

Case Report

## Successful Treatment of a Pediatric Patient with High-dose Colchicine Intake and Intoxication Findings by Hemoperfusion

### Yüksek Doz Kolşisin Alımı İle İntoksikasyon Bulguları Gelişen Çocuk Hastanın Hemoperfüzyon İle Başarılı Tedavisi

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#### ABSTRACT

Colchicine is used in treating many rheumatological diseases and is widely prescribed in children. Its use specifically aims to prevent familial Mediterranean fever (FMF) attacks and amyloidosis prophylaxis. Colchicine's therapeutic range is extremely narrow. It may cause fatal effects when taken at toxic doses. Since the plasma volume of distribution is very high, it is necessary to rapidly intervene for elimination from the body in case of toxicity with colchicine. In this case report, a 3.5-year-old patient with severe high-dose colchicine intake developed intoxication findings. Then, this patient successfully underwent hemoperfusion and recovered without sequelae.

**Keywords:** Colchicine, intoxication, hemoperfusion

#### ÖZET

Kolşisin birçok romatolojik hastalığın tedavisinde kullanılmakta olup çocuklarda özellikle Ailevi Akdeniz Ateşi (AAA) ataklarının önlenmesi ve amiloidoz profilaksisinde yaygın kullanımı mevcuttur. Terapötik aralığı son derece dar olan kolşisin, toksik dozda alındığında ölümcül etkiler meydana getirebilmektedir. Plazma dağılım hacmi çok yüksek olduğundan kolşisin ile intoksikasyon söz konusu olduğunda vücuttan eliminasyonu için hızla müdahale etmek gerekmektedir. Bu olgu raporunda şiddetli yüksek doz kolşisin alımı olup, intoksikasyon bulguları gelişen, başarılı bir şekilde hemoperfüzyon işlemi uygulanan ve sekelsiz iyileşme sağlanan 3,5 yaşındaki olgu sunuldu.

**Keywords:** Kolşisin, intoksikasyon, hemoperfüzyon

#### INTRODUCTION

Colchicine is an alkaloid commonly used in the prevention and amyloidosis prophylaxis of familial Mediterranean fever (FMF) disease attacks in children. It is also beneficial in ameliorating acute gout attacks, FMF, Behcet's disease, and inflammatory bowel diseases in adults (1, 2). Colchicine is an alkaloid with anti-inflam-

matory activity. It plays an antimitotic role by disrupting microtubule formation in cells with the ability to divide and move, preventing forming mitotic spindles. Colchicine affects the motility of neutrophils by reducing their deformity and elasticity with tubulin degradation. Although colchicine has toxic effects on all body

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cells, it usually has an earlier and a greater impact on the gastrointestinal tract and bone marrow. Hence, the first symptoms of colchicine poisoning are abdominal pain and diarrhea. Colchicine is rapidly absorbed after it enters the gastrointestinal tract. After entering the body, it first undergoes a deacetylation reaction in the liver. Then, it transforms into its more toxic 2- and 3-trimethyl-colchicine. Colchicine and its metabolites are mainly excreted using bile and feces. Colchicine has high tissue affinity and a high volume of distribution in vivo. Renal excretion of colchicine in its original form accounts for approximately 30% of the toxic load. The mortality rate with oral administration of 0.5-0.8 mg/kg is approximately 10% (3, 4). Acute poisoning may rarely occur due to the therapeutic and toxic doses of colchicine being remarkably close to each other. These poisonings can sometimes pose a life-threatening risk. Thus, all cases with suspected intoxication should be monitored in the hospital, and intensive care conditions should be provided for these cases when necessary (5).

This paper presents a three-and-a-half-year-old pediatric patient who was hospitalized in the intensive care unit of our hospital with acute colchicine poisoning and underwent hemoperfusion rapidly and complete recovery. Hemoperfusion passes the blood through a cartridge containing carbon, activated charcoal, or resin. The highly protein-bound and fat-soluble drugs undergo adhesion in the coal or resin in the cartridge and, thus, are more easily removed by hemoperfusion (6). Given this case, hemoperfusion procedures with a high colchicine dose may be appropriate sometimes.

## CASE REPORT

Three- and half-year-old male patient, weighing 17 kg, diagnosed with FMF and using colchicine, was brought to the emergency department with vomiting accompanied by nausea, which started approximately 6-8 hours before admission, 10-15 times, and diarrhea, which was 4-5 times. In the first examination of the patient, who took 18 colchicine 0.5 mg tablets (0.69 mg/kg) approximately 16 hours before admission, the general condition of the patient was moderate, conscious, but prone to sleep. The Glasgow Coma Scale (GCS) score was 12, and other system examinations were in the normal range. The patient was taken to the pediatric intensive care unit because of the toxicity of colchicine, even at low doses. Moreover, an antidote for children is absent (3,5). The patient was intubated and connected to a mechanical ventilator due to the presence of severe toxic dose intake in the monitored patient, the development of metabolic acidosis, the tendency to

