Organophosphate Poisoning

The organophosphate (OP) pesticides inhibit acetylcholinesterase. Hence, acetylcholine accumulates at nerve synapses and neuromuscular junctions, stimulating muscarinic and nicotinic receptors and the central nervous system.

They are used as pesticides but can also be used as 'nerve gas'. This is prohibited under the Geneva Convention but could be used by terrorists or rogue regimes. There is some suggestion that the use of OP pesticides may have caused some neurotoxicity and be responsible for 'Gulf War syndrome'. Certainly, insecticides were freely used, as were many other chemicals. The syndrome is inconsistent in those affected but is neither simply a post-traumatic stress disorder nor the result of acute OP poisoning and is likely to represent low-level chronic toxicity.[1, 2, 3, 4] This is supported by a case control study which reported that chronic exposure to OP pesticides can lead both to depressive and anxiety disorders and also to cognitive defects (unrelated to psychiatric disorders).[5] This is a significant problem which may also affect children and further research in this field is necessary.[4]

Epidemiology

There are no accurate figures kept about the incidence of OP poisoning.

- The vast majority of cases are accidental from the use of pesticides. There is a much higher incidence in rural areas of the third world.
- Hospital admissions for intentional OP poisoning are twice as numerous as for accidental poisoning. Intentional self-harm tends to involve much higher doses than accidental exposure.
- Fortunately, terrorist or warfare use of OP is rare but the potential exists to expose a great many people at once. Sarin is an OP poison and there are two recorded episodes of deliberate release - both in Japan.[6] One was in Matsumoto in 1994 and the other was in the Tokyo subway in 1995. These two incidents caused 18 deaths. A single drop on the skin can be rapidly fatal.

According to the World Health Organization (WHO), there are about 1 million people a year admitted to hospital with accidental poisoning and 2 million with suicidal intent. It is estimated that there could be as many as 25 million agricultural workers in the developing world suffering an episode of poisoning each year.[7] The WHO figures appear to be an underestimate and a recent call was made for more reliable data to be collected.[8]

Causes for suspicion

- If symptoms follow spraying then those who conducted the spraying should know exactly what was being released.
- If people start to get symptoms of poisoning and there is no obvious source then deliberate self-ingestion must be considered.[9]
- If there has been an accident and damage to a container then the container should have the appropriate hazard symbol on the side, giving an indication of the contents, plus a telephone number to call for further information.
- The affected person may smell of garlic, due to the OP, or of petrol due to the solvent.

Physical properties

- OPs tend to be colourless-to-brown liquids at room temperature. Some have a fruity smell but others are odourless.
- They are volatile to varying degrees and can therefore be sprayed or distributed as an aerosol and inhaled.
- The vapours are denser than air and may accumulate in low-lying areas and enclosed spaces.
- After the deliberate releases of sarin in Japan in 1994, there were secondary effects in healthcare workers who treated patients who had not been decontaminated. In emergency medicine departments, personal protective equipment (PPE) should be available for use in such cases.

Presentation

The presentation of OP poisoning depends upon whether the poisoning is mild, moderate or severe. The symptoms are basically those of excessive acetylcholine activity.

Mild

- Small or pinpoint pupils.
- Painful, blurred vision.
- Runny nose and eyes.
- Excess saliva.
- Eyes looking 'glassy'.
- Headache.
- Nausea.
- Mild muscle weakness.
- Localised muscle twitching.
- Mild agitation.
Moderate

- Pinpoint pupils, conjunctival injection.
- Dizziness, disorientation.
- Coughing, wheezing, sneezing.
- Drooling, excess phlegm, bronchorhoea, bronchospasm.
- Breathing difficulty.
- Marked muscle twitching or tremors.
- Muscle weakness, fatigue.
- Vomiting, diarrhoea, urination.

Severe

- Pinpoint pupils.
- Confusion and agitation.
- Convulsions.
- Copious excess secretions.
- Cardiac arrhythmias.
- Collapse, respiratory depression or respiratory arrest.
- Coma.
- Death.

