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Maryland Poison Center
UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY

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The Maryland Poison Center's Monthly Update: News, Advances, Information

Colchicine

Colchicine is a naturally occurring alkaloid compound harvested from the autumn crocus (*Colchicum autumnale*) with use as a natural remedy dating back to 550 A.D. Today, colchicine's primary therapeutic indications include gout and familial Mediterranean fever. Despite therapeutic benefits, colchicine is extremely toxic in overdose and after drug interactions that inhibit colchicine clearance.

Colchicine's primary mechanism of action involves its ability to inhibit microtubule polymerization. At low concentrations, colchicine prevents microtubule elongation by binding soluble tubulin fragments to form a poorly reversible complex. At higher concentrations, colchicine causes these tubules to break down. This results in the inhibition of cell replication across numerous organ systems. In overdose, the anti-mitotic effects of colchicine become indiscriminatory. Cells with the greatest cell turnover such as the bone marrow, gastrointestinal tract and hair follicles tend to be most prone to colchicine's toxic effects *(Clin Toxicol. 2010;48(5):407-14).*

Acute colchicine toxicity is associated with three sequential stages. The first occurs within 24 hours post-ingestion and is characterized by profuse nausea, vomiting and diarrhea. An initial leukocytosis is commonly observed during this time frame. A more wide-spread, multi-organ damage occurs during the second stage and can last for several days. Volume depletion and directly toxic effects to myocardial cells place patients at risk for cardiac arrhythmias and circulatory collapse, particularly within 24-36 hours after ingestion. Liver and renal failure can also occur. Following an initial leukocytosis, hematologic complications such as leukopenia and thrombocytopenia can lead to fatal infections and hemorrhagic events. Death following acute colchicine toxicity commonly occurs within 7 days. Patients surviving beyond this time frame experience bone marrow recovery and resolution of end organ damage. Alopecia develops 2-3 weeks after exposure in those that survive. Patients may experience proximal limb weakness and distal sensory abnormalities that resolve within weeks to months. Bismuth and colleagues proposed a set of prognostic criteria in which they stated patients ingesting 0.5 mg/kg or less are likely to survive with supportive care, while ingestions of ≥0.8 mg/kg are associated with 100% mortality *(J Toxicol Clin Toxicol. 2000;38(1):51-4).* Subsequent case reports have questioned these results by describing survival and mortality occurring outside of these values.

Management of colchicine toxicity relies on supportive care. In early presenting, potentially lethal ingestions, aggressive gastrointestinal decontamination using whole bowel irrigation or orogastric lavage can be considered if the patient is not already experiencing gastrointestinal symptoms. Multi-dose activated charcoal can be used to disrupt enterohepatic recirculation. Other components of initial management include fluid resuscitation and electrolyte repletion. Blood cultures and broad-spectrum antibiotics are also indicated in patients with acute colchicine toxicity, as they are at risk for significant infectious complications due to profound neutropenia. While colchicine antibodies have been studied, they are not commercially available *(Clin Toxicol. 2015;53(5):427-32)*. Colchicine is not significantly removed by hemodialysis.

Did you know?

Two recent, large, randomized, controlled trials assessed the cardioprotective effects of colchicine in patients with cardiovascular disease.

LoDoCo2 and COLCOT suggested that patients receiving colchicine experienced decreased rates of cardiovascular events compared to those receiving placebo *(Am Heart J. 2019 Dec;218:46-56, Eur Heart. 2020 Nov 7;41(42):4092-4099).* Additionally, the GRECCO-19 Randomized Clinical Trial has led some to speculate that colchicine may have beneficial effects in patients hospitalized with COVID-19 *(JAMA Netw Open. 2020 Jun; 3(6): e2013136).* While the data focusing on the use of colchicine for these indications are limited, these findings may result in an increased prescribing of colchicine and a subsequent increase in its availability.

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