



## Case report

## Colchicine overdose: A South African experience, a case report

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## ABSTRACT

**Introduction:** Colchicine overdose is uncommon but is associated with a high mortality rate. It has a narrow therapeutic index and has been described to have a 100% mortality with ingestion of > 0.8 mg/kg (Finkelstein et al., 2010; Herran-Monge et al., 2013; Aghabiklooei et al., 2014; Erden et al., 2013).

**Case report:** This is a case report of a 19-year-old male who ingested 0.4 mg/kg of colchicine in a suicide attempt. He developed multiorgan dysfunction. He was managed supportively, and the dysfunction resolved.

**Discussion:** The clinical presentation and management should be familiar to all those who work in acute care in order to be able to identify and treat it timeously thus preventing morbidity and mortality. Treatment is largely supportive. To the best of our knowledge this is the first case of colchicine overdose described in Sub-Saharan Africa.

## Introduction

Colchicine overdose is uncommon but is associated with a high mortality rate. It has a narrow therapeutic index and has been described to have a 100% mortality with ingestion of amounts > 0.8 mg/kg [1,2,4,7].

The clinical presentation and management should be familiar to all those who work in acute care in order to be able to identify and treat it timeously thus preventing morbidity and mortality. Treatment is largely supportive. This is the first case of Colchicine overdose described in Sub-Saharan Africa. Written informed consent was obtained from the patient for the publication of this case report.

## Case report

A 19-year-old male, with no known comorbidities, presented to a tertiary academic hospital with multi-organ dysfunction (MOD) after ingesting 24 Colchicine tablets and 50 tablets of Procydin (a herbal antioxidant) in a suicide attempt. This is a total of 24 mg taken which equates to 0.4 mg/kg of Colchicine ingested on the day of presentation. There was no other significant history.

The patient presented with a blood pressure of 119/60 mmHg and a heart rate of 106 bpm. He had a reduced Glasgow Coma Scale score of 14/15. The rest of the examination was unremarkable.

Blood investigations included a biochemical workup. Urine dipstick

and microscopy, cell-count and culture were done due to the risk of bone marrow suppression from Colchicine toxicity. An electrocardiogram (ECG), Chest X-Ray and an echocardiogram were also performed. Biochemical investigations revealed acute renal and liver dysfunction with thrombocytopenia, lymphopaenia and elevated cardiac markers on admission. During his admission, he developed a pancytopenia. Improvement of these abnormalities can be seen during his admission. Significant results are shown in Table 1.

The patient was managed as part of a multidisciplinary team. No acute emergency toxicological management was performed, such as activated charcoal. The patient was admitted to the medical gastrointestinal ward and management was largely supportive. Intravenous fluids were given with strict input and output monitoring to manage his acute kidney injury. The patient developed epistaxis secondary to thrombocytopenia which was treated with Tranexamic Acid. N-acetylcysteine was given. Ertapenem was given as part of the febrile neutropenic protocol and multiple platelet transfusions were given.

Serial investigations were performed, including U + E, LFT and FBC, to monitor the patient's response to the treatment provided.

The patient's MOD was improving and trending towards normal by day 7. He was discharged home.

## Discussion

Colchicine overdose is very uncommon but is associated with a high

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**Table 1**  
Relevant Patient Results

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Reference Ranges
WCC	8.64	3.77	1.84	2.08	3.28	6.60	11.73	3.9–12.6 × 10 <sup>9</sup> /L
Hb	13.9	14.1	12.5	12.8	12.6	12.7	13.1	14–18 g/dL
Platelets	96	53	33	19	18	38	76	186–454 × 10 <sup>9</sup> /L
RPI				0.2				1–2
Neutro	1.36							1.60–6.98 × 10 <sup>9</sup> /L
Lympho	0.20							1.40–4.20 × 10 <sup>9</sup> /L
Mono	1.18							0.30–0.80 × 10 <sup>9</sup> /L
Eosino	0.04							0.00–0.95 × 10 <sup>9</sup> /L
Baso	0.06							0.00–0.10 × 10 <sup>9</sup> /L
CRP	160			142				< 10 mg/L
INR	1.39	1.39	1.07	1.1			1.14	< 1.1
Na	132		136	135	136	136	136	135–147 mmol/L
K	4.6		3.9	3.6	3.6	4.0	3.7	3.3–5.3 mmol/L
Cl	93		95	95	95	96	94	99–113 mmol/L
Urea	24.4		8.6	6.7	7.1	7.2	7.9	2.6–7.0 mmol/L
Creatinine	210		87	71	64	61	63	47–90 µmol/L
TProtein	60			56	52			60–85 g/L
Albumin	35			33	30		33	35–52 g/L
TBili	6			17	14		11	0–21 µmol/L
DBili	2			7	7		5	0–6 µmol/L
ALT	1482			1354	1078		626	5–40 U/L
AST	2044			1289	683		231	5–40 U/L
ALP	388			107	104		123	40–120 U/L
GGT	50			239	240		262	0–60 U/L
Trop T	2090		1655	1868				< 14 ng/L
CKMB	222.2			21.41		11.97		0–6.22 µg/L
CK			> 20,000			3719	1688	20–200 U/L
Ca					1.85		2.10	2.15–2.50 mmol/L
Mg					0.73		0.72	0.63–1.05 mmol/L
PO <sub>4</sub>					0.6		0.82	0.78–1.42 mmol/L

mortality rate [1,2]. It has a narrow therapeutic index with 80% of patients experiencing gastrointestinal side effects with therapeutic doses [1–3]. The distinction between non-toxic, toxic and lethal outcomes is unclear and tends to be patient dependent [2]. However, some studies have defined the following as a guideline: 100% survival with a dose of < 0.5 mg/kg, 10% mortality with doses between 0.5 and 0.8 mg/kg and 100% mortality with ingestion of doses > 0.8 mg/kg [1,2,4,7].

