Lactic acidosis from metformin in Emergency Room

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Summary

Lactic acidosis is a metabolic alteration that can evolve in any reduced tissue hypoxic state in case of hepatic dysfunction, pulmonary embolism, and acute myocardial infarction. Signs and symptoms of acidosis are not always easily noticeable. In fact acidosis can be asymptomatic or can be accompanied by vague asthenia, nausea or vomiting. A distinctive symptom of acidosis is hyperpnoea, an increased depth followed by an increased frequency of breathing. Severe acidosis can determine cardio circulatory shock due to a reduced myocardial contractility or progressive sensory alteration.

KEY WORDS: lactic acidosis, metformin, type 2 diabetes.

Introduction

F.B., a 48-year-old woman, presents at Emergency Room complaining for chest and abdominal pain associated with recent vomiting episodes. In the remote pathological anamnesis the patient appears affected by type 2 diabetes mellitus treated with metformin 1000 mg at meals. She also presents high blood pressure treated with lisinopril 20 mg associated with idroclortiazide 12,5 mg, amlodipine 5 mg, daxozi- na 4 mg. The patient hyperventilates, at the chest she presents physiological murmurs, her heart rate is 75 bpm and blood pressure is 120/50 mmHg. The abdomen is globose due to adipis but it is treatable, it is not painful at superficial and deep palpation.

An ECG is performed and it shows a normal sinus rhythm. ST-T tract does not show alterations. Hematochemical examinations are performed and reveal: 4,650,000 mc/L red blood cells; 11,9 g/dl haemoglobin; 72,8 middle globular volume; 11,020 mc/l white blood cells; 331,000 mc/L platelets. Patient is submitted to a renal echography that shows regular sized kidneys, with a dense parenchymal thickness, weakly hypoechoic, without dilution of the kidney drainage system. A therapy with furosemide in high doses (250 mg e.v.) is undertaken, hydration, 15 phials of sodium bicarbonate are performed and a magnesium hydroxide for high phosphorus is given. Patient becomes oliguric.

Hematochemical examinations, that do not show any sign of improvement, and a new continuing hemogas-analysis are repeated and show lactic acidosis with an increase of lactates (14,7 mmol/L), pH 7,18. Since the patient is oliguric, a central venous catheter is inserted and she is invited to undergo a dialysis session. During dialysis the patient shows a worsening of the hemodynamic condition but she is retrieved and undergoes an only one-hour dialysis session. She is submitted to other five dialytic sessions during the confinement associating hydration and furosemide and glicemia treatment is started with low doses of rapid insulin. Creatinine values now are 3 mg/l, it is decided to continue only with hydration and diuretic. At discharge, the patient presents 1 mg/dl creatinine.

Discussion and Conclusions

This clinical case shows a rare but extremely serious metabolic complication of metformin: lactic acidosis. Drugs containing metformin show a Boxed Warning regarding this serious adverse reaction (1, 2). Life-threatening lactic acidosis can occur due to accumulation of metformin. The main risk factor is renal alteration; other risk factors include older age associated with a reduced renal function, and high doses of the medicine (> 2 g/die). Metformin is contraindicated in acute conditions associated with a potential compromise of renal function, like dehydration (3-5).

Since 1985, the Therapeutic Goods Administration has received 141 signals of lactic acidosis associated with metformin, 25 of them with a fatal result. Lots of signals described a recent story of diarrhea, vomiting or
gastrointestinal infection before the development of acidosis.

Cases of individuals with lactic acidosis treated with metformin, diuretics, ace-inhibitors that presented at first nausea, vomiting and diarrhea are reported in literature. In one case the individual died from shock; in another case the emergency dialysis proved decisive (6).

If patients who take metformin have vomiting and/or diarrhea episodes, in concomitance with a poor food intake, it should be taken into consideration the possibility to temporarily suspend metformin until the return to a normal diet. Besides, diuretic treatment should be suspended. Lactic acidosis treatment should take account of the triggering causes, adequate oxygenation and vascular perfusion of tissues, rehydration and infusion of sodium bicarbonate (only in case of severe acidosis with a ph less than 7) to elevate ph over 7.2, together with insulin and glucose. When sodium is badly tolerated, haemodialysis can be considered a useful alternative (7-9).

The mortality rate associated with this condition is > 50 per cent.

References