

Selected Topics: Toxicology



EVALUATION OF THE COLCHICINE POISONING CASES IN A PEDIATRIC INTENSIVE CARE UNIT: FIVE YEAR STUDY

Emine Polat, MD,* Nilden Tuygun, MD,† Halise Akca, MD,† and Can Demir Karacan, MD†

*Department of Pediatric Intensive Care, Dr. Sami Ulus Maternity and Childrens' Education and Research Hospital, Ankara, Turkey and †Department Pediatric Emergency Medicine, Dr. Sami Ulus Maternity and Childrens' Education and Research Hospital, Ankara, Turkey
Corresponding Address: Emine Polat, MD, Department of Pediatric Intensive Care, Dr. Sami Ulus Maternity and Childrens' Education and Research Hospital, Ankara 06110, Turkey

Abstract—Background: Colchicine poisoning is an uncommon but serious form of drug intoxication. It may produce life-threatening systemic effects. In toxic doses it produces nausea and vomiting and bone marrow suppression, often leading to sepsis, hypocalcemia, adult respiratory distress syndrome, and direct cardiotoxic effects. **Objective:** The aim of this study was to describe demographic features and the outcome of patients poisoned with colchicine. **Methods:** A retrospective study of the pediatric intensive care unit database was performed for patients ≤ 18 years of age who had colchicine poisoning between July 2008 and July 2013. **Results:** The total number of patients with drug poisoning in the study period was 144. Nine of 144 were related to colchicine poisoning. The median age was 4 years (range 20 months to 16 years) and the number of females was five. Six of the nine cases presented after ingesting <0.5 mg/kg, whereas two patients had consumed 0.5 to 0.8 mg/kg. One patient had received colchicine >0.8 mg/kg. Three patients died. **Conclusions:** Among drug intoxications, colchicines can lead to severe clinical conditions. All patients suspected of having colchicine intoxication should be managed in the pediatric intensive care unit regardless of the actual degree of poisoning. © 2016 Elsevier Inc. All rights reserved.

Keywords—child; colchicine; intensive care unit; mortality; poisoning; therapy

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INTRODUCTION

Colchicine is an alkaloid extracted from the autumn crocus (*Colchicum autumnale*) that is an old and well-known drug used for the treatment of gout, Behçet's disease, familial Mediterranean fever (FMF), sarcoidosis, and psoriasis. The anti-inflammatory effects of colchicine include prevention of neutrophil migration, activation, and degranulation. In addition, colchicine inhibits the deposition of uric acid crystals and is an inhibitor of mitosis (1–3). Colchicine poisoning is an uncommon but serious form of drug intoxication with a high mortality rate. It may produce life-threatening systemic effects at excessive doses. It may produce bone marrow suppression, often leading to sepsis, hypocalcemia, adult respiratory distress syndrome, and direct cardiotoxic effects (4–6). The aim of this study was to describe demographic features and the outcome of patients who were poisoned with colchicine and who were admitted to the pediatric intensive care unit (PICU) in a 5-year period.

MATERIALS AND METHODS

After approval from a local ethics committee, the medical records of children aged 1 month to 18 years who were hospitalized for drug poisoning at the PICU of a tertiary care research hospital between July 2008 and July 2013

were retrospectively reviewed. Among these, nine patients (four boys and five girls) with colchicine-related intoxications were evaluated. Demographic data regarding age, sex, weight, duration between drug intake and presentation to the hospital, clinical manifestations, dosage ingested, drug, duration of hospitalization at the PICU, laboratory findings, management and treatment modalities, and outcomes were recorded. Drug doses were recorded according to the declaration of the patient or family.

