Antipsychotics - Atypical

Overview

These are generally benign in OD, requiring only supportive care. Mild sedation, ↑HR, & orthostatic hypoBP common. E.g. Clozapine, risperidone, olanzapine, quetiapine, amisulpride.

Toxic mechanism

D_2, 5HT, peripheral α_1, H_1, M_1 antagonism. Risperidone & amisulpride have ↓affinity for H_1, M_1.

Toxicokinetics

Clozapine, risperidone, olanzepine: Rapidly abs. 1st pass metabolism - Cyt P450.
Olanzapine: Large Vd. Abs by SL route too and also has some hepatic conjugation to glucuronide.
Quetiapine: Large Vd. Protein bound. Hepatic met by Cyt P450
Amisulpride: 2 abs peaks (1hr, 4hr). Mod Vd. Most excreted unchanged in faeces & urine.

Clinical features

All but amisulpride: Intoxication within 4hrs. Mild confusion, sedation, ↑HR, & orthostatic hypoBP common. Miosis. Coma & cardiotoxicity, rare. EPE more common in children.
Clozapine: Hypersalivation, anticholinergic effects (incl mydriasis). Fits in 5-10%.
Olanzapine: agitated delirium & urine retention common with mod OD. 15% have non-specific ST-T wave changes.
Quetiapine: <5% fit. Although may have ↑QT, torsade de pointes very rare.
Amisulpride: Higher risk of cardiotoxicity with ↑QT & ↓HR → ↑risk of torsade de pointes up to 36h. BBB possible. Coma uncommon. Large ingestions may delay onset of toxicity.

Investigations

Screening: BSL, ECG, paracetamol
Other: Rpt ECG, cardiac monitoring. ↑QT can occur with some ODs. UEC if ECG abnormal.

Risk assessment

Clozapine& risperidone: Usually benign. OD>2.5mg/kg clozapine may → significant symptoms.

Olanzapine Dose	Effect
<40mg	Therapeutic sedation and antipsychotic effects
40-100mg (child>0.5mg/kg)	Mild-mod sedation with possible anticholinergic effects
100-300mg	Sedation with intermittent marked agitation
>300mg	Coma possible, hypoBP with peripheral alpha blockade, rarely seizures
Quetiapine Dose	**Effect**
<3g	Mild-mod sedation and sinus tachycardia
≥3g	↑Risk of CNS depression, coma & ↓BP. Delirium or seizures possible
Amisulpride Dose	**Effect**
<8g	Mild-mod sedation and sinus tachycardia. ↑QTc & TdP reported >4g
8-15g	↑Risk of delayed CNS depression, cardiotoxicity (↓BP,↑QRS,↑QTc,BBB & TdP)
>15g	Expected delayed CNS depression, cardiotoxicity (↓BP,↑QRS,↑QTc,BBB & TdP)

Management

Resus, supportive care & monitoring: ABCs incl. fluid management for ↓BP. Watch for urinary retention. Manage delirium with non-pharmacological & BDZ rather than **physostigmine**. Treat seizures with BDZ and acute dystonic reactions (EPE) with **benztropine** ± BDZ. Treat Na blockade cardiotoxicity with **bicarbonate** ± hyperventilation, and TdP with **$MgSO_4$**/pacing.
Decontamination: Activated charcoal not advised except if >4g amisulpride ingested within 1-2h.

Disposition

If remain asymptomatic at 4-6h (16h for amisulpride) post OD with normal ECG can be d/c else monitor until normal & below QT nomogram line. Advise child's parents of risk of EPE for 1wk.