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ORIGINAL RESEARCH

# Clinical Manifestations and Outcomes of Colchicine Poisoning Cases; a Cross Sectional Study

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**Abstract:** **Introduction:** Colchicine is a medication with narrow therapeutic index, leading to both accidental and suicidal poisonings incidents. This study aimed to investigate the clinical and laboratory manifestations, as well as outcomes of colchicine poisoning patients referred to emergency department. **Methods:** In this retrospective cross sectional study, demographics, clinical features, laboratory parameters, and outcomes of colchicine poisoned patients who were admitted to an academic referral center, Tehran, Iran, during 7 years were extracted from the patients' profiles and analyzed. **Results:** 21 patients with the mean age of 25.48 ± 12.65 years were studied (61.9% female; 85.7% suicidal). The mean ingested colchicine dose was 30.25 ± 21.09 mg. The most common symptoms were nausea and vomiting observed in 19 (90.5%) cases, followed by abdominal pain in 10 (47.6%) and diarrhea in 9 (42.8%) cases. 3 (14.3%) had died, the cause being disseminated intravascular coagulation (DIC) in two cases and severe metabolic acidosis in one. Prevalence of abdominal tenderness (p = 0.001) and abdominal pain (p = 0.049) was significantly different between survived and non-survived patients. There were significant correlations between systolic blood pressure (p = 0.010), diastolic blood pressure (p = 0.002), serum glucose (p = 0.031), calcium (p = 0.017), white blood cell (WBC) count (p = 0.043), aspartate aminotransferase (AST) (p = 0.001), alkaline phosphatase (ALP) (p = 0.012), prothrombin time (PT) (p = 0.006), partial thromboplastin time (PTT) (p = 0.014), $PaCO_2$ (p = 0.011), DIC (p < 0.001), and need for mechanical ventilation (p = 0.024) with survival. **Conclusion:** Based on the findings of the present study, the mortality rate of colchicine poisoning was 14.3% and there was significant correlation between lower blood pressure, lower serum glucose and calcium levels, lower $PaCO_2$, higher WBC count, higher AST and ALP levels, higher PT and PTT, need for mechanical ventilation, presence of DIC, and also abdominal pain and tenderness with survival.

**Keywords:** Colchicine; symptom assessment; toxicity; drug overdose; poisoning

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## 1. Introduction

Colchicine is a medication extracted from plants including Colchicum autumnale and Gloriosa superba. It was first approved by the Food and Drug Administration (FDA) for the treatment of familial Mediterranean fever (FMF), gout, amyloidosis, Behcet's syndrome, pericarditis, arthritis, pulmonary fibrosis, vasculitis, biliary cirrhosis, pseudogout, certain spondyloarthropathies, calcinosis, and scleroderma (1, 2). Colchicine blocks cell mitosis in the metaphase, interferes with intracellular transport pathways by preventing polymerization of tubulin into microtubules, and is a competitive antagonist of gamma-aminobutyric acid (GABA) (2).

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The maximum recommended daily dose of this medication is 1.8 mg per day (3), while the overall cumulative dose in four days should not exceed 6 mg in adults and 3 mg in the elderly (4). Colchicine is rapidly absorbed and dispersed, with serum amounts peaking at 0.5-2.0 hours following ingestion. Several studies point out the fact that the therapeutic index of colchicine is narrow, and therefore, it is difficult to discriminate between nontoxic, toxic, and lethal doses. Early identification of colchicine poisoning is crucial because sustained exposure may result in multi-organ failure and death (5). This study aimed to investigate the clinical and laboratory manifestations as well as outcomes of patients with colchicine poisoning referred to the emergency department.

## 2. Methods

### 2.1. Study design and setting

In a retrospective study, all patients with colchicine poisoning who had been admitted to Loghman-Hakim Hospital in Tehran, Iran, during 7 years (March 22, 2007, to March 21, 2014), were enrolled. The study protocol conforms to the Ethical guidelines of the 1975 Declaration of Helsinki as reflected in a prior approval by the institution's human research committee. Our local ethics committee at Shahid Beheshti University of Medical Sciences approved the study. Written informed consent was obtained from the patients for their anonymized information to be published in this article.

### 2.2. Participants

All hospitalized patients in toxicology ward or intensive care unit (ICU) with colchicine poisoning, regardless of their age or sex, were included. We excluded all patients with co-ingestion.

### 2.3. Data gathering

A self-made questionnaire containing information on the patients' demographic characteristics, the time elapsed between ingestion and hospital admission, clinical presentation on arrival, vital signs, laboratory data, duration of hospitalization, given treatment, and the final outcome was filled by a trained physician for every single patient. Diagnosis of acute colchicine poisoning was based on the history given by the patients or their relatives, and laboratory findings.

