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Case report

ACUTE METHAEMOGLOBINEMIA DUE TO NITROBENZENE POISONING: CASE SERIES

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ABSTRACT

Nitrobenzene is a nitrite compound; its toxic effects are due to its ability to convert hemoglobin to methaemoglobin by oxidizing iron. The clinical features of nitrobenzene poisoning vary based on the concentration of methaemoglobin in blood. Immediate identification based on clinical features, odour of the compound with supporting evidence of increased methaemoglobin levels will help in a timely intervention thus preventing fatal outcome. Early haemodynamic and ventilator support along with administration of methylene blue as an antidote has been proved crucial in saving some lives. An acute nitrobenzene poisoning presenting with methaemoglobinemia is becoming quite common in this part of the country. Here authors report a series of cases of nitrobenzene poisoning where immediate clinical evaluation, with repeated intravenous methylene blue saved three patients, but two patients presenting late and with heavy exposure could not be saved.

Keywords: Acute methaemoglobinaemia, Nitrobenzene poisoning, Ascorbic acid, Mechanical ventilator

INTRODUCTION

Nitrobenzene is a synthetic organic yellow oily liquid with an odour resembling bitter almonds. It is widely used in agriculture in this part of the country as a plant energizer, flowering stimulant and yield booster in variable percentages for the crops like tomato, brinjal, paddy, chilies, fruits, pulses and flowering crops. It is also used in manufacturing of dyes, inks and shoe polishes.^{1,2} The toxic effects of nitrobenzene is due to its ability to convert haemoglobin to methaemoglobin by oxidizing iron.³ The fatal dose of undiluted nitrobenzene is said to be about fifteen drops. Death usually occurs within six to seven hours of ingestion. Nitrobenzene poisoning is on the rise, due to easy access to products containing nitrobenzene.

CASE REPORT

Case report 1: A 65 year old female came with history of consumption of about 30 ml of 20% nitrobenzene [Brand name: Boom Plus(micronutrient for plants)] two hours prior to admission. She had a history of four episodes of vomiting after consumption. On examination, she was conscious and oriented; cyanosis was present, pulse rate- 80 b/m, BP -140/80 mm Hg, SpO₂ on pulse oximeter-85% on 100% oxygen. Stomach wash was given with activated charcoal in the casualty. Investigation showed Hb-12.2gm/dl, TLC-26.900cells/mm³, platelets-3.18 lakhs/mm³ and her RFT, LFT, chest X ray, ECG were all normal. ABG at admission showed pH 7.33, PaCO₂ 27, PaO₂ 60, HCO₃16.3, O₂Sa - 80%.Methaemoglobin level -17%, she had respiratory distress and saturation started falling still further, so she was intubated and put on a mechanical ventilator. We had to wait for six hours to give IV methylene

blue as it was not readily available in our hospital, but meanwhile IV vitamin C 500mg was given. She was administered IV methylene blue 50 mg as a 1% solution over five minutes after six hours of admission and immediately her SpO₂ improved to 92%, which dropped later, when 30 mg IV methylene blue was repeated. With fluctuating symptoms, IV methylene blue (50 mg TID) and IV ascorbic acid (500 mg OD) was continued for four days. The patient was extubated on the fourth day and was discharged after 10 days.

Case report 2: A 58 year old male presented with h/o consumption of 20 ml of a compound named AMRUTH which contained nitrobenzene as 50% of its constituents around two hours prior to admission. O/E: patient was restless, tachypneic, central cyanosis was present, pulse rate 94- b/m, BP- 140/90 mmHg, SpO₂-85% with high flow O₂. Investigations showed Hb-14.3gm/dl, TLC-9,300cells/mm³, platelets-1.96lacs/mm³, ABG showed pH 7.44, PaO₂ 60, PaCO₂ 28, HCO₃ 20, methaemoglobin levels - 25%, RFT, LFT, chest X ray, ECG were all normal. He was given IV methylene blue 50 mg as a 1% solution over five minutes and 50 mg IV TID for 2 days. His symptoms and SpO₂ improved immediately after giving the first dose of methylene blue. He was also supplemented with IV ascorbic acid 500mg OD; patient improved symptomatically and got discharged 5 days later.

Case report 3: A 22 year lady was referred from a primary health centre to our casualty with history of consumption of around 150 ml of 20% nitrobenzene (Boom plus) six hours prior to admission with complaints of ten episodes of vomiting, drowsiness and breathlessness. O/E she was unconscious, gasping for breath, pupils were semi dilated and sluggishly reacting to light, had central and peripheral cyanosis, pulse rate -120b/min, BP-90mmHg systole, SPO₂ -74% with 10 liters of oxygen, she was immediately intubated and connected to mechanical ventilator. Investigations Hb- 9gm%, TLC-12000cells/mm³, platelet count- 2.5laks/mm³, methaemoglobin level was 70%. ABG pH- 7.12, HCO₃-12, PaO₂ -76, PaCO₂- 38, ECG showed sinus tachycardia, RFT, LFT and chest X ray were all normal. Inj methylene blue IV 50mg as 1% solution was given, after one hour repeat ABG showed pH 7.10, PaO₂ 80mmHg, PaCO₂ 50mmHg,

HCO₃8, suggesting persistent metabolic acidosis, so Inj methylene blue IV 50mg was repeated. Over next two days patient didn't regain her consciousness, inj methylene blue 50 mg IV TID was continued and she expired on third day of admission.

