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Case Report

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Nitrobenzene Ingestion Treated with Intravenous Methylene Blue and Ascorbic Acid in a Limited Resource Condition: A Case Study

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Abstract

Acute consumption of nitrobenzene (NBZ), an aromatic oxidising nitrate compound, can result in methemoglobinemia (metHb), which inhibits oxygen delivery. NBZ consumption is a well-documented clinical condition. Treatment with intravenous methylene blue (100 mg) and ascorbic acid (500 mg) was effective. At the end of the treatment, patients showed improved signs of cyanosis and hypoxia conditions.

Keywords

Acute methemoglobinemia, Ascorbic acid, Methylene blue, Nitrobenzene

Introduction

Nitrobenzene (NBZ) is a pale-yellow colored compound, moderately water-soluble oily liquid, and odor similar to bitter almonds [1]. It is mostly used in dyes, paints, shoes, soaps, and agricultural fertilizers [2]. NBZ ingestion is rarely accidental and mostly suicidal [3]. NBZ poisoning is a rare case of acute methemoglobinemia which impairs oxygen transport. The clinical manifestation of NBZ poisoning includes cyanosis, vomiting, nausea, gastric irritation, seizures, coma, leading to respiratory failure resulting in death [4]. Therefore, early diagnosis along with aggressive treatment based on clinical investigations might drastically affect the patient's survivability. Herein, we report a fatal suicidal case of a young boy by acute NBZ poisoning.

Case Presentation

A 17-year-old boy was admitted with the history of consumption of unknown compound of unknown quantity before 3 hours of admission. He complained about severe abdominal pain followed by three episodes of vomiting prior to admission. On admission, gastric lavage was performed followed by symptomatic treatment and was discharged. The patient had no history of excessive salivation, lacrimation, and loose stools. The patient was admitted again the next day complaining about dizziness. On admission, he was conscious but non-coherent with Glasgow Coma Scale of 8 (E3V2M3), blood pressure (BP) 70/40 mm of mercury (mmHg), pulse rate (PR) 130/min, respiration rate 38 cycles/min, body temperature 97.3 °F, and SpO_2 88% with 15 L of O_2. The patient showed no pallor, icterus, cyanosis, clubbing, lymphadenopathy, pedal edema, and koilonychias. On systemic examination, abdomen was soft, non-tender, and had no organomegaly. Normal vesicular breath sounds with bilateral air entry were clear. Cardiovascular examination showed normal heart sounds (S1 and S2). The patient was drowsy but arousable and showed hypotension.

Blood investigation for Arterial blood gas (ABG) analysis was taken which

showed a dark- or chocolate-brown color. ABG results showed that all the parameters were within the normal range (Table 1) [5]. Chest CT scan showed patchy areas of consolidation and centrilobular nodules. ECG was found to be within normal limits. 2D echo showed no regional wall motion abnormality and normal left ventricular function. Hemoglobin, serum urea, serum creatinine, and serum potassium were found within limits. Whereas, white blood cells count, serum sodium, serum cholinesterase, and total bilirubin were higher. Analysis for Urine hemoglobin and urine myoglobin showed negative results (Table 2).

Based on the above findings, provincial diagnosis of NBZ poisoning with distributive shock along with metabolic acidosis, acute lung injury, and acute kidney injury was considered.

Treatment

On the day of admission, the patient was given Inj. Ceftriazone (2 g), Inj. Pantop (40 mg), Inj. Paracip (1 g), Inj. Emeset (4 mg), and Inj. 25% Dextrose (100 ml) intravenously followed by 3 units of normal saline (500 ml). O_2 support was provided at 15 ml/min. Vitals of the patient were monitored on an hourly basis.

On Day 2, it was observed that even after fluid resuscitation blood pressure of the patient was not improved. Therefore, he was given Inj. Noradrenaline (4 mg) along with normal saline (50 ml) at 10 ml/h. On further investigation, it was observed that the patient has developed cyanosis, pulse rate 101/min, blood pressure 90/60 mmHg, and SpO_2 88% with 15 L on O_2.

The patient was further administered with Inj. Methylene blue (100 mg), Inj. ascorbic acid (500 mg), Inj. ceftriaxone (2 g), Inj. Sodium bicarbonate (50 mEq) and Inj. Pantop (40 mg) along with dextrose and normal saline (500 ml) intravenously for 30 min. Patient was intubated and kept on ventilator due to persistent hypoxia for 9 days. Antibiotics were administered based on culture and sensitivity reports. Methylene blue was administered until the SpO_2 levels were stable. During the course of treatment, two sessions of hemoperfusion and one session of exchange transfusion (hemodialysis) were performed.

Table 1: ABG analysis.

Timeline	pH	SaO_2	PaO_2	PCO_2	HCO_3^-
At admission	7.30	96.0	86	36.0	20.8
6 h	7.32	96.5	92	35.5	20.4
12 h	7.36	96.9	98	39.5	21.9
24 h	7.34	97.0	103	40.3	22.3
Day 9	7.40	98.5	112	32.0	25.8

Table 2: Investigation results.

