Acute Methemoglobinemia Due to Cosumption of Nitrobenzene Compound

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Abstract : nitrobenzene is a yellow oily liquid nitrite compound, very toxic in nature, have ability to convert hemoglobin to methemoglobin. The clinical features depend on the concentration of methemoglobin level in the blood. We report two cases of acute methemoglobinemia due to consumption of nitrobenzene compound. Early management with methylene blue as antidote and hemodynamic and ventilator support will help in saving a patient and late presentation can be fatal.

Key words: Nitrobenzene, Methemoglobinemia, Cyanosis, Methylene blue,

Introduction :

Nitrobenzene is a yellow oily liquid with an almond like odour. It may be pale yellow-brown in appearance. Nitrobenzene is hygroscopic in nature. Intoxication by this compound is suicidal or accidental. The toxic effects after ingestion are due to the rapid development of methemoglobinaemia i.e. a condition in which the iron within the hemoglobin is oxidized from the ferrous state to the ferric state. This results in the brownish discoloration of the blood and its inability to transport oxygen. The diagnosis of nitrobenzene poisoning is suspected when a blood sample drawn is brown in colour and does not change even with supply of oxygen. Methemoglobinemia may be congenital due to deficiency of cytochrome B5 reductase and abnormal structure of the hemoglobin molecule or may be acquired due to oxidative stress secondary to various drugs or chemicals, commonest are nitrites or nitrates.

The clinical features due to exposure to nitrobenzene compound are inflammation of exposed area, headache, nausea, vomiting, confusion, vertigo, ataxia, tremor and coma can occur. Patient develops cyanosis, tachypnoea, and tachycardia. Patient may complain of chest pain, lethargy.

Patient may develop arrhythmia, metabolic acidosis which are life threatening. Nitrobenzene affects spleen, which may become tender and enlarged. Death usually occurs within six to seven hours of ingestion.

Case report 1:

A 15 year old female was brought to casualty by relatives after five hours of alleged history of consumption of unknown compound. At the time of presentation she had complains of nausea, vomiting approximately 2 to 3 episodes and pain in abdomen. She was conscious oriented but irritable. On examinations pulse 90 beats per minute, blood pressure was 110/70 and respiratory rate was 20 cycles per minute, central cyanosis was present with saturation of 70-75% even on supplementation of 8-10 liters of oxygen per minute. No significant systemic examination abnormalities were detected. Patient was immediately transferred to ICU. And blood examination was send immediately. Complete blood count values are normal with hemoglobin of 10.2gm/dl, total leukocyte count was 7200, liver function test and kidney function test are normal. Chest x-ray chest was also normal.

Acid blood gas were done shows

pH	pCo_2	pO_2	HCO_3-	SpO_2
7.39	30	71	18.2	94%

meanwhile relatives brought the compound called BENZ-35 (nitrobenzene compound 35%) which she consumed about 20ml. Hence test for methemoglobinemia was done, showed 14%.

Treatment : Patient was hemodynamically stable and was comfortable even though saturation was low. So patient was given intermittent non-invasive ventilation (BIPAP ventilation). Invasive ventilation avoided and close monitoring was for any signs of deterioration. Methylene blue was given as per dose of 1-2mg per kilograms. Patient weighed 40 kg. Hence 40 mg of methylene blue was given. Along with methylene blue ascorbic acid 500mg was also added and antibiotic coverage was given. Patient responded well initially to treatment, her saturation improved to 85-90%, but later on again dropped. Patient was also transfused with one packed cell volume, after 24 hours no further improvement in saturation and cyanosis was seen hence methylene blue was repeated . After second dose patient showed signs of complete improvement with 97% of saturation on room air and no cyanosis. Acid blood gas repeated

pH	pCo_2	pO_2	HCO_3-	SpO_2
7.36	34	97	20.4	98

She was kept two more days for observation and then discharged after 5 days.

Case report 2: A 45 year old male was bought to casualty after seven hours of history of consumption of 'Bloom Flower' which contains nitrobenzene compound 35% about in 100 ml. Patient was extremely restless, pulse rate 116/min blood pressure -90/60 with central cyanosis and tachypnoea with saturation of 78% on high flow oxygen. Patient immediately admitted in ICU and endotracheal intubation done as there was in respiratory distress. Investigations were done, showed Hb-14.6 TLC-9500 platelets-156000, normal chest x-ray, ABG was suggestive of

pH	pCo_2	pO_2	HCO_3-	SpO_2
7.10	38	56	16	76

Methemoglobin levels were 44%.

Methylene blue was given 65mg intravenously stat along with ascorbic acid 500mg antibiotic coverage. Supportive management was given with ionotropic support and sodium bicarbonate to correct blood pressure and metabolic acidosis. There was no improvement seen in saturation hence methylene blue repeated. Despite of all appropriate measures patient developed bradycardia and cardiac arrest within 12 hours of admission.

