A Triad of Altered Consciousness, Deep Cyanosis, with Low SpO2 and Markedly raised PaO2 on ABG: Manifestations of Rare Insecticide Poisoning (Indoxacarb)

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ABSTRACT

Indoxacarb is an oxadiazine group of insecticide and its toxicity in human is not fully reported. We are reporting a case of 30 years old urban female who presented with a triad of altered consciousness, deep cyanosis and low SpO2 and markedly high PaO2 after ingestion of unknown insecticide with suicidal intent. On strong clinical suspicion of indoxocarb poisoning, we treated her for methaemoglobinaemia with methylene blue and patient recovered fully.

Keywords: Indoxacarb, Methaemoglobinaemia, Methylene blue.

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INTRODUCTION

Indoxacarb is a new insecticide which belongs to the group of oxadiazine insecticides.1 It acts by blocking the sodium channels in the central nervous system of the insects and produces the clinical features as mild tremors, loss of appetite, and finally death in a couple of hours.2 Indoxacarb is formulated as 30% water soluble granules and proposed for use in apple, pear, brassica, sweet corn, lettuce and flowering vegetables. The contact with the substance takes place through ingestion, physical contact, translaminar action, during preening and at rewetting.2 Indoxacarb is used for control of certain lepidopteran pests including the beet army-worm in larval stage.2

Indoxacarb is designated by EPA to be a reduced risk pesticide and it is considered as organophosphorus replacement.3 It has moderate to low chronic toxicity.3 Its toxicity in humans is not yet fully identified.1,3 In our patient, we have seen a triad of altered consciousness, deep cyanosis, and low SpO2 and markedly elevated PaO2 follo-wing ingestion of indoxacarb in a suicidal attempt. The case report highlights the significance of high index of suspicion in such clinical triad as indoxacarb poisoning, as early recognition and treatment with injection methylene blue can reverse the fatal outcome, in this rare poisoning.

CASE REPORT

A 30-year-old urban female came to our emergency department with alleged history of ingestion of some unknown poison (suicidal intent). She was initially managed by physician at primary level by gastric lavage and received injection atropine. On worsening of symptoms and falling consciousness, she was referred to our hospital. On admission she was dull, drowsy, disoriented, not responding to verbal commands. Patient was cyanosed, her SpO2 on pulse oximetry was 83%. Her vitals were–pulse rate was 138/minute, and BP was 100/60. RR-14/min. Her pupils were bilaterally semidilated with sluggish reaction to light. She was immediately supported with I/N O2 6 lit/min with mask, and intravenous line was secured. As she was showing signs of dehydration CVP line was secured revealing CVP 4 mm of water, intravenous fluids were given to keep the CVP around 8 to 10 mm of water. Considering the possibility of organophosphorus poisoning injection I/V atropine 0.2 mg, injection PAM 2 gm I/V was given (Dose 25-50 mg/kg).4

As the patient was hypoventilating and her SpO2 was not improving. She was intubated and kept on ventilator CMV mode with FiO2-1.0.

On routine investigation-S. Na+ was 143, K+ was 2.8, Cl– was 106 mmol/LS. Creatinine was 0.61 mg/dl, urea was – 29 mg/dl. Her Hb% was 11.6%, TLC-16000/cumm. Total S. billirubin was 1.64 mg/dl. Direct-0.46, Indirect-1.17 mg/dl, SGOT-13u/l, SGPT-18u/l. G6PD was normal. RBS was 106 mg/dl. X-ray chest was normal. ECG was showing sinus tachycardia, urine was normal. While sampling for ABG was done, we observed that her blood was chocolate brown in colour. Her ABG report was pH 7.3, PaCO2-22.2, PaO2-260.8, HCO3-17.6. Oxygen saturation-86%. It was observed that despite continuing mechanical ventilation with 100% oxygen, her SpO2 was not improving and remain stationary at around 83 to 84% on pulse oximetry. At the same time, patient’s relatives could bring the empty bottle of consumed poison and it was indoxacarb,5 which being a nonorganophosphorus oxidiazine insecticide injection atropine and PAM was stopped.

Considering deep cyanosis, low SpO2 which remained stationary on pulse oximetry with 100% oxygen, chocolate brown coloured blood, disproportionately high PaO2 on ABG, possibility of methaemoglobininaemia was considered.6
As the facility for determination of methaemoglobin was not available at our set up, treatment with injection methylene blue on these clinical grounds was started. Injection methylene blue 150 mg was diluted in 100 ml NS (dose 1-2 mg/kg)4, was given over a period of 10 minutes intravenously. Injection ascorbic acid 1000 mg was also given in dextrose containing fluids at a rate of 100 ml/hr.4 Along with this supportive treatment with antibiotics were given. After few hours, of treatment with methylene blue patient started showing signs of improvement. Her sensorium was better, and she was arousable, SpO₂ started improving and became 90% on the same day. On day three SpO₂ was 90 to 95% on FiO₂ of 0.6%, she was switched over to SIMV mode with pressure support. Injection methylene blue was given in a dose of 150 mg 8 hourly (dose was 1-2 mg/kg 8-12 hourly), with injection ascorbic acid 1000 mg.4 On the fourth day, injection ascorbic acid 1000 mg was given in dextrose containing fluids.4 Follow-up ABG was showing pH 7.4, PaCO₂ 23.1, PaO₂-275, HCO₃⁻19.8, oxygen saturation 100%. On fifth day, the patient became conscious and ventilator was disconnected and was put on a T–piece with 5 l/min of O₂. Patient remained fully conscious and alert and her SpO₂ was 100%. On sixth day, patient was extubated and given face mask with 5 l/min O₂. Patient remained fully conscious, alert and her SpO₂ started improving and became 90% on the same day. On day three SpO₂ was 90 to 95% on FiO₂ of 0.6%, she was switched over to SIMV mode with pressure support. Injection methylene blue was given in a dose of 150 mg 8 hourly (dose was 1-2 mg/kg 8-12 hourly), with injection ascorbic acid 1000 mg.4 On the fourth day, injection ascorbic acid 1000 mg was given in dextrose containing fluids.4 Follow-up ABG was showing pH 7.4, PaCO₂ 23.1, PaO₂-275, HCO₃⁻19.8, oxygen saturation 100%. On fifth day, the patient became conscious and ventilator was disconnected and was put on a T–piece with 5 l/min of O₂. On sixth day, patient was extubated and given a face mask with 5 l/min O₂. Patient remained fully conscious, alert and her SpO₂ was 100%. Patient was observed for two more day in ICU for any signs of deterioration. On eighth day, patient was shifted to ward with stable haemodynamics and fully conscious, alert state. After two days in the ward, patient was discharged.