Case report 4: A 35 year old female patient presented with history of ten episodes of vomiting and breathlessness she was referred from local hospital after gastric lavage. She had consumed around 200 ml of 20% nitrobenzene (brand name: "Ranger" used as plant nutrient) for suicidal purpose seven hours prior to admission. O/E she was conscious, restless, irritable, central and peripheral cyanosis, extremities were cold, pupils dilated and sluggishly reacting to light, pulse rate 110/min, BP 80/60mmHg, SpO₂ on pulse oximetry: 74% with 10 liters of oxygen. Investigations Hb -11.5 gm%, TLC-15, 600cells/mm³, platelet count- 2.61 lakhs/mm³, methaemoglobin level-56%. ABG showed pH 7.06, PaO₂70, PaCO₂ 24, HCO₃16, O₂Sa -80 %. ECG showed sinus tachycardia, global ST segment depression, T wave inversion and LFT, RFT, chest X-ray was normal. There was no improvement in cyanosis even with high flow oxygen. Inj methylene blue IV 50mg as a 1 % solution was given and dopamine infusion was started. After one hour repeat ABG showed pH: 7.02, PaO₂80, PaCO₂ 50, HCO₃10, suggestive of persistent metabolic acidosis, so Inj methylene blue IV 50mg was repeated. As oxygen saturation did not improve and tachycardia persisted the patient was intubated and connected to mechanical ventilator. Twenty four hours later she developed sinus bradycardia, had cardiac arrest and succumbed to death.

Case report 5: A 25 year old lady came with history of consumption of 20% nitrobenzene substance (brand name-BOOMFLOWER-N used as plant nutrient) of unknown quantity, four hours prior to admission. O/E she was restless and in altered sensorium, pulse rate 120 /min, BP 94/60mmHg, SpO₂ on pulse oximetry 85% with 4 liters of oxygen. Investigations showed Hb- 8.3gm% ,TLC-12,400cells/mm³, platelets-2.95laks/mm³. Her RFT, LFT, Chest X ray and ECG were all normal, ABG showed pH 7.02, PaO₂ 36, PaCO₂ 36, HCO₃ 18.7, O₂Sa -80 %, methaemoglobin level-28%. She had respiratory distress and saturation started falling still further, so she had to be intubated and put on a

mechanical ventilator. Inj methylene blue IV 50mg as a 1 % solution was given, later repeated after one hour and continued tid for 2 days, she was also supplemented with IV ascorbic C 500mg every 12 hrs. Her consciousness improved over a few hours, the patient improved symptomatically and was extubated on the second day and discharged a week later.

DISCUSSION

Nitrobenzene is oxidizing nitrite compound. Nitrobenzene ingestion converts haemoglobin to methaemoglobin by oxidizing iron. Normally around 1% of methaemoglobin is present in the blood and if it exceeds more than 1% it is termed methaemoglobinemia. There are two mechanisms HMP shunt pathway and diaphorase pathway which maintain low levels of methaemoglobin in blood.⁴ These two enzyme systems require NADH and NADPH, to reduce methaemoglobin to its original ferrous state. In a condition where there is excessive oxidative stress like in nitrobenzene poisoning it will result in an increased methaemoglobin level, which is more than the capacity of the body to reduce it through the above two enzyme systems. The lethal dose in adults is about 2 to 6 gm.⁵ A normal individual will be symptomatic only when the methemoglobin level is more than 10% and present with symptoms of headache, fatigue and nausea. At methaemoglobin level of 30 -40 % patient will have symptoms of dyspnoea on exertion, palpitation and lethargy. At methaemoglobin level of 40% to 70% patient will have seizures, coma, lactate acidosis, respiratory distress and arrhythmias. Levels greater than 70% will lead to death.^{5,6} Clues for diagnosis are history of consumption of chemical compound, characteristic smell of bitter almonds, persisting cyanosis even while on oxygen therapy and normal oxygen saturation on ABG (calculated). Blood collected in syringe will be dark brown in appearance and will turn chocolate red colour after drying on a blotting paper.

Treatment: Decontamination, haemodynamic support and ventilator management. Methylene blue is the specific antidote for methaemoglobinemia induced by nitrobenzene poisoning. Methylene blue is administered if methemoglobin levels are more than 20%⁵ and it is infused intravenously at a dose of 1 – 2 mg/kg (max up to 50 mg/ dose in adults) as a

1% solution over five minutes. Injection methylene blue should be repeated after one hour if methaemoglobin levels are high and the patient is still symptomatic. Maximum dose of 7 mg/kg over 24 hours can be used, in doses of more than 7 mg/kg methylene blue itself may induce methaemoglobinemia.^{7,8} Ascorbic acid, an antioxidant can also be administered when methemoglobin levels are more than 20%.⁷

In the first three patients we have observed that the quantity consumed was less and also admission to hospital after consumption was early, but in the latter two patient amount consumed was more and hospitalization was delayed that could have been the probable reason for death. It was observed that ingestion of nitrobenzene causes very high oxidative stress as shown by increased methaemoglobin levels. In severe poisoning administration of methylene blue will slightly decrease the level of methaemoglobin on first day, but the levels will rise again high on second day due to release of nitrobenzene from gastrointestinal tract and adipose tissue stores which may be responsible for the deterioration of patients.⁴

CONCLUSION

The authors here wish to point out that nitrobenzene poisoning can be managed successfully with intravenous methylene blue and ascorbic acid with intensive hemodynamic and cardiopulmonary support, but patients presenting late and with heavy exposure, the chances of survival are less.

Patient consent: Patient/guardian consent was obtained

Competing interests: None.

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