

Lactic Acidosis Due to the Use of Metformin in Patients with Heart Failure: A Case Report

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Abstract: Metformin, commonly used in patients with type 2 diabetes mellitus (DM), is a reliable oral antidiabetic agent in the group of biguanides. These agents are effective by increasing cellular insulin sensitivity. They do not cause hypoglycaemia, even at very high doses, because they exhibit their effects with an antihyperglycemic effect from the pathway of hypoglycaemia. An eighty-year-old male patient was admitted to the emergency department with complaints of general malaise, nausea, vomiting, abdominal pain, shortness of breath. Story is that hypertension, type 2 diabetes mellitus, heart failure and chronic obstructive pulmonary disease (COPD) are diagnosed; Metformin, ramipril + hydrochlorothiazide, diltiazem and inhaler treatments. Laboratory findings: BUN: 26 mg / dL, Cr: 1,2 mg / dL, K: 4.83 mmol / L, Pco₂:46, arterial blood gas pH: 7.27, HCO₃: 13,3 mmHg, lactate level: 6.1 mg / dl. Urinalysis is glucose and ketone negatif. The patient was diagnosed with heart failure and metformin-related lactic acidosis. Metformin was cut immediately and emergency hemodialysis was planned. Parenteral 0.9% NaCl, neutralized glucose - insulin solution, NaHCO₃ infusion therapy was started. A dramatic improvement was noted in the patient's follow-up and there was no need for dialysis. In the literature, hemodialysis is the first treatment approach in cases, but we have achieved a very positive outcome without needing hemodialysis.

Keywords: biguanide, type 2 diabetes mellitus, metformin

INTRODUCTION

Metformin is a biguanide commonly prescribed in the treatment of patients with type II diabetes starting from prediabetes. It increases sensitivity to insulin action and improves glycemic control and lipid profile. Major side effects are associated with the gastrointestinal tract and include abdominal pain, diarrhea and vomiting [1]. Metformin is eliminated by the kidneys by both glomerular filtration and tubular secretion [2]. Lactic acidosis is a serious complication with high mortality and is a rare complication in patients using this drug [3]. The combination of some clinical conditions such as dehydration, hypoxemia and the use of nephrotoxic drugs may facilitate the development of lactic acidosis [4]. It is estimated that the mortality rate due to metformin-associated lactic acidosis is over 50%. As a result of the studies done, it has been stated that there is no prognostic value of lactate level and serum metformin level [5, 6].

CASE REPORT

We present a patient with deep metabolic acidosis using metformin. Clinical situation improved without supportive management and dialysis treatment. The 81-year-old man has been admitted to the emergency room for the past two days with general discomfort, agitation, nausea, vomiting, abdominal pain and shortness of breath. Type II diabetes mellitus,

hypertension, mild congestive heart failure and chronic obstructive pulmonary disease were recorded in the medical history. He was on treatment with metformin (1000 mg twice a day), diltiazem (90 mg three times a day) and besides the inhaler medications. At admission, mild mental confusion, agitation and a deep and frequent breathing pattern were noted. Arterial blood pressure was measured as 105/60 mmHg, body temperature was 36.4o C, respiratory rate was 25 breaths per minute, pulse rate was 94 beats per minute and pulse oximetry showed 87% oxygen saturation. Physical examination revealed dry appearance of mucosa, decreased turgor of skin, tachypnea, prolonged expiration during breathing, few sibilant rhonchi. His laboratory test results were as follows; blood urea nitrogen: 26 mg/dl (normal range (NR): 7-20) mg/dl, creatinine: 1,2 mg/dl (NR:0.9-1.3 mg/dl), serum glucose: 156 mg/dl (NR: 70-100 mg/dl), potassium: 4,83 mmol/L (NR:3.5-5.1 mmol/L), sodium: 141 mmol/L (NR: 136-146 mmol/L), hemoglobin: 11.6 g/dl (NR:13.5-17.5 g/dl), White blood cell count: 6630/mm³ (NR:4500-11000 /mm³), thrombocytes: 232000/mm³ (NR: 130000-400000 /mm³), arterial blood pH: 7.27 (NR: 7.35- 7.44), bicarbonate (HCO₃): 11.3 mmol/L (NR: 20-26 mmol/L), partial oxygen pressure: 74 mmHg (NR: 80-98 mmHg), blood oxygen saturation: 90%, partial carbon dioxide pressure: 19 mmHg (NR: 36-43 mmHg), lactate level: 104 mg/dl (NR: 5-22 mg/dl) and blood anion gap: 23,7 mEq/L (NR: 8-12

mEq/L). The urine examination revealed a density of 1025, but not for glucose or ketone. Renal Doppler ultrasonographic examination revealed normal-sized kidneys with mild increase in parenchymal echogenicity. The patient was considered to be suffering metformin-associated lactic acidosis (MALA). Intravenous NaHCO₃ supplementation in 0.9% NaCl solution (every 5 ml containing 1 mEq NaHCO₃) at a rate of 2 ml/kg/hour and 10% dextrose solution (containing 1 unit regular insulin for every 5 gr of glucose) at a rate of 1 ml/ kg/hour and nasal oxygen were started in the emergency room. The NaHCO₃ dosage was arranged closely with repeated pH measurements. Acute hemodialysis was planned due to the profound metabolic acidosis. On the following day, the patient was transferred to the nephrology clinic with values of pH: 7.30, HCO₃⁻: 18.4 mmol/L. The general condition was somewhat improved and the agitation decreased. He was discharged at the third day of hospitalization with the following laboratory results: pH 7.40, HCO₃⁻ 28 mEq/L.

DISCUSSION

Metformin-associated lactic acidosis (MALA) should be kept in mind in the differential diagnosis of metabolic acidosis in elderly patients with predisposing conditions [7]. Metformin is contraindicated in renal insufficiency (serum creatinine > 1.4 mg / dL in women and > 1.5 mg / dL in men), severe congestive heart failure and hepatic insufficiency have been reported [8]. Metformin should be used more carefully in clinical situations, such as dehydration, hypoxemia and concomitant nephrotoxic agents, since lactic acidosis may develop more easily. We discussed a MALA case in an old patient. Blood metformin concentration could not be measured, but there was no clinical evidence for tissue hypoperfusion and seriously disturbed tissue oxygenation suggesting metformin as the cause of lactic acidosis. In our case, the choice of the first treatment strategy in MALA cases may vary depending on the hemodynamic and respiratory failure of the patients [8]. Some reports suggested hemodialysis as the first treatment model to improve acidosis and achieve rapid drug elimination [9]. In our case, close monitoring and intravenous fluid resuscitation and sodium bicarbonate administration were positive results. In conclusion, conservative approaches, including appropriate parenteral hydration and parenteral sodium bicarbonate administration under close monitoring, may be a rescue strategy in patients with special contraindications for invasive procedures, even in the presence of severe acidosis.

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