Tricyclic Antidepressants (TCAs)

Overview

Potentially life-threatening OD with rapid onset of anticholinergic, CNS & CVS toxicity.
E.g. amitriptyline, dothiepin, doxepin, imipramine

Toxic mechanism

NA & 5HT re-uptake inhibitors, GABA-A blockers & use-dependent fast sodium channel blockers. Also block M_1, H_1, peripheral α_1, inhibit K+ channels & direct myocardial depression.

Toxicokinetics

Rapidly abs, but in OD anticholinergic effect may delay. Peak <2hrs. Large Vd 5-20L/kg. Highly protein bound (α-acid glycoprotein>albumin). Metabolised by liver P450 to active metabolites. Some enterohepatic circulation. Elim $T_{½}$ 10-81hrs, maybe ↑ in OD. Renal excretion<10%

Clinical features

Severe OD characterised by rapid onset <2hr post-OD of coma, seizures, ↓BP, arrhythmias.
CNS: sedation & coma, seizures (usually early [<2h], brief, occ status. **Note**: seizures can precip CVS collapse from ↓pH & so more free TCA from resp/met acidosis), anticholinergic delirium.
CVS: Sinus tachy & mild BP↑ may occur early. ↓BP due to blockade & myocardial depression
Broad complex tachyarrhythmias and pre-arrest broad complex bradycardias.
Anticholinergic: may be early or delayed effects (e.g. tachycardia, mydriasis, agitated delirium).

Investigations

Screening: ECG, paracetamol, BSL
Specific: Serial ECGs looking for:

- ↑PR
- ↑QRS (Na^+ Blockade: >100ms predictive for seizures, >160ms predictive for VT)
- Large terminal R (>3mm) in aVR or ↑R/S ratio (>0.7)
- ↑QTc (from K^+ blockade)
- Brugada pattern (downsloping ST↑ in V1-3 + RBBB)

Risk assessment

Dose	Effect
<5mg/kg	Minimal symptoms
5-10mg/kg	Minor toxicity: Drowsiness & some anticholinergic symptoms
>10mg/kg	Significant toxicity expected within 2-4hr. Anticholinergic effects may be masked by coma
>30mg/kg	Severe toxicity with pH-dependent cardiotoxicity & coma expected to last >24h

>15mg/kg potentially life-threatening. Dothiepin commonly causes seizures & myoclonus.

Management

Resus: Need to Mx coma, respiratory acidosis, seizures, ↓BP and cardiac arrhythmias/arrest.

- **A/B:** O_2 & intubate if airway unprotected (↓GCS), hypoventilation, refractory seizures or impending deterioration likely. Hyperventilation to max pCO_2 ≥ 30mmHg to aid alkalosis.
- **C:** Dysrhythmia Rx - **bicarbonate** (↑protein binding, ↑dissoc from Na channel as ↑non-ionised. Aim pH 7.50-7.55 with vent). If reach pH limit try: **lignocaine** 1.5mg/kg IV. Or: **hypertonic saline** (watch for hyperNa), ?**Lipid emulsion**, ??$MgSO_4$, ??glucagon. **CI:** Class Ia (e.g. procainamide), Ic (e.g. flecainide), II (BB), III (amiodarone)
- HypoBP Rx:fluids, **bicarbonate**. If refractory: **hypertonic saline**, **adrenaline** or **NA** infusions.
- **D:** Treat seizures initially with BDZs, 2nd line: **phenobarbitone**. Phenytoin discouraged.

Decontamination: Activated charcoal PO if >10mg/kg ingested and generally after airway intubated.
Antidotes: **Na bicarbonate** and possibly **IV lipid emulsion** (see Antidotes)
Elimination: MDAC not of proven benefit. May rpt AC if likely ongoing abs. Dialysis not helpful.

Disposition

If clinically well & normal ECG at 6hrs → d/c otherwise admit for obs/cardiac monitoring ± ICU.