Organophosphate Poisoning in Paediatrics

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Paediatric toxicology study (2013) USA

Most commonly fatal classes of poisoning

- Analgesics (375)
- Street drugs (124)
- Antidepressants (112)

Most common Pediatric Exposure

- Cosmetics and personal care products (13%)
- Cleaning substances (10%)
- Analgesics (7.8%)
- Foreign Bodies (7.4%)
- Topicals (7.4%)
- Cold and Cough Preparations (5.5%)
- Plants (4.6%)
- Pesticides (4.1%)

Background

- OP poisoning occurs from either ingestion, inhalation or absorption through the skin of the insecticide.
- Organophosphates and carbamates are the most frequently used insecticides worldwide.
- These compounds cause 80% of the reported toxic exposures to insecticides.
- Organophosphates produce a clinical syndrome that can be effectively treated if recognized early

Pathophysiology

- Op are AChE inhibitors
- Organophosphates form an initially reversible bond with the enzyme cholinesterase.
- The organophosphate-cholinesterase bond can spontaneously degrade, reactivating the enzyme, or can undergo a process called aging.
- The process of aging results in irreversible enzyme inactivation.

Path..

- Cholinesterases rapidly hydrolyze the neurotransmitter acetylcholine into inactive fragments.
- Acetylcholine is found in sympathetic and parasympathetic ganglia and in the terminal nerve endings of postganglionic parasympathetic nerves at the motor endplates of nerves in the skeletal muscle.
- Inactivation of the enzyme allows acetylcholine to accumulate at the synapse, leading to overstimulation and disruption of nerve impulses.
- Skeletal-muscle depolarization and fasciculations occur secondary to nicotinic stimulation at the motor endplate.

Path..

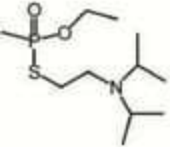
- Muscarinic effects occur at the postganglionic parasympathetic synapses, causing smooth-muscle contractions in various organs including the GI tract, bladder, and secretory glands.
- Conduction can be delayed in the sinus and atrioventricular (AV) nodes. Dysrhythmias are frequently reported; these typically include bradycardia, though tachycardia can also occur.
- Acetylcholine receptors are widely dispersed throughout the CNS. The activation of these receptors causes a wide range of effects, including CNS stimulation, seizures, confusion, ataxia, coma, and respiratory or cardiovascular depression.

Pharmacodynamics

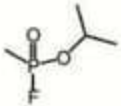
- Organophosphates are generally highly lipid soluble and are well absorbed from the skin, mucous membranes, conjunctiva, GI system, and respiratory system.
- They phosphorylate the active site of AChE
- Length of activity lasts up to thousand hours

Examples of OP

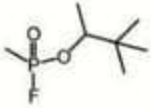
VX



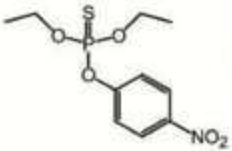
Sarin



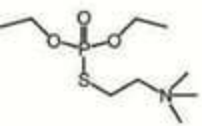
Soman



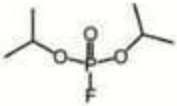
Parathion



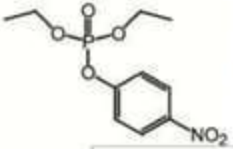
Ecothiophate



DFP



Paraoxon



Mnemonics for OP Toxidrome

- **S**alivation
- **L**acrimation
- **U**rination
- **D**efecation
- **G**I upset
- **E**mesis

- **D**iaphoresis/diarrhoea
- **U**rination
- **M**iosis
- **B**radycardia/bronchospasm
- **E**mesis
- **L**acrimation excess
- **S**alivation Excess

Evaluation

- History of poisoning
- Physical Examination
- Laboratory studies
- Gastrointestinal decontamination

Evaluation

What

- Medication
- Illicit drug
- Hazardous chemical

What form

- Pill
- Solid
- Liquid
- Gaseous

What route?

- Ingestion
- Inhalation
- Topical
- Intravenous

When?

How Much?

- Estimate amount
- Concentration

Management

- Assess the patient's airway, breathing, and circulation (ABCs).
- Secure the airway and perform cardiovascular resuscitation if needed.
- Endotracheal intubation may be necessary for airway protection and ventilatory support. (respiratory failure)
- If the patient's condition is stable, decontamination is the next priority.
- Patients who are inadequately decontaminated may expose rescue personnel and hospital staff to the toxin.
- Prehospital providers may also need decontamination.
- Gastric decontamination with gastric lavage or emesis induction should be performed in cases of ingestion (only in a conscious child)

Management

- Decontamination (emesis/gastric lavage)
- Atropine to reverse the cholinergic effects. Atropine does not bind to nicotinic receptors; hence, muscular weakness, including respiratory muscle weakness, is not affected.

- Pralidoxime (2-PAM or Protopam) a cholinesterase reactivator that reserves the neuromascular effects and restores muscle strength + respiratory effort
- 2-PAM does not cross the blood-brain barrier; hence, the central effects are not reversed.

- Anticholinergic agents should be used in doses large enough to reverse the cholinergic signs. Some authors recommend giving atropine until signs of atropinization appears. These signs include warm, dry, flushed skin; dilated pupils; and an increased heart rate

Specific rx

Atropine

- Initial dose of 0.05mg/kg IV
- Followed by 0.02mg/kg IV every 15 minutes until salivation stops and the pupil begins to dilate

Pralidoxime (16yrs or younger)

- Loading dose: 20 to 50 mg/kg iv (not to exceed 2 g/dose) over 15 to 30 minutes followed by continuous infusion
- Continuous infusion: 10 to 20 mg/kg/hour following the loading dose

- **IM**:
  Less than 40 kg:
  Mild symptoms:
  Initial dose: 15 mg/kg IM; recommend waiting 15 minutes for pralidoxime to take effect
  Second dose: 15 mg/kg IM if mild symptoms persist after 15 minutes
  Third dose: 15 mg/kg IM (total cumulative dose of 45 mg/kg) if mild symptoms persist after an additional 15 minutes

  If severe symptoms develop at any time after the first dose, 2 additional 15 mg/kg IM doses in rapid succession should be administered for a total cumulative dose of 45 mg/kg.

  Severe symptoms: Three 15 mg/kg IM doses in rapid succession should be administered for a total cumulative dose of 45 mg/kg.

  Persistent symptoms: If symptoms persist after administration of the complete 45 mg/kg regimen, the series may be repeated starting about 1 hour after the administration of the last injection.

Side effects

- Anticholinergic toxidrome

Dry mucous membranes
Mydriasis
Cyclopegia
CNS sedation
Bronchodilation
Vasoconstriction
Tachycardia
Lacrimation

Blind as a bat,
mad as a hatter,
red as a beet,
hot as Hades,
dry as a bone,
the bowel and bladder lose their tone,
and the heart runs alone...."

References

- 2003 Annual report of the American Association of Poison Control Centers Toxic Exporure Surveillance System – Watson et. al
- http://emedicine.medscape.com/article/1009888-overview#a6
- Wittenberg D.F. (2009), Coovadia's Paediatrics and Child Health. Oxford University Press Southern Africa (pty) Ltd