

A study on clinical features and outcomes of patients with *colchicum autumnale* poisoning

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ABSTRACT-*Colchicum autumnale* poisoning is rare but it is a fatal and life-threatening event. The present study is an attempt to present the clinical features and outcomes of the patients presenting with *Colchicum autumnale* plant product poisoning in a Tertiary care hospital. It is a Cross-sectional study conducted for a period of one year from February 2017 to February 2018. Aims and objectives are to identify common presentations and outcomes of colchicum autumnale poisoning. Upon admission to ICU, physical examination was performed on the patient and vital signs were noted in the supine position of the patient. All the laboratory tests were performed and a medicolegal autopsy was performed in death cases. Out of twenty three patients reported to the Inpatient Department, seventeen patients survived and six patients died. Among these six cases, three were due to consuming of Colchicum seeds and three were due to consuming roots and tubers of Colchicum. All the patients who did not survive have severe lactic acidosis, hepatic or renal dysfunction or sometimes both and some cases were presented with multiorgan dysfunction. A more severe clinical presentation should be expected in patients with pre-existing liver and renal diseases. The diagnosis could be confirmed only by toxicology analysis. Management of colchicine poisoning is restricted to supportive therapy.

Keywords: *Colchicum autumnale*, clinical features, poisoning, toxicology



INTRODUCTION:

Colchicum autumnale is a member of the family Liliaceae, known by different names like Naked Lady, Wild Saffron, Autumn Crocus and Meadow Saffron. In the southern region of Tamilnadu, it is known as 'kanneveli kalungu'. All the parts of this perennial herb that grow from a solid bulb are toxic due to the presence of alkaloid colchicine. The higher concentrations of colchicines are deposited in the plant corm and under-ground bulb. Despite serious safety concerns, *Colchicum autumnale* is used for the treatment of diseases like Gout, Arthritis and also for Familial Mediterranean Disease^{[1][2][3]}. Multi-organ toxicity is due to accidental or suicidal ingestion of *Colchicum autumnale* plant products and colchicine drug-containing overdose. Previous literature had reported several case studies of colchicine poisoning in and around several parts of the world but very few case reports pertaining to the colchicine seeds or plant products. Though colchicine poisoning is rare, it is fatal and life-threatening

event. The signs of toxicity monitor a foreseeable course and require preliminary recognition and aggressive supportive care to increase the survival chances of a patient. There is little information regarding the availability of antidotes in the market and the availability of anti-colchicine antibodies is still unavailable for human use. Death results from multiorgan failure^[4,5].

The clinical manifestations of *Colchicum autumnale* poisoning involve three different phases. The first phase of intoxication involves severe gastrointestinal irritation, watery diarrhea, burning sensation of mouth and throat, hypovolemic shock, fluid losses, vomiting, nausea, etc. In the second phase, arrhythmia, hypocalcemia, multiorgan failure (neurological, cardiovascular, pulmonary, renal,

hepatic and hematological manifestations) and death are usually seen after the third day to the seventh day of post-ingestion due to septic shock. In the third phase, if the patient survives, the recovery follows severe hair fall and it is usually seen after seven to ten days after ingestion. It crosses the placenta but there is no evidence of fetal toxicity. Colchicine is excreted into breast milk and considered compatible with lactation.

Though different mechanisms are involved in the colchicine toxicity one important mechanism is selective binding of colchicine molecules to 65 subunits of microtubules reversibly and thus altering the cell processes like cell shape, cell division by inhibiting mitosis, mobility, and cell phagocytic phenomenon, etc. There are no qualitative and quantitative standardizations for the native plant products which are used for common ailments. Prescribing these native preparations without the knowledge of the toxin levels of the ingredients may result in fatalities. Individuals and native practitioners should be made aware of the hazards of consuming unregulated medicines^[6,7,8].

Considering this ultimatum; an attempt has been made to present the clinical features and outcomes of patients presenting with *Colchicum autumnale* plant product poisoning in a Tertiary care hospital.

MATERIALS AND METHODS:

It is a Cross-sectional study conducted for a period of one year from February 2016 to February 2017. The study was performed in two different study areas in two different Tertiary care hospitals (Tamilnadu and Andhra Pradesh). Patients who were suffering from pre-existing diseases were excluded from the study. An informed consent form

was taken from the patient or from their relatives. Approval of the Institutional Ethics Committee was taken.

