Case Report

Ergotamine/Caffeine Overdose in a Female Suffering From Migraine Headache: A Case Report

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ABSTRACT

Background: Ergotamine is a very common antimigraine and is widely used in the management of headaches such as cluster and acute migraines. However, Ergotamine poisoning is an infrequent condition, and there are very few cases reported. Tachycardia and arterial spasms occasionally occur because of accidental overdosing or interactions. There are no specific antidotes, and none of the current treatments have proven efficacy.

Case Report: Here, we describe a young female who intentionally consumed approximately 20 mg of ergotamine and experienced vomiting, vasospasm, and tachycardia. Fortunately, her symptoms improved with the administration of conservation therapy, enoxaparin, nifedipine, and methylprednisolone.

Conclusion: Clinicians should be aware of the potential risk of vasoconstriction associated with ergotamine/caffeine toxicity and closely monitor patients for these side effects.

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Introduction

Evrgotamine tartrate is a medicine that belongs to the group known as ergots, which are an alkaloid produced by a fungus [1]. Ergotamine is available in various formulations, including oral, suppository, and sublingual forms, and is often combined with caffeine. Caffeine and ergotamine combinations are usually used in the treatment and inhibition of migraines or cluster headaches. Although it has not received FDA (Food and Drug Administration) approval, it is also recommended for autonomic failure because it reduces presyncopal symptoms and seated blood pressure [2, 3].

During a migraine attack, the extracranial arteries are abnormally dilated, and blood flow through them is increased [4]. Ergotamine activates serotonin receptors (5HT-1B and 5HT-1D) and induces vasoconstriction; also, at therapeutic doses, it can inhibit the uptake of norepinephrine and stimulates α-adrenergic receptors, resulting in prolonged vasoconstriction, which restricts blood flow to the extremities [5]. Caffeine works synergistically with ergotamine, enhances gastrointestinal (GI) absorption, and contracts its cerebral vasoconstriction [6-8].

The most common adverse effects of caffeine and ergotamine are GI complications, including nausea and vomiting. Cramps and insomnia can also occur [9, 10]. Ischemia, overuse headache, acroparesthesia, and ergotism are the most common adverse effects during chronic usage [11, 12]. Also, myocardial infarction and fibrotic changes have been reported [13].

One study estimated that the maximal oral bioavailability of ergotamine-caffeine combinations is approximately 5% [14]. The highest approved weekly dosage of ergotamine is 10 mg; it should not be administrated more than 6 mg for each episode [15].

Although it is a very common antimigraine, there are very few reported cases of intoxication, overdose, or poisoning by ergotamine in clinical practice compared to widely used triptans. Treatment, in some cases, initially starts with the withdrawal of ergotamine to help with symptom removal. Some studies reported the administration of sodium nitroprusside intravenously, heparin, and low-molecular-weight dextran for successful management [4, 16].

Case Presentation

On October 10th, 2023, at the Regional Centre of Clinical Toxicology hospital in northern Iran, a 19-year-old woman was hospitalized 2 hours after she took 20 tablets of ergotamine-C (containing 1 mg ergotamine tartare and 100 mg caffeine). She was a migraine sufferer for five years; still, she had not previously had severe illness. In addition to daily use of sodium valproate, she occasionally had been taking one to several tablets containing caffeine and ergotamine tartrate against migraine for a year.

During her stay in the emergency room (ER), typical symptoms of severe poisoning, including nausea, severe vomiting, dizziness, low blood pressure with a perceptible pulse, and angina, occurred.

On physical examination, she was cooperative but anxious. Upper limb pulses were present and equal. There were no ischemic changes in the extremities. Blood pressure was 120/80 mm Hg in both arms. A 12-lead electrocardiogram was obtained, which revealed sinus tachycardia. Her initial vital signs were recorded as follows: Heart rate of 96 beats per minute, respiration rate of 18 breaths per minute, blood pressure reading of 120/80 mm Hg, temperature of 37 ˚C, and pulse oximetry reading of 98% on room air. All reflexes were present and equal.

