

# Colchicine Poisoning in Children: 7 Case Reports

## Çocuklarda Kolşisin Zehirlenmesi: 7 Olgu Sunumu

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### SUMMARY

Colchicine is a drug that has been used primarily in several diseases. Colchicine poisoning is an infrequent but potentially life-threatening problem characterized by multiorgan involvement. We present seven children with colchicine poisoning. Their ages ranged between 1 and 9 years. In six children, the amount of colchicine consumed was between 0.16 and 0.39 mg/kg; the most frequent findings were diarrhea and vomiting. In one patient, the ingested amount was unknown. One of the patients died and all others recovered without sequelae. The severity of colchicine poisoning tends to be related to the dosage of ingested drug and the time of admission to hospital. Symptomatic treatment should be started as soon as possible in colchicine poisoning. (*Journal of Current Pediatrics 2009; 7: 96-100*)

**Key words:** Colchicine, children, poisoning

### ÖZET

Kolşisin, çeşitli hastalıkların tedavisinde primer olarak kullanılan bir ilaçtır. Kolşisin zehirlenmesi, sık görülmemekle birlikte, çoğul organ tutulumuna neden olarak hayatı tehdit edici karakterde seyredebilir. Kolşisin zehirlenmesi olan yedi çocuk hasta sunuyoruz. Hastaların yaşları 1 ila 9 arasında idi. Altı hastanın aldıkları kolşisin miktarları 0,16 mg/kg ile 0,39 mg/kg arasındaydı, en sık görülen bulgu kusma ve ishal idi. Bir hastanın almış olduğu miktar ise bilinmiyordu. Bir hasta kaybedildi, diğer hastalar ise sekelsiz düzeldi. Kolşisin zehirlenmesinin ciddiyeti, alınan doza ve hastaneye başvuru zamanına bağlı görünmektedir. Kolşisin zehirlenmesi sonrasında mümkün olan en kısa sürede semptomatik tedavi yapılmalıdır. (*Güncel Pediatri 2009; 7: 96-100*)

**Anahtar kelimeler:** Kolşisin, çocuklar, zehirlenme

## Introduction

Colchicine is an alkaloid that has been used primarily in Familial Mediterranean Fever, acute gouty arthritis, Behçet's disease, sarcoidosis, psoriasis, scleroderma, and amyloidosis (1). Colchicine poisoning is an uncommon form of drug overdose. However, serious complications may occur following ingestion of colchicine either accidentally or in attempted suicide. Clinical management of colchicine toxicity can be difficult because of widespread involvement of various vital organs (1).

In this report, we present the findings of seven children with colchicine poisoning, one of whom died; the others recovered without sequelae.

## Case Reports

### Case 1

A previously healthy 4-year-old girl was admitted to the emergency room (ER) 8 hours after ingesting 7 of her brother's 0.5-mg colchicine tablets (0.17 mg/kg). Her only symptom was vomiting on admission. The patient's physical examination revealed lethargy with no other remarkable findings. Laboratory values revealed elevated liver enzyme and creatine kinase (CK) levels, elevated white blood cell (WBC) count and prolongation of her coagulation parameters (Table 1). Blood gas analysis was normal. Electrocardiography and echocardiography were normal.

The patient was hospitalized. Gastric lavage was performed and activated charcoal was given just after admission to ER. Vitamin K was administered via intramuscular route. During the 4 days of follow-up, no laboratory or clinical complication developed. CK, AST (aspartate aminotransferase), ALT (alanine aminotransferase), WBC, and prothrombin time (PT) returned to normal range on the 3<sup>rd</sup> day. On the 4<sup>th</sup> day of admission the parents discharged the child from the hospital against the medical advice. On the 10<sup>th</sup> day after discharge, her physical examination and laboratory findings were normal.

### Case 2

A 4-year-old boy was brought to the ER 6 hours following ingestion of 10 colchicine tablets (0.33 mg/kg). Gastric lavage was performed and activated charcoal was given just after admission to the ER.

On admission, his physical examination was normal. His laboratory evaluation including a complete blood count (CBC), electrolytes, blood urea nitrogen (BUN), creatinine, and glucose were all unremarkable (Table 1). Electrocardiography and echocardiography were normal. Blood gas analysis was normal.

Activated charcoal was given every 4 hours for 24 hours. No abnormal findings were noted during the follow-up. He was discharged from the hospital on the 9<sup>th</sup> day of admission.

### Case 3

A 5-year-old, previously healthy boy was admitted with vomiting and fever. He was brought to the ER 30 hours after ingestion of an unknown amount of his sister's 0.5-mg colchicine tablets. Gastric lavage was performed and activated charcoal was given just after admission to the ER. The physical examination revealed state of somnolence, tachypnea, tachycardia, difficulty in breathing, and central cyanosis.

Laboratory values revealed elevated levels of liver enzymes, CK, alkaline phosphatase (ALP), BUN, and creatinine; electrolyte disturbance; and prolongation of coagulation parameters (Table 1). Blood gas analysis was normal.