The patient requires immediate hospitalization, followed by gastric lavage. The patients may develop respiratory depression, dyspnoea, shock, hypotension, marked leucopenia, thrombocytopenia, coagulation disorders, oliguria, haematuria, confusion, seizures, coma and ascending polyneuropathy. Death in severe poisoning cases occurs due to shock, metabolic derangements or respiratory failure.

Upon admission, physical examination was performed on the patient and vital signs like temperature, respiratory rate, pulse, blood pressure were noted in the supine position of the patient. All the laboratory tests like echocardiogram, chest X-ray, abdominal USG, arterial blood gas analysis, renal and liver function tests were performed and tests for rhabdomyolysis, coagulopathy, etc were also done. By taking the blood sample from the patient, the tests like RBC count, total cell count, differential count, platelet count, sodium and potassium levels, serum creatinine levels, prothrombin time and urinalysis, etc. were conducted. A medicolegal autopsy was performed in all death cases.

Results: Colchicine, the major active alkaloid is attributed to the poisoning. It has an anti-mitotic activity that arrests mitosis in metaphase. The lethal dose is about 60 mg in adults and the fatal period is about 12 - 72 hrs. The present study was conducted for a period of one year in 23 patients.

Out of 23 patients reported to the IPD, maximum patients were females i.e. 13 (57%) and 10 (43%) patients were males (Figure 1).

Upon age-wise distribution of colchicine intoxication cases, more number of cases were reported in the age group of 21-30 years which constitutes about 7 (30%) followed by in the age group of 51-60 years ie 5 (23%), 4 (17%) in 61-70 years of age group and followed by 3 (13%) in the remaining age group. A similar number of cases were reported in the age group 31-40 years i.e. 2 (9%) and 2 (9%) in 41-50 years of age group (Figure 2)

Table 1 depicted that, among the 23 cases reported, 20(87%) number of cases were represented with thrombocytopenia and very few cases showed MODS which are 3 (13%) in number.

Out of 23 patients reported to the IPD, 17 patients survived and 6 patients were dead. Among these six cases, 3 were due to consuming of Colchicum seeds and 3 were due to consuming roots and tubers of Colchicum. All the patients who did not survive have severe lactic acidosis, hepatic and renal dysfunction and the other 3 were presented with multiorgan dysfunction (Table 2) (Figure 4).

In all the 23 cases, diarrhea was the most commonly presented clinical feature followed by hematological disturbances in 20 cases (Figure 3). There is no specific

antidote that is available for the treatment. Hypovolaemic shock may lead to fluid loss, which may require fluid resuscitation and or inotropic support. The correction of the metabolic parameters and fluid balance is important for the management of such patients. Patients with respiratory depression require assisted ventilation and those with renal failure with oliguria require dialysis. Prophylactic antibiotic therapy is advisable if leucopenia is present. If the coagulation profile is abnormal, vitamin K and fresh frozen plasma should be given.

Figure 1: Gender-wise distribution of cross-sectional study

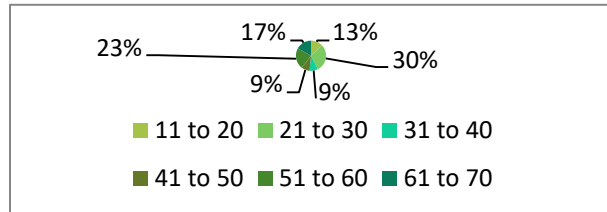
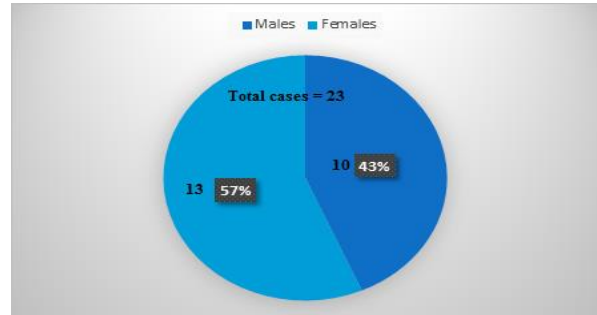


