

In large overdoses, VPA causes coma and multi-organ failure. Haemodialysis is indicated for life-threatening toxicity.

Toxicity / Risk Assessment

Large overdoses may result in delayed onset of toxicity.

Patients may present asymptomatic. Peak serum

concentration may up to 16 hours.

Toxicity may last days post massive overdose.

Predicted toxicity by ingested dose:

<200 mg/kg: mild sedation

200-1000 mg/kg: dose-dependent CNS depression

> 1000 mg/kg: coma likely to requiring intubation, cerebral oedema, multi-organ failure and death

Clinical features:

- CNS: ↓conscious state, ataxia, coma, seizures, cerebral oedema

- GI: nausea, vomiting, abdominal pain, hepatotoxicity, pancreatitis

- CVS: ↑HR, hypotension, ↑QT interval

- Metabolic: ↑ Na⁺, ↑ lactate, ↑ ammonia, ↓ Ca²⁺, ↓ glucose, metabolic acidosis

- Haematology: myelosuppression – leukopenia and thrombocytopenia

Management

Supportive care with airway protection as required

Decontamination:

Activated charcoal 50 g (Paediatric 1g/kg) within 4 hours of ingestion >200 mg/kg, OR if patient is intubated (via NGT). Repeat dose of AC if rising VPA concentration and intubated.

Consider **Whole Bowel Irrigation** if ingestion >1000 mg/kg, intubated and <4 hours post ingestion (*discuss with clinical toxicologist*)

- Check VPA serum concentration 4-6 hourly until decreasing

Extracorporeal elimination

Intermittent haemodialysis is the preferred modality.

Indications: - VPA concentration > 6000 umol/L (850 mg/L) OR

- Cardiovascular instability / cerebral oedema / metabolic acidosis pH <7.1

*Endpoint: clinical improvement AND VPA concentration < 700 umol/L (100 mg/L)

Carnitine (*discuss with clinical toxicologist*)

- Consider carnitine in patients with any of the following:

Severe metabolic acidosis (pH <7.1), NH₃ > 100 umol/L, cerebral oedema, hepatotoxicity

- Dose: 100 mg/kg IV loading dose followed by 50 mg/kg IV 8 hourly

Disposition

<200 mg/kg: observe for at least 6 hours + decreasing VPA concentrations + VPA <3500 umol/L (500 mg/L)

>200 mg/kg: observe for at least 12 hours + decreasing VPA concentrations + VPA <3500 umol/L (500 mg/L)