Case Report

Methaemoglobinaemia due to nitrobenzene poisoning

V. Manolasya, M. Soumya, G. Harshavardhan Reddy, T. Sowjanyalakshmi, B. Sreevidya, D. T. Katyarmal

Department of Medicine, Sri Venkateswara Institute of Medical Sciences, Tirupati, Andhra Pradesh, India

Abstract

An acute poisoning with nitrobenzene presenting as methaemoglobinaemia is an uncommon medical emergency. Here, we report the case of a 33-year-old male presenting with an alleged history of consumption of an unknown substance 24 h ago. On admission, he was unconscious (Glasgow Coma Scale score 3) and gasping. General physical examination revealed cyanosis of the fingers, lips and tongue, pulse: 128/min, blood pressure: 98/70 mmHg and arterial oxygen saturation by pulse oximeter (SpO_2): 70%. Pupils on both sides were dilated and sluggishly reacting to light. Respiratory system examination revealed bilateral basal crepitations. Rest of the physical examination was normal. Tracheal intubation was done, and he was initiated on mechanical ventilator support. Arterial blood gas analysis showed pH: 7.28; arterial carbon dioxide tension ($PaCO_2$): 29.9 mmHg, arterial oxygen tension (PaO_2): 45 mmHg, arterial oxygen saturation (SaO_2): 83.8% and bicarbonate: 13.4 mEq/L. In spite of mechanical ventilator support, he continued to have hypoxia and cyanosis. Saturation gap was calculated to be 13%. In view of which methaemoglobinaemia was considered and blood sample has been sent for methaemoglobin levels and started him on injectable methylene blue and ascorbic acid. After a week, hypoxia and cyanosis improved and he was discharged in a haemodynamically stable condition.

Keywords: Methaemoglobinaemia, Nitrobenzene, Saturation gap

Address for correspondence: Dr D. T. Katyarmal, Associate Professor, Department of Medicine, Sri Venkateswara Institute of Medical Sciences, Tirupati - 517 507, Andhra Pradesh, India.
E-mail: katyarmal.d.t@gmail.com

INTRODUCTION

Nitrobenzene is an oxidising nitrite compound often used in soaps, shoe and metal polishes. It is used as a solvent for lubricating oils and in petroleum refining. Exposure to nitrobenzene occurs in the community from the environment through by inhalation of ambient air, ingestion of or dermal contact with products or water containing nitrobenzene.[1] Secondary cycling of nitrobenzene from body stores can result in the recurrence of symptoms in patients after heavy exposure. Nitrobenzene causes its toxic effects by inducing methaemoglobinaemia.[2] The clinical presentation of nitrobenzene poisoning varies according to the concentration of methaemoglobin level in blood.

Herein, we report a rare case of poisoning with nitrobenzene presented with respiratory distress and cyanosis. Early institution of methylene blue as specific antidote along with haemodynamic and ventilatory support proved crucial saving the life of our patient.

CASE REPORT

A 33-year-old male was admitted with an alleged history of consumption of unknown substance 24 h ago. On

