Case Report
Eurasian Journal of Toxicology

Colchicine Intoxication In A Patient With Unilateral Renal Agenesis

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Abstract

Colchicine is an alkaloid used in the treatment of acute gout attacks, Familial Mediterranean Fever, Behçet's Disease and inflammatory bowel diseases. Depending on the dose taken, the clinic occurs in various ways. Gastrointestinal manifestations are common in colchicine intoxication, but multi-organ failure is a more rare and more serious problem. As the blood level of colchicine is determined by the kidney and the liver, toxicity may progress more rapidly in dysfunction of these organs. In this case report, we aimed to remind that colchicine intoxications may be more mortal in patients with renal insufficiency.

Keywords: renal failure, renal agenesis, colchicine intoxication

Introduction

Colchicine is an lipid-soluble alkaloid obtained from the plant 'Colchicum autumnale'[1]. It is rapidly absorbed from the gastrointestinal tract between thirty minutes and two hours after oral administration and reaches peak concentration. After absorption, approximately 50% is transported by binding to plasma proteins, so it is not possible to eliminate it by hemofiltration[2].

Colchicine is used in the treatment of acute gout attacks, Familial Mediterranean Fever (FMF), Behçet's Disease and inflammatory bowel diseases. The therapeutic dose and the toxic dose of colchicine are very close to each other and the signs of toxicity occur in acute, subacute and chronic periods[3].

In this article, we present a patient with unilateral renal agenesis who showed all periods of toxicity after high dose colchicine ingestion for suicidal purpose and showed rapid progression.

Case Report

A 21-year-old, 45 kg female patient who has been using colchicine for FMF for 5 years has took 40 colchicine dragees (Colchicine Dispert 0.5 mg) for suicide purpose.

Considering that the patient would need intensive care, she was referred to the Süleyman Demirel Medical Faculty Emergency Department four hours after taking the drug. The patient was taken to the Anesthesiology and Reanimation intensive care unit for follow-up and treatment.

From her history we learned that she had FMF, had been using colchicine for five years, and that her single kidney was agenetic. On physical examination, GKS was 15, pulse was 110 bpm and BP was 100/90 mmHg. Intestinal sounds were hyperactive, other than that physical examination findings were normal. Laboratory findings were WBC: 5800 mm3, Hb: 12.9 g/dL, Plt: 140000 mm3, BUN: 47.2 mg/dL, Kre: 3.23 mg/dL. ALT, AST and serum electrolyte values were normal. The patient was administered 1 mg/kg activated charcoal four times a day with a nasogastric tube.

6 hours after hospitalization; the patient's urine output decreased so hemodialysis was performed. On control blood samples after hemodialysis; Hb: 9.3 g/dL WBC: 2000 mm3, Plt: 76000 mm3, AST: 163 U/L, ALT: 37 U/L, creatinine: 1.98 mg / dL, BUN: 37.4 mg / dL and serum electrolytes were normal. Blood gas was pH: 7.4, pCO2: 30.6 mmHg, pO2: 78.9 mmHg, HCO3: 1 9.5. In her follow-up, hemoglobin dropped to 7 g/dL and erythrocyte suspension replacement treatment was performed. Whether there was a bleeding source was investigated and no source was detected.

24 hours after hospitalization; her condition deteriorated. Her consciousness disappeared and the pupils became anisocoric. GKS was calculated as 8. The patient was intubated. Conjunctival hemorrhage occurred. Brain CT was filmed. No pathology was detected. Since there was a hematoma in the femoral region where the dialysis catheter was present, USG was performed. It was observed that there

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Received: 14.07.2020 • **Accepted:** 26.09.2020
Cite this article as: Yagli MA, Ustun D. Colchicine intoxication in a patient with unilateral renal agenesis. Eurasian J Tox. 2021;3(2):36-38.

DOI: 10.51262/ejtox.769021

were about 1.5 units of bleeding. In follow-up, hemoglobin value dropped to 4.8 g/dL despite erythrocyte suspension replacement. No area compatible with bleeding was found in the whole body CT. Urine output stopped completely. ALT and AST rose. Laboratory results were evaluated as compatible with pancytopenia; WBC: 2100 mm3, Hb: 4.8 g/dL, Plt: 57000 mm3. Necessary transfusions were made.

