

Colchicine overdose is potentially lethal, causing severe gastroenteritis, followed by multi-organ failure. Discuss ALL cases with a Clinical Toxicologist.

Toxicity / Risk Assessment

Dose (mg/kg) & time dependent.

Symptoms progress with time

- >0.1 mg/kg: potential for toxicity including death
- >0.5 mg/kg: 10% mortality
- >0.8 mg/kg: multi-organ failure and death

Drug Interactions that can increase toxicity

CYP -3A4 strong inhibitors: amiodarone, azole antifungals, macrolide antibiotics, diltiazem, verapamil

Glycoprotein Inhibitors: amiodarone, macrolide antibiotics, cyclosporine, quinidine, verapamil

Clinical features:

- 0-24 hours: Gastrointestinal symptoms +/- fluid loss, leucocytosis, acute kidney injury
- 24-72 hours: Cardiovascular collapse, cardiac arrhythmias, respiratory depression, bone marrow failure, sepsis, renal failure, liver failure, cerebral edema, rhabdomyolysis, $\downarrow K^+$, $\downarrow Ca^{2+}$, $\downarrow Mg^{2+}$
- Late toxicity if survive >1 week: leukocytosis, alopecia, myopathy, neuropathy

Management

Early decontamination and aggressive supportive care are the mainstay of management

Decontamination:

Activated Charcoal: GIVE TO ALL PATIENTS ASAP FOLLOWING DELIBERATE SELF-POISONING

Consider **intubation & ventilation** to facilitate this in uncooperative/deteriorating patients

Activated Charcoal should be given to **all patients** following accidental exposure >0.1 mg/kg AND if ingested 0.05-0.1mg/kg with evidence of renal failure, liver failure or drug interaction.

Fluid loss and multi-organ failure

- Aggressive **fluid resuscitation** +/- inotropic support with meticulous fluid balance
- Maintain normal electrolyte and acid-base (may need invasive monitoring in high dependency unit)

Enhanced Elimination

- Following resuscitation administer **multi-dose activated charcoal** in ingestions >0.1 mg/kg
- **Renal Replacement Therapy** (haemodialysis) may be required to correct acid-base abnormalities or renal failure but does NOT eliminate colchicine

Disposition

- Patients with expected severe toxicity (>0.5 mg/kg) or multi-organ failure will need ICU
- All deliberate self-poisonings and exposures > 0.1 mg/kg are observed for at least 24 hours AND until asymptomatic with normal or stable liver function, renal function and full blood count.
- Discharge pending mental health assessment if asymptomatic >24 hours post ingestion

*Filgrastim (synthetic G-CSF) may have a role in severe neutropenia