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admission, he was unconscious (Glasgow Coma Scale score 3) and gasping. Key physical and laboratory features are described in Figure 1. General physical examination revealed cyanosis of the fingers, lips [Figure 1a] and tongue, pulse: 128/min, blood pressure: 98/70 mmHg and arterial oxygen saturation by pulse oximeter (SpO_2): 70%. Pupils on both sides were dilated and sluggishly reacting to light. Respiratory system examination revealed bilateral basal crepitations. Rest of the physical examination was normal. Peripheral venous blood sample looked dark brown in colour [Figure 1b]. Urine was found to be bluish in colour [Figure 1c]. Tracheal intubation was done, and he was initiated on mechanical ventilator support. Arterial blood gas (ABG) analysis showed pH: 7.28, arterial carbon dioxide tension ($PaCO_2$): 29.9 mmHg, arterial oxygen tension (PaO_2): 45 mmHg, arterial oxygen saturation (SaO_2): 83.8% and bicarbonate: 13.4 mEq/L. In spite of mechanical ventilator support, he continued to have hypoxia and cyanosis. Saturation gap defined as the difference between SaO_2 and SpO_2 was calculated to be 13. In view of the saturation gap, differential diagnosis considered at this point in time included methaemoglobinaemia, sulphhaemoglobinaemia and carbon monoxide poisoning. Peripheral venous blood sample was obtained for methaemoglobin level testing, and he was started on intravenous methylene blue (1 mg/kg body weight) infused over 10 min and tablet ascorbic acid 500 mg per day. The next day, the attenders of the patient brought the poison bottle labelled as Flower Bloom Plus® containing 20% nitrobenzene [Figure 2]. As there was persistent hypoxia and cyanosis, two cycles of exchange transfusion were done. Intravenous methylene blue was administered for a week in tapering dosage and was stopped on the 8th day after initiation of treatment. Cyanosis improved and hypoxia improved gradually, and the patient was weaned off from ventilator on the 3rd day of admission. He was discharged in a haemodynamically stable condition and was advised to attend psychiatry outpatient service on follow-up.

DISCUSSION

Acute ingestion of nitrobenzene leads to the development of methaemoglobinaemia which oxidises iron in haemoglobin.[3] Oxidised iron causes the characteristic brown colour which does not turn red on shaking the blood with air. Under normal physiological conditions, methaemoglobin (MeHb) constitutes <1% of total haemoglobin,[4] and levels above this are defined as methaemoglobinaemia. This low level of Me. Hb is maintained by two key innate cellular mechanisms,[5] namely hexose monophosphate shunt pathway within the erythrocyte by which oxidising agents are reduced by glutathione prior to the formation of MeHb. In the other mechanism, two enzyme systems are considered to be responsible for preventing MeHb formation. These include diaphorase I (nicotinamide adenine dinucleotide [NADH] MeHb reductase) and diaphorase II (nicotinamide adenine dinucleotide phosphate [NADPH] MeHb reductase). These two enzyme systems require NADH and NADPH, respectively, to reduce MeHb to ferrous state. Methaemoglobinaemia is clinically suspected in patients presenting with cyanosis and a normal PaO_2 levels on ABG. When SpO_2 on pulse oximetry is 5% lower than the SaO_2 on ABG, it is referred to as 'saturation gap'. In our patient, a saturation gap of 13% raised the suspicion of carboxy haemoglobinaemia or methaemoglobinaemia.[6]

Our patient, in whom MeHb levels were 49%, had presented with respiratory distress and was brought gasping to the hospital; cyanosis of the fingers, lips and tongue was evident. Cyanosis occurs when MeHb levels are >10%. At MeHb levels of 20%–30%, mild symptoms such as headache, fatigue and nausea are evident.[7] Dyspnoea on exertion, lethargy and tachycardia manifest at MeHb levels of 30%–45%. At MeHb levels 50%–70%, arrhythmias, coma, seizures, respiratory distress and lactate acidosis develop. MeHb levels >70% cause cardiovascular collapse and can be highly fatal if left untreated.[8]

