

## Curious Case of Dimethoate Poisoning with Early Onset Intermediate Syndrome, Cardiotoxicity and Hypothermia: A Case Report

Mahalingam Sasikumar, Gunaseelan R, Anuusha SS, Rajendran Ajithkumar, Manu Ayyan S, Balamurugan N\*

Department of Emergency Medicine, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India

### ABSTRACT

**Introduction:** Organophosphorus (OP) poisoning is one of the major public health concerns which accounts for about 30% suicide annually in India. Despite precautionary measures, intentional and occupational suicidal rates are higher in areas where OP is used. Though the toxidrome based approach is based on OP action on muscarinic and nicotinic receptors, it still can present in atypical ways too. Here, we describe a 37 years old male who presented with symptoms co-relating with Guillain-Barré syndrome but with discordant clinical signs. Some lacuna in the presenting symptoms prompted us to consider organophosphorus poisoning based on toxidrome which was further confirmed with plasma cholinesterase tox screen levels. Our case report highlights the importance of having a high index of suspicion for poisoning, if the clinical features are discordant with clinical history.

**Keywords:** Dimethoate poisoning; Early onset intermediate syndrome; Hypothermia; Cardiotoxicity

### INTRODUCTION

The protean manifestation of any poisoning may even confuse an experienced clinician when patient presents with altered mental status and even more when there is no history of intoxication. Approach of an unknown poisoning or suspected poisoning based on collective symptoms and signs, which can guide us through the initial treatment plan is called as toxidrome based approach. Different tox-screen investigations have come up which can later confirm the actual substance. This novel toxidrome approach had shown the way to the initial golden hour treatment concept in an unknown poisoning with a possible antidote.

Pesticides account for 1-5 million cases of poisoning and nearly 200 thousand deaths/year [1]. Organophosphorus (OP) poisoning is the most common entity responsible for pesticide poisoning. Different route of intoxication in OP poisoning occurs through ingestion, inhalation, dermal, and rarely by intramuscular, intravenous or subcutaneous route [2]. Though OP poisoning has typical manifestations due to acetylcholine overload at synaptic junction, they can present in atypical fashion like hypothermia, cardiotoxicity, atrial/ventricular arrhythmias and early onset intermediate syndrome.

Hypothermia as a manifestation of organophosphorus poisoning is rare as only a few cases have been reported in literature. This particular case had seized our attention because it presented as Guillain-Barré syndrome mimic along with hypothermia, atrial fibrillation and myocarditis which later turned out to be an OP poisoning.

### CASE REPORT

A 37 years old male chronic alcoholic presented to our emergency department (ED) with a history of abdominal pain for one day, watery diarrhoea (5-6 episodes) and vomiting (5-6 episodes) since the previous night, altered sensorium in the last 2 hours. He had a history of fried rice and heavy alcohol consumption with his friend before the onset of these symptoms. His friend also had similar symptoms such as abdominal pain, diarrhoea and vomiting. There was no history of co-morbidities. He presented to our ED in a gasping state with pulse rate of 60/min, blood pressure of 90/60 mm of Hg, saturation of 35% room air.

On primary assessment, Airway was secured with an endotracheal tube in view of gasping and oral secretions. Breathing assessment showed saturation of 96% post-intubation,

**Correspondence to:** Balamurugan N, Department of Emergency Medicine, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India, E-mail: muruganbala2006@gmail.com

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equal bilateral air entry, normal vesicular breath sounds and no bronchorrhea, wheeze, crepitations or any added sounds. Circulation assessment showed irregularly irregular pulse, with a rate of 60/min, blood pressure of 90/60 mm Hg, cold peripheries and capillary refill time >3 sec. Despite fluid resuscitation, blood pressure did not improve and point of care ultrasound (POCUS) showed reduced ejection fraction of 40%. Hence, noradrenaline infusion with maintenance fluid was started and blood pressure started improving. Disability assessment showed GCS E3 VT M2 and bilateral pinpoint pupils. In the exposure assessment, the patient's temperature was normal initially; later he developed severe hypothermia (32°C). Hence, the patient was covered with blankets and warm fluids were infused.

