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Case Report

Severe metabolic acidosis due to massive metformin overdose in a man: a case report

Aliasghar Manouchehri[1], Hale Rashidian[2] and Zakaria Zakariaei[3,*]

[1]Department of Internal Medicine, Shahid Beheshti Hospital, Babol University of Medical Sciences, Babol, Iran
[2]Departments of Emergency Medicine, Mazandaran University of Medical Sciences, Sari, Iran
[3]Toxicology and Forensic Medicine Division, Mazandaran Registry Center for Opioids Poisoning, Antimicrobial Resistance Research Center, Imam Khomeini Hospital, Mazandaran University of Medical Sciences, Sari, Iran
*Correspondence address. Toxicology and Forensic Medicine Division, Mazandaran Registry Center for Opioids Poisoning, Antimicrobial Resistance Research Center, Imam Khomeini Hospital, Mazandaran University of Medical Sciences, Sari, P.O box: 48166-33131, Iran. Tel/Fax: +981133357916;
E-mail: ali.zakariaei@yahoo.com

Abstract

Metformin-associated lactic acidosis is an extremely unusual but potentially life-threatening condition. This condition is typically observed in individuals who are suicidal or have type II diabetes mellitus (DM) and have taken an overdose of metformin. In this case, we present the instance of a 43-year-old man who had type II DM and was addicted to oral opium. Following a suicide attempt with an overdose of metformin, he experienced symptoms such as nausea, vomiting, weakness and lactic acidosis. However, prompt and effective treatment was administered, including hemodialysis and adequate hemodynamic resuscitation, leading to a successful outcome.

INTRODUCTION

Metformin is widely used as an oral hypoglycemic agent worldwide due to its efficacy in decreasing hepatic glucose synthesis and improving peripheral glucose consumption [1]. It is the primary treatment option for individuals with type II diabetes mellitus (DM). However, one of the most critical and life-threatening side effects of metformin is lactic acidosis, which is characterized by a blood lactate level of over 5 mmol/L and a blood pH of <7.35, with a mortality rate of up to 50% [2–5]. Even though metformin usage alone does not cause hypoglycemia, an overdose can result in lactic acidosis. Therefore, in cases where patients attempt suicide using drugs, particularly with comorbidities like renal failure, metformin poisoning should be considered as a potential cause of significant anion gap metabolic acidosis [6].

The mechanism of lactic acidosis following metformin overdose involves an alteration in intracellular metabolism leading to anaerobic processes. This condition leads to the lactate significant accumulation, coupled with a decrease in glucose consumption due to the suppression of hepatic gluconeogenesis. Ultimately, this results in an accumulation of lactate in the circulatory system, leading to the onset of lactic acidosis. For this reason, metformin is not recommended for use in individuals with renal or hepatic insufficiency, in very elderly patients, or circulatory dysfunction, such as congestive heart failure, dehydration, shock or sepsis, as these individuals are at an increased risk of developing lactic acidosis. The underlying cause of lactic acidosis in these instances is attributed to the disruption of renal function, secondary to tissue hypoxia caused by any of these variables [7, 8].

In this report, we describe a case of an individual with DM who presented with severe lactic acidosis and gastro-intestinal symptoms following an attempted suicide with a massive metformin overdose. The patient underwent successful resuscitation, as evidenced by hemodynamic stabilization and hemodialysis.

CASE PRESENTATION

On 8 January 2023, a 43-year-old man was brought to the emergency room (ER) of a hospital in northern Iran after attempting suicide by ingesting 90 g of metformin tablets. The patient had a history of type II DM for 8 years, which was managed with metformin (500 mg 3 times a day), and also had a history of oral opium addiction. Upon arrival at the ER, the patient was experiencing symptoms of dizziness, loss of appetite, weakness, lethargy, drowsiness, nausea and vomiting. Despite these symptoms, the patient was conscious and able to communicate verbally. On examination, the patient's vital signs were within normal range, with a blood pressure of 115/75 mmHg, a pulse rate of 90 beats/min, a respiration rate of 18 breaths/min and a temperature of 37°C.

The patient received intravenous hydration with normal saline serum and 60 g of activated charcoal through a nasogastric tube immediately. Additionally, stat doses of sodium bicarbonate (44 mEq), ondansetron (8 mg) and pantoprazole (80 mg) were administered. The results of laboratory tests conducted in ER and during hospitalization are summarized in Table 1.

Notwithstanding the administration of a continuous infusion of sodium bicarbonate for a duration of 12 h, the metabolic acidosis of the patient persisted. As of the time of assessment,

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Table 1. The results of laboratory tests performed during hospitalization

Parameter	Initial	12 h	24 h	72 h	Normal	Unit
Na	139	130	137	142	135–145	mEq/L
K	5	4	3.9	3.7	3.5–5	mEq/L
BUN	14	35	20	17	7–20	mg/dl
Cr	1.4	1.7	1.2	1	0.5–1	mg/dl
BS	180	115	147	152	80–140	mg/dl
pH	7.26	7.13	7.36	7.38	7.35–7.45	
PCO_2	57.2	33.9	37.1	41.2	35–45	mmHg
HCO_3	25.9	11.3	21	24.7	19–27	mEq/L
BE	− 2.4	−18.1	−4.6	− 0.7	0 ± 2	mEq/L
Lactate		15	–	1.9	0.5–2.2	mmol/L
Ca	9.4	–	8.9	–	8.5–10.5	mg/dl
Mg	1.8	–	2	–	1.7–2.2	mEq/L
P	3.3	–	4	–	2.5–4.5	mg/dl
LDH	–	–	–	478	140–280	U/L
CPK	–	–	–	97	20–200	IU/L
AST	–	–	–	19	10–40	U/L
ALT	–	–	–	22	<45	U/L
ALP	–	–	–	116	80–306	U/L

