

---

Elvir Mucic<sup>1</sup>, Damir Pelicic<sup>1,2</sup>

## METFORMIN – ASSOCIATED LACTIC ACIDOSIS

**Abstract:** In this paper, we provide a brief review of metformin-associated lactic acidosis in renal patients with stage 3 to 4 chronic kidney disease. A 70-year-old male patient is presented, who has been treated for type 2 diabetes for the past twenty years. Since he was taking high doses of metformin at home, without the supervision of his family or doctor, he was urgently admitted to the Nephrology Clinic of the Clinical Center of Montenegro in Podgorica, where diagnostics were immediately performed and the patient was included in hemodialysis, along with other symptomatic and conservative therapy. During hospitalization, the patient's general condition and laboratory analyses of nitrogenous substances and potassium improved. In our case, the patient's treatment with hemodialysis led to rapid correction of metabolic disorders and hemodynamic stabilization, and ultimately to recovery, so there was no need for his further hemodialysis treatment. The patient was discharged home in good general condition, and it can be concluded that timely diagnosis of metformin-associated lactic acidosis is of great importance for hemodialysis treatment, which successfully corrects a severe metabolic disorder. This case suggests the importance of early recognition and treatment of patients with lactic acidosis in diabetics and renal patients who are taking uncontrolled or inadequate metformin therapy for the treatment of type 2 diabetes.

**Keywords:** Kidney renal disease, DM 2, Lactic acid, Hemodialysis

### *Introduction*

Metformin-associated lactic acidosis (MALA) is a rare and serious adverse complication, with a high mortality rate of 30–50%. Its early recognition and timely initiation of diagnosis and treatment can reduce morbidity and mortality in patients with MALA (1).

---

<sup>1</sup> Clinic of Nephrology, Clinical Center of Montenegro, Podgorica, Montenegro

<sup>2</sup> Damir Pelicic, Faculty of Medicine, University of Montenegro, Podgorica, Montenegro, e-mail: damir.pelicic@t-com.me

It is a serious medical condition caused by the accumulation of lactic acid in the blood and a drastic drop in plasma pH (1). In the literature, MALA is a rare complication that occurs in patients treated for type 2 diabetes (DM2), which may be caused by high drug intake or comorbidities such as renal insufficiency (2).

It is manifested by gastrointestinal symptoms, altered mental status and elevated nitrogenous substances in the serum and often requires treatment with hemodialysis (2).

Although the use of metformin is recommended in the treatment of DM2, great caution is required when prescribing this drug to patients prone to systemic hypoperfusion conditions, as it may lead to the accumulation of harmful metabolic products in the patient's body and metabolic disorders that may result in metformin-related lactic acidosis (3).

### ***Presentation of the Patient***

Patient B. R., age 70, was admitted to the Nephrology Clinic via the Emergency Center late on the evening of July 4, 2026, in a life-threatening condition due to lactic acidosis. The day before admission, the patient developed gastrointestinal symptoms, such as nausea and vomiting, as well as frequent hiccups. He vomited about ten times in twenty-four hours. In the last two days, he reports less frequent urination, without dysuric disturbances.

On admission, blood findings include an elevated serum creatinine of 980 mmol/l, with hyperkalemia and lactic acidosis. He has been treated for type 2 diabetes for more than 20 years, he is on insulin therapy, but he also took metformin on his own initiative, and was not monitored by an endocrinologist for a long time.

On admission, conscious, oriented, communicative, slightly dyspneic at rest, afebrile, acyanotic, anticteric, dehydrated. Breathing normally. heart rate rhythmic, clear tones, systolic murmur above the precordium. Abdomen soft, slightly sensitive in epigastrium. The patient is a long-term diabetic, and the heteroanamnesis revealed that he was taking Metformin in high doses. Upon admission, extremely elevated values of nitrogen substances in the serum with oliguria were verified. Immediately after admission, a central venous catheter (CVC) for hemodialysis was placed in the right femoral vein and emergency hemodialysis was started. Parenteral rehydration therapy, broad-spectrum antibiotic therapy and other necessary conservative therapy were prescribed.

The prescribed therapy resulted in the recovery of renal function with preserved diuresis and serum creatinine of 248 mmol/l, optimization of diuresis and good general condition, but further continuous monitoring by a nephrologist and endocrinologist is necessary. An endocrinologist was consulted based on the glycemic profile and

modified insulin therapy was started. On the day of discharge, the CVC was removed from the right femoral vein.