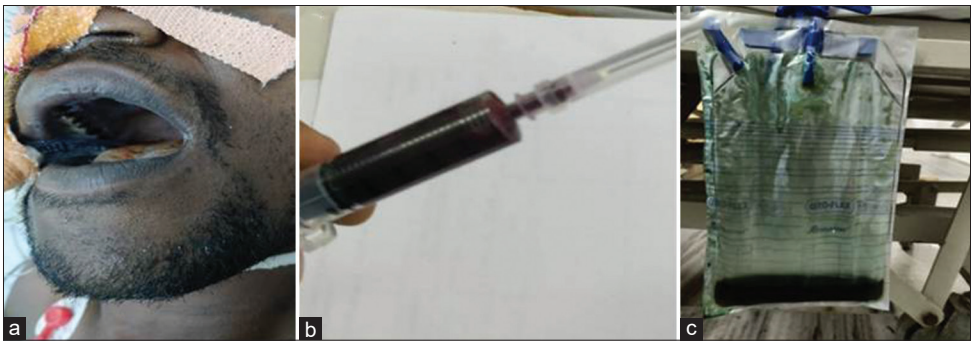

Figure 1: Clinical photograph at the time of admission showing cyanosis of lips (a). Brown-coloured blood drawn from the patient suggestive of methaemoglobinaemia (b). Urobag showing blue-coloured urine (c)

Figure 2: Flower Bloom Plus® used as a flowering fertiliser containing 20% nitrobenzene

Methylene blue is the antidote of choice for acquired methaemoglobinaemia. It acts as an exogenous cofactor which greatly accelerates the NADPH-dependent MeHb reductase system. Methylene blue is indicated for acquired methaemoglobinaemia when the MeHb level is >35% and the patient has cardiorespiratory symptoms.[9] The initial dose is 1–2 mg/kg intravenously infused over 5 min; response is usually evident within an hour. MeHb levels should be checked 1 h after infusion, and a repeat dose is indicated if MeHb levels remain high and the patient is still symptomatic.[3]

Methylene blue in higher doses itself is an oxidising agent and as little as 5 mg/kg has been reported to cause asymptomatic methaemoglobinaemia.[10] Cumulative doses >7 mg/kg have an increased risk of MeHb induction and can cause chest pain, nausea, vomiting, dizziness, hypertension, confusion, diaphoresis, tremor, dyspnoea and cyanosis.

If methylene blue is contraindicated or ineffective, ascorbic acid is often administered as an alternative therapy, but its beneficial effects are considered to occur slowly.[9] Exchange transfusion is indicated in severe cases, when both these measures fail. Exchange transfusions equal to or less than the total volume and up to greater than twice the volume have been advocated.[3]

The present case documents an uncommon occurrence of poisoning with nitrobenzene, which was managed successfully with methylene blue, ascorbic acid, exchange transfusion and other supportive management. The present case also highlights the fact that early recognition of this condition and institution of specific treatment can be life-saving.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to b`e reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Agency for Toxic Substances and Disease Registry. Toxic Substances Portal – Nitrobenzene. Toxicological Profile for Nitrobenzene. Agency for Toxic Substances and Disease Registry. CAS#: 98-95-3. Available from: https://www.atsdr.cdc.gov/toxprofiles/TP.asp?id=532&tid=95. [Last accessed on 2018 Aug 17].
2. Agrawal A, Gutch M, Arora R, Jain N. Acute cardiogenic pulmonary oedema with multiorgan dysfunction – Still to learn more about nitrobenzene poisoning. BMJ Case Rep 2011;2011. pii: bcr1020115026.
3. Schimelman MA, Soler JM, Muller HA. Methemoglobinemia: Nitrobenzene ingestion. JACEP 1978;7:406-8.
4. Mansouri A, Lurie AA. Concise review: Methemoglobinemia. Am J Hematol 1993;42:7-12.
5. Patel A, Dewan A, Upadhyay K, Patel S, Patel J. Chemically induced methemoglobinemia from acute nitrobenzene poisoning. Internet J Lab Med 2008;3:2.
6. Guay J. Methemoglobinemia related to local anesthetics: A summary of 242 episodes. Anesth Analg 2009;108:837-45.
7. Walley T, Flanagan M. Nitrite-induced methaemoglobinaemia. Postgrad Med J 1987;63:643-4.
8. Eisenkraft JB. Pulse oximeter desaturation due to methemoglobinemia. Anesthesiology 1988;68:279-82.
9. Curry S. Methemoglobinemia. Ann Emerg Med 1982;11:214-21.
10. Whitwam JG, Taylor AR, White JM. Potential hazard of methylene blue. Anaesthesia 1979;34:181-2.