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### Case report

## Metformin-related lactic acidosis: Case report<sup>☆</sup>

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#### ABSTRACT

Lactic acidosis is defined as the presence of pH <7.35, blood lactate >2.0 mmol/L and PaCO<sub>2</sub> <42 mmHg. However, the definition of severe lactic acidosis is controversial. The primary cause of severe lactic acidosis is shock. Although rare, metformin-related lactic acidosis is associated with a mortality as high as 50%. The treatment for metabolic acidosis, including lactic acidosis, may be specific or general, using sodium bicarbonate, trihydroxymethane, carbicarb or continuous haemodiafiltration. The successful treatment of lactic acidosis depends on the control of the aetiological source. Intermittent or continuous renal replacement therapy is perfectly justified, shock being the argument for deciding which modality to use. We report a case of a male patient presenting with metformin poisoning as a result of attempted suicide, who developed lactic acidosis and multiple organ failure. The critical success factor was treatment with continuous haemodiafiltration.

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### Acidosis láctica por metformina: reporte de caso

#### RESUMEN

Definimos acidosis láctica en presencia de pH <7.35, lactato en sangre >2.0 mmol/L y PaCO<sub>2</sub> <42 mmHg. Por otro lado, la definición de acidosis láctica grave es controvertida. La causa principal de acidosis láctica grave es el estado de choque. La acidosis láctica por metformina

##### Palabras clave:

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Bicarbonato de sodio  
Terapia de reemplazo renal  
Ácido láctico

es rara pero alcanza mortalidad del 50%. La acidosis metabólica incluyendo a la acidosis láctica puede recibir tratamiento específico o tratamiento general con bicarbonato de sodio, trihidroxiaminometano, carbicarb o hemodiafiltración continua. El éxito del tratamiento de la acidosis láctica yace en el control de la fuente etiológica; la terapia de reemplazo renal intermitente o continua está perfectamente justificada, donde el argumento para decidir cuál utilizar será el estado de choque. Presentamos el informe de un caso de un paciente masculino con intoxicación por metformina como intento suicida, quien desarrolló acidosis láctica y falla orgánica múltiple en cuya base para el éxito del caso fue el tratamiento con hemodiafiltración continua.

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## Introduction

Lactic acidosis is defined as the presence of pH <7.35, blood lactate >2.0 mmol/L and PaCO<sub>2</sub> <42 mmHg. However, the definition of severe lactic acidosis is controversial. Many physicians associate the severity of lactic acidosis with pH <7.2 or with deleterious effects, mainly haemodynamic, requiring immediate treatment.<sup>1-3</sup> The main cause of severe lactic acidosis is shock, associated with a mortality as high as 50% despite adequate aetiological treatment, and 100% when pH is lower than 7.0.<sup>4,5</sup>

However, an uncommon cause of lactic acidosis is metformin poisoning, with a mortality as high as 50%. The incidence is 3 cases for every 100,000 patients treated per year. The main risk factor for the occurrence of metformin-related lactic acidosis is the renal impairment present in diabetic patients. Voluntary poisoning is rare and its characteristics and prognosis are seldom reported in the literature. It appears that blood levels of metformin are not a determining factor of the outcome in the intoxicated patient, whereas blood lactate >15 mmol/L, pH <7.2, organ dysfunction (≥4 points), and lower prothrombin activity (≤50%) are considered risk factors for mortality.<sup>6,7</sup> We report the case of a patient intentionally poisoned with metformin who developed multiple organ dysfunction, in whom the critical success factor to resolve the clinical picture was continuous haemodiafiltration.

## Clinical case

We present the case of a 74-year-old male patient coming from Veracruz, Mexico, with a history of diabetes mellitus type 2 diagnosed 26 years before, treated with metformin 850 mg/day and glibenclamide 10 mg/day, a diagnosis of schizophrenia-type psychiatric disorder irregularly treated with olanzapine, and no other relevant history. Following the intentional intake of 20 tablets of metformin, the patient developed a clinical picture characterised by nausea, vomiting and drowsiness, followed 24 h later by epistaxis, diaphoresis, and loss of consciousness which prompted transfer for assessment.

Upon arrival to the emergency department, the patient was placed on invasive mechanical ventilation (IMV) because of his neurological condition, and required the use of vasopressors because of haemodynamic instability with altered

**Table 1 – Biochemical and haemodynamic variables for hospital admission.**

Biochemical		Haemodynamic	
pH	7.0	Arterial pressure	90/50 mmHg
Lactate	>15 mmol/L	Heart rate	50 lpm
HCO <sub>3</sub> <sup>-</sup>	9.4 mEq/L	Norepinephrine	0.4 mcg/kg/min
Urea	72.8 mg/dL	Dopamine	0.2 mcg/kg/min
Creatinine	2.9 mg/dL	CO	5 L/min
Potassium	6.4 mEq/L	CI	2.8 L/min/m <sup>2</sup> BS
Glucose	60 mg/dL		

pH: negative log of hydrogen ion concentrations; HCO<sub>3</sub><sup>-</sup> bicarbonate; CO: cardiac output; CI: cardiac index; BS: body surface.  
Source: Authors.

nodal-type cardiac rhythm. The initial blood work revealed hyperlactatemia (>15 mmol/L), hypoglycaemia, hyperkalemia and acute kidney injury (AKI 3) (Table 1).

The patient was admitted to the intensive care unit (ICU) with a diagnosis of severe lactic acidosis secondary to metformin intoxication, an APACHE II score of 25 and a SOFA score of 9. Slow continuous renal replacement therapy (CRRT) was started with haemodiafiltration using a Prisma-Flex<sup>®</sup> equipment; it was maintained for 48 h with an effluent dose of 25 ml/kg/h, achieving clinical and laboratory improvement characterised by a reduction in potassium levels, diminished nitrogen compounds, acidosis reversal, and lactate clearance of more than 50% in 24 h and 90% at 48 h. As a result, the patient was extubated, vasopressors were discontinued, and the patient was discharged from the ICU after 72 h (Table 2). The patient gave his consent for the publication of the case report, and approval was also obtained from the hospital's local Ethics Committee.

## Pathophysiology of metformin-related lactic acidosis

Metformin is a biguanide and the first drug of choice for blood sugar control in patients with DM type 2 because of its metabolic and cardiovascular benefits.<sup>8</sup> The most frequent adverse effects related to its use are gastrointestinal, including nausea, vomiting and diarrhoea. However, the most feared adverse effect is lactic acidosis.<sup>7,9</sup> Pyruvate-derived lactate is the end product of glycolysis in anaerobic conditions. Humans produce 1500 mmol of lactate per day (0.8 mmol/kg/h) in

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