The echocardiographic study demonstrated a systolic dysfunction. The ejection fraction and shortening fraction of left ventricle were 45% and 18%, respectively (Figure 1). The patient became hypotensive and a dopamine and dobutamine infusion was started. Unfortunately, the patient subsequently developed bradycardia, which progressed to asystolic cardiac arrest, and he died in the 3<sup>rd</sup> hour of admission. Necropsy could not be performed because permission was not granted by the parents.

### Case 4

A 9-year-old girl was brought to the ER 12 hours after ingesting approximately 30 of her mother's 0.5 mg

**Table 1. Results of Laboratory Studies**

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
WBC (K/ $\mu$ L)	11.4	11.1	49.9	8.7	8.9	9.84	23.8
RBC (M/ $\mu$ L)	4.89	5.02	5.84	5.46	5.1	4.6	
Hemoglobin (g/dL)	13.4	13.3	16.3	15.6	12.9	12.5	14.2
Platelet (K/ $\mu$ L)	331	477	403	245	393	279	773
BUN (mg/dL)	18.4	14	54	11	10	26	11
Kreatinine (mg/dL)	0.4	0.4	1.9	0.6	0.34	0.3	0.4
ALT (IU/L)	74	18	41	28	14	40	35
AST (IU/L)	42	32	510	85	43	112	273
LDH (IU/L)	283	263	6139	666	278	572	1768
CK (IU/L)	214	251	1203	171	151	99	217
PT (sec) (N:10-15.8)	18.5	13.3	44.9	19.3	14.2	21.4	32.7
PTT (sec) (N:26.5-36)	28.7	31.8	66	31.2	26.3	29.8	21.3
INR (N:0.9-1.3)	1.64	1.07	4.86	1.66	1.1	1.8	1.8

WBC: white blood cell; RBC: red blood cell; BUN: blood urea nitrogen; ALT: alanine aminotransferase; AST: aspartate aminotransferase; LDH: lactic dehydrogenase; CK: creatine kinase; PT: prothrombin time; PTT: partial thromboplastin time; INR: international normalized ratio; N: normal value

colchicine tablets (0.39 mg/kg) in a suicide attempt. Gastric lavage was performed and activated charcoal was given just after admission to the ER. The patient was hospitalized.

Her physical examination was normal. Laboratory evaluation in the hospital included a CBC, electrolytes, BUN, creatinine, glucose, and urinalysis, which were all unremarkable (Table 1). Blood gas analysis was normal. Electrocardiography and echocardiography were normal. No abnormal findings were noted during the follow-up. She was discharged from the hospital on the 5<sup>th</sup> day of admission.

### Case 5

A 1-year-old girl was admitted to the hospital 8 hours after ingestion with complaint of vomiting. She had ingested 3 of her mother's 0.5 mg colchicine tablets (0.16 mg/kg). Her physical and laboratory examinations were normal (Table 1). Electrocardiography and echocardiography were normal. She was discharged from the hospital on the 4<sup>th</sup> day of admission.

### Case 6

A 2.5-year-old girl was brought to the ER 7 hours after ingesting 7 (0.5 mg) colchicine tablets (0.3 mg/kg). Gastric lavage was performed and activated charcoal was given just after admission to the ER. The patient was hospitalized.

Her physical examination was normal on admission. Laboratory values revealed elevated liver enzyme levels (Table 1). Electrocardiography and echocardiography

were normal. No abnormal findings were noted during the follow-up. After return of elevated liver enzyme levels to normal, she was discharged from the hospital on the 4<sup>th</sup> day of admission.

### Case 7

A 3.5-year-old boy was brought to the ER 5 hours after ingesting 10 (0.5 mg) colchicine tablets (0.33 mg/kg) with complaint of vomiting and lethargy. Shortly after ingestion, the patient was given milk and provoked to vomit. Gastric lavage was performed and activated charcoal was given just after admission to the ER. The patient was hospitalized.

His physical examination revealed lethargy and frequent vomiting. Laboratory values revealed elevated WBC, platelet, liver enzyme levels, LDH, CK, and PT (Table 1). Electrocardiography and echocardiography were normal. No abnormal findings were noted during the follow-up. After return of all abnormal laboratory results to normal, she was discharged from the hospital on the 6<sup>th</sup> day of admission.

## Discussion

Colchicine is a highly active alkaloid derived from *Colchicum autumnale* and *Gloriosa superba*. It has been used in the treatment of gout disease since the sixth century.

Colchicine poisoning is an infrequent form of drug overdose with relatively few cases reported in childhood. Colchicine is rapidly absorbed from the gastrointestinal tract, mainly in the ileum, when administered orally. It is metabolized in the liver by deacetylation and biliary excretion, and excreted via the biliary tract. Up to 20% of the dose administered is excreted unchanged in the urine (1,2).

