Version 2.1 Monoamine Oxidase Inhibitor (MAOI) Antidepressants 14/08/2013

Overview

Irreversible non-selective MAOI OD (phenelzine & tranlcypromine) can cause lethal serotonin syndrome or sympathomimetic toxicity, the newer reversible selective MAO_AI [RIMAs] (moclobemide) are more benign in OD unless taken with other serotonergic agents when severe serotonin toxicity can occur. Also selegiline, an irreversible but selective MAO_BI.

Toxic mechanism

MAO_A metabolises NA, 5HT & D, MAO_B phenylethylamine & benzylamine. Irreversible inhibitors require new enzyme synthesis over days to regain MAO function. The accumulation of active amines and 5HT can result in prolonged sympathomimetic and serotonin toxicity.

Toxicokinetics

Rapidly abs. Peak 2-4hrs. Considerable 1st pass metab. Mod V_d 5-20L/kg. Metabolised by liver to active metabolites (phenelzine, tranylcypromine and selegiline) that are renally excreted.

Clinical features

Phenelzine & tranylcypromine: Monoamine toxicity develops after 6-12h. Heralded by agitation, ↑HR, involuntary movements, grimacing, clonus & hyperreflexia followed by a rapid ↓LOC. Muscle rigidity may → hyperthermia, rhabdo, respiratory compromise and hypoxia. Autonomic instability, DIC and multiple organ failure may ensue.
Other adverse reactions can be a classical serotonin syndrome. Or the tyramine reaction (e.g. after cheese) where hypertensive crises can follow sweating, agitation, mydriasis & headache.
Moclobemide: in isolated OD only minor nausea, anxiety & ↑HR. However frequent serotonin syndrome occurs if other serotonergic agents co-ingested usually within 6-12h.

Investigations

Screening: ECG, paracetamol, BSL
Specific: Serial ECGs (moclobemide) looking for mild ↑QTc at 6hrs.
Other as indicated: UEC, FBC, CK, troponin, ABG, CXR, CT brain, EEG

Risk assessment

Moclobemide: Generally minor symptoms. If OD>3g may ↑QTc. <5% mild serotonin syndrome unless other serotonergic co-ingestant.
Phenelzine & tranylcypromine: potential life-threatening serotonin or sympathomimetic toxicity.

Management

Resus & Supportive Care: Attend to ABCs. Address sympathomimetic & serotonin toxicity:

- ↑BP/HR: initially use BDZ. Severe ↑BP may require **GTN** or **nitroprusside** IV or **phentolamine** 2-3mg q10-15min. BB are **CI** (unopposed α effects → ↑↑BP)
- BDZs also for agitated delirium or seizures.
- Aggressive Mx of hyperthermia (T>38.5°C: continuous core T monitoring, BDZ, fluid resus. T>39.5°C: paralyse & intubate)
- Specifically treat serotonin syndrome (see Toxidromes).

Decontamination: Charcoal if >1mg/kg tranylcypromine or >2mg/kg phenelzine if alert & <2hr post-OD.
Antidote: **cyproheptadine** if mild-mod serotonin syndrome not responding to BDZ.

Disposition

If clinically well & no serotonin syndrome at 6h (moclobemide) or 12h (others) → d/c. If severe sympathomimetic/serotonic toxicity→ICU.