International Journal of Biomedical Research

ISSN: 0976-9633 (Online)
Journal DOI:10.7439/ijbr
CODEN:IJBRFA

Case Report

A fatal case of nitrobenzene poisoning with severe methemoglobinemia and ARDS due to Drowning

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Abstract

A 32 Year old male farmer was brought by relative in unconscious state. He had severe cyanosis and laboured breathing. There was history of suicidal consumption of nitrobenzene compound [Bloom Flower] followed by drowning. He was diagnosed to have severe methemoglobinemia [MetHb] with aspiration pneumonitis. Immediately he was started with aggressive treatment in the form of ventilatory support, IV methylene blue, parentral ascorbic acid, higher antibiotics, IV steroids and supportive therapy. After initial improvement in first three days, he developed ARDS and died on fourth day of admission.

Keywords: Nitrobenzene Poisoning [NB], Methemoglobinemia [MetHb], Methylene blue, Acute Respiratory Distress Syndrome [ARDS].

1. Introduction

Acute poisoning with NB causing significant MetHb is uncommon but life threatening emergency. It leads to severe oxidative stress as suggested by increased level of methemoglobin. Delayed release of NB from stores in the adipose tissue and gastrointestinal tract is commonly seen after severe poisoning and may be responsible for delayed catastrophe. We present here a fatal case of acute nitrobenzene poisoning with drowning as a suicidal attempt by a farmer.

Fig. No.1 – Bloom Flower – n Nitro Benzene 20% v/v

2. Case History

A 32 years old male patient was brought to Casualty of Bharati Hospital, Sangli, in unconscious state and laboured breathing .He had alleged history of consumption of 'Bloom Flower' a fertilizer containing NB followed by drowning. Patient was cyanosed, had pulse rate of 110/min, respiratory rate of 30/min, SpO_2 66% at room air and 73 % after O_2 inhalation (8L/min) for 10 minutes. Blood pressure was 90/60mmHg .Patient was deeply comatose with semi dilated pupils, sluggishly reacting to light. Patient had bilateral crepitations. Patient was immediately intubated and was taken on ventilator with 100%FiO_2 after which SpO_2 rose to 85 % after ½ hour.

On detailed history, patient had informed his relatives on phone that he had consumed some poison approximately ½ liter with suicidal intention. He was found 60 minutes later in a pond nearby with head submerged in water. Container brought by relatives was 'Bloom Flower' containing 20% v/v NB. Smell of patient's breath and container being similar confirmed consumption of NB. Blood samples drawn were chocolate brown in colour which did not turn red on exposure to air. This confirmed MetHb as a result of NB poisoning complicated with drowning.

Chest x-ray showed hazy opacities suggestive of aspiration pneumonitis. ECG showed sinus tachycardia. Arterial Blood Gas (ABG) was suggestive of mild compensated metabolic acidosis$_{(T1)}$. Liver function tests, Renal Functions and electrolytes were within normal limits$_{(T2)}$. Clinical diagnosis of acute severe MetHb due to NB poisoning with aspiration pneumonitis was established.

Stomach wash with activated charcoal was given immediately. Broad spectrum antibiotics, IV fluids and Inj. Noradrenaline infusion were started. Intravenous Methylene blue 50 mg in 100 ml NS over 10 minutes followed by every 4 hourly for first day, then 8 hourly from 2nd day onwards, along with paraenteral ascorbic acid 500mg OD. Fresh blood was administered to increase oxygen carrying capacity severed by MetHb. Spo_2 rose to 90-93 % after methylene blue administration and blood transfusion. Patient became conscious 10 hours later, responding to verbal commands, cyanosis improved. Patient maintained spo2 of 90-92% for next few hours after which Spo_2 again dropped to 87% and remained constant for next few hours. Serial ABG's were done which showed improvement $^{(T1)}$. Patient became fully conscious within next 24 hours. However third day onwards patient started going into respiratory distress and x-ray picture worsened showing bilateral extensive pneumonitis. Inj Methyl Prednisolone was added 1gm OD in view of developing ARDS. Inj methylene blue was stopped on 4th day. ABG also showed decreased in PaO_2 levels.On the 4th day patient started detoriating with worsening of ARDS. Patient expired later on fifth day on account of respiratory failure.

