Sodium Valproate (VPA, valproic acid)

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 conc. may occur up to 16 hours post ingestion.

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 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, ↓ Ca^{2+}, ↓ glucose, metabolic acidosis
- Haematology: myelosuppression – leukopaenia and thrombocytopaenia

Management: Airway protection as required. Call clinical toxicology for all ingestions 500 mg/kg

Decontamination

Activated charcoal 50 g (paediatric 1g/kg) within 4 hours of ingestion >200 mg/kg, OR at any time if the patient requires intubation (via NGT or orogastric tube).

Consider **Whole Bowel Irrigation** if ingestion >1000 mg/kg, (discuss with clinical toxicologist)

Investigations - Check VPA serum concentration 4-6 hourly until decreasing

Meropenem: (discuss with clinical toxicologist)

- 1g intravenous 8 hourly may have a role in ingestions > 400 mg/kg or patients with severe toxicity

Carnitine (discuss with clinical toxicologist & see separate *Carnitine guideline*)

- Consider carnitine in patients with any of the following:

Severe metabolic acidosis (pH <7.1), NH_3 > 100 µmol/L, cerebral oedema, hepatotoxicity

- Dose: 100 mg/kg IV loading dose (max 6 g) followed by 50 mg/kg IV 8 hourly (max 3 g per dose)

Enhanced elimination (discuss with clinical toxicologist)

Intermittent haemodialysis is the preferred extracorporeal toxin removal modality.

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

- Severe toxicity including CVS instability/cerebral oedema/ metabolic acidosis pH <7.1

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

Disposition:

>200 mg/kg: observe for at least 8 hours + decreasing VPA concentrations + VPA <3500 µmol/L (500 mg/L)

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