Figure 2: Demographic variable

able age-wise distribution of study cases

Table 1: Laboratory investigations of study cases

Parameters	Number of positive cases	Percentage	Number of negative cases	Percentage
Thrombocytopenia	20	87%	3	13%
Leucocytopenia	13	57	10	43
Renal dysfunction	15	65	8	35
Hepatic dysfunction	12	52	11	48
Hemodynamic instability	11	48	12	52
Lactic acidosis	10	43	13	57
CK-MB isoenzyme elevated levels	6	26	17	74
Multiple organ dysfunction syndrome (MODS)	3	13	20	87
Statistics:				

t-value: -0.13, degree of freedom: 7, p-value: 0.89 (Insignificant)

Figure 3: Representation of the clinical features of the cross-sectional study

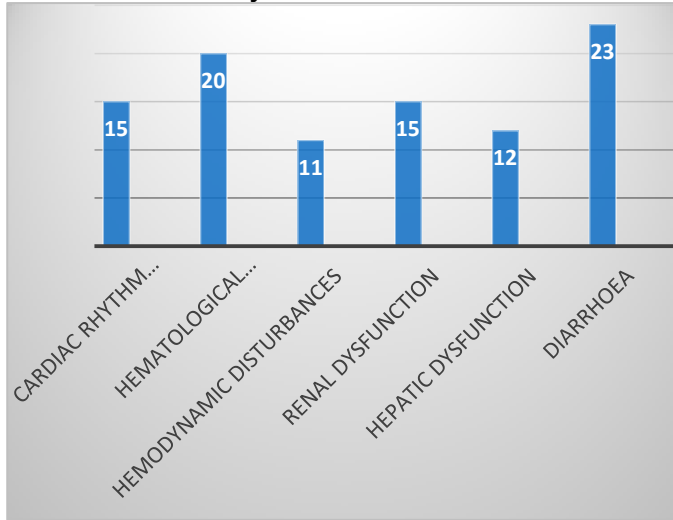


Figure 4: Number of dead and alive cases showing clinical features

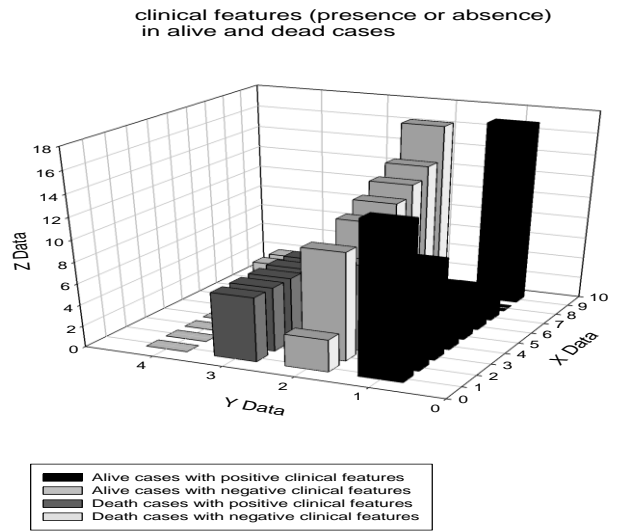


Table 2: Outcome of the study

Independent variables Number of study cases (n=23)

	Alive (n=17)	%	Dead (n=6)	%
Seeds	13	76.4	3	50
Roots and tubers	4	23.5	3	50
Lactic acidosis	4	23.5	6	100
Hepatic dysfunction	6	35.2	6	100
Renal dysfunction	9	53	6	100
CK-MB Elevation	3	17.6	3	66.6

One way ANOVA (Analysis of variance):
Uncorrected for the mean of the observations:

	DF (Degree of freedom)	SS (sum of square)	MS (Mean square)
Regression	2	121.5306	60.7653
Residual	4	13.4694	3.3673
Total	6	135.0000	22.5000

Corrected for the mean of the observations:

	DF	SS	MS	F (Fischer test value)	probability value ('p' value)
Regression	1	0.0306	0.0306	0.0091	0.9286
Residual	4	13.4694	3.3673		
Total	5	13.5000	2.7000		

Table showing number of dead and alive cases showing clinical features

Clinical features	Total number of alive cases (n=17)		Total number of dead cases (n=6)	
	Positive	Negative	Positive	Negative
Thrombocytopenia	14	3	6	0
Leucocytopenia	7	10	6	0
Renal dysfunction	9	8	6	0
Hepatic dysfunction	6	11	6	0
Haemodynamic disturbances	5	12	6	0
Lactic acidosis	4	13	6	0
CK-MB elevation	3	14	3	3
Diarrhoea	0	17	3	3

