Indoxacarb Poisoning Presenting as Methemoglobinemia and Seizure

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Abstract
We are reporting a case of poisoning with a non-organophosphate pesticide (indoxacarb) resulting in methemoglobinemia and seizures, and successfully treated with ventilator care and intravenous ascorbic acid. Since there are limited data concerning the human toxicity of indoxacarb, physicians in emergency rooms should be aware of this rare poison and also its clinical presentations.

Introduction
Acute, deliberate self-poisoning with agricultural pesticides is a global public health problem. Most estimates of the extent of acute pesticide poisoning have been based on data from hospital admissions, which would include only the more serious cases and hence merely reflect a fraction of the real incidence. The majority of deaths occur due to exposure to organophosphates, organochlorines and aluminium phosphide.

Indoxacarb is a broad spectrum non-organophosphorus oxizidaine pesticide. Although toxic effects of indoxacarb in humans are not described in any of the pesticide data base (no toxic effects or antidote mentioned in package tin), studies in animals have shown various complications. Many case reports have shown neurological, cardiovascular and hematological manifestations in humans. These include methemoglobinemia, hemolytic anemia, rhabdomyolysis, acute respiratory distress syndrome (ARDS), altered mentality, peripheral neuropathy, seizures, acute renal failure, arrhythmias, heart failure and cardiac arrest.

Case Report
A 55 year male patient was brought to casualty with history of consumption of unknown poison with suicidal intent, followed by altered sensorium. On presentation to casualty, pulse was 84/min and regular, blood pressure 130/80 mmHg, respiratory rate of 12/min. On central nervous system examination, patient was drowsy not responding to oral commands with normal sized pupils, equal and reactive to light and bilateral flexor plantar response with no muscle fasciculations. Other systemic examinations were normal. Patient had bluish discolouration of the mucus membranes with oxygen saturation of 84% on 6 lit/min of oxygen and poor respiratory efforts and hence a decision was taken to intubate the patient and commence mechanical ventilation. Patient was given gastric lavage. During drawing blood for ABG analysis, arterial blood was noted to be chocolate brown in colour. ABG analysis showed pH: 7.310, pCO2: 40.9 mmHg, pO2: 266 mmHg, BEEcf: -6 mmol/l, TCO2: 22 mmol/l, SO2: 82%.

After one hour of admission, patient developed one episode of generalized tonic-clonic seizures for which Inj. Phenytoin 1000 mg in 10 ml normal saline was given. Blood investigations showed pseudocholinesterase level of 6,974 IU/L (normal range is 4500-7500). Other routine investigations including liver and renal function tests, PT and aPTT were unremarkable.

On persistent asking, patient attenders brought the tin bottle of poison and it came out to be indoxacarb compound. Our suspicion of methemoglobinemia with chocolate brown coloured arterial blood was confirmed and inj. ascorbic acid 2 gm in 500 ml of 5% dextrose at a rate of 100 ml/hour was started, with other supportive care. Since patient had poor respiratory efforts, mechanical ventilation was continued. ABG on second day showed pH: 7.253, pO2: 198 mmHg, pCO2: 40.8 mmHg, BEEcf: -9 mmol/l, TCO2: 19 mmol/l, SO2: 100%. Bluish discoloration of mucus membranes completely disappeared on second day. Methemoglobin levels was 7.1% on first day and on fourth day, it was 1.21%. Patient was extubated on fourth day without any complications. CT scan brain done to rule out other causes of seizure was normal. Patient was discharged on 6th day of admission with no complications. Patient follow up after 2 weeks was normal.

Discussion
Our patient had consumed a 14.5% indoxacarb solution containing indoxacarb (14.5% w/w), inactive enantiomers (6% w/w), distilled methyl soyate, amorphous silicon dioxide, polyethoxylated polyaryl phenol and polyethoxylated polyaryl phenol phosphate. Indoxacarb affects insects by either direct exposure of spray droplets or through ingestion of treated foliage and fruits. Once absorbed, it acts by blocking the flow of sodium ions in central nervous system.

Methemoglobinemia is a common manifestation of indoxacarb poisoning. Methemoglobin is generated by oxidation of the heme iron moieties to the ferric state, causing a characteristic bluish-brown muddy colour resembling cyanosis. Methemoglobinemia has such high affinity for haemoglobin that virtually no oxygen is delivered to the tissue and the O2 dissociation curve is shifted to the left. Methemoglobinemia should be suspected in patients with hypoxic symptoms, who appear cyanotic but have a Po2 sufficiently high to saturate normal hemoglobin with oxygen.

In humans, methemoglobin levels are normally less than 1%.

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Methemoglobinemia often causes symptoms of cerebral ischemia at levels >15%; levels >60% are usually lethal.\textsuperscript{1} Seizure in a case of methemoglobinemia is usually seen at levels of >10%, but our patient had seizure at a level of 7.1%. This can be explained by direct effect of indoxacarb on central nervous system. Methemoglobinemia is treated with methylene blue 1–2 mg/kg, administered slowly. If cyanosis persists, the dose may be repeated at an hourly interval to a maximum of 7 mg/kg/day. Mild and follow up of severe cases can be treated with oral methylene blue (60 mg thrice daily) or ascorbic acid.\textsuperscript{1}

Viswanathan et al from Pondicherry has described non-methemoglobinemic presentation of indoxacarb poisoning in the form of ARDS, quadriplegia, hemolysis and seizures.\textsuperscript{2} However, there is little data on toxicity profile in humans. Only few cases are reported till now in literature about indoxacarb poisoning and its toxicity in the form of methemoglobinemia and seizures. One report from Korea shows methemoglobinemia and acute renal failure following indoxacarb poisoning, which was treated successfully with hemodialysis.\textsuperscript{3} A few Indian case reports are also available about indoxacarb poisoning, where methemoglobinemia was the only manifestation. Nirmala et al from Bangalore treated a case of indoxacarb poisoning with methylene blue 2 mg/kg in 100 ml normal saline and ascorbic acid 500 mg in 5% dextrose which were continued for two days along with non-invasive ventilation.\textsuperscript{4} Chhabra et al from Delhi treated a patient with indoxacarb poisoning with similar dosing regimen but patient was on invasive ventilation for one day.\textsuperscript{5}

Our case presented with seizure and methemoglobinemia. Methylene blue could not be given because of non-availability. However he responded well with ascorbic acid. Further studies are required for defining the benefit of methylene blue and ascorbic acid in a given case.

Increasing resistance to pyrethroids and the high mortality/morbidity associated with organophosphates poisoning has led to indoxacarb being marketed as a safe and effective replacement. However, physicians in emergency rooms should be aware of this rare poison and also its clinical presentations. Early recognition and treatment of complications can be lifesaving and hence we report this case.

References


