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Lactic acidosis in a patient treated with metformin

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Abstract

Metformin is widely recognized as the first-line therapy for type 2 diabetes due to its low cost, safety profile, and potential cardiovascular benefits. However, complications of its use may occur in daily clinical practice, including lactic acidosis, which, although rare, is characterized by relatively high mortality. The clinical case described involves a 63-year-old patient treated with metformin for 3 weeks. She was diagnosed with acute kidney injury and severe lactic acidosis requiring renal replacement therapy in the ICU setting.

Keywords: Metformin; Lactic acidosis; Renal failure.

Introduction

Lactic acidosis is a heterogeneous disturbance of acid-base balance associated with increased lactate levels. It manifests with significant deterioration in the general condition accompanied by consciousness disorders; nausea, vomiting, abdominal pain, and Kussmaul breathing may occur. Lactic acidosis can be easily diagnosed based on blood gas analysis, with characteristic deviations: blood pH<7.35 and lactate concentration >5 mmol/L [1]. The key is to diagnose and remove the cause of increased lactate levels.

Two types of lactic acidosis are distinguished: Type A is associated with tissue hypoxia and increased anaerobic metabolism leading to increased lactate production. Type B accompanies other diseases such as diabetes and liver and kidney diseases, or may result from ethylene glycol or salicylate poisoning or metformin use.

Metformin, a dimethyl biguanide derivative, is one of the basic and commonly used drugs in the treatment of type 2 diabetes. Its mechanism of action is complex, based on mechanisms including decreased glucose absorption in the gastrointestinal tract, increased glucose utilization by peripheral tissues by increasing their sensitivity to insulin, and inhibition of gluconeogenesis. The detailed mechanism of reducing hepatic glucose production is still debated, considering influences such as gene expression, inhibition of glycerol-3-phosphate dehydrogenase, and effects on the redox potential, leading to changes in the NAD+ to NADH ratio (inhibiting gluconeogenesis in redox potential-dependent pathways, including lactate conversion to pyruvate). Additionally, inhibition of complex I activity of the respiratory chain may occur, but there is no certainty about the clinical significance of this mechanism, possibly occurring only with high doses of metformin that are never used in practice [2,4,7].

In the treatment of lactic acidosis, it is essential to determine the cause that needs to permanently restore the acid-base balance. In addition to this, sodium bicarbonate infusion and hemodialysis (intermittent or continuous) are used; metformin is easily dialyzable due to its low molecular weight and lack of protein binding. Renal replacement therapy should be continued until lactate concentration drops below 2 mmol/L and pH is above 7.35 [5,7].

Case report

A 63-year-old patient in a severe general condition was admitted to the Emergency Department of the Clinic of Nephrology, Transplantology, and Internal Medicine in Szczecin due to deteriorating consciousness, nausea, and vomiting since the

previous day, along with significantly elevated renal parameters (creatinine level of 11 mg/dL reported in the emergency room of the district hospital from which she was transferred). According to the patient's husband and medical documentation (the patient was unable to provide information), she had an uncomplicated laparoscopic cholecystectomy two weeks earlier, as well as suffered from hypertension and type 2 diabetes. Current medications included indapamide, bisoprolol, and metformin at a dose of 3 x 850 mg (the latter drug was initiated about three weeks earlier).

Upon admission, the patient was conscious, but with a delayed response to commands. Physical examination revealed signs of dehydration, pale skin, intensified vesicular murmur with Kussmaul breathing, regular heart rate of 85/min., blood pressure of 100/58 mmHg, soft, painless abdomen without signs of peritoneal irritation, sluggish peristalsis, negative Chelmonski's and Goldflam's signs, no signs of lateralization in neurological examination, and negative meningeal signs. Body temperature was 35°C, oxygen saturation was 100% without oxygen supplementation.