DISCUSSION: Colchicine poisoning is a rare but serious and potentially fatal event seen in food poisoning cases or overdose with drugs containing colchicine, or in persons who want to do suicidal attempts but currently no specific antidotes are available in the market. Preliminary measures, such as gastric lavage, decontamination of skin surfaces and maintenance of airway, breathing, and circulation, are strictly followed in all cases of Colchicum poisoning to reduce the mortality rates. However, the literature survey showed many case histories of Colchicum intoxication and the majority of them reported death was the main outcome in Colchicum poisoning cases. In our study, the number of death cases was six out of 23 cases reported to IPD and the death was mainly due to renal failure, hepatic failure and multiorgan dysfunction syndrome which is similar to the findings of Brncic et al. (2001)^[6] reported two cases of *Colchicum autumnale*, in which the patients had identical initial symptoms but developed extremely different clinical courses. One patient recovered

in spite of severe gastroenteritis and liver injury, whereas the other died of rapid progressive multiple organ failure 52 hrs after the plant ingestion. They recommend that all patients suspected of colchicine intoxication due to its unpredictable outcome should be managed according to the principles of intensive care, irrespective of the actual degree of poisoning. The findings of the current study were also correlated with the study conducted by Brvar et al. (2004)^[9] which reported a death case of a 76-year-old man mistakenly ingested *Colchicum autumnale* presented with nausea, vomiting, diarrhea, and dehydration 12 hours after ingestion. The echocardiogram showed dilatation with diffuse hypokinesia. Laboratory tests also revealed rhabdomyolysis, coagulopathy, and deterioration of renal function and hepatic function. Therapy was supportive of hydration, vasopressors, mechanical ventilation and antibiotics. On the third day, the patient died due to cardiac arrest. Danel et al. (2001)^[10] found a 44-year-old man ingested about 40 flowers of *Colchicum autumnale*. The patient presented with nausea, vomiting, and abdominal pain 2 hours after ingestion and had diarrhea 14 hours after ingestion. Hematological values remained within the normal range. The treatment was mainly supportive. The outcome was favorable. The intoxication was confirmed by high-performance liquid chromatography-mass spectrometry. Nagesh et al. (2011)^[11] reported a colchicine poisoning case and the patient is a 24-year-old man presented with severe vomiting, diarrhea and epigastric pain. He died on the third day of ingestion due to multiorgan failure. Chemical analysis of blood and viscera obtained postmortem confirmed the presence of colchicine. However, in all the cases, the death was due to MODS but the present study differs from the previous studies in terms of the number of cases handled in a period of one year. Most of the previous studies were concerned with case histories of Colchicine poisoning but the present research presented 23 cases of Colchicine poisoning in a period of one year. Management includes only intensive support therapy. A more severe clinical presentation should be expected in patients with pre-existing liver and renal diseases. The main reasons for death are cardiovascular collapse, respiratory failure and leukopenia with infection. Although the etiological diagnosis does not implicate specific measures in the management of the poisoning, it determines the pattern of the medical approach, which must include early intensive support measures irrespective of the expressed level of toxicity. Fab fragment antibodies produced in rabbits or goats have been effective in treating colchicine poisoning when tested in mice and rabbits. Colchicine-specific fab fragments have been successfully used to treat a life-threatening, intentional overdose of colchicine tablets in a 25-year-old woman. However, fab fragments of anticolchicine antibody are not commercially available. Pancytopenia in patients surviving the initial stages of autumn crocus poisoning has been successfully treated with granulocyte colony-stimulating factor, which may help prevent life-threatening sepsis^{[12][13][14][15]}. A diagnosis could be confirmed only by toxicology analysis. Management of colchicine poisoning is restricted to supportive therapy.

CONCLUSION: Seeds are the most commonly used plant products for poisoning. The most common presentation is gastrointestinal symptoms which are present in all patients (100%). Plant roots and stem are also equally toxic. MODS is the most common cause of death. GM-CSF is helpful in pancytopenia patients. Specific therapy such as colchicine antibodies is reported in some case reports as well as in animal studies but it is not yet commercially available. A more severe clinical presentation should be expected in patients with pre-existing liver and renal diseases. The main reasons for death are cardiovascular collapse, respiratory failure and leukopenia with infection. Hepatic and renal dysfunction could worsen the prognosis of poisoning with colchicine.

Conflict of Interest: None

Source of support: Nil

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