Clinical presentation and management of organophosphate poisoning: clinical study of five cases

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ABSTRACT
It is well documented, though not widely appreciated, that organophosphate poisoning has a spectrum of severity and chronicity. In this study, four cases with organophosphate poisoning are presented, followed by a discussion of their presentation and management.


Keywords: Organophosphate compounds, variable presentation, cholinesterase, cholinergic stimulation, atropine, pralidoxime.

Organophosphates are derivatives of phosphorous acid and contain carbon. They were synthesized at the beginning of this century, but commercial interest in such compounds did not start until late in the Second World War, when human scientists developed tetraethyl pyrophosphate (TEPP). A variety of organophosphates including sarin, tabun and parathion have been used since then in chemical warfare and some are still widely used as agricultural pesticides.1 Poisoning by organophosphates can happen either accidentally or internationally. The clinical presentation can be perplexing but an accurate diagnosis can save a lot of suffering by the patient and embarrassment to the treating physician. Diagnosis is made primarily from the clinical picture, the whole landmark of which is the excessive cholinergic stimulation which affects the central, as well as the peripheral, nervous system2 and possibly direct effect on the myocardium.3 The diagnosis can be confirmed by estimation of red blood cell or plasma cholinesterase level. Both acute and chronic manifestations can be seen in organophosphate poisoning4 and more recently an intermediate syndrome of neurotoxicity has been described.5

Case Reports. Case 1. A 26 year old Sudanese man, was brought to the emergency room in a comatose state not responding to painful stimuli. No obvious signs of external trauma were seen. At the time of presentation it was not certain whether he had overdosed himself or ingested any poisons but he was known to be working as a shepherd and a camel driver on a farm and apparently there was no past medical history or relevance. He was noted to have a spontaneous fluctuating pulse rate and blood pressure. He was tachypnoeic most of the time with a rate of 20/minute. He was not cyanosed or jaundiced, but he was noted to be sweating and salivating excessively with pinpoint pupils bilaterally. He was also having generalised fasciculation seen in the muscles of upper and lower limbs, gag and corneal reflexes were present. Rest of physical examination was normal. Full blood count, urea and electrolytes, serum glucose, urgent liver function tests, serum calcium, ECG, chest and skull x-ray, arterial blood gases, (CT) computerised tomography scan of brain were all normal. Lumbar puncture revealed normal CSF pressure with normal chemistry and microscopy. Red blood cell cholinesterase showed a level of 0.1 U/ml (normal range 4.7-14.4 U/ml). He was treated with intravenous atropine infusion and the dose was titrated according to the clinical response. He was also given intravenous pralidoxime. He showed good recovery and his level of consciousness improved and his secretions dried up, but he started to have respiratory failure due to hypoventilation. This necessitated intubation and ventilation. Over the next few days, however, he had a fluctuating level of consciousness but this settled eventually while he

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was maintained on atropine. His serum toxicological screen for organophosphates detected a high concentration of diazinon. He admitted to having ingested the insecticide in a suicide attempt. The patient was discharged three weeks after admission after full clinical recovery, his RBC cholinesterase rose up to 0.9 U/ml and diazinon level in serum was not detected at the time of discharge.

**Case 2.** A 17 year old Saudi girl was brought to the emergency room by her parents after she intentionally ingested a spoonful of an insecticide solution mixed in a glass of milk. The nature of the insecticide was not known to the parents. However, a few minutes after ingestion, she started to vomit violently. At the time of presentation she looked very anxious and frightened and was slightly dehydrated. She had good colour. Pulse rate was 120/min, respiratory rate was 18/min. Blood pressure was 110/70. No signs of external trauma were noted. Rest of physical examination was normal. Full blood count, electrolytes, blood sugar and, chest x-ray were normal. Electrocardiogram (ECG) showed sinus tachycardia, otherwise normal. Red blood cell cholinesterase was markedly depressed to 0.1 U/ml (normal 4.7 - 14.4 U/ml). No organophosphate compounds were detected on toxicological analysis of serum and urine. She was admitted for observation. No ill effects were noted over a three day period and the patient was discharged home after full psychiatric consultation.

**Case 3.** An 18 year old boy who came from an agricultural town was admitted with a one week history of gross psychosis, not easy to manage in the community. He was restless and talkative throughout most of the day and night and completely irrational with paranoid delusion. He was intermittently disoriented in time, place and person, and memory was disturbed. However, he was reported two days prior to admission, to having had fluctuated levels of consciousness with periods of deep unconsciousness and unresponsiveness to painful stimuli. He was also reported to have had jerky and twitchy movements in limbs and profuse sweating. There was a definite history of exposure to insecticide spray on the farm on multiple occasions. No history of drug abuse. Physical examination was only possible after heavy sedation, which confirmed the excessive sweating and lacrimation. He had bilateral pinpoint pupils and fasciculation was noted in the thighs. Rest of cranial nerve examination was normal. He was flaccid in all limbs after sedation, but all reflexes were normal. Cardiovascular examination revealed tachycardia with a rate of 110/min regular. Blood pressure was recorded initially as 120/70 but fluctuation was observed later on, up to 160/90. Rest of cardiovascular and respiratory examination was normal. Examination of the abdomen was normal.

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<tr>
<th>Table 1 - Level of pseudocholinesterase U/ml</th>
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<td>Admission</td>
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Serial measurements of his pseudocholinesterase a week later is shown in the table.

Patient responded well initially to intramuscular injection of atropine 1.2 mg with disappearance of all neuropsychiatric disturbances and control of sweating and lacrimation. Tachycardia however persisted but no arrhythmias were observed. He was maintained on regular injections of atropine 1.2 mg every 4 hours for the first week. This was gradually reduced and eventually stopped after two weeks with complete clinical recovery.