36 hours after hospitalization; distention developed in the abdomen. On physical examination, she had defence in the abdomen and there was no intestinal sounds by listening. Air-fluid levels were observed on the lateral decubitus radiograph. It was diagnosed as ileus related to colchicine. Hemodynamics remained stable. Urine output stopped. Hemofiltration was performed to the patient whose laboratory values were BUN: 34 mg/dL, Creatinine: 2.46 mg/dL, blood gas pH: 7.31, pCO2: 37.8 mmHg, pO2: 36.6 mmHg, HCO3: 18.7.

48 hours after hospitalization; AST and ALT increased to 2803 U/L and 1534 U/L respectively. D-dimer was 1468 mg/dL and Fibrinogen was 220 mg/dL. Disseminated intravascular coagulation (DIC) was considered. Inotropic support therapy was started for the patient who developed multiple organ failure. Thrombopheresis was applied. The patient's fever was also high so cultures was sent considering neutropenic fever. Empiric antibiotic treatment was started. Except for ionized calcium, electrolyte follow-ups were observed at normal levels.

On the third day; the patient who developed septicemia, had resistant deep metabolic acidosis and did not respond to inotropics died. Staphylococcus Aureus growth was reported in the blood cultures after the patient died.

Discussion

Colchicine intoxication shows progression by dose. When colchicine is taken at doses below 0.5 mg/kg minor toxicity develops and there is 100% improvement, when taken at doses between 0.5-0.8 mg/kg major toxicity develops and %10 mortality is observed, and when taken at doses above 0.8 mg/kg it has been reported that patients are lost as a result of cardiogenic shock within 72 hours. However, the risk of toxicity in acute intake of these doses is higher than the risk of toxicity in patients using it chronically[4-5]. Although the degree of toxicity is evaluated according to the dose range, there are cases that reported death at low doses and improvement at high doses[6]. In our case, although the patient had been using for colchicine five years with the diagnosis of FMF and who ingested colchicine at a dose of 0.5 mg/kg for suicidal purpose, so no significant toxicity was expected, she died.

Colchicine is metabolized in the liver within 48 hours of being absorbed from the gastrointestinal tract. Their metabolites are excreted in urine and faeces. It enters enterohepatic recirculation before its excretion. The application of activated charcoal in the first 48 hours and in repeated doses is important in this respect[7]. We applied activated charcoal to the patient at a dose of 1 mg/kg, 4 times a day.

The main effect of colchicine is observed in tissues where mitosis is rapid. One of the places where these tissues are found most is the gastrointestinal tract. As a result of this, ileus can occur in colchicine intoxications. In the acute period of intoxication, nausea vomiting becomes abdominal pain. In the following stages, erosive hemorrhagic gastritis, dehydration, electrolyte disorders and paralytic ileus may develop[8-9]. In our case, severe abdominal pain, abdominal distention and ileus was observed on the second day of hospitalization.

One of the tissues where the cell cycle is fast is bone marrow. It causes pancytopenia by causing hypoplasia in the bone marrow, and as a result septicemia can occur. These septicemias are quite mortal[8]. In this case, neutropenic fever was caused by leukopenia. There was no growth from the first set of cultures. Staphylococcus Aureus growth occurred in blood cultures taken on the third day.

Colchicine toxicity is divided into three periods. First period; begins hours after taking the drug. It is characterized by symptoms of the gastrointestinal tract, such as nausea, vomiting, abdominal pain and diarrhea. There is peripheral leukocytosis. The second period is seen 24 to 72 hours after drug intake. Multiple organ failure, leukopenia, thrombocytopenia, anemia, liver failure, electrolyte imbalance is observed. The third period is seen after the 10th day following toxic intake. In this period, patients may develop septicemia and alopecia may be observed. (10) Similar periods were observed in our case. However, the progression was much faster. The patient, who spent the acute period with gastrointestinal system symptoms, had pancytopenia within hours. Ileus developed afterwards. The patient entered multiple organ failure within 2 days. Then, blood pressure dropped and inotropic support was initiated. Septicemia that is normally expected after the tenth day occurred on the third day. The patient who developed cardiac collapse did not respond to inotropics and died.

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