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Case Report

Diagnosis and management of nitrobenzene poisoning in a low-resource setting: A case report

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ABSTRACT

Background: and Importance: Nitrobenzenes are aromatic oxidizing nitrate compounds, acute ingestion of which can cause methemoglobinemia (metHb) that impairs oxygen transport. Clinical presentation ranges from cyanosis to asphyxia depending on the level of methemoglobin in the blood. Lack of improvement of hypoxia despite administration of oxygen can also be a clue to the diagnosis.

Case presentation: A 23-year-old male with accidental ingestion of nitrobenzene presented with multiple episodes of vomiting, headache, and dyspnea. His venous blood was dark brown in color and oxygen saturation was not improving despite high-flow oxygen. He was managed with methylene blue and Vitamin C on this background with an appropriate history of nitrobenzene ingestion.

Discussion: Acute nitrobenzene poisoning results in methemoglobinemia which is diagnosed by Co-oximeter but in resource-limited settings, clinical findings such as no improvement in SpO_2 despite supplemental oxygen and chocolate brown appearance of blood aid in the diagnosis. Prompt treatment of methemoglobinemia with methylene blue along with Vitamin C has shown successful and effective outcomes.

Conclusion: Diagnosis of acute nitrobenzene poisoning can be made with proper history, physical and bedside examinations in resource-limited settings even without the aid of a co-oximeter.

1. Introduction

Nitrobenzenes are aromatic oxidizing nitrate compounds used in agricultural fertilizer, soaps, shoes, paints, and dye. Acute ingestion of nitrobenzene can cause methemoglobinemia (metHb) which impairs oxygen transport [1]. Clinical presentation ranges from cyanosis to asphyxia depending on the level of methemoglobin in the blood. Lack of improvement of hypoxia despite administration of oxygen can also be a clue to the diagnosis. Though the gold standard of diagnosis is by co-oximeter which may not be available in resource-limited settings, clinical findings such as no improvement in SpO_2 despite supplemental oxygen and chocolate brown appearance of blood aid in the diagnosis [2].

We report such a case of accidental ingestion of nitrobenzene managed with the infusion of methylene blue and ascorbic acid after diagnosing methemoglobinemia clinically due to the unavailability of a co-oximeter. This case has been reported in line with SCARE criteria [3].

2. Case report

A 23-year-old male presented in the emergency department 3 h after accidental ingestion of approximately 50 ml of Nitrocin, a Nitrobenzene solution (20%) used as agricultural fertilizer. The patient had 3-4 episodes of non-projectile, non-bilious, and non-blood mixed vomiting following ingestion of nitrobenzene associated with headache and dyspnea. He did not have any significant past medical/surgical or family history.

On examination, he had both central and peripheral cyanosis. His heart rate was 64 beats per min, respiratory rate of 24 breaths per min, and blood pressure was 120/80 mmHg. His oxygen saturation (SpO_2) was 82% which was not maintained even with high flow oxygen at 15 L per minute. His chest was clear and no murmur was heard on

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auscultation. His bilateral pupils were 2mm and reactive to light. After his presentation at the ER, a nasogastric tube was inserted and gastric lavage was done. His venous blood was dark brown in color when blood was drawn for the investigation. His arterial blood gas analysis (ABG) reported pH: 7.47; pO2: 257; pCO2: 33.1; SaO2: 100; HCO3: 25.6. His blood parameter revealed mild leukocytosis with normal hemoglobin and renal function tests. The patient was admitted to the intensive care unit (ICU) for further care and management. Due to the lack of tests available for detecting metHb, the patient was clinically diagnosed with probable methemoglobinemia and was treated accordingly. In the ICU, a solution of methylene blue 8 ml in 100ml of normal saline was injected over 30 minutes (1ml = 10 mg methylene blue). A solution of 1 gm of vitamin C was also injected over 30 minutes. The patient's cyanosis decreased and his symptoms improved significantly after the treatment. His oxygen saturation increased to 93% decreasing the requirement of high flow oxygen and arterial blood was repeated which showed pH, 7.43; pO2, 85; pCO2, 41.5; bicarbonate, 27.1; SaO2,95%. The patient was transferred to the ward on the 4th day of admission and was subsequently discharged with oral vitamin C. On follow-up after two weeks of discharge, the patient was doing well and had no symptoms.