BS: blood sugar; Cr: creatinine; BUN=blood urea nitrogen; CPK=creatine phosphokinase; LDH: lactate dehydrogenase; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALP: alkaline phosphatase; HCO_3: bicarbonate; BE: bass excess; P: phosphorus; Ca: calcium; Mg: magnesium

the measurements obtained revealed that the pH of the individual was quantified at 7.13, the HCO_3 value was determined to be 11.3 mmol/L, the BE ascertained to be −18.1 and the PCO_2 evaluated to be 33.9. Furthermore, the individual's blood lactate level was detected to be 15 mmol/L (reference range, 0.5–2.2 mmol/L). Due to the progressive deterioration of the patient's health status, a decision was made to initiate intermittent hemodialysis utilizing a double-lumen subclavian dialysis line. Blood flow was adjusted to a rate of 180 ml/min, with the procedure being carried out over a period of 4 h. Following the initial session of hemodialysis, the patient's metabolic acidosis demonstrated marked improvement.

On the second day following hemodialysis, the patient demonstrated notable clinical and laboratory improvements. After 4 days, the patient was discharged from the hospital in good general condition and with controlled blood sugar levels. Written informed consent was obtained from the patient for the publication of this report. This study was conducted in accordance with the principles outlined in the Declaration of Helsinki, and the CARE guidelines and methodology were followed throughout.

DISCUSSION

Upon admission to the ER, the patient's arterial blood gas levels were mildly impaired. However, serial blood gas monitoring and worsening clinical symptoms ultimately led to a diagnosis of metformin-related metabolic acidosis, which was determined to be the result of a drug overdose suicide attempt. It is noteworthy to acknowledge that in patients who have previously shown signs of addiction to oral opium and present clinical indications such as weakness, nausea, vomiting and loss of appetite, lead poisoning should be considered in the differential diagnosis. This is imperative as the condition may be linked to compromised adherence to therapeutic regimens and an augmented prevalence of morbidity [9].

Metformin overdose should be considered as a potential cause of significant anion gap metabolic acidosis in diabetic patients. Accurate diagnosis can be challenging in cases where patients have an uncertain medical history, have overdosed on an unknown drug or multiple drugs or are experiencing gastrointestinal symptoms. Additionally, it is important to note that diabetic patients who do not use insulin or oral antidiabetic agents to increase insulin production may still be at risk of drug-induced hypoglycemia. When metformin is combined with drugs that stimulate insulin production, severe physical exercise, fasting or comorbidities such as renal failure, metformin-induced hypoglycemia should be taken into consideration. Appropriate laboratory tests such as blood sugar and arterial blood gas should be conducted to confirm the diagnosis and guide appropriate treatment [10].

In cases of metformin toxicity, the primary step in treatment involves improving ventilation and circulation. If recent ingestion is suspected, it may be necessary to consider gastrointestinal decontamination. For patients who are well-ventilated but experiencing acidosis, administration of bicarbonate is recommended. However, it should be noted that sodium bicarbonate infusions alone are not sufficient for balancing acid–base metabolism. In such cases, hemodialysis is advised for the purpose of clearing metformin and correcting acidosis. In particular, for patients like our own who are presenting with lactate and metformin in circulation, intermittent hemodialysis can be an effective means of elimination [11].

Minor gastrointestinal symptoms and hyperlactataemia are frequently observed as side effects in cases of acute overdose. Patients who consume >50 g of the metformin may suffer from severe toxicity, which manifests as severe metabolic acidosis, hyperlactatemia and hypotension [12]. Metformin overdose can lead to elevated lactate production and impaired hepatic lactate metabolism. Although there have been several published cases of metformin-associated lactic acidosis, acute overdose incidents have been less frequently reported. In a systematic review by Dell'Aglio *et al.*, 22 cases of acute metformin ingestion were analyzed, and it was found that patients with a blood pH of 6.9 or lactate levels exceeding 25 mmol/L had an 83% mortality rate. Furthermore, individuals who consumed metformin doses above 50 g had a mortality rate of 38% [13].

The reversible conditions of hypoglycemia, hypothermia and lactic acidosis resulting from metformin overdose can be effectively addressed through prompt diagnosis and treatment. In

particular, early diagnosis of lactic acidosis and its management through hemodialysis, alongside cardiovascular support, blood glucose control and stabilization of vital signs, can significantly enhance the chances of a successful outcome.

CONCLUSION

For patients with a prior occurrence of significant metformin overdose, expeditious diagnosis and timely intervention in the form of hemodialysis for metabolic acidosis, coupled with sufficient hemodynamic resuscitation, and proper management of blood glucose and core body temperature, can yield satisfactory outcomes. Hence, emergency clinicians and toxicologists must maintain a high level of suspicion for drug poisoning in any patient presenting with marked metabolic acidosis or displaying symptoms related to the gastrointestinal and respiratory systems.

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CONFLICT OF INTEREST STATEMENT

None declared.

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DATA AVAILABILITY

The data are available with the correspondence author and can be achieved on request.

AUTHORS' CONTRIBUTIONS

Z.Z. involved in the collecting of samples and data. H.R. and A.M. comprised in the interpretation writing, editing of the manuscript. Z.Z. prepared the draft and submitted the manuscript. All authors reviewed and approved the final version of the manuscript.

ETHICS APPROVAL

The study was approved by our local ethics committee.

INFORMED CONSENT

Written informed consent was obtained from the patient for publication of this case report.

GUARANTOR

Aliasghar Manouchehri.

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