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Case Report

Naphthalene Toxicity Resulting In Severe Multiorgan Failure

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Abstract

Naphthalene, a widely used industrial chemical and a popular household insecticide or repellent is an uncommon agent of poisoning worldwide. The usual toxic manifestations range from mild gastrointestinal symptoms like recurrent vomiting, and pain abdomen to severe multiorgan failure including severe haemolysis, acute kidney injury (AKI), hepatitis and methemoglobinemia. The commonest causes of poisoning include deliberate self-harm and accidental industrial overdose. We report a successful management of a rare case of naphthalene toxicity presenting with severe haemolysis, methemoglobinemia and multiorgan failure.Prompt identification of methemoglobinemia and immediate administration of specific antidote methylene blue along with blood transfusions and other supportive care holds the key to successful outcomes.

Keywords: Naphthalene toxicity; methylene blue; methemoglobinemia; haemolysis; acute kidney injury; jaundice.

Introduction

Mothballs are among the most popular domestic insecticides or repellents used worldwide. Naphthalene, the active ingredient of mothballs is well absorbed following ingestion, dermal contact, or inhalation.[1] The most common causes of toxicity are deliberate self-harm [2] with suicidal intent [3] and accidental industrial overdose. The lethal dose of acute naphthalene toxicity is 5–15 g for adults and 2–3 g for children,[2] with the standard weight of one mothball being 4 grams. Naphthalene toxicity causes severe intravascular haemolysis, acute kidney injury, haemolytic jaundice, methemoglobinemia, respiratory failure and occasionally central nervous system manifestations like confusion, restlessness, irritability and rarely coma.[1]Methaemoglobin levels of more than 15% are fatal and more than 20% usually result in 100% mortality.[4]

Case report

An 18-year-old female patient presented 48 hours after consumption of 8 naphthalene balls with suicidal intent. She was initially managed in a local hospital with decontamination and supportive measures. The patient was referred on day 3 with severe anaemia, haemolysis, jaundice and AKI.

On presentation, the patient was tachypnoeic, irritable and restless. She was desaturating with room air SpO2 of 68% which increased to 73% on the reservoir bag with 100% FiO2. She was pale and jaundiced. Further evaluation revealed severe anaemia with haemoglobin of 4.5g/dL. She had severe intravascular haemolysis and conjugated hyperbilirubinemia with AKI. Arterial blood gas (ABG) revealed a gross Spo2-Pao2 gap which led to the suspicion of methemoglobinemia. Methaemoglobin levels assessed as per co-oximetry were14.8%. She was managed by Inj.Methylene blue 75mg (1.5mg/kg) intravenously (IV) 6th hourly, Inj. Ascorbic acid 100mg IV 8th hourly and Inj.N-Acetylcysteine (NAC) 1.2gm over 24 hours.

Supplemental oxygen was continued. The patient was transfused 4 units of compatible packed cells. Daily serial monitoring of her haemoglobin (Hb%), bilirubin, creatinine, SGOT, SGPT levels and urine microscopy was done & tabulated as shown in Table-1

She gradually improved following methylene blue and blood transfusion. Serial methaemoglobin levels showeda steadily falling trend from 14.8% on day 1 to less than 2 by day 5.Similarly,her serum creatinine steadily decreased from 2.8 on day 1 to baseline values by day 5 and haematuria settled by day 5. SGOT/SGPT levels also proportionately had a downward trend. CNS manifestations like irritability, restlessness, and confusion settled within 24 hours. She was severely hypoxic on admission with a wide SpO2-PaO2 gap which is classically described as acquired methemoglobinemia. The patient was continued on an oxygen mask with a reservoir bag for 48 hrs gradually the oxygen requirement steadily decreased and the patient was off oxygen by day 5. Sherecovered well and had no clinically appreciable signs of haemolysis or jaundice. She was hemodynamically stable and her urine output was adequate by day 6 and was shifted to the ward.

Discussion

Naphthalene toxicity is not uncommon however the majority of the cases usually present with mild symptoms. The clinical manifestations may vary from mild **gastrointestinal effects like** nausea, vomiting, abdominal pain or diarrhoea to severe renal impairment, hepatic dysfunction, hypoxia and even coma.[1] Toxic manifestations of naphthalene are due to enhanced production of free oxygen radicals, resulting in lipid peroxidation and deoxyribonucleic acid damage resulting in severe intravascular haemolysis, severe anaemia, conjugated bilirubinaemia and acute kidney injury.[5] Intravascular haemolysis resulting in severe jaundiceandacute kidney injury has been reported in several earlier published case reports.[1,6]Severe forms of hepatocellular failure and haemolytic jaundicemay also need exchange transfusion. Our patient received a total of 4 units of packed cell transfusion after which haemolysis resolved spontaneously as seen in the peripheral blood smear. Serial LDH and bilirubin levels showed a decreasing trend and became normal over aperiod of 5 days to 1 week.