Colchicine is directly toxic to tissues with rapid turnover like the intestinal mucous membrane and bone marrow. The acute toxicity of colchicine is well known: abdominal pain, gastroenteritis with vomiting and diarrhea, hypokalemia, metabolic acidosis, aplastic anemia complicated by hemorrhage, and infection can result (1,3-6). Gastrointestinal side effects (e.g. crampy abdominal pain, nausea, vomiting, diarrhea) are frequent and occur in up to 80% of the patients receiving colchicine in full therapeutic doses (6). In six of our pa-

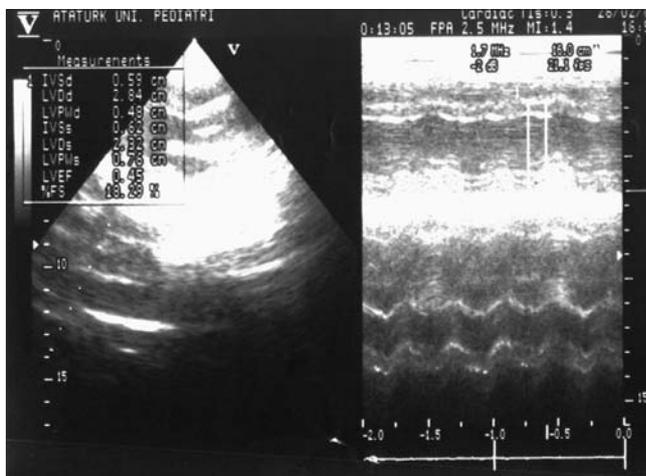


Figure 1. Case 3. Functions of left ventricle in echocardiographic study (Left ventricular systolic dysfunction)

tients, the dosage of colchicine was between 0.16-0.39 mg/kg, and all of them had only gastrointestinal side effects such as vomiting; none was observed to have hematologic, cardiac or central nervous system side effects during the follow-up.

Colchicine poisoning may cause severe coagulation disturbances (7). In one series of colchicine poisonings, coagulation disturbances were prominent (8). In three of our patients, the coagulation parameters, especially PT, were disrupted. All four patients with disrupted coagulation parameters had elevated liver enzymes. The elevated liver enzymes and the prolonged PT are thought to occur as a result of hepatotoxic effect of colchicine poisoning. Of the four patients, three received vitamin K injection (patients 1,4 and 7) and the levels of PT returned to normal. Patient 3 was treated with vitamin K and fresh frozen plasma, but he died 3 hours after admission to ER.

Colchicine may affect the cardiovascular system, and cardiovascular collapse is an important cause of morbidity in patients with severe colchicine toxicity (9). An initial decrease in cardiac performance is associated with poor prognosis. Echocardiography was performed in all of the patients, and in five of them it was normal. In one patient (patient 3), ejection fraction and shortening fraction were low. He was monitored due to hemodynamic and respiratory status, and fluid replacement therapy was started immediately. Unfortunately, the patient died with multiorgan failure.

Prognosis of colchicine poisoning is mainly associated with the dose of ingestion and the time of admission after ingestion of the drug. In one series with colchicine poisoning, all 38 patients who had ingested less than 0.5 mg/kg of colchicine survived with supportive therapy alone, while all patients who had ingested more than 0.8 mg/kg died within 72 hours (7). In our six patients who survived, the dosage of colchicine was less than 0.5 mg/kg. The time of admission to the hospital of these six patients was between 6-12 hours. One of the seven patients, who was admitted to the hospital 30 hour after ingestion, died. In one series of patients with colchicine toxicity, a relation was determined between the time of admission to hospital after drug ingestion and mortality (10). Our findings are compatible with this study.

Treatment of colchicine poisoning is generally supportive because no antidote exists. Although specific therapy such as with colchicine antibodies has been reported in some case reports and animal studies, it is not

yet commercially available (11). Primary decontamination with gastric lavage and activated charcoal should be performed as early as possible. Multiple-dose activated charcoal may have important utility because of enterohepatic recirculation of the drug (12). Gastric lavage and activated charcoal were performed in our patients. In four patients with abnormal coagulation parameters, activated charcoal was continued for 24 hours.

Following oral administration, colchicine rapidly and extensively diffuses into tissue. Although approximately 50% of circulating colchicine is bound to plasma proteins and the plasma half-life is short, colchicine has been demonstrated in leukocytes 9 days after its administration (13,14). Hemodialysis or hemoperfusion are not particularly effective due to the large volume of distribution of colchicine (15).

For technical reasons, few reports have been published measuring the value of colchicine levels in blood, its components (white blood cell), or urine (14). We could not measure the levels of colchicine because of technical insufficiency.

In conclusion, the severity of colchicine poisoning tends to be related to the dosage of ingested drug and the time of admission to hospital. Although gastrointestinal system side effects are usually seen in patients with ingesting lower doses of colchicine, cardiovascular and hematological side effects can be seen with relatively higher doses. Although a specific treatment is not yet available in colchicine poisoning, symptomatic treatment should be started as soon as possible. Efforts to develop specific treatment for colchicine intoxication should be strengthened in order to reduce mortality in patients ingesting a high dose.

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