

# Lactic acidosis after metformin use in chronic hemodialysis patient

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## ABSTRACT

**Objectives:** Metformin is a biguanide and is used especially in metabolic syndrome where insulin resistance is at the forefront and in Type 2 diabetes mellitus, both by suppressing the endogenous glucose production in the liver and increasing the sensitivity of insulin in peripheral tissues such as fat and muscle tissue.<sup>1</sup> The most rare but life-threatening side effect of metformin is the development of lactic acidosis. Therefore, the glomerular filtration rate is 30 ml/min. its use is contraindicated in patients with chronic kidney disease.<sup>2</sup> Lactic acidosis is the cause of metabolic acidosis with increased anion gap; occurs when the plasma lactate concentration exceeds 4-5 millimol /Liter (mmol /L) (Normal range: 0.5-1.5 mmol /L).<sup>3</sup> Here, we present the development of lactic acidosis due to metformin use in an 84-year-old female patient who has been on chronic hemodialysis treatment for 4 months. The patient applied to the emergency department twice because of confusion. The patient, who was found to have acidosis in the blood gas, regained consciousness after he was taken to hemodialysis and was referred to the nephrology outpatient clinic, considering that she might have dialysis insufficiency. The patient, who learned that she used metformin in his anamnesis, did not recur after the drug was stopped. The use of metformin in advanced age and renal failure may cause fatal complications. Glomerular filtration rate 45 ml/min. metformin should be used with caution in patients with should not be given to those below.

**Keywords:** metformin, lactic acidosis, type-2 diabetes mellitus, hemodialysis

Metformin is a biguanide and is used especially in metabolic syndrome where insulin resistance is at the forefront and type 2 diabetes mellitus (DM) by suppressing endogenous glucose production in the liver and increasing insulin sensitivity in peripheral tissues such as fat and muscle tissue.<sup>4</sup> Metformin has some advantages over sulfonureas. For example; It does not cause hypoglycemia, does not increase weight gain and hyperinsulinemia, and contributes positively to blood lipid levels. Because of these advantages, metformin is widely used in the treatment of type 2 diabetics alone or in combination therapy. The most important side effect of met-

formin is the development of lactic acidosis. Although it is expected that there is a predisposing factor, especially abnormal renal function, lactic acidosis may develop in individuals with normal renal function.<sup>5</sup> Although lactic acidosis due to metformin is a very rare clinical condition, it can be fatal at a rate of approximately 50%.

## CASE REPORT

In this case, an 84-year-old female patient was admitted to the emergency department with complaints

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of nausea, dizziness and vomiting for a week. The patient, who was followed up with type-2 diabetes mellitus for 10 years, was using metformin 1000 mg 1\*1 and vildagliptin tablet 1\*1 in her treatment. In the vital signs checked in the emergency room, TA: 160/80 mmHg, pulse: 90 beats/minute, SpO<sub>2</sub>: 68 %, respiratory rate 25/minute. Laboratory parameters were as follows: PH: 7.12 mmHg, HCO<sub>3</sub>: 10.50 mmol/L, PCO<sub>2</sub>: 33.0 mmHg, SO<sub>2</sub>: 53.60 %, BE: -17.4 mmol/L, and c-lac: 13.0 mmol/L. The patient, whose general condition was moderate, conscious and oriented-cooperative, was admitted to the ward. In other tests, wbc: 22,4 10<sup>3</sup>/uL, CRP: 9 mg/L, BUN: 94 mg/dL, creatinine: 5.7 mg/dL and blood glucose: 147 mg/dL (table 1). The patient is on hemodialysis 3 days a week. The patient's acidosis and clinic did not improve despite hemodialysis. According to the information received from the relatives of the patient, the patient was using 1000 mg of metformin. Metformin was stopped and crystallized insulin was administered to the patient according to her blood glucose. In the follow-ups, the patient whose acidosis and clinical condition improved in arterial blood gas, and whose lactate level returned to the normal range, was prescribed insulin and the patient was discharged with full recovery.

## CONCLUSION

Metformin-induced lactic acidosis is a rare, preventable, but life-threatening side effect when it develops. Its total incidence has been reported as 2-9 cases per 100,000 patients per year.<sup>6, 7</sup> Especially in

the presence of renal dysfunction, lactic acidosis may develop due to metformin use. However, the fact that there are very few cases reported to date, leads to the fact that lactic acidosis developing due to metformin is easily missed, especially in individuals without renal dysfunction. We think that this oral antidiabetic drug, which is widely used today, should be used by evaluating the complication risks for selected patients. In our case, metformin-induced lactic acidosis developed in the presence of renal failure. In the presence of renal insufficiency, the clearance of both lactate and metformin decreases and the risk of lactic acidosis increases.<sup>8</sup> Therefore, metformin should not be started in patients with creatinine levels higher than 1.4 mg/dL in women and 1.5 mg/dL in men. The development of severe metabolic acidosis without ketosis in patients treated with biguanides was first reported by Walker and Linton in 1959, and the precursor of metformin, phenformin, was withdrawn from the market in 1982 due to its high lactic acidosis-inducing effect. Lactic acidosis is a clinical emergency that requires prompt diagnosis and prompt treatment. A 42.5% mortality rate was reported in the series of Misbin *et al.*<sup>9</sup> Recovery is possible even in very serious cases, thanks to early diagnosis and prompt initiation of treatment. It has been reported that especially patients with chronic renal failure benefit from dialysis.<sup>10</sup> As a result, metformin, which can be used alone or in combination in the treatment of type 2 DM, has the potential for side effects such as lactic acidosis, especially due to its positive effects on insulin resistance. We believe that in the absence of absolute contraindications, there is no obvious reason to deny patients clinical benefits

**Table 1. Laboratory parameters of the patient while using metformin and after discontinuation**

Parameter	When using	After stopping
WBC (10 <sup>3</sup> /uL)	22.4	18.3
BUN (mg/dL)	94	41
Creatinine (mg/dL)	5.7	2.3
Glucose (mg/dL)	147	118
CRP (mg/L)	9	9
PH (mmHg)	7.12	7.29
PCO <sub>2</sub> (mmHg)	33	36
HCO <sub>3</sub> (mmol/L)	10.5	18.1
Lactate (mmol/L)	13.0	2.7
SPO <sub>2</sub> (%)	68	92

of metformin therapy. Clinicians who start metformin treatment should assess renal function and instruct patients to discontinue the medication and consult their doctor in case of severe vomiting and/or diarrhea, or other hypovolemic conditions. Although it is a very rare and preventable side effect, it can be a mortal side effect when patient selection is not done well. For this reason, we recommend that it should not be preferred in patients with type 2 diabetes who are at an advanced age and have serious diabetic complications.<sup>11</sup>

#### *Authors' Contribution*

Study Conception: MB,; Study Design: MB,; Supervision: MB,; Materials: FB,; Data Collection and/or Processing: MB,; Funding: FB,; Statistical Analysis and/or Data Interpretation: FB,; Literature Review: MB,; Manuscript Preparation: FB and Critical Review: FB.

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