Laboratory investigations were within normal limits, including electrolyte levels and a complete blood count, coagulation studies, and liver function tests, except for venous blood gas (Table 1). Based on these assessments, the patient was transferred to the toxicology ward for further management.

Our patient consumed a significant dose and experienced a violent process of poisoning. Because specific antidotes were out of reach, the possibility of dangerous complications, and there was a lack of efficient methods of extracorporeal elimination, we initially discontinued all ergotamine and caffeine-containing drugs. Then, symptomatic treatments along with supportive therapy were applied. We used antiemetic medications, such as metoclopramide, to control the patient's nausea and vomiting. Also, due to the patient's severe condition, fluid therapy and sodium bicarbonate were applied.

One day after the onset of symptoms, the patient developed acute pain, pallor, and feeling of cold in her arms and cyanosis, refrigeration of fingers, and narrowing of the blood vessels in the limbs (peripheral vasoconstric-

Table 1. Initial laboratory data in the emergency department

Lab Data Parameters	Result	Reference Range
pH (NA)	7.48	7.35-7.45
PCO_2 (mm Hg)	17.9	38-52
HCO_3 (mEq/L)	13.5	21-28
SpO_2 (%)	98	>98
BE (Mmol/L)	-7.2	-1.5 to +3.0
BS (mg/dL)	150	<110
Respiratory rate (RR/min)	18	
Temperature (°C	37	
Blood pressure (mm Hg)	120/80	
Pulse rate (pulse/min)	96	
Troponin-rapid (ng/mL)	negative	<0.5
AST (U/L)	21	<31
ALT (U/L)	14	<31
Blood urea (mg/dL)	26	
Creatinine (mg/dL)	0.8	0.6–1.3
ALP (U/L)	238	64–306
WBC (10^9/L)	12.3	4.5 to 11.0
RBC (10^6/µL)	4.86	4.7 to 6.1
HB (g/dL)	13.6	10.5–13.5
HCT (%)	44.2	37-45
PLT (10^3/µL)	319	150-450
INR	1	
PT (second)	13.5	10-15
Na (sodium) (mEq/L)	139	135-145
K (potassium) (mEq/L)	3.7	3.5-5.5

PBR

Abbreviations: WBC: White blood cells; PLT: Platelet count; Hb: Hemoglobin; HCT: Hematocrit; AST: Aspartate aminotransferase; ALT: Alanine transaminase; ALP: Alkaline phosphatase; K: Potassium; Na: Sodium; pH: Power of hydrogen; BE: Base excess; Cr: Serum creatinine; BS: Blood sugar.

tion). Arterial spasm induced by ergotamine, which was not considered initially, was contemplated.

She was treated with bed rest and maintained at room temperature. Both upper and lower extremities were kept warm with the help of a hot bag. Therapeutic doses of enoxaparin (4000 IU) were administered to prevent possible thrombotic complications. Improvement was achieved by 10 mg three times daily oral nifedipine and a 1-hour infusion of 70 mg methylprednisolone. Cyanosis decreased, and livid discoloration and impaired arm movement improved (Table 2).

Table 2. Post-treatment laboratory data, demonstrating an improvement after treatments

Lab Data Parameters	Result	Reference Range
pH (NA)	7.42	7.35-7.45
PCO_2 (mm Hg)	33.7	38-52
HCO_3 (mEq/L)	24	21-28
SpO_2(%)	99%	>98
BE (mmol/L)	-2	-1.5 to +3.0
BS (mg/dL)	110	<110
RR (RR/min)	18	
T (˚C)	37	
BP (mm Hg)	120/80	
PR (Pulse/min)	90	
Troponin-rapid (ng/mL)	Negative	<0.5
WBC (10^9/L)	11.3	4.5 to 11.0
RBC (10^6/µL)	4.86	4.7 to 6.1
HGB (g/dL)	15	10.5–13.5
HCT (%))	45.2	37-45
PLT (10^3/µL)	319	150-450

PBR

Abbreviations: WBC: White blood cells; PLT: Platelet count; Hb: Hemoglobin; HCT: Hematocrit; AST: Aspartate aminotransferase; ALT: Alanine transaminase; ALP: Alkaline phosphatase; K: Potassium; Na: Sodium; pH: Power of hydrogen; BE: Base excess; Cr: Serum creatinine; BS: Blood sugar.

