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Case Report

Colchicine Poisoning: Case Report and Literature Review

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Abstract

Colchicine is an active alkaloid that is commonly used for treatment of multiple diseases including gout, primary biliary cirrhosis and familial Mediterranean fever. Less commonly, it has been implicated in cases of fatal overdose owning to its narrow therapeutic index. Clinical presentation of colchicine poisoning follows a well described but swift course with gastrointestinal symptoms being the earliest manifestation. Death usually occurs either directly due to multiorgan failure or indirectly due to secondary sepsis. We report an extreme case of colchicine ingestion by a 22 years old female who intentionally ingested 45 to 50mg of colchicine. Six hours later she presented in local hospital where gastric lavage was performed. Four days later, on continual deterioration of her condition, she presented with poor prognosis in the tertiary care emergency. She exhibited symptoms of coagulopathy, respiratory distress, multiple organ failure and eventually suffered fatal cardiopulmonary collapse approximately 14 hours after admission. Use of Colchicine specific Fab fragments have been shown to reverse symptoms of Colchicine poisoning in experimental settings however they are not available for general use. Currently treatment options are limited to specific supportive measures.

Keywords: Colchicines; Poisoning; Multiple organ failure; Cardiopulmonary resuscitation; Respiratory distress syndrome

Introduction

Colchicine is a neutral lipophilic alkaloid which has weak anti-inflammatory properties. As such it has been designated as a prophylactic agent for gout and a treatment of familial Mediterranean fever (FMF) [1]. Cases of colchicine overdose are rarely seen in the clinic. Its narrow therapeutic index makes it an erratic drug to work with, with no clear distinction between lethal and therapeutic doses. Doses exceeding 0.5 mg/kg, in acute cases, have been associated with a high death rate [2]. Though the lowest lethal doses vary between 7-26 mg [3].

Colchicine overdose can cause multi-organ pathological processes, but these have not been comprehensively summarized in the literature to date There are only few case reports explaining details of accidental and intentional overdoses and their prognosis [4-6]. In this case, a 22 years old female presented with high dose colchicine poisoning. Colchicine ingestion and the subsequent course of her condition during her 14 hour hospital stay has been discussed.

Case Report

A 22 year old female presented to a local hospital with history of ingestion of 95 to 100 tablets of 0.5 mg colchicine drug, six hours prior with intent to end her life. She was not on any regular medications and past medical history was unremarkable. She presented with symptoms of abdominal pain, nausea and vomiting. Gastric lavage was performed with activated charcoal but her condition continued to deteriorate. She was then transferred to another local hospital for further management. She had several episodes of vomiting, diarrhea and hematemesis and also developed bleeding from multiple orifices, including vagina, urethra and rectum.

After four days, she presented to our tertiary care hospital for further treatment with complaints of diffuse body pains, shortness of breath, hematemesis and hematuria. Her vitals at presentation were: blood pressure of 90/60 mm Hg, respiratory rate of 22/min, heart rate of 126/min, body temperature of 37°C and oxygen saturations of 88% without oxygen. On examination she was delirious, pale and dehydrated. Auscultation of the chest revealed decreased breath sounds throughout both lung fields, with inspiratory crackles. Other findings were: bilateral conjunctival hemorrhage, and parenteral bleeding.

Emergency blood tests reports shown in table 1, 2, 3 and 4; revealed low platelet count deranged INR low potassium bicarbonate, calcium high blood urea nitrogen creatinine and uric acid. Moreover, urine R/E report revealed presence of large amount of glucose, protein, blood, cells (red blood cells, white blood cells, epithelial cells) and casts.

Hematology, INR and CPK	***Reference values***	***At presentation***
RBC trillion cells/mcL	3.9-5.0	4.5
Hemoglobin g/dL	12.0-15.5	11.9
Platelet count /mcL	150,000-450,000	83,000
WBC /mcL	3,500-10,500	5,500
INR	0.9-1.2	1.7
Creatine phosphokinase U/L	22-198	15631

Table 1: shows emergency test reports of hematology, INR and CPK.

Electrolytes	***Reference values***	***At presentation***
Potassium mmol/L	3.5-5	3.3
Sodium mmmol/L	135-145	136
Chloride mmol/L	95-105	103
Bicarbonate mmol/L	22-28	17
Magnesium mmol/L	1.5-2	1.8
Calcium mg/dL	8.5-10.2	5.9
Urea mmol/L	1.2-3	123
Blood urea nitrogen mg/dL	8-21	57
Creatinine mg/dL	0.8-1.3	2.7
Uric acid mg/dL	3.5-7.2	11

Table 2: shows emergency test reports of electrolytes.

Liver	*Reference values*	*At presentation*
Albumin g/dL	3.5-5.5	2.8
Aspartate aminotransferase (AST) IU/L	5-30	576
Alanine aminotransferase (ALT) IU/L	5-30	66
Alkaline phosphatase IU/L	30-120	451
Direct bilirubin mg/dL	0.1-0.4	0.3
Total bilirubin mg/dL	0.1-1.1	0.48

Table 3: shows emergency test reports of liver function.