Differential diagnosis

The essential features of this type of acute poisoning are those of excessive cholinergic activity. There are a number of other possibilities to consider when deliberate poisoning is suspected:

**Could this be cyanide?** Very rapid onset of symptoms in seconds or minutes with gasping, air hunger and acidosis. There are confusion, convulsions, collapse and coma. There is decreased respiratory rate, respiratory arrest or sudden death. Cyanosis is unusual but there may be cherry pink skin (only seen post-mortem in carbon monoxide poisoning). Pupils are dilated or normal with no fasciculation and secretions are normal.

**Could this be a nerve agent or organophosphate?** Rapid onset of cholinergic symptoms, including small or pinpoint pupils, painful dim vision, increased respiratory rate, breathing difficulty and bronchospasm. There are excess secretions, saliva and sweat. There is muscle twitching, convulsions, coma, arrest.

Carbamates have a similar effect to OPs but they are less of a problem as they are more easily reversed.[10]

**Could this be lewisite?** Rapid onset of burns or blistering within minutes of exposure.

**Could this be mustard gas?** Burns or blistering usually beginning 2-12 hours after exposure.

**Could this be phosgene?** No history of exposure to chlorine. Rapid-onset eye and/or skin irritation with rapid or delayed respiratory symptoms.

**Could this be chlorine, other irritant gas, or a riot control agent?** Exposure to pungent greenish yellow gas (chlorine) or other irritant. Rapid-onset eye and/or skin irritation and choking/coughing/wheezing.

**Is chemical exposure still a possibility?** Unexplained sudden death in a healthy adult. Unexplained reduction in level of consciousness. Patient reports unusual sight, smell or taste. A number of patients with the same symptoms. Symptoms in a family or group with common exposure. Known incident or exposure or cause unknown.

Investigations

A&E departments have been supplied with toxicological analytic sampling kits and these kits should be used, where possible, for toxicological sampling.

- Decontaminate the patient before obtaining any samples.
- Collect samples as early as possible, preferably before treatment; however, do not delay life-saving treatment to obtain them.
- Do NOT clean the venepuncture site with alcohol or proprietary skin wipes or swabs, as these contain solvents that can interfere with some assays. Use sterile water or, if the skin is visibly clean, dry cotton wool.
- Label all specimens as high-risk.

If there is difficulty in obtaining specimens, the following are given as order of priority:

- 10 ml blood in plastic lithium heparin tube; 5 ml for children.
- 5 ml blood in glass lithium heparin tube; may be omitted for children.
- 4 ml blood in EDTA tube, adults and children.
- 30 ml urine with no preservative, adults and children.
Plasma cholinesterase level may be used to screen for exposure. RBC cholinesterase level correlates better with severity and prognosis or a mixed cholinesterase ratio is best for determining if sufficient pralidoxime is being given.

Management[11]

General principles
When aiding those who have or may have been exposed to dangerous chemicals, it is important to consider not just the welfare of the patient but your own safety. It is one of the axioms of disaster management that those who are there to rescue should not add to the problem by becoming victims.

- Ensure either that you are wearing chemical PPE and/or that the patient has been decontaminated.
- Decontaminate the patient in the NHS decontamination unit or decontamination area if this has not already been done. Do not attempt to do it in the A&E department or GP surgery.
- If there has been ingestion of an OP or carbamates within the previous two hours, activated charcoal may be used.
- Stabilise the airway with oxygen by mask, intubate and ventilate if needed, control any haemorrhage and set up intravenous (IV) access if needed.
- Assess the cause, give antidotes if appropriate, reassess, and in the UK alert the local Health Protection Team (HPT), and seek expert advice if needed from HPT, Toxbase[12] or the Public Health England (PHE) poisons helpline.[13]
- Hydrocarbon solvents used with OPs often persist after decontamination and can lead to fear that OP is still present. These solvents can lead to symptoms too, including headache and nausea.
- Lipophilic compounds can cause delayed or persistent toxicity as they slowly move out of the tissues.
- Remember that accurate, contemporaneous notes are essential.
 Specific aspects

