Isoniazid

Overdose can cause rapid onset of seizures, coma, and severe metabolic acidosis. Pyridoxine is the specific antidote.

Toxicity / Risk Assessment

Isoniazid inhibits pyridoxine metabolism, preventing the conversion of glutamate to GABA. Reduction in central nervous system GABA leads to seizures.

Toxicity is dose dependent.

Onset of clinical effects is rapid (30 – 120minutes).

>1.5 g (20mg/kg): severe toxicity possible

Clinical features:

- **CNS:** lethargy, blurred vision, slurred speech, ataxia, mydriasis, confusion, coma, seizures
- **GI:** nausea and vomiting
- **CVS:** tachycardia and hypotension (late)
- **Metabolic:** severe lactic acidosis
- **Other:** complications of prolonged seizures – hyperthermia, pulmonary aspiration, rhabdomyolysis, weak MAO inhibitor effects

Isoniazid levels do not correlate with toxicity and are not routinely available.

Management Discuss all cases with a clinical toxicologist.

Patients with coma or seizure activity should be treated with prompt intubation and ventilation.

Decontamination:

Activated charcoal 50 g (1g/kg children) via NGT if intubated

Antidote: (Pyridoxine)

Pyridoxine is the specific antidote – *see separate pyridoxine guideline.*

Indications: seizures, coma, metabolic acidosis.

Seizures

Whilst pyridoxine is being sourced administer IV diazepam 5-10mg and repeat if seizures continue.

If refractory seizure activity despite treatment with pyridoxine and benzodiazepines – Propofol or phenobarbitone (20mg/kg [max. 2 g] IV over 20 minutes) are suitable second line treatments

Enhanced elimination: There is no role for extracorporeal elimination techniques unless pyridoxine is not available (or there is inadequate supply) and the patient has ongoing seizure activity refractory to the above treatments.

Disposition:

Discharge pending mental health assessment if asymptomatic at 6 hours post-exposure.

All patients with neurotoxicity should be admitted to a HDU environment.