed dermally,[3] this is unusual[4] and nil further precautions were advised by the specialist poisons service.

She was treated with adrenaline boluses, sodium bicarbonate, 100% oxygen and calcium gluconate. Following early conversations with the specialist toxicology unit at St Thomas' Hospital, the patient was treated with methylene blue initially 100mg (2mg/kg) given intravenously over five minutes. A venous blood gas reading recorded the methaemoglobin level at 81% with severe mixed respiratory and metabolic acidosis, a haemoglobin of 125 and a lactate of 11.9. The patient sustained spontaneous circulation for fourteen minutes before returning to PEA arrest. The methylene blue dose was then repeated. The emergency department team achieved sustained cardiac output after 20 minutes. A further dose of 50mg methylene blue was then given (250mg in total) and an adrenaline infusion was started. At this time the patient's cyanosis had improved.

A CT head demonstrated global cerebral oedema with reduced grey-white matter differentiation and significant effacement of the sulci and descent of the cerebellar tonsils through the foramen magnum. This was felt to be consistent with hypoxic-ischaemic encephalopathy, reflecting an extreme cellular hypoxia. Following this, the patient was admitted to the intensive care unit for oxygenation, neuroprotection and monitoring of organ function.

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Methaemoglobin was undetectable (< 3%) on repeat blood gas monitoring four hours following the administration of the final dose of methylene blue.

On the second day of admission, brainstem testing confirmed brain death. The patient's prognosis was discussed with the family. In light of her extensive brain injury and poor functional response, her next of kin consented for her organs to be donated. Following discussions between our specialist nurses for organ donation, our local transplant centre and the coroner, this was deemed appropriate despite the hypoxic hit in light of extensive evaluation revealing nil acute organ impairment beyond the central nervous system.

Discussion

Sodium nitrite is used industrially as a food additive and colour fixative[5] and as a mammalian pesticide due to its toxic qualities.[6] Poisoning has occurred in industrial settings from nitrogenous contamination of water supplies[7] as well as in individual cases of deliberate[1,2] or accidental (through contamination)[5] ingestion. Ingestion of large quantities of nitrites produces a corresponding methaemoglobinaemia.[4,8]

The iron in haem-groups in haemoglobin (Hb) is able to bind and transport oxygen in its reduced ferrous state. In methaemoglobinaemia, iron is present in its oxidised ferric form which is unable to bind oxygen.[9] Thus high percentages of methaemoglobin (metHb) impede oxygen transport in the blood. In addition to this, the resulting increased oxygen availability for ferrous iron shifts the oxygen dissociation curve to the left,[9] leading to an increased affinity and reducing oxygen dissociation at the tissue level, thus worsening cellular ischaemia and producing a hypoxia refractive to supplemental oxygen. Under ordinary physiological conditions, any methaemoglobin spontaneously arising from oxidative stress is reduced.[8]

Methaemoglobinaemia is seen with a deficiency of reducing enzymes or in poisonings of substances acting as electron donors (amyl nitrate, nitrites, benzocaine, etc.[9]) and rarely in recessive genetic disorders producing defects in reducing endogenous reducing enzymes or defects in globin proteins[9] as with the 'Blue Fugates' of Kentucky in the 19th and 20th centuries, so named for their pronounced hereditary cyanosis.[10] In acquired cases of methaemoglobinaemia ingestion of oxidising substances overwhelms the endogenous cytochrome b5 reductase (NADPH-metHb reductase) enzymes[7] otherwise responsible for reducing ferric haemoglobin.

Elevated methaemoglobin is defined as being above 1.5%[7] and may be detected on blood gas sampling. Methaemoglobin is expressed as a percentage and needs to be interpreted in light of the haemoglobin of which it is a percentage. Thus 15% metHb with Hb of 160 represents a greater quantity of abnormal haemoglobin than 20% metHb with Hb 80, for example, and may produce a more severe clinical picture.[9] Symptoms typically appear at 10% metHb and include cyanosis,[7] then dizziness and headache at metHb of 30%[9] followed by dysrhythmias, seizures and coma seen at levels greater than 70% metHb.[7]

Treatment of methaemoglobinaemia aims to support the patient with oxygen while reducing haemoglobin ferric iron to ferrous iron, the recommended agent for this being methylene blue,[4,9] which works alongside innate reducing enzymes by acting as a cofactor and an electron acceptor.[7] This increases the rate of reductase enzyme activity converting ferric iron to ferrous iron and hence metHb to haemoglobin. Methylene blue is given 1-2mg/kg intravenously over five minutes where metHb is greater than 30%.[4]

Conclusion

To conclude, we reported a fatal case of severe methaemoglobinaemia secondary to sodium nitrite poisoning. As well as accidental industrial poisonings, sodium nitrite poisonings may present with intentional ingestion, reflecting its wide availability online. Severe methaemoglobinaemia is rapidly fatal, with fast diagnosis and treatment associated with improved outcomes. Clinicians should be suspicious of methaemoglobinaemia in cases of cyanotic hypoxia refractory to supplemental oxygen.

Declarations of interest

none

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