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CRITICAL CARE AND RESUSCITATION

CASE REPORT: CLINICAL CASE

Colchicine Overdose

Challenges With Venoarterial Extracorporeal Membrane Oxygenation and Microaxial Flow Pump Support

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ABSTRACT

Colchicine has an expanding role in cardiovascular disease treatment. Colchicine overdose is a toxicologic emergency. Direct cellular toxicity interferes with myocardial contractility, leading to cardiovascular collapse. We present a case of a patient with a colchicine overdose supported with venoarterial extracorporeal membrane oxygenation, highlighting the challenges and limitations. (JACC Case Rep. 2024;29:102580) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 29-year-old man presented with an intentional overdose of colchicine and carvedilol prescribed to treat a recent episode of myopericarditis. He initially reported ingestion of 12 pills of 6.25 mg carvedilol 4 hours prior to presentation to counteract the stimulatory effects of cocaine. He subsequently admitted to ingesting half a bottle of colchicine tablets (0.6 mg) in a suicide attempt. In the emergency department (ED), the patient was afebrile, was tachycardic to 104 beats/min, and had a blood pressure of 99/73 mm Hg.

TAKE-HOME MESSAGES

- Although VA-ECMO has an increasingly recognized role in the treatment of overdoses, its role in colchicine toxicity may be limited.

PAST MEDICAL HISTORY

The patient had a history of polysubstance use disorder (cocaine and methamphetamine), depression with suicidal ideation, and recent myopericarditis a month prior to current presentation. During that admission, a transthoracic echocardiogram demonstrated a left ventricular ejection fraction of 45% and a coronary angiogram was free of obstructive disease. Colchicine and carvedilol were prescribed.

INVESTIGATIONS

Initial laboratory studies on ED arrival included a creatinine of 1.2 mg/dL, sodium of 143 mmol/L, potassium of 3.7 mmol/L, and aspartate aminotransferase and alanine aminotransferase of 10 and 9 U/L, respectively. The venous blood gas revealed a pH of 7.4 and lactate of 1.1 mmol/L. The white blood cell count was 4.2 × 1,000/μL, hemoglobin was

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ABBREVIATIONS AND ACRONYMS

ARDS = acute respiratory distress syndrome

CI = cardiac index

ED = emergency department

SVR = systemic vascular resistance

VA-ECMO = venoarterial-extracorporeal membrane oxygenation

13.7 × 1,000/μL, and platelets were 317 × 1,000/μL. Following 8 hours of observation and stable vitals, he was transferred to the psychiatric service. While on the psychiatric service, he was noted to have altered mental status, hypotension, and tachycardia and was transferred back to the ED. Repeat labs at hour 22 postingestion demonstrated a white blood cell count of 41.6 × 1,000/μL, pH of 7.29, partial pressure of carbon dioxide of 47 mm Hg, lactate of 4.3 mmol/L, creatinine of 2.2 mg/dL, aspartate aminotransferase of 325 U/L, and alkaline phosphatase of 350 U/L. Transthoracic echocardiography showed a left ventricular ejection fraction of 20% and right ventricular dysfunction. On re-evaluation by the toxicology team at 25 hours, and in the context of the patient now endorsing colchicine ingestion in addition to carvedilol, it was felt that the patient's presentation was most consistent with colchicine toxicity given abdominal symptoms, profound leukocytosis, shock, and multisystem organ injury.

The patient was admitted to the cardiac intensive care unit and a pulmonary artery catheter was inserted to delineate the hemodynamic profile. Initial data revealed a central venous pressure of 5 mm Hg, pulmonary artery pressure of 25/13 mm Hg (mean 17 mm Hg), pulmonary artery wedge pressure of 12 mm Hg, mixed venous oxygen saturation of 58%, and cardiac index (CI) of 1.5 L/min/m^2. A dobutamine infusion was initiated at 2.5 μg/kg/min and calcium and high-dose insulin euglycemic therapy were started to treat the beta-blocker overdose. Rapid progression of hypoxemia and increased work of breathing lead to endotracheal intubation.