Discussion: Nitrobenzene is a nitrite compound which is oxidising nature. Acute consumption of this compound leads to speedy development of methaemoglobinaemia Nitrobenzene oxidizes iron in hemoglobin and forms methaemoglobin(MeHb)[1]. In 1886 first case was reported with nitrobenzene poisoning and which was subsequently followed by many casulties.[2,3] Modes of intoxication may be due to accidental or suicidal consumption.[2] Patients consuming well water with very high levels of nitrites and nitrates leads to accidental toxicity .[4]

The MeHb is maintained at low level by two mechanisms.[7] in erythrocyte there is hexose monophosphate shunt pathway, by which glutathione reduces oxidizing agents before formation of MeHb. This is first mechanism. The second mechanism consists of two enzymes systems which act against formation of MeHb : Diaphorasel (nicotinamide adenine dinucleotide, NADH MeHb reductase) and diaphorase II (nicotinamide adenine dinucleotide phosphate, NADPH, MeHb reductase). NADH and NADPH respectively are required by these two enzyme systems to reduce MeHb ferrous state. MeHb constitutes normally < 1% of the total Hemoglobin in physiologic state. Increase in levels of methemoglobin is defined as methemoglobinemia. The estimated lethal dose ranges from 2 gm to 6 gm in adults; and doses less than 0.8 mg/kg/day does not normally cause methemoglobinemia.[5]

Clinical features of acute intoxication usually depend on level of methemoglobin. Usually patient is asymptomatic up to the level of 10 – 15% of methemoglobin, showing only cyanosis. More 20%, patient experiences headache, dyspnoea, chest pain, tachypnoea, and tachycardia develop. At the level of 40 – 50%, confusion, lethargy, and metabolic acidosis occur leading to coma, seizures, bradycardia, ventricular arrythmias, and hypertension. Level around of d 70% is deadly. Patients with anemiac or G6PD-deficiency patients present with severe symptoms.[2,4] There is leukocytosis with relative lymphopenia.[6]

Patient may other features include hepatosplenomegaly, abnormal liver function test, and Heinz body haemolytic anaemia.2,6 p-nitrophenol and aminophenol are metabolic products of nitrobenzene of which up to 65% is excreted in urine and up to 15% in stools after five days of ingestion. These are gradually released from liver, stomach, blood, and brain.

Diagnosis can be reached with history of chemical ingestion, the characteristic smell of bitter almonds, cyanosis persisting even after oxygen therapy without in patient without any underlying cardiopulmonary disease, normal ABG (calculated) oxygen saturation, with low arterial oxygen saturation. Methaemoglobinemia is suggested by failure Dark brown blood to turn bright red on shaking. This is also supported by evidence that dried blood is chocolate red in colour. Spectrophotometry confirms presence of nitrobenzene compounds and butanone test of Schrenk,2 estimates methemoglobin levels in the blood, and presence of p-nitrophenol and p-aminophenol in urine.[2,7,8]

Patient's treatment is aimed at decontamination, giving symptomatic and supportive care. In acquired (toxic) methaemoglobinaemia Methylene blue is the treatment of choice. NADPH-dependant methemoglobin reductase system is accelerated by methylane blue while acting as exogenous cofactor. Use of methylene blue is indicated if the methemoglobin levels > 30%.5 It is administered intravenously at 1 – 2 mg/kg (up to 50 mg dose in adults,) as a 1% solution over five minutes; with a repeat in one hour, if necessary. Methylene blue acts as

an oxidant at levels of more than 7 mg/kg, hence may cause methaemoglobinaemia susceptible patients. G6PD deficiency is contraindication to methylene blue because it may lead to severe haemolysis. Ascorbic acid acts as antioxidant can be used in patients with methemoglobin levels of more than 30%.[9] In recent advances, for methaemoglobinaemia can be treated with N-acetylcysteine, as it has been effective to reduce methemoglobin, but it is not yet an approved treatment.[8] second line treatment includes exchange transfusion and hypebaric oxygen. In severe cases exchange transfusion is indicated.[5,9] Hyperbaric oxygen for patients with a methemoglobin level > 50%.[2]

In these 2 case, that are presenting, in first use low dose of methylene blue and appropriate time helped patient overcome fluctuations in symptoms secondary to release of nitrobenzene from the body stores. Transfusion with packed cell volume improved her oxygen carrying capacity, improving the patient symptomatically. Patients care regarding hydration, nutrition and hepatoprotection prevented renal failure and liver failure, these may resulted as long term complications of nitrobenzene poisoning.[2,7]Forced dieresis was given to lower methemoglobin levels rapidly and improving discoloration.[6] Antioxidants were given for follow-up management of methemoglobinaemia.[10]

Second patient presented late, after seven hours so despite of all supportive measures unfortunately couldn't survive.

Conclusion : Nitrobenzene poisoning is a dangerous condition, but it is treatable with aggressive management with methylene blue ,ascorbic acid and if needed ventilator support. But late presentation can be fatal.

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