Urine R/E	*Reference values*	*At presentation*
pH	4.5-8	5.5
Glucose	-	+++
Protein	-	++
Red blood cell /HPF	≤2	Numerous
Cast	None	Present

Table 4: shows emergency test reports of urine.

She presented with symptoms of respiratory insufficiency, hypotension, acute liver failure, acute renal failure, and coagulopathy. Considering her acute renal failure and unstable circulation, she was treated with continuous renal replacement therapy, frozen plasma, and broad spectrum intravenous antibiotics. Despite continuous supportive treatment the patient's respiratory function continued to deteriorate for which she required end tracheal intubation. After a few hours she suffered 2 episodes of asystole. The first was successfully reverted after minutes of Cardiopulmonary Resuscitation (CPR) but the second proved fatal. She was declared dead after 30 minutes of CPR, 14 hours after initial presentation in Emergency Department.

Discussion

Colchicine works by arresting mitosis of cells in metaphase. It achieves this by binding to intracellular protein tubulin causing disruption of the micro tubular network. This disturbs cellular functions like exocytosis and endocytosis, cellular proliferation, assembly of Golgi apparatus and maintenance of cell shape. The cells affected most are those with the highest rates of proliferation that is hair follicles, gastrointestinal tract and bone marrow [7].

Following oral ingestion colchicine is readily absorbed from the gastrointestinal tract. However, subsequently it undergoes extensive first pass effect followed by entry of the metabolites into the enterohepatic recirculation. Due to colchicine's protracted course in this recirculation multi dose activated charcoal may be considered even in late presentations [8]. After absorption colchicine is widely distributed to all tissues and binds strongly to proteins, hence haemodialysis and haemoperfusion are not effective [9]. In addition to excretion via bile and feces, 10-20% of colchicine experiences renal clearance. Thus hepatic and renal disturbances can greatly reduce the therapeutic range [10].

The clinical course of colchicine poisoning usually follows a sequence of three phases. The first gastrointestinal phase occurring 0-24 hours after ingestion is signified by the patient developing nausea, vomiting, diarrhea, abdominal pain, anorexia, electrolyte imbalance, hypovolemia. This is representative of the mucosal damage of the gastrointestinal tract. The second multiorgan phase, developing 1-7 days after ingestion, is characterized by respiratory distress, cardiac arrhythmias and arrest, encephalopathy, convul-

sions, renal failure, hepatic failure, metabolic derangements (metabolic acidosis, hypokalemia, hyponatremia, hypocalcemia, hypophosphatemia), myopathy, neuropathy, rhabdomylysis and secondary sepsis. If not properly managed death can occur, otherwise the patient moves to the third recovery stage evidenced by rebound leukocytosis and resolving of multiorgan failure with no longterm complications. Death is mostly noted to be due to cardiac arrhythmias, circulatory collapse or sepsis. The stages can be successive or more commonly overlapping [3, 4].

At time of presentation our patient was well into the second stage of multiple organ failure as evidenced by her deranged blood chemistry that includesraised serum creatinine (ahallmark of the second stage) hypokalemia, hypocalemia, metabolic acidosis,raised urea and uric acid levels [11]. Such symptoms of prerenal azotemia coupled with gastroenteritis, hypotension and lactic acidosis are suggestive of colchicine poisoning [12]. In our patient gastric lavage was redundant as she presented in our hospital 4 days after ingestion. Excessive parentral bleeding was observed due to thrombocytopenia caused by bone marrow suppression by colchicine [2].

The antimitotic activity of colchicine on the respiratory system caused respiratory distress in our patient for which she needed intubation. There she suffered two incidences of asystole and she also had very high serum creatinine phosphokinase levels which indicated cardiac damage. Colchicine is postulated to have a direct cardiotoxic effect by interfering with conduction and contraction of cardiac cells. Cardiac failure is associated with poor prognosis [13-14]. Our patient also showed evidence of renal and hepatic dysfunction and damage as seen by her elevated serum liver enzyme and creatinine levels, hyperuricemia and presence of abundant glucose, protein and cellular elements in urine. It is hypothesized that colchicine can cause this damage directly through its antimitotic effect as well as indirectly by rhabdomylysis [15]. Renal and hepatic damage also reduced clearance of colchicine further increasing its toxicity in the patient's body.

At the present the mainstay of management of Colchicine poisoning is mostly supportive. A multifaceted approach of early diagnosis, prompt gastric lavage and use of activated charcoal, aggressive specific supportive therapy and long term follow up of patient have been shown to bring about complete recovery even in cases of massive overdose [5]. Our patient presented too late for such measures to be effective. Use of Granulocyte colony-stimulating factor (to counter bone marrow suppression) and N-acetylcysteine have shown to have favorable outcomes [5, 16]. The only definitive treatment is the use of Colchicine specific Fab fragment antibodies which bind to the drug tightly and prevent its action on the patient's cells [9]. However its limited availability for non-experimental use hinders its effective utilization in the health care system.

Our case exhibited the typical features of severe colchicine poisoning, with the ingested dosage of approximate 50 mg. Supportive measures taken aided in prolonging life of patient. However timely diagnosis, quick presentation to hospital for gastric lavage, a more holistic multifaceted approach in early period and prompt referral to tertiary care hospital might have altered the outcome.

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