

## CASE REPORT

## Colchicine Poisoning: A Case of Deliberate Self Poisoning, Late Presentation and Fatal Outcome

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### Abstract

Colchicine poisoning is relatively uncommon, but potentially life threatening event due to the high toxicity of the drug and ability to precipitate severe multi-organ failure in overdose. Colchicine is used primarily in the treatment of acute attacks of gout and inflammatory diseases. We report a the first case of a 18 -year-old Libyan female who presented to the emergency department approximately 20-28 hours after ingesting 30 mg of colchicine in a suicide attempt. In spite of gastric lavage, use of activated charcoal and supportive measures, multi-organ system failure developed over the following two days, and patient died on the third day after admission. Salient toxicological and clinical aspects of colchicine poisoning are discussed.

**Keywords:** Colchicine, Toxicity, Death, Poisoning

### Introduction

Colchicine is an alkaloid derived from *Colchicum autumnale* (Figure 1) and is used primarily in the treatment of acute gouty arthritis. The drug recently became more widely used for the treatment of more rheumatological and non-rheumatological conditions including pseudogout, familial Mediterranean fever, amyloidosis, scleroderma, sarcoidosis, Bechet's disease, Paget's disease, psoriasis, primary biliary cirrhosis and alcoholic cirrhosis (2-7). Although colchicine poisoning

is an uncommon form of drug overdose, it can lead to severe multi organ failure when taken in excessive doses (8). The amount of colchicine required for considerable morbidity and mortality varies greatly. A lethal outcome has been reported after ingestion of 7 mg over a 4-day period, whereas patients have survived after ingestions of more than 60 mg (9, 10). Suicidal attempts with colchicine are uncommon. We report a case of an intentional ingestion of colchicine and discuss the toxicological and clinical aspects of the subject.



**Figure 1.** *Colchicum autumnale* redrawn from internet-based resources (Courtesy of Miss Noor Beshyah, The Bateen Secondary School, Abu Dhabi, United Arab Emirates).

## Case Report

### Initial presentation

A previously healthy 18-year-old Libyan female presented to the emergency department with abdominal pain, nausea, diarrhea (watery stools) and severe generalized weakness. The family reported history of a suicidal attempt with anti-inflammatory drugs of her father over previous 20-28 hours and she received treatment as gastritis in the referring hospital. On physical examination, she looked well, was conscious and oriented. Her vital signs were normal; blood pressure 110/60 mmHg; heart rate showed was regular at 100 beats/min, respiratory rate was 30 breaths/min, and temperature was 37.3°C. There was mild epigastric tenderness. Rest of the physical examination was unremarkable. Laboratory studies including a complete blood count, electrolytes, blood urea nitrogen creatinine, glucose, and urine analysis, were within normal range except for leukocytosis (WBC 26,800/mm<sup>3</sup>) and increase creatinine level (2.4 mg/dL). The electrocardiogram confirmed sinus tachycardia with no other pathological abnormalities. Chest X-ray was normal. Urethral catheterization produced a small quantity of urine.

### Management and progress

Gastric lavage was performed in the emergency department and the patient was admitted to the hospital for further management. The management plan was to rehydrate her and correct any electrolyte disturbances that may ensue. She remained hemodynamically stable during the first 8 hours of hospitalization. Subsequently, she became distressed, shocked and needed transfer to the intensive care unit for closer observation and further treatment. On the second day, the family brought a drug bottle that should have contained colchicine tablets of 0.6 mg strength suggesting that the patient took nearly 30 mg.

Treatment options were limited and only supportive care could be given. Over the following 12 hours, the patient's clinical condition and hemodynamic status deteriorated progressively. She became confused, febrile, and more distressed; laboratory values showed leukocytosis, thrombocytopenia, mild electrolyte disturbances and elevated liver enzyme levels (white cell count 24x10<sup>9</sup>/l, platelets 130x10<sup>9</sup>/l, urea 54 mmol/l, creatinine 3.1 mg/dL, INR 3.5). Arterial blood gas results confirmed a metabolic acidosis (pH 7.2, pCO<sub>2</sub> 21.8 mmHg, pO<sub>2</sub> 68.8 mmHg, HCO<sub>3</sub><sup>-</sup> 9.9 mEq/L). She received bicarbonate infusions to maintain plasma pH with some improvement (pH 7.3, HCO<sub>3</sub><sup>-</sup> 18mEq/L).

