

### Overview

C19-diterpenoid alkaloids incl aconitine, mesaconitine, and hypaconitine found in plants of *Aconitum* species, e.g. *A. napellus* (wolfsbane, monkshood). Content in roots and root tubers > flowers > leaves and stems. Used in trad Chinese Medicines (chuanwu, caowu & fuz) for analgesic, indigestion, agitation, anti-inflammatory & many other purposes). Should be processed (heating & hydrolysis) to reduce aconite content (by 65-90%) before use, but may not occur.

### Toxic mechanism

Aconite alkaloids bind with high affinity to the open state of the voltage-sensitive sodium channels at site 2, blocking their inactivation. Thus continuing sodium influx and sustained depolarization, the sodium channels become refractory to excitation. In heart,  $\text{Na}^+$  influx into the cytosol, increases intracellular  $\text{Ca}^{2+}$ , via  $\text{Na}^+-\text{Ca}^{2+}$  exchange system → positive inotropy and induces triggered activity/ectopics. Also has anticholinergic effects mediated by blocking the vagus. Neurotoxicity: Central autonomic control - activation of the ventromedial nucleus of the hypothalamus → hypotension and bradycardia. Peripherally - persistent voltage-sensitive sodium channel activation leads to a block with decreasing ACh quanta released.

### Toxicokinetics

Rapid absorption from GI (onset of symptoms 10-120min). Also absorbed easily through skin. Metab: Hydrolysis with esterases and demethylation by CYP450 (esp CYP3A) enzymes to much less toxic compounds. Elim: Urine, bile & faeces. Cleared from blood <24hr, but may be detectable in urine for a week.

### Clinical features

*Neurological:* sensory (paraesthesia and numbness of the face, perioral area, and the four limbs), motor (muscle weakness in the four limbs), or both.

*Cardiovascular:* ↓BP, palpitations, chest pain, ↓HR, sinus tachycardia, ventricular ectopics, VT, TdP, VF, and junctional rhythm.

*GI:* nausea, vomiting, abdominal pain, and diarrhoea.

*Other:* dizziness, ↑RR, sweating, difficulty breathing, confusion, headache & lacrimation.

### Investigations

*Screening:* ECG, paracetamol, BSL

*Other:* lab assays for *Aconitum* alkaloids (not widely avail)

### Risk assessment

Est fatal dose = 2mg aconitine, 5ml aconite tincture or 1g of plant.

### Management

*Mainly supportive:* incl ABCs,  $\text{O}_2$ , fluids, replace  $\text{K}^+$  loss, DC cardioversion may be ineffective, cardiopulmonary bypass/ECMO

*Decontamination:* rapid abs reduces any benefit from activated charcoal

*Elimination:* lipid soil & large molecule so dialysis not useful. ?charcoal haemoperfusion

*Specific:* Atropine if bradycardia. Amiodarone or flecainide may help if ventricular arrhythmias  
Magnesium sulphate has been advocated.

*Prevention:* Education/regulation of herb preparation.

### Notes

Mortality of order of 5%, much higher if unprocessed plant ingested,