Chemically Induced Methemoglobinemia From Acute Nitrobenzene Poisoning

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Citation

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Abstract

Methemoglobinemia is an unusual and potentially fatal condition in which hemoglobin is oxidized to methemoglobin lowering its ability to bind and transport oxygen. The most common cause of methemoglobinemia is the ingestion or inhalation of oxidizing agents such as nitrates and nitrites. A rare case of self-poisoning with nitrobenzene following oral ingestion is reported. On presentation to the hospital, altered sensorium and cyanosis were observed in a young male who ingested about 75 ml of an unknown liquid in the previous 6 hrs. Timely identification of the compound and the estimation of methemoglobin (MeHb) were helpful in saving the patient. The importance of laboratory support activity of a poison information center in evading death due to unknown poisoning has been highlighted.

Organizations involved in the work:

(i) Poison Information Centre,
National Institute of Occupational Health (NIOH)
Ahmedabad-380 016, Gujarat, INDIA
(ii) Civil Hospital,
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INTRODUCTION

Suicide is a major cause of premature mortality globally and 113914 suicides are recorded annually from India [1] for which variety of chemicals are used. The primary mission of poison control centres has always been an improvement in the poisoned patients' care and poison prevention. The need to reach this mission implies that many functions and roles must be accomplished. However, two of the main challenges of poison centres in developing countries are still treatment information and laboratory services. The treatment of poisoning caused by an unknown compound is a challenge to a treating physician. The situation becomes graver when the laboratory support for certain specific poison is unavailable. Thus, laboratory support is an essential component of a poison control centre providing analytical services on emergency basis to help in diagnosis and management.

Nitrobenzene, an aromatic nitro-compound, occurs as a pale yellow moderately water-soluble oily liquid with an odor resembling that of bitter almonds. It is slightly soluble in water, readily soluble in organic solvents such as alcohol, ether and benzene [2] and highly soluble in lipids. It is used in the manufacture of aniline, benzidine, quinoline, azobenzene, rubber chemicals, pharmaceuticals and dyes [3]. It is also used as a solvent in shoe and metal polishes and in screen-printing. Its toxic effects are due to its ability to induce methemoglobinemia. An acute poisoning with nitrobenzene presenting with methemoglobinemia is an uncommon medical emergency. We describe here an unusual case of acute nitrobenzene poisoning in a suicidal attempt by a young boy.

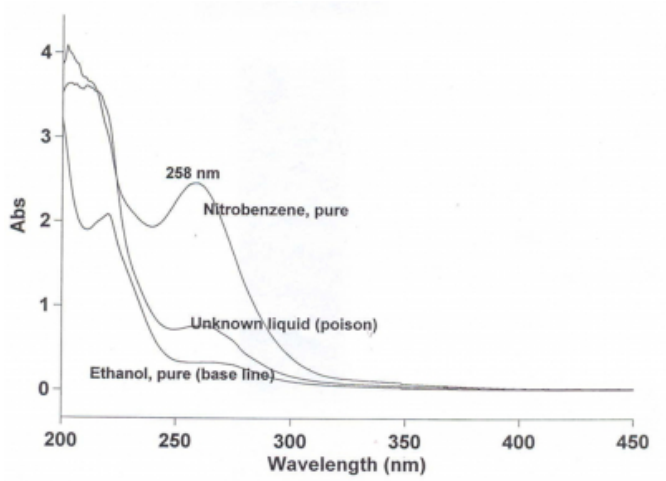
CASE REPORT

A 20-year boy, associated with screen printing work, ingested an unknown liquid used for screen printing at around 6:00 hours in the morning in an intentional poisoning out of anger following some conflict with his family members. He had vomiting and epigastric burning sensation after about 40 minutes. He was admitted to the Civil Hospital, Ahmedabad at 12:00 hours. Physical examination of fingers and tongue revealed a cyanosis with poor respiratory effort. His pulse rate was 120/min and blood pressure 100/70 mm of mercury. Pupils were bilaterally dilated. On admission, the hemoglobin level was 13.7 g/dl (normal: 14-18 g/dl) and total leucocyte count (20,000/cu mm) showed polymorphonuclear leucocytosis. The patient was immediately given oxygen using venti-mask at the rate of 6-8 liters/min. There was no jaundice and toxicity profile

for cannabis, morphine, cocaine, amphatamine, benzodiazepine and phenobarbitone gave negative results. Routine urine examination, ECG, X-ray chest and biochemical profile which included SGPT, RBS, blood urea, serum-billirubin,-sodium and –potassium were within normal limits. Arterial blood gas analysis showed pH 7.34, PaO2 70.6 mm of mercury, PaCO2 31.8 mm of mercury, HCO3 16.4 meq/l. The unknown pale yellow liquid used for consumption was sent to the Poison Information Centre, NIOH, Ahmedabad for identification and the blood samples for MeHb analysis. From the absorption spectra (Fig.-1) which showed wavelength peak of 258 nm matching with the pure nitrobenzene and its typical bitter-almond smell, it was identified as nitrobenzene. Serum and RBC cholinesterase levels were within normal limits excluding the involvement of organophosphate pesticide.