The patient was prescribed a broad-spectrum antibiotic immediately after obtaining blood and urine for culture and sensitivity. Despite crystalloid solutions and fresh frozen plasma to maintain adequate perfusion pressures, the patient became hypotensive and unstable. She required a dopamine infusion to maintain blood pressure and few hours later the patient developed respiratory distress and required endotracheal intubation and mechanical ventilation. The patient became less responsive progressively and eventually arrested. Resuscitation started, but she continued to deteriorate and she died on the third day of hospitalization.

### Discussion

Colchicine poisoning is an unusual form of drug toxicity and constitutes a toxicological emergency where rapid intervention is required. However, as it is not suspected readily, late diagnosis exemplified by our case may lead to grave outcome.

**Table 1.** The three stages of clinical presentation of colchicine poisoning.

Stage	Time Post-ingestion	Characteristics
One	< 24 hour	This is marked by the onset of nausea, vomiting, and severe diarrhea with hypovolemia.
Two	2-5 days	They may include involvement of any organ with multi organ failure system includes bone marrow depression (pancytopenia) and also respiratory, renal and cardiac failure (2,14).
Three	Recovery	This is seen in patients who recover from colchicine poisoning and is manifested by transient alopecia and a rebound leukocytosis. Colchicine toxicity can lead to severe coagulation disturbance (17).

Deliberate overdose is very unusual as the medication is not readily available as common household medication. Only 369 entries were found in response to a search on PubMed using the search item of “colchicine poisoning”. There are no reports from any other Arab countries. Indeed, this is the first case to be reported from Libya.

Colchicine is rapidly absorbed in the ileum after its oral ingestion and is metabolized in the liver by deacetylation to the more toxic oxydicolchicine and excreted with its metabolites via the biliary tract. The more toxic metabolites may be responsible for the early gastrointestinal symptoms. Up to 20% of the quantity used is also eliminated in the urine (14,15). Colchicine toxicity is based on its antimitotic activity as it binds to cell protein tubulin (which acts as a receptor for colchicine) and inhibits mitosis in metaphase by blocking spindle formation by disrupting microtubules (16). Characteristically, colchicine has a short plasma half-life of twenty minutes, due to high affinity to tissues as kidney, liver and spleen where they contain high concentrations of colchicine, while it is apparently largely excluded from cardiac and skeletal muscle as well as brain tissue (16). Colchicine has a direct toxic effect to the abdominal mucous membrane layers and hematopoietic stem cells, causing severe diarrhea, related to the rapid turnover of intestinal mucosal cells and decreasing absolute number of short-living blood cells granulocytes and thrombocytes. In acute colchicine poisoning, there is a delay of 1-6 hours between ingestion and the development of toxic symptoms. The three stages of its clinical presentation are described in table 1. In one case of colchicine poisoning, coagulation disturbance was prominent (18). Colchicine concentration in the brain is low, and can affect the heart causing heart failure, which is considered as an important cause of morbidity in patients with severe colchicine toxicity (18). Echocardiography should be performed in all patients

(19). Prognosis of colchicine poisoning is mainly dependent on the amount of consumption and the duration after ingestion of the medication (20).

The treatment of colchicine poisoning is mainly supportive because of lack of specific antidote. Although treatment with monoclonal antibodies to colchicine has been reported in but it is not yet widely available. This may prove particularly useful in the future (21). Intensive gastrointestinal decontamination with gastric lavage and activated charcoal should be instituted as early as possible (but perhaps even in later presentation). It has a significant value because of the enterohepatic circulation of the medication (22). Neither hemodialysis nor hemoperfusion is particularly effective because of the large cell distribution of colchicine (23). The value of colchicine levels in blood or urine has not been well elucidated for technical reasons. A successful result after the use of colchicine-specific Fab fragments has been revealed in the treatment of a woman who had ingested 60 mg of colchicine (10). Colchicine-specific Fab fragments are derived from goats and consist of the light chain and variable region of the heavy chain (6). The mechanism of action is similar to digoxin-specific Fab fragments, it has high affinity to colchicine and allows redistribution into the intravascular compartment and this acts for elimination of important quantities of drug from peripheral sites (24). In our patient, several factors could have contributed to her demise including the late diagnosis, the uncommon nature of the offending agent, the inherently aggressive nature of the poisoning and the lack of national advisory services.

In conclusion, this case exemplifies the colchicine overdose and its associated high morbidity and mortality rates due to multi-organ failure in a setting of limited resources. The severity related to the dosage of ingested drug and the time of admission to hospital was illustrated. Although a specific therapy is not yet

available for colchicine poisoning, the symptomatic treatment should be started as soon as possible. An effort to create particular strategy to colchicine intoxication should be strengthened in order to decrease mortality rate in patients taking the drugs in a large amount.