Laboratory results primarily indicated non-respiratory acidosis with a pH below the detection threshold in this laboratory (6.8) with indeterminately low bicarbonate levels, indeterminate base deficit, and lactate concentration above 15 mmol/L. Creatinine level was 11.4 mg/dL, and urea level was 186 mg/dL. Toxicological analysis confirmed only therapeutic levels of the aforementioned drugs; no salicylates or alcohols were detected.

Fluid infusion, sodium bicarbonate administration, establishment of dialysis access, and attempted hemodialysis were immediately initiated; however, due to low arterial pressure values after the start of the procedure (BP 60/40 mmHg), the patient was qualified for continuous techniques and transferred to the ICU of the current hospital.

The applied therapy resulted in rapid correction of acid-base imbalances, restoration of diuresis, and improvement in the patient's condition. Imaging studies (abdominal ultrasound and CT) revealed only a small hematoma in the gallbladder fossa. Surgical consultation did not indicate the need for surgical intervention. After stabilizing the general condition, the patient was transferred to the Department of Nephrology, where her condition remained stable, renal parameters were within normal limits, and she did not require dialysis therapy. The patient, in good general condition, was discharged home. Considering the entire clinical picture after excluding other causes, the symptoms indicate metformin-induced lactic acidosis.

Discussion

As long as renal function is stable and the patient is regularly monitored, metformin does not increase the risk of lactic acidosis in individuals with mild or moderate chronic kidney disease (eGFR 30-60 ml/min/1.73 m²). The risk of lactic acidosis during metformin therapy is significantly higher in the presence of additional factors such as impaired renal function, dehydration, conditions associated with decreased blood oxygenation, or systemic infection. Metformin should not be initiated for eGFR below 30 ml/min/1.73 m² and its discontinuation should be considered if eGFR falls below 45 ml/min/1.73 m² [6].

It is difficult to unequivocally determine what contributed to the occurrence of lactic acidosis in the described patient. Analysis of postoperative results from two weeks before the described hospitalization showed normal renal parameters and the patient's condition after the surgical procedure was good. Some sources distinguish two types of lactic acidosis in patients using metformin: MALA – metformin-associated lactic acidosis occurring in patients with the aforementioned risk factors; and MILA – metformin-induced lactic acidosis when no additional risk factors are present [7]. The described clinical case was most likely MILA, as no additional factors leading to lactic acidosis were identified and the daily dose of the drug was quite high (2550 mg).

Metformin is widely regarded as the first-line therapy for type 2 diabetes due to its low cost, safety profile, and potential cardiovascular benefits (reduction of cardiovascular and microvascular risk). However, complications of its use may occur in daily clinical practice, including lactic acidosis, which, although rare (2-9 cases/100,000 patients per year), has a mortality rate of 25%-50% [3].

References

1. Di Mauro S, Filippello A, Scamporrino A, Purrello F, Piro S, Malaguarnera R. Metformin: When Should We Fear Lactic Acidosis? Int J Mol Sci. 2022; 23(15): 8320.
2. Fadden EJ, Longley C, Mahambrey T. Metformin-associated lactic acidosis. BMJ Case Rep. 2021 Jul 8;14(7):e239154.
3. Królik PW, Rusinek B, Dobrzańska-Pielech T, Rudnicka-Drożak E. Kwasica mleczanowa związana z leczeniem metforminą. Geriatria. 2018; 12: 117-125.
4. LaMoia TE, Shulman GI. Cellular and Molecular Mechanisms of Metformin Action. Endocr Rev. 2021; 42(1): 77-96.
5. Rahman F, Tuba S. Lactic Acidosis Associated with Metformin in Patients with Diabetic Kidney Disease. Med Arch. 2022; 76(4): 297-300.
6. Standards of Care in Diabetes Abridged for Primary Care Providers American Diabetes Association. 2023.
7. Visconti L, Cernaro V, Ferrara D, Costantino G, Aloisi C, Amico L, Chirico V, Santoro D, Noto A, David A, Buemi M, Lacquaniti A. Metformin-related lactic acidosis: is it a myth or an underestimated reality? Ren Fail. 2016; 38(9): 1560-1565.