

## CASE STUDY

# Methemoglobinemia Due To Nitrobenzene Poisoning; A Rare Case Series

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### ABSTRACT

*An attempt to commit suicide with toxic substances is common. Though, acute poisoning with nitrobenzene for suicidal purposes or accidental consumption is very rare. Hereby we report three cases of such rare occurrence in which two cases of suicidal attempt and one of accidental ingestion. Both suicidal cases were saved with appropriate management while third case was presented to emergency department very late and unfortunately he succumbed to the poisoning. We would like to highlights in our case series that timely management with intravenous methylene blue helped to save the life.*

**Keywords;** Nitrobenzene, Methemoglobinemia, Methylene blue, Thinner Poisoning, Suicidal Attempt

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## INTRODUCTION

Nitrobenzene is an aromatic nitro compound, pale yellow in colour and moderately water-soluble oily liquid with an odour of bitter almonds. It is readily soluble in organic solvents such as alcohol, ether, and benzene while highly lipid soluble. It has an oxidizing property and used in the manufacturing of aniline, pesticides, rubber chemicals and printing materials etc.[1] Nitrobenzene ingestion may cause acute methemoglobinemia which often presents as a life threatening emergency requiring immediate treatment.[1,2] Early aggressive management with methylene blue improves the outcome of a patient.

## CASE 1

Twenty one-year-old unmarried female with history of consumption of 100 ml thinner following altercation with her elder sister was presented to our emergency with complaints of vomiting, restlessness and breathlessness. At the time of presentation, she had passed more than 2 hours. Central cyanosis was present [Figure 1] and her spO<sub>2</sub> was 60-65 % despite high flow oxygen administration. Her BP 110/80 mmHg, pulse rate 100/M were recorded. Gastric lavage was done immediately and supportive therapy was started.

Her cardiac, respiratory and CNS examinations revealed no abnormality. She had no significant past history. Blood of ABG sampling was chocolate brown in colour and revealed 23% Methemoglobin while LFT, KFT and Electrolytes were within normal limit. Patient was managed with methylene blue 1mg/kg infusion over 15 minutes. Following which her spO<sub>2</sub> became normal and ABG revealed only 3% Methemoglobin.[Table 1] Central cyanosis also disappeared. Her recovery during hospitalisation was uneventful. She discharged on 5<sup>th</sup> day of hospitalization with proper counseling by psychiatry department.

Table 1; Significant ABG analysis reports

Blood chemistry during Hospitalisation	Case 1			Case 2				
	At admission	1 hour	2 hour	At admission	1 hour	2 hour	3 hour	5 hour
pH	7.42	7.41	7.41	7.36	7.38	7.36	7.40	7.41
sPO <sub>2</sub> (%)	62	88	94	50	60	86	88	92
pCO <sub>2</sub> (mmHg)	33.3	36.6	38.0	46	40	38	34	36
HCO <sub>3</sub> (mmol/L)	21.3	22.0	22.2	22	22	21.6	22.0	21.6
MetHb (%)	21.6	3.0	1.3	32	13	2.2	2.0	1.4

### CASE 2

The twenty eight years old married male patient was brought in emergency with nausea, laboured breathing, and discomfort in chest, following ingestion of unknown amount of unknown substance. On general examination, he was drowsy and cyanosis was present on face and extremities [Figure 2] while no pallor or ecchymosis. His vitals were as: blood pressure- 130/80 mmHg, pulse rate- 112/min and respiratory rate-22/min, spO<sub>2</sub> 50%. Systematic examination was unremarkable. Immediately gastric lavage was done and high flow oxygen was started with supportive therapy. He was still not maintaining normal spo<sub>2</sub> even on high flow oxygen, therefore tracheal intubation was done. Presence of central cyanosis, chocolate brown colour of blood and low spO<sub>2</sub> despite high FiO<sub>2</sub> was clinched a clinical diagnosis of Methemoglobinemia. In arterial blood gas analysis, methemoglobin level was found to be 32%. Meanwhile this unknown substance was identified as nitrobenzene by seeing container brought by family members with patient.

