

Overview

Narrow therapeutic range. Acute or acute on chronic OD tolerated better than chronic OD.

Toxic mechanism

Direct GIT irritant, cation interference in ion-dependent transport processes in kidneys & nerves. ↑Serotonin syn, ↓5-HT_{1a} receptors, ↓2nd messenger activity (via inositol & G-protein).

Toxicokinetics

Rapidly absorbed, but in OD may be saturatable. Peak levels in <4hrs, longer with sustained-release preps. V_d ~0.6L/kg. Distributes into cells (incl CNS) slowly over days/weeks. Excreted unchanged in urine (RF, dehydration, hypoNa and distally-acting diuretics reduce Li clearance). T_½ 1-3 days in OD. Therapeutic range=0.6-1.4mmol/L. (May be as low as 0.4-0.8mmol/L)

Clinical features

Acute: Often asymptomatic, larger OD → GIT upset, delayed mild neurological symptoms (mainly tremor), rarely delayed seizures. Severity doesn't correlate with serum level.

Chronic: Mainly neurologic. Progression from Grade 1 (tremor, hyperreflexia, agitation, muscle weakness, ataxia), through Grade 2 (stupor, rigidity, hypertonia, hypotension) to Grade 3 (coma, fits, myoclonus). Other chronic effects: GI upset, hypothyroidism, QT prolongation, nephrogenic DI, renal impairment, SILENT (irreversible Li-effectuated neurotoxicity commonly cerebellar dysfn, but many types).

Investigations

Screening: BSL, ECG, paracetamol

Other: Serial [Li⁺] (confirm OD & progress, but doesn't correlate with sev well), UEC, TFT

Risk assessment

In absence of RF, even with large OD, Li often excreted before it distributes sig into the CNS. Dehydration, NSAIDs, thiazides, ACEI, DI, Age>50, RF, hyperthyroid ↑risk of chronic toxicity. In acute OD <25g is benign and if good urine output maintained, then neurological symptoms are uncommon even with OD>25g. Chronic OD is more severe than acute for the same serum level.

Management

Resus & Supportive care:

- Fluid replacement, maintain good urine output (>1ml/kg/hr) & [Na⁺] in normal range
- Observation & serial UEC, Li levels q4-6h or more often if severe OD.
- Rx for DI incl free water, thiazide, salt restriction. ?thiamine for neuroprotection.

Decontamination:

- Charcoal doesn't effectively adsorb Li. Na polystyrene sulfonate resin does, but →?↓K⁺
- WBI has been advocated in massive acute OD with SR preps but little proven benefit.

Enhanced Elimination:

- Haemodialysis/CVVHD if:
 - RF, seizures/coma, or intractable hypoBP. Also [Li⁺]>2.5mmol/L in chronic OD.
 - Beware rebound Li blood levels.

Disposition

Acute OD with Li<2.5mmol/L and no neurotoxicity can be d/c. Admit all with chronic toxicity. ICU may be required if CNS symptoms, RF, or chronic OD blood level >1.5mmol/L.

Note

Chronic OD recovery may be delayed 2-3 weeks despite falling levels.