General examination, cardiovascular, respiratory and Per abdomen examinations were normal. Central nervous examination showed improvement in GCS to E3VTM6 after a few hours, pinpoint pupils, quadriparesis with upper limb weakness (3/5) greater than lower limb weakness (4/5), neck flop, bilateral hand grip 50%, areflexia and no neck rigidity. Thus, we initially considered acute gastroenteritis with hypokalemia or GBS as a possible differential diagnosis but certain features like pinpoint pupil and hypothermia did not fit in. So, other possible differential diagnosis like OP poisoning, barbiturate poisoning, botulism, mushroom poisoning was considered. Atropine challenge test (1 mg atropine caused ill-sustained rise in heart rate dropping back to baseline immediately) was done which favored organophosphorus poisoning. If rapid and persistent atropinisation (pulse rate rises by 20% of baseline or >25-30/min) occurs after a small dose of 1 mg atropine suggest it's not OP poisoning. Hence, serum acetylcholinesterasetox screen levels were sent.

Investigation showed blood sugar of 248 mg/dl, ketones were negative, ECG showed ST depression (lead 1, avl, 2, 3, avf, v6) with atrial fibrillation, troponin T was positive, potassium level was 3.5 mEq/l, POCUS revealed an ejection fraction of 40% and ABG revealed mixed acidosis. Renal function test, Chest Xray, CT brain were normal.

Meanwhile, treatment was mainly aimed at supportive care, vitals stabilization, ventilator and hypothermia management. He was treated with warm saline through intravenous route and nasogastric route, atropine boluses, noradrenaline infusion. Plasma acetylcholinesterase levels (55 u/l, 1700 - 5778 reference value) favored organophosphorus poisoning and hence, patient was started on atropine therapy immediately. The compound consumed was traced to be dimethoate. Though the patient initially responded to treatment, he went into severe refractory hypotension probably due to cardiotoxicity and sepsis during ICU stay and expired despite our efforts.

## DISCUSSION

Pesticides are classified according to their chemical properties as organophosphates, carbamates, organochlorine compounds, and pyrethroids. OP poisoning often tends to be severe and takes longer time to recover because they bind irreversibly to acetylcholinesterase (AChE) as opposed to carbamates [3]. Symptoms and signs, following organophosphate exposure,

depend on the existent balance between muscarinic and nicotinic receptors and also amount of the poison consumed, it's concentration and the route of administration.

Muscarinic receptors are located in central nervous system (CNS) and in peripheral nervous system (PNS) at parasympathetic neuroeffector junction whereas nicotinic receptors are located in CNS, PNS at both sympathetic and parasympathetic ganglia, neuromuscular junction (NMJ) and also in the adrenal medulla. Thus, typical presentation of OP poisoning includes a) PNS muscarinic effects (diarrhoea, urination, miosis, bronchospasm, bronchorrhea, bradycardia, emesis, lacrimation, salivation, secretion, sweating) b) PNS and neuromuscular junction nicotinic effects (mydriasis, tachycardia, twitching, weakness, hypertension, hyperglycaemia, fasciculation) c) CNS muscarinic or nicotinic which can be acute (confusion, convulsion and coma), subacute (intermediate syndrome) or delayed (neuropathy due to chronic exposure).<sup>1</sup> There are few case reports which mention different route of OP exposure like intravenous, intramuscular and subcutaneous route which tend to cause cellulitis, necrotizing fasciitis and cutaneous abscess due to co-formulated hydrocarbons in OP compounds.

OP poisoning can have predominant muscarinic symptoms or nicotinic symptoms depending on the level of free muscarinic and nicotinic receptors. Lack of intoxication history, bronchial secretions or pulmonary findings and fasciculations in our patient caused the diagnostic uncertainty. Toxidromes are a constellation of symptoms and signs seen in poisoning. Different toxidromes are cholinergic, anticholinergic, sympathomimetic, sedative and opioids. Thus, we can find the toxidrome based on patients' clinical features and initiate treatment. Atypical features of acute OP poisoning range from hypothermia, atrial/ventricular arrhythmias, early onset intermediate syndrome, cardiotoxicity. Thus, our patient developed acute early onset intermediate syndrome which mimicked like Guillain-Barré syndrome. Literature also suggests OP can result in typical GBS in chronic phase due to toxic demyelination.