Detailed history revealed that patient was a case of bipolar disorder, but he had stopped treatment for one year. After which he developed depression and started expressing frequent suicidal ideas to family members since last 2 months. One night when family members were sleeping, he consumed unknown substance.

His serum electrolytes, random blood sugar, renal function tests and liver function tests were within normal limits. His chest x-ray was normal and his ECG revealed sinus tachycardia.

On the basis of history and examination, patient was managed as a case of nitrobenzene induced Methemoglobinemia and intravenous methylene blue in dose of 1mg/kg body weight was infused over 15 minutes. Arterial blood gas analysis was repeated after one hour which showed Methemoglobinemia level to be 13%. Methylene blue infusion in same dose was repeated, it resulted to normalise Methemoglobinemia level. Subsequently he became conscious after 7 hours with spO<sub>2</sub> of >90% and disappearance of cyanosis. He was extubated after 24 hours. Further recovery was uneventful. He was discharged after 8 days and advice to follow psychiatry OPD properly.

### CASE 3

Thirty five years old married male, painter by occupation was brought to medical emergency in unconscious state at around 8 AM. On examination, pulse and blood pressure were not recordable. Central cyanosis was present.[Figure 3] Immediately, cardiopulmonary resuscitation was started and tracheal intubation was done. Intravenous fluids and other emergency drugs were administered instantly. Unfortunately patient could not be revived despite our best effort.

On elaboration of history from wife, it was found that patient was chronic alcoholic and was drinking alcohol daily. In previous mid-night, she noticed that patient was having nausea, vomiting, restlessness, difficulty in breathing and bluish discoloration of hands as well. She found these symptoms quite unusual and at the same time she got empty bottles of nitrobenzene nearby patient. So patient was brought to community health centre immediately, where after primary management patient was referred to higher centre, though patient's condition was deteriorating.

On the basis of history (empty bottles of nitrobenzene) and clinical presentation, clinical diagnosis of nitrobenzene induced methemoglobinemia was made and patient succumbed to death. He could have been revived if he would have been brought in time and appropriately managed with methylene blue.

### DISCUSSION

Methemoglobin (MHb) is called when the oxidation of ferrous iron (Fe<sup>2+</sup>) to ferric iron (Fe<sup>3+</sup>) takes place within the hemoglobin molecule. It impairs the oxygen carrying capacity of hemoglobin which leads to tissue hypoxia or may be fatal if severe.[3] Methaemoglobin is normally present in the body as less than 1% of the total haemoglobin.[4] Nitrobenzene intoxication leads to rapid development of methaemoglobinaemia.[4] The first case of nitrobenzene poisoning was reported in 1886 and

subsequently many cases have been reported.[5] According to review of published articles, the lethal dose of nitrobenzene ranges from 1 g to 10 g.[6]

The causes of methemoglobinemia may be genetic or acquired, with the latter being much more common. The congenital causes of methemoglobinemia are NADH cytochrome-b5 reductase enzyme deficiency (autosomal recessive), cytochrome-b5 enzyme deficiency (autosomal recessive), and hemoglobin M disease due to globin chain mutation (autosomal dominant).[1,7] Though, most of methemoglobinemia cases are due to exposure to exogenous oxidizing agents including Chloroquinine, Clofazimine, Dapsone, Dimethyl Sulfoxide, Dinitrophenol, Ferricyanide, Lidocaine, Methylene Blue, Metoclopramide, Maphthalene, Nitrates, Nitrites, Nitrobenzene, Nitroglycerin, Nitroprusside, Paints, Phenacetin, Phenazopyridine, Phenytoin, Primaquine, Prilocaine, Resorcinol, Rifampicine, Smoke Inhalation, Sodium Valproate, Sulfasalazine, Sulphonamides and Toluidine.[2] Clinical manifestations according to methaemoglobin level [8] are as

- a) Level up to 10- 15% of methemoglobin- usually asymptomatic or only cyanosis.
- b) Beyond 20%-headache, dyspnea, chest pain, tachypnea, and tachycardia.
- c) At 40 - 50%- confusion, lethargy, and metabolic acidosis occur which may lead to coma, seizures, bradycardia, ventricular dysrhythmia, and hypertension.
- d) Level around 70%- this high level is fatal.

