



A Case Report on Nitrobenzene Poisoning

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Abstract

Acquired methemoglobinemia may be frequently encountered in rural India. This case report throws light on the essence of timely diagnosis and intervention where the immediate administration of the cost effective but life saving antidote of methylene blue can make a difference in saving the patient's life and preventing further complications.

Keywords: Methemoglobinemia, nitrobenzene, methylene blue.

Introduction

Acute poisoning with nitrobenzene is not an uncommon case, especially in rural India where toxic compounds are easily available in the form of insecticides. However, its significance lies in timely identification of symptoms, availability of antidote and prevention of complications as early aggressive management has a great impact on the outcome of the patient.

Case Report

A 32 year old female was brought to the emergency with alleged history of unknown insecticide poisoning. She was referred from local primary health centre after being administered preliminary care. On examination she was found to be conscious with evidence of central cyanosis,

blood pressure 100/60 mmHg, pulse rate 102/min, pupils reacting to light and a saturation of 90%, that improved with oxygenation. She complained of dizziness and gave history of three episodes of vomiting immediately after consuming the poison. In the emergency, she was administered gastric lavage. Arterial blood gas analysis revealed oxygen saturation gap with metabolic acidosis. A clinical diagnosis of methemoglobinemia was made and she was shifted to critical care for further management. However, on the second day of admission, the container with the toxic compound was brought by the patient's husband and it proved to be a nitrobenzene composition. Blood samples drawn were chocolate brown in colour, reinforcing our diagnosis. An ultrasound of the abdomen and pelvis revealed normal study.

Chest radiograph and ECG were also normal. Liver & renal function tests, serum electrolytes, coagulation profile proved to be normal. However hemoglobin which was 9.8g/dL at the time of admission, dropped down to 4 g/dL after a week. Subsequent peripheral smear done revealed microcytic hypochromic anemia with no evidence of hemolysis. Echo revealed mild dilatation of all chambers of heart with trivial mitral regurgitation and normal ejection fraction. Toxicology analysis showed a normal serum cholinesterase value of 10,454 and a high methemoglobin value of 12.3% (day 3). Unfortunately, it could not be repeated due to financial constraints.

She was administered methylene blue 50mg (5mL@1 mg/kg) for every 12 hours immediately on admission and thereafter continuously for 5 days after assessing the need clinically. Care was taken not to exceed the critical dose which was not more than 7 mg/kg/day. Parenteral vitamin K, tablet vitamin C, intravenous fluids, dextrose infusions and antibiotics were given. Two units of packed cell were transfused on day 7 & day 9 of admission to correct anemia. Patient responded well to the treatment and improved symptomatically. She was transferred to regular ward and was offered counseling for suicidal tendencies. She was discharged after two weeks with supplemental iron, folate, ascorbic acid and other nutrient supplements and is doing well on regular follow-up.

Discussion

Methemoglobinemia is characterized by excessive amount of hemoglobin in which the ferrous (Fe^{2+}) of heme is oxidized to the ferric (Fe^{3+}) form. Methemoglobin is useless as an oxygen carrier and causes varying degree of cyanosis. This condition may be genetic or acquired.

Hereditary methemoglobinemia is a recessively inherited disorder due to deficiency of reduced nicotinamide adenine dinucleotide (NADH) cytochrome b_5 reductase. Normal red blood cells have a system to convert useless methemoglobin to functional hemoglobin, the mechanism for

which resides in the soluble NADH cytochrome b_5 reductase. The gene regulating the synthesis of cytochrome b_5 reductase is located in chromosome 22q13 and this gene, when mutated, can cause severe methemoglobinemia, which is of two types: type I-erythrocyte and type II – generalized.^{1,2}

Acquired methemoglobinemia is caused by exposure to some specific drugs or toxins, which may be from food or work - related. Cyanosis resulting from drug administration has been recognized since 1890³. The most common cause of methemoglobinemia overall is due to accidental ingestion or exposure to oxidizing agents. There are two mechanisms involved:

- 1) Oxidation of hemoglobin to methemoglobin
- 2) Reduction of oxygen to free radical O_2 , which in turn oxidizes hemoglobin to methemoglobin.

Outbreaks of methemoglobinemia have been reported due to nitrite poisoning from water contamination.⁴

The physiologic level of methemoglobin in the blood is 0% to 2%.² Toxicity is expressed according to the level of methemoglobin in blood as follows:

10% - 20% - Well tolerated.

30%-50% -Dyspnoea, nausea, tachycardia

55%-70% - Lethargy, stupor, cardiac arrhythmias and circulatory failure.

>70% - Death

Drugs like dapsone, sulfasalazine, or phenacetin cause hemolytic anemia, characterized by Heinz bodies and fragmented red blood cells. Sometimes this acute intravascular hemolysis can precipitate renal failure.

With regards to treatment, supportive therapy like oxygen supplementation and decontamination with activated charcoal (for long acting drugs like dapsone) is initiated. In a symptomatic patient, methylene blue is administered intravenously, 1 mg/kg over 3–5 min. Repeat dose can be administered in 30 minutes if cyanosis does not improve.⁵ Methylene blue, which has a active form leukomethylene blue, acts as an electron

donor to the ferric iron, reducing it back to ferrous state. The main contraindication is G-6PD deficiency. In this condition, NADPH is not produced and methylene blue cannot activate the alternate pathway to reduce methemoglobin.⁶ Another reason is that oxidative stress caused by methylene blue can induce hemolysis. At levels of more than 7 mg/kg, methylene blue is an oxidant and hence can cause methaemoglobinaemia in susceptible patients.

Ascorbic acid can be administered to patients with methemoglobin levels of more than 30%. It acts as an anti-oxidant. Recently, N-acetylcysteine has been shown to reduce methemoglobin (Studies are ongoing; its use is not approved till date). In severe cases, exchange transfusion is indicated.⁷ Hyperbaric oxygen is used only for those patients who have a methemoglobin level above 50% and for those who do not respond to routine treatment.⁸

In this case, timely identification and repeated low dose methylene blue helped in managing the fluctuating symptoms caused by the release of nitrobenzene from the body stores. Adequate hydration and nutrition therapy helped in preventing kidney and liver failure, which have been cited as late effects.⁹

Conclusion

Timely diagnosis and availability of methylene blue goes a long way in bettering the mortality and morbidity of the patients. Steps should be taken to curb the easy and cheap availability of toxic insecticides in rural India. Should such scenarios arise, physicians should avail the utility of cheap and life saving drug, which is easily available in the hospital laboratories or even with the local chemists.

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