



Clinical Pharmacology & Toxicology Pearl of the Week

~ Colchicine ~

- ✓ Colchicine is a plant alkaloid isolated from the Autumn Crocus and Glory Lily flowers
- ✓ Used in Gout, Pseudogout, Behcet's disease, Pericarditis, Familial Mediterranean Fever, idiopathic vasculitis and Sweet syndrome
- ✓ It exerts anti-inflammatory effects by inhibiting leucocyte function & recruitment

Pharmacokinetics

- Colchicine's pharmacokinetics contribute to its narrow therapeutic window:
- Absorption: well absorbed orally, efflux from enterocytes and hepatocytes via P-Glycoprotein (P-GP)
- Distribution: very lipophilic, distributes rapidly into all major organ systems
- Metabolism: high first-pass metabolism, primarily by liver CYP3A4
- Elimination: 40-65% renal excretion as unchanged drug; enterohepatic & biliary clearance

Pathophysiology and Toxicity

- Colchicine binds to several sites on cell microtubules and inhibits proper function, leading to inhibition of mitosis (cell division) in the metaphase stage. This leads to cellular dysfunction and death
- Historically, the toxic dose was reported to be 0.8 mg/kg. However, ingestions of 0.5 mg/kg and lower have resulted in fatalities and reported ingestions greater than 0.8 mg/kg have survived. The inability to properly quantify the toxic dose in humans is due in part to inaccuracies in reported dose ingestion by patients
- Colchicine toxicity may occur in the setting of:
 - Concurrent use of CYP3A4 inhibitors: protease inhibitors, imidazoles, clarithromycin, grapefruit juice
 - Administration of P-GP inhibitors: clarithromycin, tacrolimus, cyclosporine
 - Renal and/or liver impairment
 - Co-prescription of statin medications, specifically: pravastatin, fluvastatin, lovastatin
 - Overdose (intentional vs. unintentional) or ingestion of the Autumn Crocus or Glory Lily

Treatment may involve the following:

- ED observation for at least 8-12 hours if asymptomatic. Admit for at least 24 hours if symptomatic
- Aggressive GI decontamination
 - may include gastric lavage, single dose activated charcoal
- Multi-dose activated charcoal to interrupt enterohepatic recirculation
- IV fluids
- Antibiotics if infection suspected
- Dialysis if AKI is present
- G-CSF if neutropenia

Table 1: Phases of Colchicine Toxicity

Early Phase (0-24h)	Multi-organ failure Phase (1-7 days)	Recovery Phase (7-21 days)
Nausea Vomiting Diarrhea Abdominal pain Dehydration	Respiratory: Respiratory Distress Syndrome	Recovery of organ failure(s)
	Cardiovascular: Congestive heart failure Cardiac arrhythmia, cardiac arrest	Leukocytosis Alopecia
	Neurologic: Seizures Encephalopathy Cerebral edema Neuropathy, myopathy	Neuropathy Myopathy
	Hematologic: Cytopenias Bone marrow suppression Hemolysis, DIC	
	Metabolic: Metabolic acidosis HypoK, hypoNa, hypoP04, hypoglycemia/hyperglycemia	
	Other: Renal failure, Liver failure Immune compromise & Sepsis	

The Clinical Pharmacology (CP) physician consultation service is available Mon-Fri, 8am-5pm, excluding stat holidays. The on-call physician is listed in ROCA on the AHS Insite page. CP consultations are also available through Netcare e-referral, Specialist Link, and RAAPID. You can also find us in the [Alberta Referral Directory](#) (ARD) by searching “Pharmacology” from the ARD home page. Click [HERE](#) for more details about the service.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414 (AB and NWT) or 1-866-454-1212 (SK). Information about our outpatient Medical Toxicology Clinic can be found in [Alberta Referral Directory](#) (ARD) by searching “Toxicology” from the ARD home page.

More CPT Pearls of the Week can be found [HERE](#).

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