## References

- Insel AP. Drugs employed in the treatment of gout. In: JG Hardman, AG Gilman and LE Limbird (Eds). *The Goodman and Gilman's: The Pharmacokinetics Basis of Therapeutics*, Saunders Co., New York (1999); PP: 647-9.
- Milne ST, Meek PD. Fatal colchicine overdose: report of a case and review of the literature. *Am J Emerg Med* 1998;16:603-8.
- Ghayad E, Tohme A. Behcet's disease in Lebanon: report of 100 cases. *J Med Liban* 1995;43:2-7.
- Naidus RM, Rodvien R, Mielke CH, Jr. Colchicine toxicity: a multisystem disease. *Arch Intern Med* 1977;137:394-6.
- Seideman P, Fjellner B, Johannesson A. Psoriatic arthritis treated with oral colchicine. *J Rheumatol* 1987;14:777-9.
- Kaplan MM, Alling DW, Zimmerman HJ, Wolfe HJ, Sepersky RA, Hirsch GS, et al. A prospective trial of colchicine for primary biliary cirrhosis. *N Engl J Med* 1986;315:1448-54.
- Quijano-Pitman F. Colchicine in the treatment of liver cirrhosis. *Gac Med Mex* 1998;134:610.
- Miller MA1, Hung YM, Haller C, Galbo M, Levsky ME. Colchicine-related death presenting as an unknown case of multiple organ failure. *J Emerg Med* 2005;28:445-8.
- Macleod JG, Phillips L. Hypersensitivity to colchicine. *Ann Rheum Dis* 1947;6:224-9.
- Baud FJ, Sabouraud A, Vicaut E, Taboulet P, Lang J, Bismuth C, et al. Brief report: treatment of severe colchicine overdose with colchicine-specific Fab fragments. *N Engl J Med* 1995;332:642-5.
- Kirchin VS SH, Beard RC. Colchicine: an unusual cause of reversible azoospermia. *BJU International* 1999; 83:156.
- Wilbur K, Makowsky M. Colchicine myotoxicity: Case reports and literature review. *Pharmacotherapy* 2004;24:1784-92.
- Altman A, Szyper-Kravitz M, Shoenfeld Y. Colchicine-induced rhabdomyolysis. *Clin Rheumatol* 2007;26:2197-9.
- Putterman C, Ben-Chetrit E, Caraco Y, Levy M. Colchicine intoxication: clinical pharmacology, risk factors, features, and management. *Semin Arthritis Rheum* 1991;21:143-55.
- Achtert G, Scherrmann JM, Christen MO. Pharmacokinetics/bioavailability of colchicine in healthy male volunteers. *Eur J Drug Metab Pharmacokinet* 1989;14:317-22.
- Hurlburt KM. Unclassified therapeutic agents, in Dart RC (eds): *Medical Toxicology*. Philadelphia, Lippincott Williams & Wilkins, 2004;ed 3:1033-4
- Murray SS, McMichan JC, Mohr DN. Acute toxicity after excessive ingestion of colchicine. *Mayo Clin Proc* 1983;58:528-32.
- Standardized prognosis evaluation in acute toxicology its benefit in colchicine, paraquat and digitalis poisonings. *J Toxicol Clin Exp* 1986;6:33-8.
- Bismuth C, Baud F, Dally S, Sauder P, Kopferschmitt J, Jaeger A, et al. Hemodynamic studies in eight cases of acute colchicine poisoning. *Hum Toxicol* 1983;2:169-73.
- Ataş B, Caksen H, Tuncer O, Kirimi E, Akgün C, Odabaş D. Four children with colchicine poisoning. *Hum Exp Toxicol*. 2004;23:353-6.
- Scherrmann JM, Sabouraud A, Urtizberea M. Clinical use of colchicine-specific Fab fragments in colchicine poisoning. *Vet Hum Toxicol* 1992; 34:334
- Niel E, Scherrmann JM. Colchicine today *Joint Bone Spine*. 2006;73:672-8.
- Borron SW, Scherrmann JM, Baud FJ. Markedly altered colchicine kinetics in a fatal intoxication: examination of contributing factors. *Hum Exp Toxicol* 1996;15:885-90.
- Schaumann W, Kaufmann B, Neubert P, Smolarz A. Kinetics of the Fab fragments of digoxin antibodies and of bound digoxin in patients with severe digoxin intoxication. *Eur J Clin Pharmacol* 1986;30:527-33.