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Case Report

Atropine Induced Delirium in Organophosphate (OP) Insecticide Poisoning: A Case Report

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ABSTRACT

Delirium is a condition associated with disturbances in mental abilities attributing to the reduced awareness of one's environment. The onset of delirium is usually rapid, which may last for hours or even few days. Organophosphate poisoning (OP poisoning) is one of the leading causes associated with suicidal attempts and major admissions in the intensive care unit. Few literatures have been reported regarding the use of atropine and the concurrent risk of adverse reactions. Manifestations of atropine overdose and misuse includes dryness of the mouth, tachycardia and in addition, psychotic symptoms such as restlessness and excitement, hallucinations, delirium etc. A 14 year-old female patient who manifested with delirium and associated symptoms after atropine administration during the management of OP poisoning. Atropine administrations should be monitored based on the acetyl cholinesterase enzyme estimation and the dose may be titrated to prevent the worsening of the present conditions. Monitoring of the signs and symptoms is the key element to prevent the adverse effects.

Key words: Atropine, Organophosphate, Poison, Delirium, Adverse drug reaction, Acetyl cholinesterase estimation.

Key message: Atropine induced delirium is rarely observed as an adverse event in patients receiving higher doses. Hence, atropine administration should be titrated based on the acetylcholine estimation to prevent the excess atropinisation and monitoring of signs and symptoms is essential to prevent the adverse effects.

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INTRODUCTION

Organophosphates were first discovered in 1930s with insecticidal properties, and in 1940s and 1970s witnessed its high demand for pesticide use.[1] Organophosphates are insecticidal pesticides that are highly toxic in nature. Furthermore, it inhibits acetyl-cholinesterase (AchE) resulting in high concentration of the neurotransmitter acetylcholine, the chemical responsible for the activation of muscular functions, rendering the importance of drugs that affect the neurotransmitter and which may intern lead to serious clinical impacts such as seizures and paralysis.[2] They are found in the muscarinic receptors of the nerves, muscle and the grey matter of brain. Acetylcholine also plays an important role in the autonomic nervous system, as in the sympathetic nervous system as well as in parasympathetic nervous system. As such accumulation of acetylcholine at neuromuscular junctions leads to the excitation of the central nervous system, which results in delirium, hallucinations and altered behaviour.[3]

Organophosphate compounds are the organic derivatives of acids, which contains phosphorous. The usual outcome of death after OP poisoning results from respiratory depression.[4] Symptoms of acute organophosphate poisoning usually develops during or after exposure, it can be in minutes or in hours depending upon the method of exposure. Usually exposure by the means of inhalation results in the fast occurrence of toxic symptoms followed by oral and dermal route.[5]

Because of the easy availability of organophosphates, it has become a very common approach for committing self-harm, attributing to the significant cause of morbidity and mortality in developing countries including India. According to W.H.O (World health Organisation), every year about 200,000 people die because of organophosphate poisoning and most of these deaths had occurred in developing countries.[6]

Atropine is an anticholinergic agent, which inhibits the muscarinic effects of acetylcholine. Widely employed for other health conditions and yet a drug of choice in the management of organophosphate poisoning.[7] Varying doses are employed depending upon the severity and the amount of poison ingestion. However, chronic use and over dose has led to the rising incidences of adverse events and the atropine side effects including headache, drowsiness, weakness, dizziness and nervousness,[8] emphasizing the need of impactful guidelines in the use of atropine for the management of OP poisoning.

CASE REPORT

A 14-year-old girl with an alleged history of Organophosphate consumption (EKALUX) was admitted to the ICU (Intensive care unit). On examination, it was noted that the patient was drowsy yet arousable, afebrile, and CVS with S1S2 +, RS with NVBS + however with B/L Crepts being noted positive. Per Abdomen was noted soft while the pupils were noted constricted? Blood Pressure was observed at 80/60mmHg which was low for the patient's condition and the patient was diagnosed with OPC Poisoning. (Table 1)

Table 1: Laboratory Investigation report.

Blood parameters	Lab Findings	Reference Ranges
White blood cells	$20.0x10^3$cells/mm^3	3.2-9.8 $x10^3$cells/mm^3
Red blood cells	$5.17x10^6/mm^3$	3.5-5.0 $x10^6/mm^3$
Haemoglobin	13.2g/dL	12-16g/dl
Haematocrit	41.1%	33-43%
Mean cell volume	79.5fL	76-100m^3
Mean cell haemoglobin	25.5Pg	27-33pg/cell
Mean cell haemoglobin concentration	32.1g/dL	33.37g/dL
Platelet	$433x10x10^3/mm^3$	$130-400x10^3/mm^3$
Randon blood sugar	115mgs%	<200mg/dL

