

Nitrobenzene Induced Methemoglobinemia with Paroxysmal Atrial Fibrillation Treated with Single Volume Exchange Transfusions

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INTRODUCTION

Methemoglobinemia is a lethal but rare disorder which may occur either due to genetic defect in red blood cells/hemoglobin or other acquired exposures to oxidants/toxins including nitrobenzene.^{1,2} Nitrobenzene compounds are commonly used in paint-thinners or in agriculture as a plant growth nutrient and have a bitter-almond smell.^{3,4} Acute intoxication with nitrobenzene can be asymptomatic or present with cyanosis, headache, dyspnea, tachypnea, and tachycardia.⁵ Severe intoxication can produce confusion, lethargy, seizure, bradycardia, ventricular dysrhythmia, etc. and is possibly fatal.⁵ Its poisoning is treated with methylene blue as an antidote, ascorbic acid, riboflavin, and exchange transfusion in severe cases.⁶⁻⁹ In this study, we presented a case report of a female with this rare

ABSTRACT

Methemoglobinemia is a potentially fatal condition if left untreated. Conventional treatment of nitrobenzene induced methemoglobinemia dictates the use of methylene blue, which is the antidote of choice. However, its availability in our setting is limited only to the laboratory use. We present a case of a 21-year-old female with intentional ingestion of nitrobenzene. Clinical history and supportive investigations revealed methemoglobinemia and it was successfully managed with single volume exchange transfusions in absence of specific antidote. While exchange transfusions are indicated for severe cases, it may be useful as an alternative treatment in acute life-threatening conditions where methylene blue is not available.

KEY WORDS

Exchange transfusion, Methylene blue, Nitrobenzene, Whole blood

condition with paroxysmal atrial fibrillation treated with single volume exchange transfusions.

CASE REPORT

A 21-year-old female, intended to suicide, presented to the Emergency Department (ED) of Dhulikhel Hospital (DH) with an alleged history of ingestion of a poison (nitrobenzene 20%). The informant (her brother-in-law) explained her history of loss of consciousness for 3 hours with frothing through the mouth. The Glasgow coma scale (GCS) score was 4/15 and she was pale and cyanosed at presentation. Her recorded vitals were pulse 78 beats

per minute irregularly irregular, blood pressure of 100/60 mmHg, SpO₂ 83% (room air), afebrile and tachypneic.

In the auscultation process of the chest, we heard the bilateral equal air entry on both lungs in all lung-fields. She received high flow oxygen (O₂) through the O₂ mask. The unimproved O₂ situation in the high flow led the case to get intubated. The baseline samples such as complete blood count, renal function test, liver function test, urine routine and microscopic examination, urine pregnancy test, electrocardiography, chest x-ray, arterial blood gas (ABG) analysis were sent for the investigations. The laboratory reports were normal. The ABG report showed pH of 7.0, pCO₂ of 24 mmHg, pO₂ of 335 mmHg, HCO₃ of 6 mmol/L and lactate with 17.9 mmol/L. Based on all the clinical history and laboratory investigations, her diagnosis was stated as nitrobenzene induced severe acute methemoglobinemia. This case possessing all these characteristics has been reported as pioneer in DH.

She received infusion of injection sodium bicarbonate while she had severe metabolic acidosis. Her ECG reading showed the atrial fibrillation. After the seventh day, she was extubated, and her urine output was maintained at 40-50ml/kg/hr. She was supplemented with riboflavin (2.5 mg PO BD) and ascorbic acid (1.5 gm PO TDS) as well.

While she was admitted in intensive care unit (ICU), total 7 pints of blood (2 pints of fresh blood and 5 pints of whole blood each containing 350 ml) were transfused over 5 days preceded by equivalent volume of phlebotomy before each transfusion. This was followed by gradual improvement of her SpO₂. The monitored differences of SpO₂ and PaO₂ in the case exhibited progressively condensed differences from 15.8 to 2. Following the progress, patient was shifted to the ward on the eighth day and discharged on the subsequent day along with supportive medication and psychiatry consultation with the impression of dissociative disorder.

The author had obtained informed consent from the case to present this case study, assured voluntary participation and maintained confidentiality and privacy throughout the study.

DISCUSSION

Nitrobenzene is usually used as intermediate in the synthesis of solvents like paint remover with its pale-yellow oily liquid. This is commonly used as a flavoring agent in the rubber industry and in the plant growth nutrient and its physiological level is 0-2%.^{4,10} The symptoms of nitrobenzene poisoning differ with the level of methemoglobinemia. Within 10-15%, the cases may develop cyanosis however many of them are asymptomatic. After the level rises to 20-40%, the symptoms such as headache, dyspnea, and chest pain with signs of tachycardia and tachypnea develops. When the level reaches 40-50%, the symptoms such as confusion, lethargy and metabolic acidosis leading to

coma, seizure and arrhythmia appears and the level above 70% is considered fatal.⁵

In the index case, the patient was comatose at presentation and her methemoglobin level could be predicted to be above 50%.¹⁰ She also developed paroxysmal atrial fibrillation during the management, and this could be due to her severe metabolic acidosis condition. This is a unique case of nitrobenzene induced methemoglobinemia in DH with contrasting characteristics.

The diagnosis of methemoglobinemia was done based on the clinical history, examination, and laboratory findings. This case was diagnosed based on her history of chemical ingestion, presence of her bitter almond smell, cyanosis on general physical examination and low arterial SpO₂ with normal ABG.

Methylene blue is considered as rare antidote of choice in methemoglobinemia, especially in the resource limited settings.⁶ Thus, the exchange transfusion is a substitute and an alternative to this setting.⁹ Despite the absence of the methylene blue, the case was well managed adopting the alternative method i.e., by repeated exchange transfusions with fresh and whole blood. After this intervention, she recovered and was discharged from the hospital. An editorial with similar setting mentioned the improvement in a case of 60 years old male with poor Glasgow coma scale after transfusion in three different cycles.^{13,14} Another case in a different study indicated that a case with similar characteristics expired, giving contrasting outcome.¹⁵ The improved in this study received 700 ml (II-pint) fresh blood and 1750 ml (V pint) whole blood transfusion exchange. In a similar study, upon unavailability of methylene blue, the case received 3800 ml of therapeutic whole blood exchange as the emergency intervention.¹⁴ The case improved significantly, and methemoglobin was diminished to 5.2%.¹⁴ The systematic review paper also summarized the median value of the amount of blood exchanged as 3000 mL among 24 cases.¹⁴

The use of N-acetylcysteine to minimize the methemoglobinemia is not yet permitted to treat methemoglobinemia.^{11,16} Hence, this was not adapted in the management of this case.

The case received the Ascorbic acid and Riboflavin as the supplement. Some studies suggested to use both supplements.¹⁷ While few also mentioned about avoiding ascorbic acid in the acquired causes.^{7,8}

The study of the case is a first kind in DH and thus will be an evidence for the future researchers and physicians. This study could have expressed more investigations and reports for further detailing of the case. The future researchers may explore more and have wider coverage of the required information. The case report study design has its own several limitations, thus the future researchers might adapt other study designs to obtain more precise and comprehensive findings. This can be helpful to design

effective interventions. The findings of the case study of the methemoglobinemia cannot be generalized as the case setting is limited to DH only.

The limited settings may have scarce availability of all the required management of the nitrobenzene poisoning induced methemoglobinemia. The single volume exchange

transfusions alternative to methylene blue may perhaps save a life of the female case in emergency. Thus, the resources limitation could have been enhanced, if not, the substitutes should be explored to prevent acute life-threatening conditions in nitrobenzene poisoning emergencies.

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