After 2 days, the patient's condition gradually resolved, and discharged from the toxicology ward and transferred to the psychiatric and neurological department for further evaluation and proper and safe administration of migraine treatment strategies, including triptans.

Discussion

Ergotamine tartrate is a medicine that belongs to the group known as ergots, which are an alkaloid [17]. Ergotamine, in combination with caffeine, is sometimes administered for the treatment and prevention of migraine [1, 18].

The range of ergot poisoning symptoms is usually classified into circulatory and neurological. In severe cases, the circulatory group is often related to vasoconstriction in the extremities, which may cause claudication, paresthesia, vesicle formation, and gangrene. The neurological manifestations include headache, vertigo, psychotic disorders, seizure, and coma. The gastric complication that our patient experienced has also been noted [4, 10].

Instead of frequent ergot toxicity in chronic usage, acute toxicity may also occur from intentional high-dose ingestion, usually in suicide attempted cases. Fever, sepsis, malnutrition, pregnancy, hepatic disease, and renal failure can escalate the vasospastic effects of ergots [19, 20].

Vasospasm is a well-recognized but rare adverse effect of ergotamine tartrate, which mainly involves the lower extremities; however, vasospasm alone did not cause gangrene. Derivatives of ergot alkaloids often block α-adrenergic and serotonin receptors plus a direct stimulating action on medium-sized arteries arteriole smooth muscles [21].

Although optimal therapy for ergotamine poisoning has not yet been published, complete withdrawal of the ergot compound and maintaining adequate circulation in

the affected areas to prevent ischemic damage are indicated [21]. Coldness and numbness of the extremities are early symptoms of toxicity. Immediate withdrawal of the ergotamine and careful observation plus conservative treatment are expected to be sufficient in most patients [4]. If symptoms continue, pharmacologic therapies may be applied. Pharmacologic therapy includes nitroprusside, prazosin, streptokinase, calcium channel blockers, intra-arterial infusion of prostaglandin E1, heparin, nitroglycerin, or intra-arterial nifedipine. In severe cases, surgical sympathectomy may be instituted [12, 22].

An alternative option would be to reduce blood viscosity with low-molecular-weight dextran (Rheomacrodex) to increase tissue perfusion. Heparin has been used in severe cases to reduce the risk of thrombosis. Hyperbaric oxygen is reported to help critical patients [4].

Surgical and chemical blockades of sympathetic, low molecular weight dextran, anticoagulants, and vasodilators such as tolazoline are used to treat ergot toxicity. In addition, sodium nitroprusside has been used to manage ergotamine-induced ischemia [23]. Captopril, an angiotensin-converting enzyme inhibitor, was suggested in some patients with increased peripheral venous renin activity [5, 21, 24].

Oral captopril rapidly responds within three hours by the increase of peripheral pulsations. Captopril may be the primary choice in severe peripheral ischemia induced by ergotamine because it is easily administered and is associated with low risk at minimum doses [24].

Conclusion

Ergotamine poisoning is an infrequent but potentially reversible condition. Based on this case, it is possible that ergotamine/caffeine toxicity can lead to the occurrence of peripheral vasospasm. Prompt administration agents such as nifedipine, captopril, methylprednisolone, heparin, and benzodiazepines can improve symptoms. Clinicians should be aware of the potential risk of vasoconstriction associated with ergotamine/caffeine toxicity and closely monitor patients for these side effects. Conservational therapy may be necessary to minimize the occurrence of vasospasm and improve patient outcomes. This case report can be a basis for completing future research and clinical trials about poisoning with triptans and better treatment.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of Mazandaran University of Medical Sciences, Sari, Iran. This study followed the principles outlined in the Declaration of Helsinki and the CARE guidelines.

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Authors' contributions

Samples collection, and data collection: Amir Hasan Farzaneh; Writing and final approval: All authors.

Conflict of interest

The authors declared no conflict of interest.

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