AKI following naphthalene toxicity is multifactorial and is said to be due to haemolysis, haemoglobinuria and also as a result of direct toxic effect on the kidney resulting in interstitial nephritis. Haemodialysis has been initiated in one of the earlier published studies in a patient with naphthalene toxicity[3] and AKI was seen in the majority of the patients in earlier published reports.[1,6] Todate, no randomised controlled trial or high-quality retrospective studies have been done to ascertain the incidence of dialysis requiring AKI in these patients. Our patient responded to a conservative line of management for AKI with blood transfusion, NAC and other supportive measures though the patient was oligo anuric on admission, she gradually responded with steadily increasing urine output and serumcreatinine levels which returned to normal by day 5 without patient requiring any intervention in the form of haemodialysis.

Most of the time acquired methemo globinemia is usually easily diagnosed at the bedside by way of disproportionate fall in SpO2 assessed by the finger pulse oximeters as opposed to near normal PaO2 values measurement by ABG.[7] The SpO2 will stay at 85% without increasing further with supplemental oxygen because of the differential absorption of methaemoglobin at different wavelengths which is the principle behind pulse

Table1: Trend of parameters during the hospital stay

	Day 1	Day 2	Day 3	Day 4	Day 5
Haemoglobin g/dl	4.5	6.3	7.8	9	-
Methemoglobin %	14.2	-	7.2	-	2
Hematuria	++++	+++	++	+	-
Creatinine mg/dl	2.8	2.6	1.8	1.5	1.1
SPO2	68%	78%	90%	94%	100%
Total Bilirubin	6	5.2	4	2	0.8
Serum LDH	1848	1000	534	200	157

oximetry.[8] Co-oximetry is the gold standard for the detection of methemoglobinemia. Methemo globinemia is almost always seen in naphthalene toxicity. Methaemoglobin is an abnormal haemoglobin in which the iron moiety of haemoglobin is in the oxidized form of a ferric (Fe^{+3}) state rather than a ferrous state (Fe^{+2}), thus not able to bind to oxygen causing severe hypoxia. Normal methaemoglobin levels are less than 2%. Patients usually become symptomatic after methaemoglobin levels reach 5%.[9]Cyanosis is usually evident when methaemoglobin reaches 10%. The classic appearance of "chocolate brown blood" and haematuria occurs when can it reaches 15%. As the percentage of methemoglobinemia approaches 20%, the patient may experience anxiety, light-headedness, and headaches. At methaemoglobin levels of 30%, there may be tachypnoea and CNS manifestations like confusion, lethargy, vertigo, fasciculations, convulsions and rarely coma. The outcome is usually fatal once the level reaches 60-70% because of persistent seizures, dysrhythmias, metabolic acidosis, and coma.[4]

The gold standard for the treatment of naphthalene toxicity is Inj methylene blue which is given at a dose of 1 to 1.5 mg/kg body weight for adults, in a 1% sterile aqueous solution via slow intravenous infusion.[4]Methylene blue increases the rate of conversion of met Hb to Hb by accepting an electron (in the presence of nicotinamide adenine dinucleotide phosphate [NADPH] and metHb reductase), to form leucomethylene blue, which can then donate this electron to reduce metHb.[9]

Various other adjunctive measures including the administration of NAC and antioxidants including vitamin C have been advocated by many authors.[10]The mechanism of action of NAC is similar to methylene blue which increases the reduced form of NADPH from NAD thereby reversing free radical super oxygen mediated haemolysis and acute liver injury. Vitamin C and antioxidants reduce free radical-mediated direct cellular injury. In our case patient was given inj methylene blue 1.5mg/kg along with inj.vitamin C 300mg IV 8^{th} hourly and inj. NAC 1.2g.Supportive measures like blood transfusion, oxygen therapy and other medications were continued till recovery.

Limitations

Methaemoglobin levels with co-oximetry were done only after 8-10 hrs of admission and hence might have even shown falsely lower values following initiation of treatment. G6PD deficiency was not ascertained before initiation of inj methylene blue, which is stated as a prerequisite by many authors. [1,6,11]

Conclusion

Naphthalene poisoning is not uncommon but becomes challenging to manage in the backdrop of multiorgan involvement like severe anaemia, methemo globinemia, haemolysis, AKI, hypoxia, CNS manifestations and jaundice.[12] Mortality is very high in these cases. A multipronged strategy involving timely identification, initiation of specific antidotes, and aggressive management of haemolysis and AKI is vital to successful outcomes.

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