sleep, and the decrease in GCS to 9. The hemogram and biochemical parameters of the patient were in the normal range of the intensive care unit examinations. Blood gas: pH: 7.25, pCO<sub>2</sub>: 38 mmHg, HCO<sub>3</sub>: 17 mmol/L lactate: 6.6 mmol/L hemoperfusion procedure was started rapidly for four hours. During the hemoperfusion, the patient had massive diarrhea, followed by hypotension (70/45 mmHg). The patient was tachycardic, desaturated, and isotonic. In the blood gas taken from the patient whose vital parameters returned to normal, pH: 7.15 pCO<sub>2</sub>: 43 mmHg HCO<sub>3</sub>: 15.4 mmol/L lactate: 8.9 mmol/L. For the patient whose metabolic acidosis with increased anion gap on the first day of hospitalization gradually deepened and who had resistant hypotension requiring inotropic support. Noradrenaline started, bone marrow suppression was present, thrombocytopenia developed, liver function tests were increased, and three therapeutic plasma changes and four hemodialysis procedures were performed to reverse the picture of thrombocytopenia-associated multiple-organ failure (TAMOF) by colchicine after the hemoperfusion procedure (7). No pathology was present in the echocardiographic examinations performed at intervals during the patient's hospitalization. The patient, whose aspartate aminotransferase (AST), alanine aminotransferase (ALT), and lactate dehydrogenase (LDH) values decreased gradually in the following days, was discontinued by reducing inotropic and sedative drugs and extubated on the sixth day of hospitalization. The laboratory parameters of the patient during admission to the intensive care unit and externalization from the intensive care unit are in Table 1. On the tenth day of hospitalization, the patient was transferred to the pediatric clinic, whose general condition was normal and vital findings were stable. Consent from the patient's parents was obtained for this case study.

## DISCUSSION

Colchicine intoxication is a multiorgan toxicity. Its severity and mortality are directly proportional to the amount taken. In a study with forty-three patients, patients were in survival and death groups according to the prognosis, and clinical data were analyzed. Colchicine uptake doses were  $\leq 0.5$ , 0.5-0.8, and  $\geq 0.8$  mg/kg, and survival rates were 100%, 83.33 and 28.60%, respectively (8). In our patient, although our hospital did not determine colchicine levels, the following results support that the patient received the dose expressed by the family: metabolic acidosis with an elevated anion gap, significant increase in liver function tests, thrombocytopenia, and a 3-unit decrease in GCS. In this con-

text, our patient had a significant risk ratio in mortality with an intake rate of 0.69 mg/kg.

**Table 1.** Laboratory Values of the Patient with Colchicine Poisoning in the Pediatric Intensive Care Unit

	DAY 1	DAY 1 CONTROL	DAY 3	DAY 5	DAY 7	DAY 9
Hgb (g/L)	11.8	9.9	11.8	12.3	10.6	11.8
Plt (10 <sup>3</sup> /uL)	358	66	39	23	165	223
WBC (10 <sup>3</sup> /uL)	12	6.21	6.95	5.84	13.91	14.15
CRP (mg/L)	44	128	190	117	10	6.3
Urea (mg/dL)	0	22	6	16	29	28
Creatinine (mg/dl)	0.26	0.31	0.23	0.41	0.28	0.3
ALT (U/L)	29	2077	1054	828	385	267
AST (U/L)	192	HIGH	1804	774	77	46
LDH (U/L)	1491	4237	1532	880	477	430
aPTT (seconds)	42	55	33	39	28	29
INR	2.03	2.03	1.8	1.38	1.17	1.1

Hgb: hemoglobin, Plt: platelet, WBC, white-blood-cell, CRP: C-reactive protein, ALT: alanine aminotransferase, AST: aspartate aminotransferase, LDH: lactate dehydrogenase, aPTT: activated Partial Thromboplastin clotting Time, INR: International Normalized Ratio

Typical symptoms of acute colchicine poisoning can have three consecutive and overlapping phases. Phase I (within 24 hours of ingestion) reflects gastrointestinal mucosal damage characterized by abdominal pain, severe vomiting, diarrhea, and gastrointestinal bleeding. Phase II (usually 1-7 days after intake) has multiple organ dysfunction: metabolic acidosis, shock, myelosuppression, oliguric renal failure, liver dysfunction, and respiratory failure. Phase III (7-21 days after ingestion) has bone marrow hematopoietic recovery and resolution of organ system disorders (9). In our patient, Phase I, II, and gastrointestinal complaints were present at admission.

At the end of approximately 24 hours, impairments in liver function tests and hematological parameters occurred. The risk of toxicity in acute high-dose colchicine intake is higher in patients who routinely use colchicine, as in this patient (10). The kidneys and liver excrete colchicine and its metabolites from the body. The

elimination half-life of colchicine in humans is 9.3-30 hours. (9) Approximately 50% of colchicine is bound to plasma proteins. The volume of distribution is 2.2 l/kg, which corresponds to a larger volume than the total body fluid (6).

The first applications of sorbent hemoperfusion in treatment have been successfully applied in treating some acute drug intoxication. In specific cases, hemoadsorption is much more efficient than hemodialysis. This has been frequently achieved by coal adsorption or resins. Such devices typically contain between 100 and 300 g of activated charcoal or between 300 and 650 g of resin. Blood flow for effective drug removal is approximately 300 mL/min to 450 mL/min, and intermittent hemoperfusion is usually performed for 4 hours (11). In our patient, an activated charcoal hemoperfusion procedure was performed for four hours approximately 16 hours after intake, and then, sequelae-free survival was achieved with hemodialysis, plasmapheresis, and supportive treatments. There is a case report in the literature with lethal dose colchicine intake and survival after the hemoperfusion procedure (12).

As a result, toxicity due to using colchicine may develop even at low doses and require intensive care follow-up. The administration of hemoperfusion to acute selected cases in the fastest way can be life-saving. However, patients and their relatives should be informed in detail about colchicine and its side effects when it is a critical component of preventive health services. This drug is a component of treatment regarding its side effects.

**Patient Consent Form / Hasta Onam Formu**

The parents' of this patient consent was obtained for this study.

**Conflict of Interest / Çıkar Çatışması**

The authors declared no conflicts of interest with respect to authorship and/or publication of the article.

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