3. Discussion

Nitrobenzenes are oxidizing nitrite compounds that can oxidize ferrous iron (Fe++) to ferric iron (Fe+++) in the hemoglobin molecule resulting in methemoglobinemia. Methemoglobinemia is diagnosed when 1% of hemoglobin is oxidized. This results in an inability of hemoglobin molecules to carry oxygen leading to tissue hypoxia [4]. The cause of methemoglobinemia can be congenital or acquired. Acquired methemoglobinemia can be due to exposure to oxidizing agents such as benzocaine, prilocaine, nitrates, aniline, and dapsone [5].

Symptoms of methemoglobinemia correspond with the concentration of methemoglobin. Methemoglobin concentration of <1.5 g/dL (<10%) have no symptoms, 1.5–3.0 g/dL (10–20%) present with cyanosis, 3.0–4.5 g/dL (20–30%) presents with anxiety, lightheadedness, headache, tachycardia, 4.5–7.5 g/dL (30–50%) presents with fatigue, confusion, dizziness, tachypnea, increased tachycardia, 7.5–10.5 g/dL (50–70%) presents with coma, seizures, arrhythmias, acidosis and >10.5mg/dl (>70%) are presented dead [6].

Co-oximeter is the gold standard for the diagnosis of methemoglobinemia [2]. It uses a peak absorbance of light at 630 nm to detect methemoglobin and accordingly uses different wavelengths to detect hemoglobin, deoxyhemoglobin, oxyhemoglobin, and carboxyhemoglobin [6]. ABG result interpretation without co-oximetry can result in misdiagnosis of saturation of oxygen (SaO_2) as it is calculated from PaO_2 which is dissolved arterial oxygen which is normal in methemoglobinemia resulting in falsely elevated SaO_2. In contrast, pulse oximetry measures oxygen saturation (SpO_2) using wavelength to detect oxyhemoglobin and deoxyhemoglobin, and methemoglobinemia results in depressed and inaccurate SpO_2 due to wavelength interference. As a result, patients present with refractory hypoxemia, and also the saturation gap (SaO_2- SpO_2) is more than 5% in methemoglobinemia [5,7,8].

In addition, bedside tests such as placing 1–2 drops of blood on white filter paper and the appearance of dark brown color can help in the diagnosis of methemoglobinemia [6]. In our case, due to the absence of a co-oximeter, clinical findings of cyanosis not improving upon supplemental oxygen, bedside test of chocolate brown color blood and saturation gap of 15% with history of nitrobenzene ingestion were substantial evidence to diagnose methemoglobinemia. A differential diagnosis of sulfhemoglobinemia was made initially, however, all these mentioned facts made robust evidence for the diagnosis of methemoglobinemia.

Treatment of acquired methemoglobinemia includes oxygen with an infusion of methylene blue. Methylene blue uses NADPH produced from Glucose-6-phosphate dehydrogenase-dependent hexose monophosphate shunt to convert to leukomethylene blue, an electron donor which reduces methemoglobin to hemoglobin. Therefore, dextrose can be given in methemoglobinemia, it can make methylene blue more effective as it is essential to form NADPH through hexose monophosphate shunt. In cases of acquired methemoglobinemia, symptomatic patients can be started on treatment if methemoglobin is 30% but asymptomatic patients can also be started on treatment if metHb is 20% [5,9]. The recommended dose of methylene blue is 1–2mg/kg IV over 5 minutes which can be repeated in 30–60min if there is no improvement in symptoms [5].

In conditions in which methylene blue is contraindicated or ineffective, high dose ascorbic acid (Vitamin C) (10g IV) can be given but has a slow reducing capacity. Hyperbaric oxygen therapy is another alternative treatment. Exchange transfusion can be opted in severe cases and when other methods of treatment fail [4,5,10]. Our patient was managed with methylene blue as well as Vitamin C.

4. Conclusion

Nitrobenzene poisoning can result in methemoglobinemia, a life-threatening condition that can be diagnosed clinically and by bedside tests in a low-resource setting where co-oximeter and detection of methemoglobin are often difficult. Treatment with oxygen, methylene blue along with vitamin C has a rapid recovery and good outcome.

Ethical approval

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Author contributions

Rupesh Ramtel- Study concept, data collection and treatment of the patient.
Bibhuti Adhikari- Study concept, data collection and treatment of the patient.
Mijjal Shrestha- Study design, writing, and reviewing the paper.
Niroj Hirachan- Study design, data collection and writing the paper.
Elisha Poddar- Study design, writing, and reviewing the paper.
Suraj Shrestha- Study design, data collection and writing the paper.

Registration of research studies

Name of the registry.
Unique Identifying number or registration ID.
Hyperlink to your specific registration (must be publicly accessible and will be checked).

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Consent

Written informed consent was obtained from the patients for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Declaration of competing interest

None to declare.

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