**Differential counts reported: Polymorphs: 84%, Lymphocytes: 08%, Monocytes: 08%.

After admission, the patient was kept on Nil per oral (NPO) and gastric lavage was performed for the decontamination. Intravenous fluids were administered such as RL (Ringer Lactate), DNS (Dextrose normal saline) 1pint each. Followed by the administration of Inj. Atropine 20 ampoules (0.6mg/ampoule) IV STAT and Inj. Atropine 30 ampoules IV with normal saline IV infusion. Additionally, Injection Ranitidine 50mg IV BD and Inj. PAM (Pralidoxime) 2gm IV STAT. The next day, patient was found to be conscious yet irritable. On examination CVS (Cardiovascular system) noted with S1S2 +, RS with NVBS + however with B/L Crepts still being noted positive. Per abdomen was noted soft while the pupils were noted constricted? Blood Pressure was noted at 90/60mmHg, Bilateral pupils noted at 4mm, Temperature at 98.4'F, Pulse rate at 98/min, Respiratory rate at 22/min and partial oxygen saturation at 92% in room air. I/O chart was noted as Input- 2000ml/Output- 1750ml. Patient was given with IVF RL and DNS each 2 pint and NS 1 pint. Inj. PAM 500 mg IV 8^{th} hourly, Inj. Ranitidine 50mg IV BD and Inj. Atropine 3 ampoules IV BD.

At this point of time, the patient developed signs of delirium and hallucinations, with dilations noted in the pupils. The adverse event that followed atropine administration and the consecutive evidence of atropine-induced delirium suggested a remarkable association. Furthermore, ruling out the probability of delirium with any of the drug administered rather than atropine and subsequent control of delirium within three hours of drug stoppage. The toxic reaction that followed atropine administrations clearly indicates over dosing and an irrational approach of disease management. However, due to the deteriorating health of the patient, she was referred to a multispecialty hospital for further management.

DISCUSSION

The wide use of organophosphates in agriculture as pesticides or insecticides is quite evident with their significant impact on the enzyme acetylcholinesterase.[9] Where acetyl cholinesterase is the key enzyme responsible for the metabolism of acetylcholine into choline and acetate. Acute inhibition of acetyl cholinesterase can be life threatening and can occur within few minutes.[10]

Manifestations of OP poisoning may include fever, tachycardia, tachypnea, confusion, delirium and occasionally seizures. Cases of severe intoxication may also include CNS depression, respiratory failure, coma, and death. However, this case report reflects the absence of dosage corrections and an absence of an individual patient-based approach.

Organophosphate poisoning is a significant cause of morbidity and mortality across the world. Acute organophosphate intoxication is frequently associated with suicidal usage, accidental ingestion or inhalation while in use.[11]

Primary approach includes the cardiopulmonary support, gastric wash and the use of activated charcoals.[12] In case of skin contact, skin should be washed properly, and clothes should be removed to provide further spreading.

This case signifies the importance of atropine dosage in the management of OP poisoning. The dosage adjustment needed for atropine may be based on patient's tolerability and risk for development of adverse events (Personalized dosage tailoring). Additionally, the extent of cholinesterase enzymes inhibition may also indicate the burden of the damage. However, the concentration of cholinesterase enzymes may vary depending upon the race and or comorbidities. Therefore, blood colorimetry should usually be employed to analyze the cholinesterase enzyme levels in different sub populations. This in turn would help in designing a better evidence-based therapy.[13]

Recent evidence suggests the use of galantamine in OP poisoning cases. Galantamine is an irreversible competitive inhibitor of AChE and up lights the possible outcomes of galantine use in OP poisoning. Furthermore, the property of Galantamine in the prevention of neurodegeneration is ideal for OP poisoning cases.[13] However, atropine and pralidoxime have been widely employed for intoxication. Atropine competitively antagonizes acetylcholine only at muscarinic receptors while being ineffective on the nicotinic receptors attributing to its inefficacy in the prevention of clinical manifestations involving muscle weakness,[14] respiratory depression, convulsion and coma where supportive care should be initiated.[15]

CONCLUSION

Early diagnosis and treatment of OP Poisoning is a lifesaving approach. The use of anticholinergic such as atropine, scopolamine and glycopyrolate has widely been applied. However, caution needs to be applied in justification with the increasing number of case reports addressing the events of delirium and associated side effects in patients with atropine therapy. Additionally, the need of guidelines addressing such events and proper management approaches should be implemented in the global scenario.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATION USED

AchE- Acetyl-cholinesterase; OP poisoning- Organophosphate poisoning; WHO- World Health Organisation; RL- Ringer Lactate; DNS- Dextrose normal saline; CVS- Cardiovascular system; NPO- Nil per oral.

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