The patient was discharged on July 10, 2027 with a good general condition. Therapy is prescribed and a control examination is scheduled with an endocrinologist and a nephrologist in outpatient settings.

## ***Discussion***

Metformin has been used in the treatment of DM2 for more than 60 years, and the balance between its benefits and side effects remains a matter of debate (4).

The literature suggests that lactic acidosis is indeed a rare and very serious adverse event in diabetic patients treated with metformin, with an incidence of 0.03–0.1 cases per 1000 patient-years and a high mortality rate of approximately 50% (5).

The liberalization of metformin prescribing guidelines in the United States of America and the European Union, particularly with regard to its use in advanced stages of chronic kidney disease (CKD), has led to renewed interest in the subject of MALA (6).

Despite adjusting the dose of metformin in patients with impaired renal function, patients with diabetes and stage III-IV renal insufficiency have a higher risk of rapid decline in renal function, and metformin toxicity may occur if the drug is administered uncontrolled and without regular monitoring by endocrinologists and nephrologists. In our case, the patient's treatment with hemodialysis led to a rapid correction of metabolic disorders and hemodynamic stabilization, and finally to recovery, so there was no need for his further treatment with hemodialysis (6).

The literature also suggests that MALA accounts for a smaller proportion of cases than non-metformin-related lactic acidosis (7–9).

## ***Conclusion***

In our case, the patient's hemodialysis treatment led to rapid correction of metabolic disorders and hemodynamic stabilization, and ultimately to recovery, so that there was no need for his further hemodialysis treatment. The patient was discharged home in good general condition.

It can be concluded that timely diagnosis of MALA is of great importance for hemodialysis treatment, which successfully corrects severe metabolic disorders.

This case suggests the importance of early recognition and treatment of patients with lactic acidosis in diabetics and renal patients who are uncontrolled or inadequately taking metformin therapy for the treatment of DM2.

### ***Conflict of Interest***

The author declares no conflict of interest.

### ***References***

1. van Berlo-van de Laar IRF, Gedik A, van 't Riet E, de Meijer A, Taxis K, Jansman FGA. Identifying patients with metformin associated lactic acidosis in the emergency department. *Int J Clin Pharm*. 2020 Oct; 42(5): 1286–1292.
2. Lalau JD, Kajbaf F, Protti A, Christensen MM, De Broe ME, Wiernsperger N. Metformin-associated lactic acidosis (MALA): Moving towards a new paradigm. *Diabetes Obes Metab*. 2017 Nov; 19(11): 1502–1512.
3. Ávila E, Roessler B E. MALA: Acidosis láctica asociado al uso de metformina, una revisión a propósito de casos clínicos [MALA: Lactic acidosis associated with the use of metformin, review of clinical cases]. *Rev Med Chil*. 2023 May; 151(5): 618–627. Spanish.
4. Bicsak TA, Walsh B, Fineman M. Metformin-associated lactic acidosis: Moving towards a new paradigm? *Diabetes Obes Metab*. 2017 Nov; 19(11): 1499–1501.
5. *Metformin and other antidiabetic agents in renal failure patients*. Lalau JD, Arnouts P, Sharif A, De Broe ME. *Kidney Int*. 2015; 87: 308–322..
6. Moioli A, Maresca B, Manzione A, Napoletano AM, Coclite D, Pirozzi N, Punzo G, Menè P. Metformin associated lactic acidosis (MALA): clinical profiling and management. *J Nephrol*. 2016 Dec; 29(6): 783–789.
7. Lalau JD, Kajbaf F, Protti A, Christensen MM, De Broe ME, Wiernsperger N. Metformin-associated lactic acidosis (MALA): Moving towards a new paradigm. *Diabetes Obes Metab*. 2017 Nov; 19(11): 1502–1512.
8. Huang W, Castelino RL, Peterson GM. Adverse event notifications implicating metformin with lactic acidosis in Australia. *J Diabetes Complications*. 2015 Nov–Dec; 29(8): 1261–5.
9. DeFronzo R, Fleming GA, Chen K, Bicsak TA. Metformin-associated lactic acidosis: Current perspectives on causes and risk. *Metabolism*. 2016 Feb; 65(2): 20–9.