Parameter(s)	Observed Result(s)	Remark(s)
Hemoglobin	13 g/dL	13.2 to 16.6
White blood cells count	19,300 cells/µl	4,500 to 11,000
Serum urea	19 mg/dL	6 to 24
Serum creatinine	0.91 mg/dL	0.74 to 1.35
Serum sodium	148 mEq/L	135 to 145
Serum potassium	4.0 mEq/L	3.5 to 5.5
Serum cholinesterase	20.36 U/ml	8 to 18
Urine hemoglobin	Negative	No hemoglobinuria
Urine myoglobin	Negative	No muscle damage
Total bilirubin	1.7 mg/dL	0.1 to 1.2

At the end of Day 9, the patient was extubated and removed from ventilator. The patient has shown improved hypoxia and cyanosis conditions. ABG values were found to be within the normal range at the time of discharge (Table 1).

The management has two aspects: first, to restore normal physiological condition with supportive management and second, to attempt to decrease the methemoglobin level. The first includes administration of sodium bicarbonate and intermittent hemodialysis to attenuate metabolic acidosis, endotracheal intubation and IPPV for oxygenation and use of vasopressors for tissue perfusion. The second entails the usage of methylene blue and rarely exchange transfusion. Although ample evidence of intravenous methylene blue is present in literature supporting its use, we had to resort to enteral administration due to its unavailability. Very limited experience is present for the use of oral methylene blue in NBZ poisoning. The bioavailability for oral methylene blue has been found to be around 72% and based on its usage for other therapies, a dose of 2 mg/kg (100 mg) which has been found to be both safe and effective was chosen for our patient. Vitamin C further decreases the oxidative stress acting as an oxygen scavenger which too was administered orally due to its unavailability in intravenous form. The patient's improvement after oral methylene blue administration is suggestive that this route of administration is a viable option for treatment when the intravenous preparation is not available.

Discussion

In general, NBZ will be readily absorbed from the skin, gastrointestinal, and respiratory tracts following accidental or intentional exposure [4]. NBZ is highly lipophilic in nature; hence it is accumulated in stomach, blood, brain, and liver in high concentrations [4]. Once absorbed into blood, it will oxidize the iron (Fe) moiety present in hemoglobin (Fe^{+2}) resulting in the formation of methemoglobin (Fe^{+3}) (metHb) which will be incapable of oxygen transportation leading to hypoxia condition [2, 3]. In general, less than 1% of metHb is observed in blood under normal physiological conditions. Low levels of metHb are regulated by erythrocytes through innate-cellular mechanisms (via disphorase and hexose monophosphate pathways) [1, 6]. If exposed or ingested NBZ at higher concentrations will lead to increased oxidative stress therefore overwhelming the erythrocytes' ability to regulate metHb levels resulting in acute methemoglobinemia [4]. Therefore, even at high PaO_2 levels, a decrease in SpO_2 will be observed resulting in the occurrence of dark- or chocolate-brown colored blood which is a characteristic feature of NBZ poisoning [3, 4].

Methemoglobinemia symptoms are graded based on the levels of metHb: (i) no symptoms will be observed at <1.5 g/dL (<10%), (ii) cyanosis at 1.5 - 3.0 g/dL (10 - 20%), (iii) tachycardia, headache, light-headedness, and anxiety at 3.0

- 4.5 g/dL (20 - 30%), (iv) increased tachycardia, tachypnea, dizziness, confusion, and fatigue at 4.5 - 7.5 g/dL (30 - 50%), (v) lactate acidosis, arrhythmias, seizures, and coma at 7.5 - 10.5 g/dL (50 - 70%), and finally (vi) cardiovascular collapse and death at >10.5mg/dL (>70%) [2, 6]. G6PD deficit and anemic individuals suffer more severely [7]. It was reported that concentrations in the range of 1 - 10 gm will be lethal [4].

Even though measurement of metHb levels was not possible, features such as (i) cyanosis with low SpO_2 and normal PaO_2, and (ii) lack of SpO_2 levels improvement even after administering supplemental O_2 were sufficient to determine the severity of methemoglobinemia clinically. The patient was administered with methylene blue in combination with ascorbic acid to combat methemoglobinemia condition. Most cases report the usage of either methylene blue or ascorbic acid [2, 4, 6]; whereas a steady recovery with no secondary effects was observed when these antioxidants were used in combination. The bioavailability for methylene blue was found to be ~72%. Additionally, a dose of 2 mg/kg (i.e., 100 mg) was found to be both effective and safe for the patient based on its usage during other therapies [4]. Administration of sodium bicarbonate and hemodialysis was performed to attenuate metabolic acidosis.

In conclusion, NBZ ingestion in excess amounts will lead to methemoglobinemia, a life-threatening condition which can be treated with O_2, methylene blue, and ascorbic acid. The present case reports a successfully managed NBZ poisoning with intravenous methylene blue and ascorbic acid along with cardiopulmonary and hemodialysis support.

Conclusion

Nitrobenzene poisoning in a resource limited setting can cause therapeutic inadequacies due to unavailability of intravenous methylene blue and vitamin C preparations. However even oral preparations can be effective in successful management as evident in our case.

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