In our case, alcohol intoxication, dimethoate poisoning and hypotension could have been the contributing factors for hypothermia. Temperature changes in the setting of OP poisoning is probably due to hypothalamic homeostatic alteration, which commonly causes hyperthermia and rarely hypothermia. It has been observed that hypothermia occurs initially (first 48 hours) followed by normothermia/hyperthermia [1,4]. Literature also suggests that hypothermia was associated with higher doses whereas hyperthermia was seen only with lower doses, which can also be attributed to the use of anticholinergics and concomitant sepsis during ICU stay [5]. Only very few cases had been reported in the literature which describe the occurrence of hypothermia in OP poisoning. The most common ECG abnormality seen in hypothermia is QTC prolongation (62%). Severe hypothermia can cause severe cardiac dysfunction, global hypokinesia which can trigger atrial/ventricular tachyarrhythmias which can worsen the patient's condition further. So, treating them early with intravenous

warm saline, passive external rewarming (PER) can give us extra time to resuscitate them effectively.

Ludomirsky et al.[6] described three phases of OP induced hypercholinergic cardiac crises (OIHC) namely

- Initial Pheochromocytoma-like pattern - Due to nicotinic stimulation of adrenal medulla, catecholaminergic surge occurs leading to initial period of hypertension and sinus tachycardia.
- Second phase Parasympathetic overflow - Due to muscarinic stimulation of neuroeffector junction, parasympathetic overflow occurs leading to sinus node and atrioventricular conduction disturbances. This can cause ST-T changes, bradyarrhythmia, complete heart block.
- Third phase is characterised by QT prolongation, polymorphic tachycardia, Torsades de Pointes and sudden cardiac death which can occur in initial few hours up to 15 days of exposure

On initial presentation, our patient had atrial fibrillation and left ventricular dysfunction but was found to be normothermic. Patient developed hypothermia later. So, the cardiac dysfunction could possibly be explained by OIHC rather than hypothermia. This can also induce coronary artery spasm, severe left ventricular dysfunction and even acute myocardial infarction. Cardiac manifestations can vary from asymptomatic ECG abnormalities to life threatening complications such as cardiac arrhythmias, hypertension, hypotension, myocardial ischemia, and noncardiogenic pulmonary oedema. Among these, hypotension and prolonged QTc are independent predictors of mortality [1]. The postulated mechanisms include parasympathetic/sympathetic imbalance and direct cardiotoxicity. Catecholamines and vasoactive amines surge due to OP poison can cause myocardial damage by penetrating the myocardial collagen matrix and also by endothelial erosions and plaque rupture [1].

Dimethoate, methamidophos, and oxydemeton methyl are distinct from other OP compounds because they are lipophobic, with small volumes of distribution and high serum concentrations [7]. The co-formulated hydrocarbons namely xylene or cyclohexanone can decrease systemic vascular resistance which can result in distributive shock. Hence, dimethoate tend to cause direct cardiotoxic effects (cardiogenic shock) and peripheral vasodilation (distributive shock) which could have resulted in refractory hypotension in our patient. Studies regarding dimethoate poisoning showed that peripheral NMJ dysfunction can occur simultaneously with the cholinergic syndrome leading to early onset intermediate syndrome [8]. It had been also noted that oxime therapy is not much effective in dimethoate poisoning [9]. Dimethoate poisoning has 3-fold increase in case fatality rate than other OP compounds. Literature search revealed nearly 40% of patients dying from

dimethoate poisoning had systolic blood pressure less than 80 mm of Hg when compared to 5% of chlorpyrifos poisoning. Case fatality rate among dimethoate poisoning presenting with SBP less than 80 mm of Hg is around 80% [7].

Though our case diagnosis was initially like “searching a needle in a haystack” due to presence of atypical features and lack of adequate clinical history, we still managed to find the diagnosis. Hence, we thought reporting this exemplary case would add value to current literature and existing knowledge regarding OP poisoning.

## CONCLUSION

Clinicians should always have a high index of suspicion for poisoning, if the clinical features are not in concordance with clinical history. This case report brings a new insight into the various atypical presentations in dimethoate poisoning like early intermediate syndrome, cardiotoxicity and hypothermia. Recognizing the toxidrome using clinical features and trying to fit the pieces of puzzles (atypical features) together will help us grab the diagnosis and initiate treatment early.

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