Figure 1

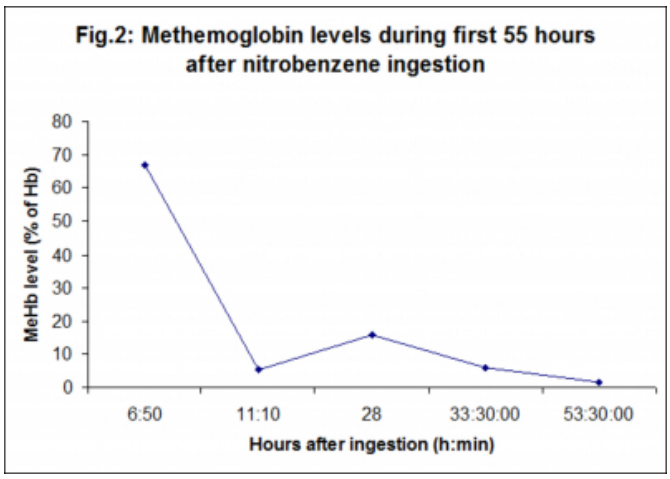
Figure 1: Absorption Spectra of the Unknown Liquid used by the patient for ingestion.



NB:Unknown liquid (poison) and Nitrobenzene, pure were diluted 1:14,000 and 1: 30,000 respectively with ethanol 99.9% for scanning

The MeHb levels from the blood samples were analyzed on the same day at 15:50 hrs by the method of Evelyn and Mallay [4] as modified by Henry [5]. The levels were found to be 66.7 % of Hb (normal: 0-3 % of Hb). On confirmation of chemically induced methemoglobinemia, he was administered 100 mg methylene blue i.v. over 10 minutes at 16:10 hrs. He also received DNS (i.v.) and two units of PCV over 6 hrs. The MeHb level reduced to 5.4 % after 1 hour of methylene blue administration and gained consciousness at 22:00 hrs. Next day morning at 10:10 hrs, MeHb levels rose a little higher (15.8%) which again reduced to 6.0 % at 15:30 hrs. On the third day morning (11:30 hrs), patient's condition was better with MeHb levels reducing to the normal (1.63%). He was discharged home on hospital day four without apparent sequelae.

Figure 2



DISCUSSION

Hemoglobin molecule is composed of four polypeptide chains associated with four heme groups containing an iron molecule in the reduced state or ferrous form (Fe 2+). Hemoglobin can accept and transport O_2 only when the iron atom is in its ferrous form. When hemoglobin becomes oxidized, it is converted to the ferric state (Fe 3+) or methemoglobin resulting in to a condition called methemoglobinemia in which there is inhibition of binding and delivery of oxygen by a red blood cell [6]. MeHb lacks the electron that is needed to form a bond with oxygen and thus is incapable of O_2 transport. This condition is mainly caused by the intentional or non-intentional exposure of oxidizing agents such as nitrates and nitrites including occupational exposures [7].

Blood normally contains approximately 1% MeHb levels. The low level of MeHb is maintained by two important mechanisms. One is the hexose-monophosphate shunt pathway within the erythrocyte by which oxidizing agents are reduced by glutathione prior to the formation of MeHb. The second mechanism against MeHb formation uses two enzymes systems: diaphorase-I (nicotinamide adenine dinucleotide methemoglobin reductase) and diaphorase -II (nicotinamide adenine dinucleotide phosphate methemoglobin reductase). These two enzyme systems require NADH and NADPH respectively to reduce MeHb to its original ferrous state. Diaphorase II quantitatively contributes only a small percentage of the reducing capacity

of RBC. Methemoglobinemia occurs when excessive oxidative stress produce methemoglobin at a rate that overwhelms the capacity to reduce it through enzyme systems. Methylene blue is used as the antidote for acquired (toxic) methemoglobinemia. It acts as an exogenous cofactor which greatly accelerates (about 5 times) the NADPH dependent methemoglobin reductase system i.e. diaphorase II.

Although not completely understood, reduced nitrobenzene metabolites are believed to be responsible for nitrobenzene-induced methemoglobinemia. Studies with laboratory animals demonstrated that orally administered nitrobenzene is reduced in the intestine and that intestinal microfloral metabolism is essential for the production of methemoglobin [89]. Literature review showed several cases of acute poisoning through certain industrial/household products containing nitrobenzene. A fatal case of self poisoning involving nitrobenzene following oral ingestion by a 28-year-man with severe methemoglobinemia showing MeHb levels as high as 70% has been reported by Martinez et al [10]. A 5-year-old boy, who accidently ingested a screen printing material containing nitrobenzene, revealed cynosis, hyperpnea, methemoglobinemia and died after 18 hrs due to cardio-respiratory arrest [11]. A fatal case of intentional poisoning in a 46-year-female has also been reported after ingestion of a floor cleaner containing nitrobenzene with MeHb 68% [12]. Similarly, cases of acute poisoning with leucocytosis and methemoglobinemia after injection of India Ink containing nitrobenzene into a median cubital vein and that of a 21-year-man after ingestion of a screen printing-dye containing nitrobenzene have been reported in suicidal attempts [13]. We have observed extremely high levels of methemoglobin (66.7%) and these levels reduced near to normal after a dose of methylene blue (100 mg, i.v.). The levels again rose after 18 hrs of antidote administration. Delayed release of nitrobenzene from stores in the adipose tissue and gastrointestinal tract is commonly seen after severe poisoning [11]. This delayed rise in the MeHb levels may be attributed to the release of nitrobenzene stores from the adipose tissue. This report highlights the importance of laboratory-activity of a poison information centre in the management poisoning cases.

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