- If you suspect exposure to a nerve agent or OP, ensure that either they have been decontaminated or that you are wearing PPE.
- Maintain an airway, give oxygen, use suction on secretions.
- Remove the patient's clothing if not already done (place in a double bag, sealed, labelled and stored securely). Shower, wash down or rinse-wipe-rinse with liquid soap and water, or dilute detergent. Remove any contact lenses if present and irrigate the eyes with lukewarm water or normal saline solution.
- Check triage tags for details of prehospital treatment.
- For severe or moderate symptoms, establish IV access, arrange assessment by an anaesthetist and, as soon as possible, give atropine:[14]
  - An adult requires atropine, between 0.6 mg and 4 mg IV and a child needs 20 micrograms per kg IV. Give every 10-20 minutes until secretions dry up and the heart rate rises to 80 to 90 beats per minute. This may need as much as 20 mg to achieve this. Do NOT rely on reversal of pinpoint pupils as a guide to adequate atropine administration. Normalisation of cardiovascular parameters and absence of oropharyngeal secretions are better clinical markers of adequate atropine administration.

- Pralidoxime is given at 2 g or 30 mg/kg IV for an adult, over 4 minutes. Then continue with the same every 4-6 hours or infuse IV at 8 to 10 mg/kg/hour. The rate of fixing of the bond between cholinesterase and the OP varies between compounds and so the window of opportunity for pralidoxime varies but is usually between 12 and 36 hours. Pralidoxime may be continued for 7 days or until atropine is not required for 24 hours. However, recent studies have suggested that pralidoxime with atropine therapy does not offer any appreciable benefit over atropine in the management of OP poisoning although further trials are needed to explore different dosing regimens of pralidoxime in order to further determine its efficacy in OP poisoning.[15, 16]
- Diazepam is given at 5-10 mg IV for an adult or 1-5 mg IV for a child. Repeat as required.[17]
- Intubate and ventilate if there is apnoea or severe respiratory distress but avoid succinylcholine.
- Check arterial blood gases, U&E, and glucose. Monitor the ECG and treat any arrhythmias.
- Contact the PHE Poisons Information Service for advice if there is no response, or slow response, to antidotes. Paralysis may mask seizures. Consider electroencephalogram (EEG) monitoring.
- For mild symptoms only with eye signs but no bronchospasm, bronchorrhoea or fits, observe for 2 hours after exposure, consider atropine or 0.5% tropicamide eye drops for painful or blurred vision and, if there is no progression of symptoms, complete a chemical exposure record form and discharge the patient with an information sheet.

Progression of symptoms suggests continued exposure, inadequate decontamination or inadequate treatment.

Late effects

Between 1 and 4 days after exposure to OPs, acute respiratory failure can occur with flaccid paralysis. It is refractory to pralidoxime and ventilation is required.

An intermediate syndrome can occur as proximal weakness presents after resolution of the initial crisis. This is different from a potentially permanent peripheral neuropathy.

Expert advice

Expert advice may be sought from PHE which has helplines for Chemicals 0844 8920555 and Poisons 0844 892 0111.

Prognosis

- Later effects of acute exposure include EEG changes, poor concentration and memory and post-traumatic stress disorder.[18]
- The respiratory system is often the first to be affected, as the agent is usually inhaled; however, there do not appear to be long-term respiratory problems.[19]
- Chronic, usually industrial exposure, gives a lower exposure but for a longer time.
- The long-term neuropsychological effects in orchard sprayers in England have been examined and it is difficult to obtain a clear result.[20] A survey of agricultural workers in the USA found a more clear relationship with cumulative dose of OPs.[21]
- A survey from Spain was also quite clear about a cumulative dose effect.[22] Studies have also suggested that sheep farmers are at increased risk of neurological abnormalities.[4, 23]

Further reading & references

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