**Case 4.** A 63 year old lady had been bedridden for four years due to generalised weakness. She was seen frequently at home due to attacks of dyspnoea, and on a few occasions a high blood pressure was recorded. She was maintained on frusemide and nifedipine for treatment of pulmonary oedema and hypertension. The family also reported intermittent periods of confusion. She was obese and tachypnoeic at rest with shallow breathing. She was centrally cyanosed but well perfused. She also had twichings in small muscles of the hands. Pulse rate was 110/ min bounding in character and blood pressure initially recorded as 180/100. There was a soft ejection systolic murmur at lower left parasternal area. Jugular venous pressure was elevated and mild pitting ankle and sacral oedema was observed. There were bilateral soft inspiratory and expiratory crepitations despite the poor inspiratory effort and faint widespread rhonchi. Examination of the abdomen was unrevealing. Neurologically she was oriented and rational. She was noted to be drowsy but easily rousable. Both pupils were equal in size and reactive to light. Eye movements and fundoscopy were normal. Rest of cranial nerve examination was unrevealing. She was flaccid in all four limbs with grade 2/5 power in all four limbs. Sensation was intact and all reflexes were present. Chest radiography showed poor inspiratory effort with possibly enlarged heart, congested pulmonary hila with upper lobe venous congestion. Her serum creatinine kinase was normal and serum pseudocholinesterase was markedly reduced to 0.9 (4.7 - 14.4 U/ml). Reviewing the history, she told of definite exposure to insecticide fumes in closed rooms of her apartment on multiple occasions over the past few years prior to presentation. Arterial blood gases showed hypoxia with mild hypercapnoea. She was
managed on controlled oxygen via nasal canals, but initially this caused elevation of Pco². She
could only tolerate 1/2 litre/minute of oxygen, which was effective in alleviating the hypoxia
without worsening of hypercapnoea. Physical rehabilitation program was initiated to improve
her muscle power but with little success. Patient
was sent home on controlled domiciliary oxygen.

Discussion Organophosphate poisoning is not
rare and a spectrum of clinical manifestations can
be produced. In the United States alone the
annual incidence of organophosphate poisoning
exceeds 30,000. The serious clinical picture of
the first patient was due to neurotoxicity of the
organophosphates. The patient was acutely
intoxicated and responded well to pralidoxime
plus atropinisation. The second patient was
fortunate in that she had severe gastric upset after
ingesting the poison which possible cleared off,
most of it spontaneously. As a result, no clinical
ill effects were observed, despite the marked
depression of her RBC cholinesterase. She
possibly ingested an organophosphate or a
carbamate pesticide.

Neurotoxicity in acute poisoning is due to
excessive cholinergic stimulation which results
from irreversible covalent bonding of the
organophosphate esters to the enzyme
cholinesterase, which in turn leads to inactivation
of the enzyme and excessive accumulation of
acetylcholine, which causes the continuous and
excessive cholinergic activity and interrupts the
normal neurotransmission across cholinergic
neuro-junctions. The latter includes the
postganglionic parasympathetic nerve endings,
preganglionic nerves to parasympathetic and
sympathetic ganglia, somatic motor nerve endings
to striated muscles and certain synapses in the
CNS. Due to the slow rate of regeneration of
cholinesterase, chronic and delayed neurotoxicity
can be encountered, especially in certain
occupational groups at risk of toxicity, such as
farmers, ground and air personnel involved in
spraying of organophosphate pesticides. Patient
number 5 was chronically intoxicated with
marked depression of her plasma cholinesterase.
Fortunately it was possible to manage her on long
term controlled domiciliary oxygen only, without
the need for ventilatory support. Red blood cell,
cholinesterase is similar to neural cholinesterase
and the level of the two enzymes are closely
related. The normal range of cholinesterase in
the population is wide, and caution has to be taken
when interpreting results of cholinesterase in an
individual from a single measurement. This can
be overcome by doing serial measurements and
looking for a statistically significant rise over a
period of time as demonstrated for patient number
4.

Management is supportive and specifically
aimed at antagonizing the excessive cholinergic
stimulation by adequate atropinization plus the
specific antidote of pralidoxime aimed at
preventing and reversing covalent bonding of
organophosphates with tissue enzyme.

Pralidoxime, however, is only effective if given in
acute intoxication during the first 36-48 hours and
some authors have even doubted the usefulness of
the compound in affecting the outcome of acute
poisoning, when compared to treatment with
atropine alone. However, these authors did not
demonstrate that they had used an adequate dose
of pralidoxime to maintain an adequate blood
therapeutic level of about 4 mg/l, which
necessitates infusion of up to 500 mg/hour.

Pralidoxime is expensive and may not be widely
available especially in rural centres, where most of organophosphate poisoning is encountered.

In severely intoxicated patients, especially those who have cardiac arrhythmias and conduction defects who may not have responded to the above management, total exchange blood transfusion may offer considerable improvement of the cardiac dysfunction, as this intervention provides cholinesterase in the fresh blood which may be responsible for alleviating the clinical ill effects resulting from deficiency of the enzyme. Supportive therapy should be aimed to counteract serious complications such as cardiac arrhythmias, respiratory failure, central nervous system depression, seizures and peripheral neuropathy.14

Conclusion It is essential to have a high index of suspicion of organophosphate poisoning in patients at high risk and to be aware of the spectrum of chronicity between acute, sub-acute and chronic intoxication. Rapid diagnosis will guide physicians to institute appropriate measures to treat the poisoning and initiation of support therapy and accordingly will reduce mortality and morbidity.

References