RESULTS

The total number of patients with drug poisoning in the study period was 144. Nine of 144 patients had colchicine poisoning. The median age was 4 years (range 20 months to 16 years), and the number of females was five. Six of the nine cases presented after ingesting a dose range of 0.11 to 0.60 mg/kg of colchicine. They all recovered uneventfully and were discharged on hospital day 7. On follow-up they showed no sequelae. Three patients who had consumed doses between 0.5 and 0.84 mg/kg died after developing disseminated intravascular coagulopathy (DIC), shock, and multiorgan failure. These three patients were treated with inotropic agents; two underwent plasma exchange and one had continuous renal replacement therapy (CRRT). They all had bone marrow involvement (one had hemophagocytic lymphohistiocytosis and two had leukocytosis). Two of them developed complete heart block and even underwent temporary transvenous pacemaker implantation; both remained completely unresponsive to cardiopulmonary resuscitation.

Demographic features, clinical and laboratory findings, treatment modalities, and outcome of the patients are summarized in Table 1.

DISCUSSION

Colchicine is a highly active alkaloid that has been commonly used for the treatment of FMF and other rheumatologic diseases (1–6). In Turkey, colchicine is available in blister packs of 60 coated tablets. It has a narrow therapeutic index, with a 9- to 16-hour half-life (3–5). There is no definite limit in the toxic effects of the drug. A correlation was reported between the clinical process and the ingested dose. It has previously been reported that minor toxicity with only gastrointestinal tract symptoms appears with an oral intake of <0.5 mg/kg, from 0.5 to 0.8 mg/kg results major toxicity (e.g., myelosuppression and multiorgan failure), and an oral intake of >0.8 mg/kg can be lethal after developing cardiogenic shock (7). Our three patients died because of shock, hematologic complications, and

Table 1. Demographic Features, Clinical and Laboratory Findings, Treatment Modalities, and Outcome of the Patients

Case No.	Age, Years	Sex	Period Hour*	Dose, mg/kg	Reason	Presenting Symptoms	Hb, g/dL	WBC, K/ μ L	PLT, K/ μ L	AST, U/L	ALT, U/L	CPK, U/L	LDH, U/L	PT, sec	aPTT, sec	INR	Therapy	Outcome
1	10	F	24	0.12	Accidental	Nausea and vomiting	13.3	8.1	409	63	43	99	312	15.9	94	1.47	GL and AC	CR
2	4	M	1	0.11	Accidental	Absent	14.1	7.9	349	31	25	190	16	12.3	28	1.12	GL and AC	CR
3	2	M	5	0.3	Accidental	Absent	12.1	17.4	410	35	15	161	216	10.8	33.7	0.98	GL and AC	CR
4	4	M	2	0.6	Accidental	Absent	12.2	14.1	304	33	21	128	315	11.6	22.6	1.10	GL and AC	CR
5	4.5	F	2	0.6	Accidental	Vomiting	11.9	10.5	334	27	15	113	184	11.9	25.3	0.98	GL and AC	CR
6	1.5	F	1	0.16	Accidental	Absent	12.2	13.2	352	46	19	647	293	14.5	27	1.20	GL and AC	CR
7	8.5	F	96	0.5	Suicidal	Nausea, vomiting, and diarrhea	13.6	1.9	57	613	56	5536	7565	26.1	43.8	2.31	EP, PE, and IA	Death
8	8	M	24	0.52	Accidental	Nausea, vomiting, and diarrhea	16.9	87.7	449	500	48	926	6135	33.9	86.5	3.27	EP, AA, and IA	Death
9	16	F	14	0.84	Suicidal	Nausea, vomiting, and diarrhea	11.0	66.3	310	175	41	691	2393	25.0	58.8	1.88	PE and IA	Death

AA = antidysrhythmic agents; AC = activated charcoal (multidose); ALT = alanine aminotransferase; aPTT = activated partial thromboplastin time; AST = aspartate aminotransferase; CPK = creatinine phosphokinase; CR = complete recovery; EP = external pacemaker; GL = gastric lavage; Hb = hemoglobin; IA = inotropic agents; INR = international normalized ratio; LDH = lactate dehydrogenase; PE = plasma exchange; PLT = platelet; PT = prothrombin time; WBC = white blood cell. Laboratory values are those provided at the time of admission. * Time between drug ingestion and admission to the hospital.

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