

Dialysis requiring acute kidney injury and lactic acidosis in a young patient with normal renal function after high-dose metformin use

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Abstract: Metformin (MTF) is an anti diabetic agent used for the treatment of metabolic syndrome and type 2 diabetes mellitus which are characterized with insulin resistance. The most important side effect of MTF is lactic acidosis (LA). A 23 year old male without any health problems, had taken his father's 4 tablets of 1000 mg metformin for head ache, accidentally. 8 hours after taking the pills, he admitted to the emergency service with abdominal pain, diarrhea, nausea. The patient was evaluated as MTF- associated LA and taken to the intensive care unit. Hydration with isotonic saline began and hemodialysis (HD) treatment was executed. Although LA is seen especially in patients with impaired renal function, but may also occur in patients with normal renal function. With rapid diagnosis and treatment, improvement may be achieved.

Keywords: Metformin, acute kidney injury, lactic acidosis.

INTRODUCTION

Metformin (MTF) is an anti diabetic agent from the biguanide group, and its glucose lowering effect is mainly due to decreased hepatic glucose output and increased insulin-mediated glucose uptake of skeletal muscle and adipocytes. In addition to these effects, it reduces the intestinal glucose absorption, increases the insulin sensitivity in peripheral tissues, and thus it is used for the treatment of disorders characterized with insulin resistance such as metabolic syndrome and type 2 diabetes mellitus [1].

The most important side effect of MTF is lactic acidosis (LA). Although this side effect is seen especially in patients with impaired renal function, but may also occur in patients with normal renal function [2,3]. Although MTF- associated LA is a rare condition, but may be mortal in about 50% of cases. MTF-associated LA may occur in patients with previously normal renal functions, even in young patients. Patients with severe LA induced by MTF can survive when fluid replacement, iv sodium bicarbonate and haemodialysis treatments are initiated rapidly. Conditions and/ or diseases that affect renal perfusion can precipitate lactic acidosis [4].

CASE REPORT

A 23 year old male patient without any health problems, had taken his father's 4 tablets of 1000 mg metformin for head ache, thinking them as analgesic

pain. Eight hours after taking the pills, he admitted to the emergency service with abdominal pain, diarrhea, nausea and fatigue. Physical examination findings were as follows; arterial tension: 110/70 mm Hg, heart rate: 95/ min, respiratory rate :25 min, and laboratory examination values were as follows; blood glucose: 65 mg/ dL, urea: 70 mg/ dL, creatinine: 4.2 mg/ dL, pH: 7.28, HCO₃: 21 mmol/ L, pCO₂: 37 mmHg, lactate:12.4 mmol/ L and no significant pathological values were detected in complete blood count and urinalysis. Repeated blood tests from a new sample were consistent with the first evaluation. His laboratory values of 3 months ago were completely normal and there was no metabolic or renal dysfunction. The patient was evaluated as MTF- associated LA and taken to the intensive care unit. Hydration with isotonic saline began and hemodialysis (HD) treatment was decided. Abnormal laboratory parameters were partially ameliorated with HD, but in the next few days HD was executed 2 more times. With supportive therapy and 3 sessions of HD, clinical and laboratory findings of the patient were improved within following week and, values were as follows; urea: 44 mg/ dL, creatinine: 0.9 mg/ dL, pH: 7.43; HCO₃: 23.7 mmol/ L, pCO₂: 38 mmHg, lactate: 2.2 mmol/ L respectively. On abdominal ultrasound, size of both kidneys were found to be below normal. After being discharged from the hospital, control examinations did not reveal any abnormal value (Figure 1).

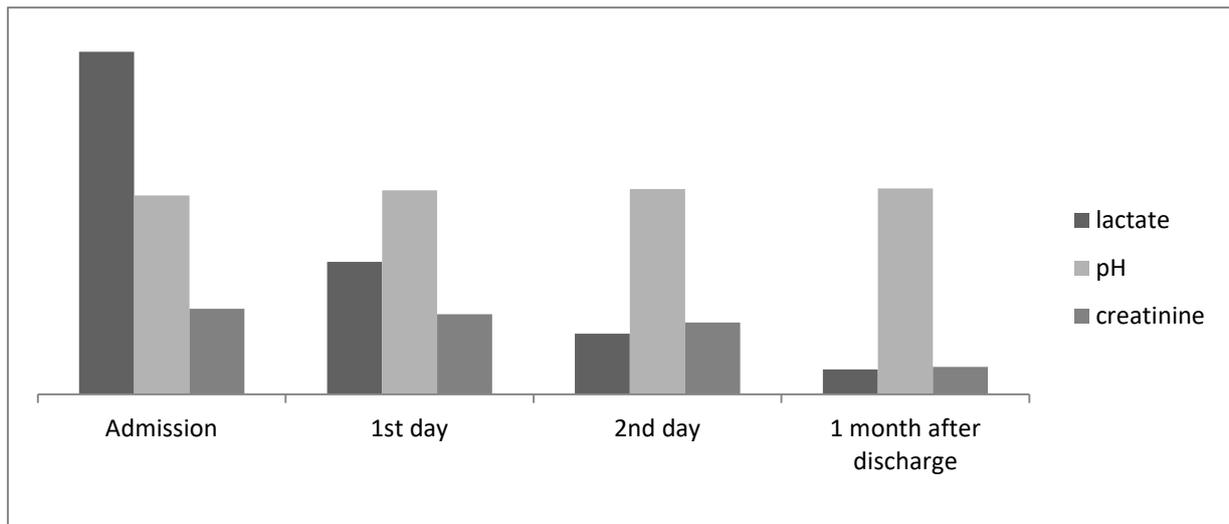


Fig 1: Survey of laboratory values of the patient

DISCUSSION

MTF is a generally well-tolerated, effective and inexpensive anti-diabetic agent. In addition to its oral anti-diabetic property, its numerous positive effects on cardiovascular system has been shown in patients with diabetes and insulin resistance. Unchanged MTF molecule is mainly excreted by the kidneys, via filtration and active tubular secretion [1, 2].

In fact, MTF possesses a low risk of severe LA in the general diabetic population. On the other hand, MTF should be used with caution in patients with kidney dysfunction. In patients with a glomerular filtration rate (GFR) below 30 ml/min, the use of MTF is also associated with a high risk of LA [5]. LA is seen in the incidence of 4.3 per 100,000 patient year among patients using MTF. LA is characterized with arterial lactate concentrations of ≥ 5 mmol/L, blood pH of ≤ 7.35 and usually occurs in hypoxic conditions. LA is divided into type A and B. Type A is more common and occurs in patients with impaired tissue perfusion. On the other hand, type B occurs due to some drugs, toxins or genetic disorder that causes lactate accumulation. One of the reasons of type B LA has been reported as MTF. LA is an urgent clinical situation that requires rapid diagnosis and treatment and has a mortal course in 50% of the cases. Treatment includes fluid replacement, iv sodium bicarbonate and haemodialysis [6].

In particular, patients with kidney failure are known to benefit from HD. Richy FF *et al*; [7]. Determined that LA incidence did not differ significantly between MTF using patients with normal and various degrees of renal dysfunction in their study published in 2014 that they investigated a total of 77,601 patients treated with metformin for type 2 diabetes.

CONCLUSION

In our case, the use of Metformin is considered to be the factor that induced lactic acidosis. Because no ischemic, renal or metabolic problem, that may cause this state, was determined in this patient. With rapid diagnosis and treatment, improvement was observed.

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