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Case Report

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NITROBENZENE POISONING WITH SEVERE METHEMOGLOBINEMIA: A CASE REPORT

Dr. Uday S. Bande, Dr. Ishwar Hasabi, Dr. Basith Lateef K.*, Dr. Basavaraj B. Baligar and Dr. Praveen Kusubi

Department of General Medicine, Karnataka Institute of Medical Sciences, Hubli, (K.I.M.S. Hubli.).

***Correspondence for Author: Dr. Basith Lateef K.**

Department of General Medicine, Karnataka Institute of Medical Sciences, Hubli, (K.I.M.S. Hubli.).

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ABSTRACT

A rare fatal case of self-poisoning with nitrobenzene and organophosphorous poisoning is presented following oral ingestion is reported. 20 year old, irritable, anxious male presented to emergency referred from secondary center with respiratory failure and cyanosis, A clinical diagnosis of severe acute methhemoglobinemia of nitrobenzene and organophosphorous compound was made. Methylene blue and exchange transfusion were the therapeutic methods applied in the treatment of the Methemoglobinemia. Patient was discharged on13 days with iron folate .ascorbic acid, antibiotics, physiotherapy and psychiatric counseling. Conclusion Poisoning with nitrobenzene can cause life-threatening methemoglobinemia that can be reversed by methylene blue.

KEYWORDS: Nitrobenzene Poisoning, Methemoglobinemia, Methylene blue.

INTRODUCTION

Nitrobenzene is an organic compound with the chemical formula $C_6H_5NO_2$. It is a water-insoluble pale yellow oil with an almond-like odor. It is highly toxic with Limit Value 5 mg/m^3. Nitrobenzene is considered a likely human carcinogen by the United States Environmental Protection Agency, and is classified by the IARC as a Group 2B carcinogen which is "possibly carcinogenic to humans".[1]

Its toxicity induces methemoglobinemia. The first report of poisoning due to nitrobenzene was in 1886 and subsequently several cases have been reported.[2] The lethal dose is reported to range from 1 to 10gm[3] the toxic dose resulting in methemoglobinemia was estimated in one case study at 4.3 to 11gm based on urinary p-nitrophenol levels.[4]

Recommended treatment is based on the principles of decontamination and symptomatic and supportive management. To review the clinical features of acute toxicity of aromatic amino and nitro compounds 1240 cases of acute toxicity induced by aromatic amino and nitro compounds from 1979 to 2013were studied. Methemoglobinemia was found in 1146 cases, while cases of poisonings with 5-nitro-o-toluidine, 2-methyl-4-nitroaniline, and 3-chloro-2-methyl aniline were not found to have methemoglobinemia.[5]

Acute poisoning with nitrobenzene is uncommon but life threatening emergency. Early aggressive management of severe poisoning, strongly suspected on clinical grounds may change outcome of a patient.

CASE REPORT

20 year old, irritable, anxious male presented to emergency referred from secondary center with respiratory failure and cyanosis, poor respiratory efforts 10 cycles per minute, BP120/70, pulse 120/min, pupils 4mm reactive to light, spo2 81%. there was a history of vomiting, increased salivation, pain abdomen, and uneasiness. At the secondary referral center, stomach wash, injection atropine, and PAM was given. in view of the low saturation, poor respiratory efforts the patient was intubated and put on ventilator, blood drawn for the samples showed chocolate brown color, saturation did not improve even with 100% oxygen, abg showed compensated metabolic acidosis ray chest was normal, ECG was within normal limits blood urea serum creatinine were normal.

Hemoglobin at admission was 11.1 gm%, 9.3 gm %, the next day and 5.9 on the third day. Bilirubin on admission was 0.6 raised to 2.4 on next day.

A clinical diagnosis of severe acute Methemoglobinemia of nitrobenzene and organophosphorous compound was made.100 mg methylene blue repeated after 12 hours, along with atropine 2cc half hourly and PAM were given 2gm iv stat followed by 600mg/kg/hour, Vitamin C, intravenous fluids, prophylactic antibiotics, anxiolytics were given. Urine output was maintained at 100ml/hour and a normal central venous pressure was maintained. Three pints of whole blood were transfused.

