

Acute Nitrobenzene Poisoning with Severe Methemoglobinemia: A Case Report

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ABSTRACT

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Introduction: Nitrobenzene, an aromatic organic compound used in paints and printing industry. Its toxicity induces methemoglobinemia. **Clinical Sequelae:** A 42 year female patient survived a suicidal consumption of 250ml of 20% Nitrobenzene. On presentation to the hospital, the patient was unconscious and showed typical signs of cyanosis, abnormal arterial blood gas (ABG) showing metabolic acidosis with SpO₂ of 83%, and the arterial blood sample was chocolate brown in colour. The patient suspected of methemoglobinemia showed the formation of 17.7% methemoglobin (normal: 0-2 % of Hb). **Management:** She underwent supportive treatment and was given 1% methylene blue and 1gm ascorbic acid which acts as an oxygen scavenger. The patient eventually made a complete recovery and the ABG was entirely normalized after 17 days due to intensive treatment. **Conclusion:** Acute Methemoglobinemia is usually associated with high mortality; hence early identified and aggressive management of poisoning should be attempted. RBC exchange transfusion and hyperbaric oxygen therapy are usually reserved for patients who are resistant to standard treatment.

Keywords: Ascorbic Acid, Cyanosis, Methylene Blue, Nitrobenzene, Methemoglobinemia, ABG.

INTRODUCTION

Intentional exposure is a major cause of premature mortality globally and 113914 suicides are recorded annually from India for which a variety of chemicals have been used.¹ Nitrobenzene also known as nitrobenzol or oil of mirbane is used in dyes, paints, printing, lubricating oil and synthetic rubber. In India, 20% nitrobenzene emulsion is widely used as pesticides and marketed under the brand name Synflower offered by Mandar agrotech. The lethal dose is reported to range from 1 to 10gm by different studies.²⁻⁴ Nitrobenzene ingestion primarily induces methemoglobinemia. The toxic dose resulting in methemoglobinemia was estimated in one case study at 4.3 to 11gm based on urinary p-nitrophenol levels.⁵

CASE REPORT

A 42 year old woman consumed 250ml 20% Nitrobenzene Pesticide in a suicide attempt. An hour later she was rushed to a local hospital with progressive cyanosis, gasping and unconsciousness. She was quickly transferred to a mission hospital and intubated. Her arterial blood sample drawn was found to be chocolate brown in colour which suspected of methemoglobinemia. Her blood sample analysis suggested

metabolic acidosis with pH: 7.10, PaO₂: 134mmHg, PaCO₂: 42.6mmHg, and HCO₃: 12.9meq/L. Gastric lavage was done via naso-gastric (NG) tube with sodium bicarbonate, followed by administration of activated charcoal (1g/kg of 20% suspension) and started with IV fluids. Her blood sample analysis after 4 hours showed respiratory alkalosis with pH-7.49, PaO₂-273mmHg, PaCO₂ -33mmHg, and HCO₃ -20.2meq/L. Her SpO₂ was 83% and had respiratory distress. Due to non availability of intravenous methylene blue; specific antidote could not be given and was referred to a tertiary hospital. She was brought to tertiary care hospital on ventilator and was drowsy. On examination, her pulse was 106beats/min, blood pressure 90/60mmHg, and her SpO₂ was still 85% with FiO₂ -100%.^[6] Urine was dark coloured, WBC count was 21,500/dL while all the other parameters were normal. *MetHb* spectrophotometry values gave the result as 13.8% (Normal 0-2% of Hb). It was diagnosed as Acute Nitrobenzene Poisoning with Severe Methemoglobinemia and treated with 1% solution of methylene blue 2mg/kg intravenously over a period of 5 minutes and slow intravenous infusion of 1gm ascorbic acid in 5% dextrose thrice a day. She developed ventricular bigeminy and was treated accordingly. She was extubated after 51 hours of ventilation. *MetHb* spectrophotometry values on the 10th day gave the result as 17.7% and SpO₂ was 90%. After five days of ICU stay patient condition was stabilized, slowly recovered, SpO₂ gradually increased and was discharged on the 17th day.