### 2.4. Statistical Analysis

Data were analyzed using the Social Package for Statistical Analysis (SPSS) software version 20. The findings were presented as mean ± standard deviation for continuous variables and frequency (%) for categorical variables. Chi-square and Fisher's exact tests were used to analyze categorical variables. Statistical comparison was made using Mann–Whitney U-test for non-parametric variables and independent t-test for parametric variables. Multivariate analysis was performed on demographics, vital signs on arrival, and laboratory panels to assess their correlation with patients' survival. A p-value of 0.05 or less was considered to be statistically significant (Two-tailed).

## 3. Results

### 3.1. Baseline characteristics of studied case

21 patients with the mean age of 25.48 ± 12.65 (range; 7 to 68) years were admitted with colchicine poisoning during the study period (61.9% female). 11 (52.4%) patients had underlying diseases, including Familial Mediterranean Fever (FMF), hypothyroidism, gout, psychotic disorder, glucose-6-phosphate dehydrogenase (G6PD) deficiency, rheumatoid arthritis, and Behcet's disease. 18 (85.7%) had ingested colchicine to attempt suicide, and the other three (14.3%) had consumed it inadvertently. The mean ingested colchicine dose was 30.25 ± 21.09 mg. The most common symptoms were nausea and vomiting, observed in 19 (90.5%) cases, followed by abdominal pain in 10 (47.6%) and diarrhea in 9 (42.8%) cases.

### 3.2. Outcomes

The mean duration of of hospital stay was 3.64 ± 3.84 (Range: 1 to 14) days. 9 (42.8%) cases were in need of intensive care unit (ICU) admission (Mean ICU stay was 2.78 ± 1.98 days). 3 (14.3%) had died, and 18 (85.7%) had been discharged from the hospital without any complications. The three non-survivors had ingested 20, 38, and 40 mg of colchicine. Cause of death was disseminated intravascular coagulation (DIC) in two patients and severe metabolic acidosis in one. Table 1 and figure 1 compare the baseline characteristics, clinical findings, and laboratory findings of patients between survived and non-survived groups. Nausea and vomiting were present in all three patients who died. Prevalence of abdominal tenderness ($p = 0.001$) and abdominal pain ($p = 0.049$) was significantly different between survived and non-survived cases. Sinus tachycardia was present in four survivors and one non-survivor ($p > 0.05$).

There were significant correlations between systolic blood pressures ($p = 0.010$), diastolic blood pressures ($p = 0.002$), serum glucose ($p = 0.031$), calcium ($p = 0.017$), white blood cell (WBC) count ($p = 0.043$), aspartate aminotransferase (AST) ($p = 0.001$), alkaline phosphatase (ALP) ($p = 0.012$), prothrombin time (PT) ($p = 0.006$), partial thromboplastin time (PTT) ($p = 0.014$), $PaCO_2$ ($p = 0.011$), DIC ($p < 0.001$), and need for mechanical ventilation ($p = 0.024$) with survival.

**Table 1:** Comparing the baseline characteristics, vital signs and laboratory findings of survivors and non-survivors

| Variable | Survived (n = 18) | Died (n = 3) | P value |
|---|---|---|---|
| **Age (year)** | | | |
| Mean ± SD | 26.11 ±12.75 | 21.67±13.87 | 0.690 |
| **Sex** | | | |
| Male | 7 (38.9) | 1 (33.3) | 0.858 |
| Female | 11 (61.1) | 2 (66.7) | |
| **Ingestion to hospital time (hours)** | | | |
| Mean ± SD | 13.52 ± 17.09 | 8.50 ± 3.50 | 0.3 |
| **Ingested colchicine dose (mg)** | | | |
| Mean ± SD | 29.82 ± 22.63 | 32.67±11.01 | 0.473 |
| **Hospitalization time (day)** | | | |
| ICU | 0.9 ± 1.8 | 4 ± 1.7 | 0.008 |
| Toxicology ward | 3.3 ± 2.1 | 0 | 0.006 |
| Total hospital stay | 4±3.4 | 4±1.7 | 0.44 |
| **Blood pressure (mmHg)** | | | |
| SBP | 116.94 ±13.41 | 93.33 ±7.63 | 0.010 |
| DBP | 76.67 ±10.43 | 46.67 ±27.53 | 0.002 |
| **Laboratory findings** | | | |
| Serum Glucose (mg/dl) | 123.83 ± 71.26 | 69.67 ± 13.42 | 0.031 |
| WBC ($\times 10^9$/L) | 9.07 ± 3.94 | 24.67 ± 6.09 | 0.043 |
| Calcium (mg/dL) | 8.97 ± 0.83 | 7.53 ± 0.64 | 0.017 |
| AST (U/L) | 71.04 ± 82.94 | 357 ± 231.61 | 0.001 |
| ALP (U/L) | 297.41 ± 233.01 | 1085.33 ± 650.42 | 0.012 |
| PT (seconds) | 14.47 ± 2.34 | 29.00 ± 4.24 | 0.006 |
| PTT Time (seconds) | 28.92 ± 3.47 | 39.00 ± 6.55 | 0.014 |
| **Need for mechanical ventilation** | | | |
| Number (%) | 1 (5.5) | 3 (100) | 0.024 |
| **DIC** | | | |
| Number (%) | 0 (0) | 2 (66.6) | < 0.001 |

SD: standard deviation; ICU: intensive care unit; SBP: systolic blood pressure; DBP: diastolic blood pressure; AST: Aspartate Aminotransferase; PTT: Partial Prothrombin Time; PT: Prothrombin time; ALP: Alkaline Phosphatase; WBC: White Blood Count; DIC: disseminated intravascular coagulation.