Over the next day, the patient developed worsening mixed cardiogenic and vasodilatory shock. By hour 46, the CI had dropped to 1.4 L/min/m^2 on dobutamine 7.5 μg/kg/min, norepinephrine 16 μg/min, and vasopressin 0.04 U/min, with an arterial lactate of 3.8 mmol/L (**Table 1**). The patient displayed evidence of worsening end-organ dysfunction including acute renal failure, hepatic failure, mixed metabolic and respiratory acidosis, and acute respiratory distress syndrome (ARDS), as evidenced by diffuse bilateral infiltrates on chest x-ray film and partial pressure of arterial oxygen/fraction of inspired oxygen ratio under 100 (**Figure 1**).

DIFFERENTIAL DIAGNOSIS

The differential for patient's profound shock included both beta-blocker and colchicine overdose. Ultimately, due to the time course of beta-blocker elimination, the lack of significant bradycardia, and the presence of early multisystem injury along with leukocytosis, it was felt that colchicine was the more likely culprit. The diagnosis was further substantiated by the mixed cardiogenic and vasodilatory shock, multiorgan failure, acidemia, and ARDS.

MANAGEMENT

After discussion as a multidisciplinary shock team, at hour 42, the decision was made to proceed with venoarterial-extracorporeal membrane oxygenation (VA-ECMO) and Impella (Abiomed) insertion for left ventricular unloading to support the patient's biventricular failure and concomitant respiratory failure. Postcannulation, the patient experienced bleeding from multiple access sites. Repeat echocardiography showed biventricular dysfunction and an ejection fraction of 5% (Video 1).

OUTCOME AND FOLLOW-UP

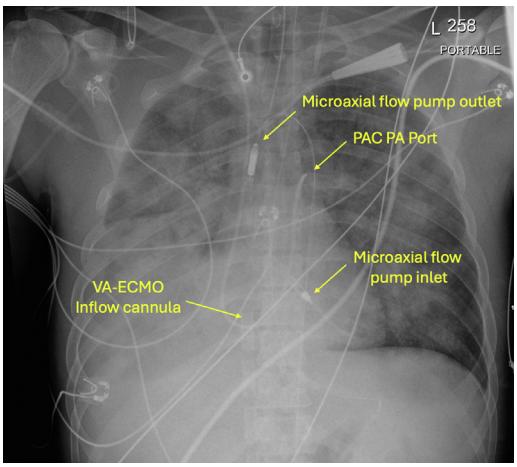
At hour 58 postingestion, despite escalating doses of vasoactive agents and frequent administration of intravenous fluid boluses, ECMO flows were unable to be maintained due to access insufficiency. The patient's arterial lactate continued to rise up to 13.4 mmol/L (**Figure 2**). At hour 62 postingestion,

TABLE 1 Clinical Time Course

Time Since Ingestion (h)	Arterial Lactate (mmol/L)	Cardiac Index (L/min/m^2)	Dobutamine (μg/kg/min)	Norepinephrine (μg/min)	Vasopressin (U/min)	Epinephrine (μg/min)	Mechanical Circulatory Support
4	1.1	–	–	–	–	–	–
29	4.4	1.6	2.5	5	–	–	–
34	3.8	1.3	5.0	5	0.04	–	–
54	10.5	1.0	7.5	30	0.04	–	VA-ECMO + Impella
58	13.4	0.9	10	30	0.04	30	VA-ECMO + Impella

VA-ECMO = venoarterial extracorporeal membrane oxygenation.

FIGURE 1 Chest X-Ray Film With Diffuse Infiltrates



PA = pulmonary artery; PAC = pulmonary artery catheter; VA-ECMO = venoarterial-extracorporeal membrane oxygenation.

despite VA-ECMO and vasoactive support, the patient expired.