DISCUSSION

Indoxacarb is an oxidiazine group of insecticide and produces toxicity by blocking Na channels in the central nervous system. Our patient had ingestion of indoxacarb for suicidal intent and we diagnosed this rare poisoning on clinical triad of altered consciousness, deep cyanosis, with low SpO₂ and markedly raised PaO₂ on ABG: Manifestations

In physiological condition-methaemoglobin is present below 1%. Methaemoglobinemia occurs when its level reaches above 1%.7 This occurs either due to congenital changes in methaemoglobin affecting synthesis and metabolism or from exposure to toxins that acutely affect redox reaction affecting methaemoglobinemia. There are few causes of methaemoglobinemia given below:

1. Inorganic agents:
   - Nitrites—fertilizers, preservatives, industrial products.
   - Chlorates.
   - Copper sulphate (fungicides).

2. Organic nitrites/nitrates:
   - Amyl nitrite, isobutyl nitrite, sodium nitrite
   - Nitroglycerine
   - Nitroprusside
   - Nitric oxide

3. Local anaesthetic agents—benzocaine, lidocaine, prilocaine, phenazopyridine (pyridium).


5. Antineoplastic agents—cyclophosphamide, ifosfamide, flutamide.


7. Antibiotics—sulphonamide, Nitrofurantoin, P—aminosalicyclic acid, dapsone.

8. Industrial/household agents—aniline dyes, nitrobenzene, napthelene (moth balls), nitroethene (nail remover).

Symptoms are proportional to the methaemoglobin level in blood. Skin colour changes (cyanosis with blue or greyish discoulouration) and blood colour changes to chocolate brown at levels upto 15%. Above 15% levels neurologic and cardiac symptoms arise due to hypoxia. Levels above 70% are usually fatal.8

Methaemoglobin has oxidized ferric iron (Fe⁺³) rather than reduced ferrous form (Fe⁺²) found in haemoglobin. This structural change is responsible for methaemoglobin’s inability to bind oxygen. In addition ferric iron has greater affinity for oxygen due to its chemical structure, thus shifting the O₂ dissociation curve of partially oxidized haemoglobin molecule to the left, resulting in decreased release of O₂ in tissues.8,9

In physiological state, methaemoglobin level is maintained below 1% by red cell NADH and cytochrome B₅ reductase enzymes. This is known as diphorase pathway. So MethHb Fe⁺³ is converted to Hb Fe⁺².10 NADPH is responsible in cytochrome B₅ reductase enzyme deficiency. This utilizes glutathione and G₆PD to reduce methaemoglobin to haemoglobin. Methylene blue accelerates the NADPH-dependent methaemoglobin reduction pathway,10,11 and can clear about 15% per hour. Failure of 100% oxygen to correct cyanosis is suggestive of methaemoglobinemia.

G₆PD deficiency is important to clarify. Bedside diagnostic tests to diagnose methaemoglobinemia is when we put 1 to 2 drops of patient blood on a white filter paper, deoxyhaemoglobin brighten in colour after exposure to O₂ but methaemoglobin will not change colour.12 There is difference between O₂ saturation measured on pulse oximetry and on ABG.

Methylene blue is given in dose of 1 to 2 mg/kg, administered as 1% solution in I/V saline in 3 to 5 minutes. Dose may be repeated at 1mg/kg every 30 minutes to a total dose not more than 7 mg/kg. Methylene blue requires G₆PD to
work, so may not be effective in G6PD deficient patients. Exchange transfusion can be considered in these patients, severely symptomatic patients, or when methylene blue is not effective. Other supportive measures should be used to correct acidosis. NADPH dependent methaemoglobinaemia requires glucose for clearance of methaemoglobinaemia, so I/V fluids containing 5% dextrose in water is appropriate. Dose of ascorbic acid is 500 to 1000 mg/day.

In our patient methaemoglobinaemia occurred following ingestion of indoxacarb which was suspected on clinical history and, clinical triad and was successfully treated with methylene blue, supportive treatment and ventilator support for few days and patient was discharged without any sequel. Further studies reported few cases in past.\textsuperscript{13-16} So because there are various industrial and household causes of methaemoglobinaemia its important to recognise this poisoning as early diagnosis on strong clinical ground can reverse the fatal outcome.

REFERENCES


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