**Table 2:** Comparing the clinical manifestations of survivors and non-survivors

| Variable | Survived (n = 18) | Died (n = 3) | P value |
|---|---|---|---|
| Nausea/Vomiting | 16 (88.89) | 3 (100) | 0.729 |
| Diarrhea | 8 (44.44) | 1 (33.33) | 0.447 |
| Abdominal pain | 2 (11.11) | 3 (100) | 0.049 |
| Abdominal tenderness | 7 (38.89) | 3 (100) | 0.001 |
| Hyperactive bowel sound | 1 (5.56) | 0 (0.00) | 0.8 |
| Headache | 1 (5.56) | 0 (0.00) | 0.857 |

Data are presented as number (%).

## 4. Discussion

Based on the findings of present study, the mortality rate of colchicine poisoning was 14.3% and there was significant correlation between lower blood pressure, lower serum glucose and calcium levels, lower $PaCO_2$, higher WBC count, higher AST and ALP levels, higher PT and PTT, need for mechanical ventilation, presence of DIC, and abdominal pain and tenderness with survival.

Most of our patients were young females. However, in previous studies, male patients were more commonly involved (6). The mortality rate was 14.3%, which is relatively low in comparison to lethal poisonings. Ozdemir and colleagues had studied childhood poisoning in Turkey and had stated that colchicine was the second leading cause of deadly poisonings after carbon monoxide when narcotics were excluded (7).

Our lowest lethal dose was 20 mg in an accidental intake in a 10-year-old boy with G6PD deficiency. Other studies reported death due to ingestion of colchicine doses higher than 0.5 mg/kg and especially more than 0.8 mg/kg (8). Although we found reports of complete recovery following consump-

tion of doses higher than 1 mg/kg (9), there were fatalities after the ingestion of doses as low as 0.5 mg/kg. Starting treatment later than two hours after the ingestion of colchicine can therefore, significantly impair the course of therapy (10). In contrast to previous studies, in the present study surviving cases had taken longer to reach the hospital compared to non-survivors. The reason could be that some patients were referred to Loghman Hospital after their treatment had initiated in other hospitals. Yet, the consumed amount of colchicine was significantly lower in survivors. We observed early-onset leukocytosis within 24-72 hours in non-survivors. According to Erden et al., early onset of leukocytosis in the initial stages of colchicine poisoning is a useful factor to predict poor prognosis (10).

In our study, non-survivors had higher values of liver enzymes, PT, PTT, WBC, and ALP and decreased calcium, blood sugar, and $PaCO_2$ levels. Metabolic acidosis was also more prevalent in non-survivors compared to survivors, however the difference was not significant. All of the mentioned findings are consistent with the results of previous researches. Appropriate and timely treatment can prevent death (11). In our study, injection of packed cells and fresh frozen plasma were needed in two patients with bone marrow suppression and DIC who eventually died. However, it should be mentioned that we performed transfusion in another patient who ultimately survived. Intravenous bicarbonate was indicated in two patients to correct metabolic acidosis, one of whom recovered, and the other died after going through progressive metabolic acidosis and emergent hemodialysis. The need for intubation was another poor prognostic factor in our cases.

Accidental colchicine poisoning may occur quite often. This poisoning is accompanied with a high mortality rate if it remains undiagnosed, and therefore, it should be suspected when clinical signs and symptoms imply the ingestion of an anti-mitotic medication. We observed that nausea and vomiting, abdominal pain, and abdominal tenderness, and DIC were associated with poor prognosis. Moreover, we revealed that systolic and diastolic blood pressures, serum glucose, calcium, and $PaCO_2$ were significantly lower in non-survivors. Besides, AST, ALP, PT, and PTT measures were considerably higher in dead patients. Intubation and mechanical ventilation significantly correlated with poor prognosis. Supportive treatments are recommended to be initiated as soon as possible when indicated.

## 5. Limitation

Since the study was retrospective, we could only review patients' records, which could be considered as a limitation. Also, it was not possible for us to confirm colchicine toxicity by analyzing its serum level.

## 6. Conclusion

Based on the findings of present study, the mortality rate of colchicine poisoning was 14.3% and there was significant correlation between lower blood pressure, lower serum glucose and calcium levels, lower $PaCO_2$, higher WBC count, higher AST and ALP levels, higher PT and PTT, need for mechanical ventilation, presence of DIC, and abdominal pain and tenderness with survival.

## 7. Declarations

### 7.1. Acknowledgements

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### 7.2. Author contribution

All the authors meet the standard criteria of authorship based on recommendations of the international committee of medical journal editors.

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### 7.4. Conflict of interest

The authors declare that there is no conflict of interest.

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