Table 1: Table of ABG ١

	pH	$PaCO_2$	Pao_2	HCO3	SpO_2
On admission	7.31	30	64	15.2	80
12 hours	7.41	31	120	18.5	84
24 hours	7.45	33	112	20.4	88
36 hours	7.48	35	116	23.4	90
48 hours	7.30	45	86	28	76
72 hours	7.32	51	80	26	68

Table 2: Table of Investigations ٢

	Hb	TLC	SGOT	SGPT	Urea	Creat	Na+	K+	HIV	HBsAg
On admission	12.1	14000	52	68	26	0.8	138	4.2	Non reactive	Negative
24 hours	10.2	18000	64	74	23	0.9	135	3.8		
48 hours	11.5	20000	60	72	30	0.8	136	4.2		

3. Discussion

NB, a pale yellow oily liquid, with an odour of bitter almonds is used as an intermediate in the syntheses of solvents, like paint remover. It was first synthesized in 1834 by reacting benzene and fuming nitric acid and was made commercially available in England by 1856. It serves as an intermediate in the syntheses of aniline dyes, a solvent for the manufacture of cellulose ethers and acetate, a flavoring agent, a perfume for soap, and in rubber industry[1]. Exposure to these products through respiratory and cutaneous route leads to intoxication in workers. Other etiology leading to MetHb includes consumption of herbiside accidentally or as a suicidal attempt, as these products are now available easily[10].

The first report of NB poisoning came in 1886[2] and subsequent fatality reports followed[2,3] Intoxication can be accidental or suicidal or the side effect of some drugs including metoclopromide[3]. Accidental toxicity can occur in patients consuming well water with dangerously high levels of nitrites and nitrates[4].

MetHb impart a chocolate hue to the blood which does not turn red on exposure to air. The lethal dose is reported to range from 1 - 10 gm by different author[5,6]. Concentration of MetHb upto 20% are generally well tolerated although values above 40% are associated with cardio respiratory symptoms. Life threatening MetHb is rare and is usually the result of acute poisoning by oxidizing compounds[7]. Lethal concentration of MetHb is probably greater than 70%.

The metabolism route of NB is oxidation to p- nitrophenol and reduction to aniline which is further oxidized to P-aminophenol Nitrobenzene and phenylhydroxylamine, highly toxic compounds are believed to be produced as intermediates in the reduction of NB to aniline,which oxidise Hb to methemoglobin. Normal level of methemoglobin in blood is about 1% and level above this is called MetHb[10].

The toxic effect of NB is due to rapid development of MetHb. A condition in which the iron within the haemoglobin is oxidized from the ferrous (Fe2+) state to the ferric (Fe3+) state resulting in the inability to transport oxygen and causes a brownish discolouration of the blood[3]. Once formed, methemoglobin can be reduced enzymatically either via an Adenine dinucleotide (NADH) – dependent reaction, catalyzed by cytochrome b5 reductase, or an alternative pathway utilizing the nicotine adenine dinucleotide phosphate (NADPH) – dependent methemoglobin reductase system[2].

Methylene blue is the antidote of choice for acquired (toxic) MetHb. It acts as an exogenous co-factor which greatlt accelerates NADPH dependent Methemoglobin reductase system. The initial dose is 1-2 mg/kg or 0.1-0.2ml/kg of 3% solution given intravenously over 5 minutes. In higher doses, methylene blue itself is an oxidizing agent and as little as 5mg /kg has caused asymptomatic MetHb. Cumulative dose greater than 7 mg/kg have an increased risk of methemoglobin induction. Methylene blue is contraindicated in patient with G6pd deficiency, because it can lead to severe haemolysis. Ascorbic acid acts as an antioxidant. N-acetyl cysteine is shown to reduce MetHb, but not yet approved for treatment. Exchange transfusion and hyperbaric oxygen is reserved for severe cases[12].

Treatment of MetHb is based on principles of decontamination, symptomatic and supportive management. In our case patient had consumed NB in high doses causing severe MetHb complicated by aspiration pneumonitis due to drowning. Initially patient responded to Inj. methylene blue and ventilator support, he showed improvement in level of consciousness. His cyanotic tinge was also improved after fresh blood transfusions. But on fourth day he started detoriating with worsening of ARDS which may be the result of drowning or delayed release of nitrobenzene from stores in the adipose tissues and GIT. We discontinued Inj. Methylene blue on fourth day as patient redeveloped cyanosis which may be the result of toxicity of Inj. Methylene blue itself. His serial ABGs showed worsening hypoxia. We lost the patient on fifth day inspite of all aggressive therapeutic interventions. It would have been ideal to measure serum MetHb levels at repeated intervals in this patient, but this couldn't be done due to unavailability of this investigation in our area. The mortality can be explained due to additive effect of heavy consumption of NB and ARDS due to drowning.

4. Conclusion

- Heavy doses of NB self poisoning is rare but fatal due to severe MetHb.
- Inj methylene blue is recommended for reversal of severe MetHb.
- There are evidence that exchange transfusion may be beneficial when methylene blue is ineffective[12].
- In case of non availability of IV methylene blue, methylene blue powder can be use which is available in gynecological outpatient departments, and can be made into 1% solution and sterilized in CSSD. [*Central Sterile Services Department*]

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