Above features may worse if patients are known case of anemic or G6PD-deficiency. Hepatosplenomegaly, altered liver functions, and Heinz body haemolytic anaemia are also reported in some cases. Nitrobenzene is metabolized to p-nitrophenol and aminophenol and It is excreted largely through urine up to 65% while remaining in stools. Nitrobenzene may accumulate in liver stomach, blood, and brain which is then released gradually.[8] Following points may be helpful to reach diagnosis of methemoglobinemia-

- a) History of nitrate chemical ingestion and the characteristic smell of bitter almonds.
- b) Persisting cyanosis even though patient is on oxygen therapy. It is necessary to rule out severe cardiopulmonary disease.
- c) Low arterial oxygen saturation, despite normal ABG (calculated) oxygen saturation
- d) Dark Brown discolouration of blood that fails to turn bright red on shaking.
- e) Associated acidosis can worsen the symptoms

The diagnosis is confirmed by quantitative estimation of blood methemoglobin levels by a co-oximeter.[9] and the presence of nitrobenzene compounds may be confirmed spectrophotometry.[8] A case of symptomatic methaemoglobinaemia require intensive monitoring until symptoms clear or the methaemoglobin level is below 15%.[4]

Management of nitrobenzene acute intoxication is based on the principles of decontamination and symptomatic therapy. Methylene blue is the antidote of choice for acquired methemoglobinemia. The initial dose of methylene blue is 1 to 2 mg/kg or 0.1 to 0.2ml/kg of the 3% solution which is given intravenously over five minutes.[4] It acts immediately and response occurs within 1 hour. Methaemoglobin levels should be checked 1 hour after infusion level. If methaemoglobin level remains high and patient is still symptomatic, repeat dose of methylene blue is indicated.[4] By the way, methylene blue is contraindicated or ineffective, ascorbic acid is an option as an alternative therapy. Though its reducing effect is too slow to have significant benefit.[4] In more severe cases or both above therapies are failed, exchange transfusion is beneficial. [4,8]. Recently some studies have been shown beneficial effect of N-acetylcysteine in methemoglobinemia but it is not yet approved.[8] Hyperbaric oxygen is reserved for patients having methemoglobin level > 50% or patients not responding to standard treatment. Forced diuresis has been shown to reduce methemoglobin level and improve discolouration.[8]

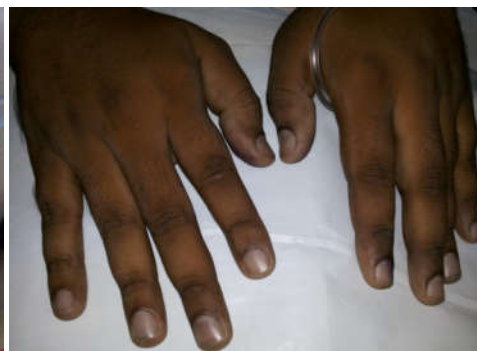
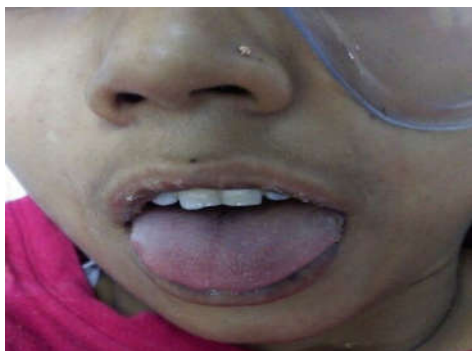


Figure 1; Bluish discolouration of tongue      Figure 2; Bluish discolouration of fingers



Figure 3; Bluish discoloration of hand

### CONCLUSION

Acute poisoning of nitrobenzene causes significant methemoglobinemia and it is life threatening emergency. Early diagnosis and optimal emergency management with methylene blue improves the outcome of a patient.

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