Organophosphates & Carbamates

Overview

Organophosphates are highly toxic with ~15% OD mortality & 300,000 deaths/yr worldwide generally caused by respiratory failure. Dimethyl OPs: e.g. fenthion, dimethoate. Diethyl OPs: e.g. chlorpyrifos. Carbamates are similar but less lethal: e.g. carbazine Nerve gases: Sarin, VX.
N.B. Some solvents used for OPs may be toxic themselves.

Toxic mechanism

Phosphorylation and so inactivation of acetylcholinesterases (AChE) → ↑ACh at CNS/autonomic receptors & NMJ depolarising block. 2-36h after binding, the OP-AChE bond 'ages' , making the complex irreversibly bound. Ageing doesn't occur with carbamates.

Toxicokinetics

Well abs by oral, also abs by dermal & inhalation routes too. Variation in inhibition onset speed (diethyl generally faster than dimethyl OP: chlorpyrifos a few min, most <4h, fenthion may be up to 48h), lipid solubility (prolonged action/delayed toxicity e.g. thiones: malathion, chlorpyrifos, fenthion), speed in aging the OP-AChE bond (dimethyl faster than diethyl), and whether requiring metabolism (by hepatic CytP450 e.g. 3A4) to form the active oxon (e.g. fenthion). Carbamates distribute less to CNS. Most metabolised by serum esterases (paraoxonase) and have renal elim.

Clinical features

Acute effects: Early *Muscarinic* (DUMBBELS/SLUDGE, ↓HR, ↓BP), *CNS* (agitation, coma, fits), ±*Respiratory* (chemical pneumonitis [HC carrier]) & *Nicotinic* effects (weakness, fasciculations).
Intermediate syndrome: delayed (2-4d) NMJ *Nicotinic* effects mainly proximal paralysis or paresis ± CN lesions caused by prolonged AChE inhibition/ACh stim at nicotinic receptors.
OP induced delayed neuropathy (OPIDN): Rare. After 1-5wk. Asc. sensorimotor neuropathy.
Chronic OP-induced neuropsychiatric disorder (COPIND): Acute or chronic exposure. BDZ may help if given in during acute poisoning.

Investigations

Screening: ECG (QT), paracetamol, BSL, CXR if severe poisoning (looking for aspiration)
Specific: RBC (correlates with severity, progress) and plasma (sensitive exposure marker only) cholinesterase levels. RBC test not widely available, so use a mixed (plasma) cholinesterase test (50:50 mix of patient & control serum – if mixed sample level < mean of separate samples then unbound OP present & more oxime required). ECHO if myocarditis suspected.

Risk assessment

Dermal/inhalational exposure rarely lethal unlike deliberate oral OD. May be delayed onset for ≥12hr. No known cases of 2° poisoning of staff however carrier fumes→headache/dizziness. Impaired GCS (<13) at presentation best predictor of death, but note delayed for fenthion.

Management

Resus & Supportive Care: ABCs. Fluids. Treat hypoBP, coma, respiratory failure & seizures.
Decontamination: AC if <2hrs post ingestion. Well ventilated area, universal precautions. Bag clothes, wash skin with soap/water. Nosocomial poisoning by the OP is not a risk.
Antidotes: Escalating doses of **atropine**. Possibly **pralidoxime**. Also **BDZs** and potential for neuromuscular blockers (e.g. **rocuronium**) to protect the NMJ.

Disposition

Min 12h obs. If intoxicated→ICU. Pralidoxime may be req for ≤7d, d/cif OK 24h after stopped. Follow up for intermediate or delayed syndromes.