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DISCUSSION

Methemoglobinemia is a condition in which the ferrous (Fe^{2+}) state of iron within haemoglobin gets oxidized to ferric (Fe^{3+}) state, which results in the incapability in oxygen transport and chocolate brown discoloration of blood.⁷ Two different mechanisms define the low level of methemoglobin. The first mechanism happens during the hexose-monophosphate shunt pathway in the erythrocyte which reduces oxidizing agents by glutathione before forming methemoglobin. The other mechanism which is contrary to methemoglobin formation utilizes diaphorase –I and diaphorase –II enzyme systems which necessitate NADH and NADPH enzymes respectively reducing methemoglobin to its ferrous state. The cytochrome b5 reductase enzyme catalyses the NADH-dependent reaction.^{8,9}

Normal level of methemoglobin is 0 to 2% and acute intoxication shows 10 to 15% methemoglobin which is usually asymptomatic sometimes with only cyanosis. Beyond 20% headache, dyspnea, chest pain, tachypnea, and tachycardia develops and above 40% confusion, lethargy, and metabolic acidosis leading to coma, seizures, bradycardia, ventricular dysrhythmia, and hypertension. More than 70% is highly fatal and leads to death. Nitrobenzene is a very lipid soluble compound and a higher concentration accumulates in the adipose tissues. Nitrobenzene turnover is sufficiently slower and its release from these tissues varies from hours to days. Hence, the methemoglobin levels also vary.^{3,9}

It also causes hepatosplenomegaly, elevated liver function, and haemolytic anaemia. Tools of diagnosis include distinguishing smell of bitter almonds, persevering cyanosis on continuous hyperbaric oxygen therapy without pre-existing cardiopulmonary disease, minimal arterial oxygen saturation, and atypical arterial blood gas (ABG) analysis. Chocolate brown colour of arterial blood which fails to turn bright red on shaking is the distinctive feature indicating methemoglobinemia. Pulse-oximeter, co-oximetry, Evelyn-Malloy method and enzyme assay are different spectrophotometric techniques employed to detect the presence of nitrobenzene.⁸⁻¹⁰ Methemoglobinemia can be congenital or acquired; antidote of choice for acquired (toxic) methemoglobinemia is methylene blue, 1-2 mg/kg administered as a 1% solution undiluted as direct IV over 3-5 minutes, repeated at 1 mg/kg in 1 hour as necessary to control fluctuating symptoms. Methylene blue is also known to cause erroneous SpO_2 levels and the antidote is toxic at doses more than 7mg/kg which can cause dyspnea, chest pain, and hemolysis.^{3,12,13} Methylene blue is an exogenous cofactor that donates electron which rapidly reduces methemoglobin to ferrous state through NADPH (nicotinate adenine dinucleotide phosphate) -dependent methemoglobin

reductase system. Methylene blue is contraindicated in patients with G6PD (glucose-6-phosphate dehydrogenase) deficiency leading to severe haemolysis and it can swap its action causing methemoglobinemia at higher doses. Other uses of methylene blue include treatment of urolithiasis, cystitis, herpes simplex infection and antidote of choice in cyanide poisoning.^{3,8,9}

Adjuvant treatment includes ascorbic acid an antioxidant; free radical scavenger which reduces the NAD^+ at doses of 0.5-1gm given 8th hourly.^{2,8} There is very less evidence from recent studies that suggested N-acetyl cysteine is effective in reversing methemoglobin. RBC exchange transfusion and hyperbaric oxygen therapy are usually reserved for patients who are resistant to standard treatment and for those with severe symptoms.⁹ Dextrose should be administered as it's the major source of NADH in the erythrocyte which catabolises sugar through glycolysis and also a source of NADPH through the hexose-monophosphate shunt, which is necessary for enhanced effectiveness of methylene blue.¹⁴

CONCLUSION

The treatment of poisoning caused by an uncommon compound is a challenge and the situation becomes graver when the patient does not respond properly on treatment. Acute Methemoglobinemia is usually associated with high mortality; hence an early aggressive management of poisoning should be attempted.^{10, 12} Methylene blue and ascorbic acid are the treatment of choice, while RBC exchange transfusion and hyperbaric oxygen therapy are usually reserved for patients who are resistant to standard treatment. The authors wish to point out the non availability of intravenous methylene blue should not be a hindrance, as methylene blue powder is available and can be made into 1% solution and sterilized in CSSD (Central Sterile Supply Department).⁹

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