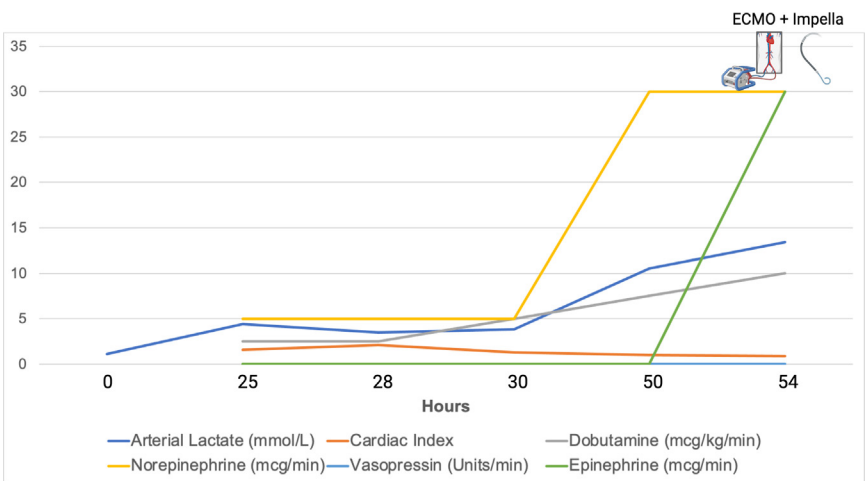
DISCUSSION

Colchicine is an anti-inflammatory medication used as a treatment in pericarditis.[1] Beyond the treatment of pericarditis, colchicine has a variety of indications in the management of cardiovascular disease including recent investigations into its role in post-operative atrial fibrillation, acute myocardial infarction, and coronary artery disease.[2,3] Colchicine binds to intracellular tubulin, preventing its polymerization into microtubules, thereby affecting multiple intracellular functions including disruption of the cytoskeleton, mitosis, and intracellular transport. It is thought to have broad anti-inflammatory effects through the inhibition of neutrophil migration to inflamed foci.[4]

Colchicine has both a narrow therapeutic window and a long half-life of elimination. Due to being a major substrate of CYP3A4 and P-glycoprotein, it has a wide range of drug interactions, including carvedilol (a P-glycoprotein inhibitor). The most common side effect of colchicine is gastrointestinal toxicity. In overdose, it can cause a range of toxicities including myelosuppression, disseminated intravascular coagulation, ARDS, and most saliently, cardiotoxicity and multiorgan failure.[5] Severe overdose has high mortality and there is no currently available antidote. A prior study of 8 patients with hemodynamic compromise due to colchicine overdose showed 4 patients with reduced CI and increased systemic vascular resistance (SVR) and 4 patients with hyperdynamic hearts and reduced SVR with the former phenotype leading to mortality.[6] Our patient, with a reduced CI and SVR, was unique in that he displayed a mixed cardiogenic and vasoplegic shock phenotype.

