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Case report

How to explain a PaO2 of 140 mmHg in a venous line?

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Abstract. Metformin is a commonly used oral antidiabetic drug which can cause lactic acidosis. Although rare, this condition carries a high mortality risk. Correction of metabolic acidaemia is essential for treatment and dialysis with bicarbonate replacement is the gold standard approach. A 53-year-old man with diabetes on metformin therapy was admitted to the intensive care unit with severe lactic acidosis and acute renal failure suggesting metformin intoxication. The lactic acidosis was treated with bicarbonate haemodialysis and his pH normalized after 10 hours, but he died because of myocardial infarction due to severe hypotension. At ICU admission an aortic dissection was also hypothesized but TEE did not evidence aortic dissection. The dilemma in this patient was represented by the abnormal PaO2 value (140 mmHg) in the venous blood gas analysis. Considering that metformin acts on mitochondrial respiration, the dilemma may be explained by hypothesizing a cellular respiration block caused by metformin or severe acidosis. (www.actabiomedica.it)

Key words: Metformin, lactic acidosis, acute renal failure, dialysis, cellular respiration, blood gas analysis, oxygen partial pressure

Introduction

Metformin is a biguanide oral hypoglycaemic agent that is commonly used in the treatment of diabetes mellitus (1). Lactic acidosis is the major toxic effect of metformin and it is associated with high mortality (2). Bicarbonate haemodialysis is the gold standard treatment and should be performed early in the course of management, especially in patients with severe metabolic acidosis who fail to respond to intravenous bicarbonate therapy or in whom renal failure is present (3-5). We report a fatal case of severe lactic acidosis and acute renal failure in a diabetic patient treated with metformin.

Case report

A 53-year-old patient with severe lactic acidosis was admitted to the intensive care unit for resuscitation and renal replacement therapy with a diagnosis of metformin intoxication.

The medical history showed multiple coronary stenting, hypertension, atrial fibrillation and diabetes on oral medications (metformin 850 mg TID). Serum creatinine was 1.2 mg/dl (106,08 μmol/L) thirty days before and 13 mg/dl (1149,2 μmol/L) at hospital admission, documenting acute renal failure.

On ICU admission the striking findings were represented by: lactate 30 mmol/L, creatinine 13 mg/dl (1149,2 μmol/L), non invasive arterial pressure 60/30 mmHg (with dopamine 20 μg/kg/min) and pH 6.5. The patient was unconscious (GCS=3), anuric and anemic (Hb=8.6 g/dl).

Aortic pressure rose to 90/50 mmHg with norepinephrine 0.4 μg/kg/min and epinephrine 0.4 μg/kg/min administration.

Right femoral vein was cannulated under ultrasound guidance and a dialysis catheter was inserted. Right and left internal jugular veins were cannulated for fluid and drug infusion. Left femoral artery was cannulated but showed no pulse. Before starting the dialytic treatment we checked the blood gas analysis from the right femoral venous vascular access and obtained a PaO2 of 140 mmHg: this value was confirmed several times. The same result was repeatedly reported from the other venous vascular accesses and dialysis was started.

The picture was complicated by the suspicion of ascending aortic dissection: PaO2 140 mmHg in a non pulsatile vascular access (false lumen?), severe hypotension with anemia, right radial artery as the only arterial access with a pulse wave, TEE with a mirroring effect resembling aortic dissection type A (with no involvement of the descendent tract). A repeated TEE examination by a second operator excluded the diagnosis of aortic dissection.

In order to explain the abnormal findings of blood gas analysis we considered the hypothesis of mitochondrial dissociation (similar to that of carbon monoxide intoxication) but a PubMed search did not confirm our hypothesis.

PH normalized 10 hours later with bicarbonate haemodialysis. After 24 hours of renal replacement therapy the blood gas analysis performed from the in situ vascular access evidenced venous values (PaO2=40 mmHg).

TEE showed a normal kinesis (under high dose cathecolamines) at ICU admission, but the patient died 40 hours after because of myocardial infarction due to severe hypotension (cardiac troponin I=25 ng/ml (25 μg/L)).

Post-mortem examination did not evidence aortic dissection and confirmed that the venous cannulae were correctly positioned.

Discussion

Metformin is a biguanide and its glucose-lowering effects are mainly a consequence of reduced hepatic glucose output (primarily through inhibition of gluconeogenesis, but also of glycogenolysis) and increased insulin-stimulated glucose uptake in skeletal muscle and adipocytes (1).

Metformin can cause lactic acidosis by peripherally increasing lactic acid production while impairing its removal by the liver and kidney. Although rare, this condition carries a high mortality risk (2). Correction of metabolic acidaemia is central to treatment. Sodium bicarbonate is the most commonly used agent in mild forms, even if well-known problems associated with its use including leftward shift of the haemoglobin dissociation curve, excess sodium load, rebound metabolic alkalosis, disturbances in serum potassium and calcium, decreased myocardial contractility and increased carbon dioxide production are present. Considering that metformin is excreted unmetabolized from the kidney, dialysis with bicarbonate replacement fluid is the gold standard treatment in severe cases because it not only corrects the acidosis but it also removes this drug from plasma, preventing further lactate over-production (3-5).

In our patient metformin intoxication was properly treated with bicarbonate haemodialysis and the pH normalized (7.43) after 10 hours of treatment.

The dilemma was represented by the abnormal PaO2 value (140 mmHg) in the venous blood gas analysis. Considering that metformin acts on mitochondrial respiration (1), could this problem be explained by hypothesizing a metformin-related cellular respiration block or by severe acidosis? A disruption of the respiratory chain in the hepatocyte mitochondria with an ensuing reduction of gluconeogenesis appears a possibility.

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