Meth hemoglobin estimation was done which was high (5.1 units as compared to normal values of

<1.5).methylene blue was continued till the urine colour and blood changed to normal colour.

Patient was extubated after6 days and maintained on oxygen at 6l/min. He improved rapidly after 6 day with an sp02 of 92% at room air. Patient was discharged on13 days with iron folate .ascorbic acid, antibiotics, physiotherapy and psychiatric counseling.

3. DISCUSSION

Nitrobenzene is an oxidizing nitrite compound. Acute ingestion of nitrobenzene leads to rapid development of methaemoglobinaemia. Methaemoglobin is normally present as less that 1% of the total hemoglobin under physiologic conditions. Levels above it is defined as methaemoglobinaemia. The estimated lethal dose ranges from 2 to 6 gms in adults; and doses less than 0.8mg/kg/day does not normally cause methaemoglobinaemia.

The toxic effects after ingestion are due to the rapid development of methaemoglobinaemia,[4] a condition in which the iron within the haemoglobin is oxidized from the ferrous (Fe2+) state to the ferric (Fe3+) state, resulting in the inability to transport oxygen and causes a brownish discoloration of the blood.[3] Once formed, methemoglobin can be reduced enzymatically either via an Adenine dinucleotide (NADH)-dependent reaction, catalyzed by cytochrome b5 reductase, or an alternative pathway utilizing the nicotine adenine dinucleotide phosphate (NADPH)-dependent methemoglobin reductase system.[6]

Methaemoglobin is formed by oxidation of ferrous (FeII) haem to the ferric (FeIII) state and the mechanisms by which this occurs are complex. Most cases are due to one of three processes. Firstly, direct oxidation of ferrohaemoglobin, which involves the transfer of electrons from ferrous haem to the oxidising compound. This mechanism proceeds most readily in the absence of oxygen. Secondly, indirect oxidation, a process of co-oxidation which requires haemoglobin-bound oxygen and is involved, for example, in nitrite-induced methaemoglobinaemia. Thirdly, biotransformation of a chemical to an active intermediate that initiates methaemoglobin formation by a variety of mechanisms. Methaemoglobinaemia presents clinically with symptoms and signs of tissue hypoxia. Pulse oximetry is unreliable in the presence of methaemoglobinaemia. Arterial blood gas analysis is mandatory in severe poisoning and reveals normal partial pressures of oxygen (pO2) and carbon dioxide (pCO2,), a normal 'calculated' haemoglobin oxygen saturation, an increased methaemoglobin concentration and possibly a metabolic acidosis. Following decontamination, high-flow oxygen should be given to maximize oxygen carriage by remaining ferrous haem. No controlled trial of the efficacy of methylene blue has been performed but clinical experience suggests that methylene blue can increase the rate of methaemoglobin conversion to haemoglobin some 6-fold. Patients with features and/or methaemoglobin concentrations of 30-50%, should be administered methylene blue 1-2 mg/kg/bodyweight intravenously (the dose depending on the severity of the features), whereas those with methaemoglobin concentrations exceeding 50% should be given methylene blue 2 mg/kg intravenously.[7]

Acute oral exposure of NB has resulted in MetHb, cyanosis, anemia and neurological effects including headache, nausea, vertigo, confusion, unconsciousness, apnea, coma and death. Signs and symptoms may be delayed several hours because some chemicals do not directly produce MetHb, but require biochemical transformation to toxic metabolites. MetI-Ib imparts a chocolate hue to the blood. The diagnosis should be suspected when a blood sample is brown colored and does not redden on exposure to air. The aetiology of MetHb may be congenital because of deficiency in cythocrome b5 reductase and structural abnormalities in the hemoglobin molecule or could be acquired as the result of the oxidant stress from various drugs or chemicals, most commonly nitrites or nitrates.[8]

Methylene blue: initial dose adult/child: 1 to 2 mg/kg/dose (0.1 to 0.2 mL/kg/dose) IV over 5 minutes with a 30 mL flush of normal saline as needed every 4 hours. Improvement is noted shortly after administration if diagnosis is correct. Methylene blue may also be given by intraosseous infusion if intravenous access cannot be established. Additional doses may be required neonates: DOSE: 0.3 to 1 mg/kg.[9]

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