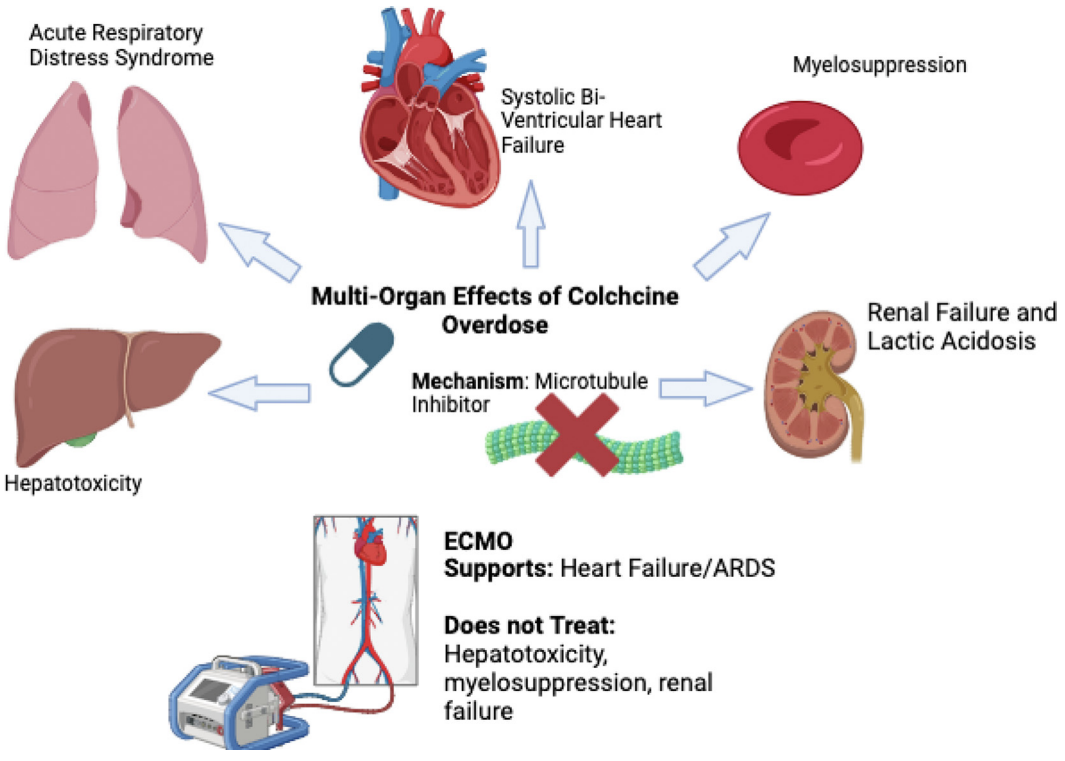
VA-ECMO is a form of mechanical circulatory and respiratory support in which venous blood is drained

FIGURE 2 Graphical Clinical Timeline



ECMO = extracorporeal membrane oxygenation.

FIGURE 3 Multiorgan Effects of Colchicine Overdose



ARDS = acute respiratory distress syndrome; ECMO = extracorporeal membrane oxygenation.

by means of an extracorporeal blood pump and passed through a membrane whereby oxygen is added and carbon dioxide is removed with the oxygenated blood being returned to the arterial circulation. VA-ECMO is increasingly being used in cases of toxicity and overdose.[7] Data supporting the use of VA-ECMO in toxicology are encouraging, with those receiving VA-ECMO for overdose experiencing better outcomes compared with the use of VA-ECMO for alternative indications.[7] Most reported cases of VA-ECMO for overdose focus on cardiovascular medications, including antiarrhythmic medications and psychotropic agents with off-target cardiovascular effects.[7]

Prior case reports have shown mixed success of VA-ECMO for colchicine overdose.[8,9] Two previously described cases of successful VA-ECMO for colchicine overdose occurred in a 4-year-old girl and 68-year-old woman. In both cases, the patients experienced multiorgan failure; however, those patients were able to be supported through their illness. A prior failure of VA-ECMO was reported in a 50-year-old woman who presented with severe cardiogenic shock in the setting of polysubstance ingestion with colchicine, beta-blockers, and anticholinergic agents. Despite VA-ECMO, the patient expired from mixed hemorrhagic and cardiogenic shock.[10] A recent case also reported failure of VA-ECMO and exchange transfusion in a 13-year-old boy with colchicine overdose.[11]

CONCLUSIONS

Although VA-ECMO has an increasingly recognized role in the management of cardiotoxic medication overdose, the efficacy of VA-ECMO in colchicine overdose may be compromised due to multiorgan failure with both cardiogenic and vasodilatory shock phenotypes (**Figure 3**). Due to the propensity for disseminated intravascular coagulation with colchicine overdose, there is likely an increased bleeding risk with large-bore cannulation. This case suggests that although for many cardioselective medications VA-ECMO may be a viable strategy to support patients through an acute overdose, its role in colchicine overdose may be limited. Because colchicine has no effective antidote currently available to providers, it

is important to screen patients for depression and suicide attempts prior to prescribing colchicine.

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KEY WORDS cardiogenic shock, colchicine, mechanical circulatory support

APPENDIX For a supplemental video, please see the online version of this paper.