Colchicine has multiple indications the most common being used for acute gout [1].

Colchicine is taken orally and is rapidly absorbed, undergoing “extensive first pass metabolism” [1] in the liver and wide distribution to bind to intracellular elements [1]. It undergoes “significant enterohepatic re-circulation” [1] and 10–20% is renally excreted [3,5]. Toxicity occurs when colchicine binds to tubulin and disrupts the microtubular network. This leads to a decrease in protein assembly and decreased endocytosis and exocytosis. It changes cell morphology, phagocytosis and leukocyte migration. It intervenes in the production of prostaglandins, changing the activity of COX-1 and COX-2 [9] as well as being a “competitive antagonist of GABA<sub>A</sub>” [4]. Decrease in cellular motility, cessation of mitosis and disruption of cardiac myocyte conduction and contractility occur [1] as well as “inhibition of the release of histamine and secretion of insulin, depression of the central respiratory system, stimulation of the central vasomotor system inducing hypertension, and increased reaction to the sympathomimetic agents” [4]. This ultimately results in multi-organ failure [1].

Signs and symptoms of Colchicine overdose usually present in 3 phases [1]. The first phase is within 4–24 h and includes: gastrointestinal disturbances, dehydration, hypovolaemia, reactive leucocytosis and electrolyte imbalance. The second phase is within 24 h to 7 days and includes MOD. The last phase is within 7–14 days and includes recovery of bone marrow depression, rebound leucocytosis and transient alopecia [1].

The main causes of death include MOD and sepsis [1]. Other noted causes of death are sudden arrhythmias [4,9], acute cardiac failure, cardiogenic shock, haemodynamic collapse and haematopoietic complications such as myelosuppression [4,7].

Management of Colchicine overdose predominantly involves monitoring and supportive therapy. Management can be divided into six stages [1,2]: prompt recognition of Colchicine overdose, determination of dose ingested in mg/kg, admission for observation in a high care area, early gastric decontamination, aggressive case dependent supportive management and specific treatment if available.

Early gastric decontamination includes multidose activated charcoal due to the high enterohepatic re-circulation [3]. Gastric lavage can be performed if a high dose is ingested, preferably within < 60 min of the ingestion [3].

Aggressive supportive management includes monitoring and symptomatic management. Continuous vitals and ECG monitoring should be done. Serial investigations including bloods, Chest X-Ray, echocardiogram and urinalysis should be undertaken. Symptomatic management includes anti-emetics, intravenous fluids, correction of electrolyte and acid-base disturbances and broad-spectrum antibiotics. Blood products, vasopressors, antiarrhythmics, intubation and febrile neutropaenic protocol can be given on a case to case basis. N-acetylcysteine can be considered. It was used in another case study which proposed that the antioxidant properties decreased oxidant-induced cell damage and apoptosis [1]. Dialysis can be considered for organ support, but clearance of Colchicine is not possible due to its high volume of distribution.

Specific treatment includes Granulocyte-Colony-Stimulating Factor (GCS-F) and Fragment-Antigen-Binding (Fab) antibodies. GCS-F assists “regeneration of suppressed bone-marrow” [6] by accelerating production of neutrophils within the bone marrow and preventing sepsis [1]. Fab fragment antibodies are the only treatment that specifically targets Colchicine toxicity; however, it is not produced commercially.

Fab antibodies consist of “the light chain and variable region of the heavy chain of antibodies derived from goats immunized with a conjugate of Colchicine and serum albumin” [1]. Fab antibodies work by binding to Colchicine, thus decreasing the levels of toxicologically active fractions, and removing the drug from peripheral sites. There are no recorded side effects to Fab antibodies thus far. The limitations to the use of this treatment are limited availability, no known correct dosage and the high costs involved in preclinical trials [8]. Fab antibodies have only been used in a few cases of Colchicine overdose and further research is needed. There is very limited data on this as an effective and realistic treatment method.

With regards to this case, the management was in keeping with that described in the literature. It was not noted whether early gastric decontamination was performed. The effect of Procydin is not known. GCS-F or Fab antibodies were not given as they are not available at the institution. The dose ingested was 0.4 mg/kg and the good outcome is consistent with the toxic dose ingestion guideline mentioned above.

## Conclusion

Colchicine overdose is uncommon but carries a high mortality rate. This appears to be the first case described in Sub Saharan Africa. It is important to be able to identify and promptly treat the condition to minimize mortality. Treatment is largely supportive. Specific agents are available but require further research.

## Authors' contribution

Authors contributed as follow to the conception or design of the work; the acquisition, analysis, or interpretation of data for the work; and drafting the work or revising it critically for important intellectual content: JE contributed 70%, SG contributed 20%, and AM contributed 10%. All authors approved the version to be published and agreed to be accountable for all aspects of the work.

## Declaration of competing interest

Authors declared no conflict of interest.

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