CASE REPORT

Lactic acidosis in diabetic ketoacidosis

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SUMMARY

We describe the case of a 22-year-old man with insulin-dependent diabetes, who was admitted to the emergency department with hypotension, unconsciousness and a severe combined diabetic ketoacidosis (DKA) and lactic acid acidosis. In the discussion, we focus on the pathophysiological mechanisms underlying lactic acidosis in DKA, and we elaborate on the prognostic value of hyperlactataemia on such occasion.

BACKGROUND

Lactate acidosis is a common finding in diabetic ketoacidosis (DKA). Although hyperlactataemia is generally thought to result from anaerobic glycolysis due to (relative) tissue hypoperfusion, other pathophysiological mechanisms may also be responsible for the extremely high lactate values sometimes found in patients with ketoacidosis.

CASE PRESENTATION

A 22-year-old man with insulin-dependent diabetes was admitted to the emergency department (ED) by the Helicopter Emergency Medical Service (HEMS) after having been found unconscious. He was on insulin (Lantus and Humalog), and used no other medications. When the HEMS physician arrived, he had a marked Kussmaul's breathing pattern, a sinus tachycardia of 117 bpm and a blood pressure of 67/30 mm Hg. His Glasgow Coma Scale was 1-1-1, and he had dilated pupils that were unresponsive to light. Otherwise, physical examination was unremarkable; in particular there was no evidence of a systemic infection. During examination he started having a tonic clonic seizure that was terminated with midazolam and propofol, after which he was intubated, ventilated and transported to the hospital. Since hypotension was refractory to normal saline infusion, repeated epinephrine boluses (10 µg) were administered during transport.

INVESTIGATIONS

First arterial blood gas analysis after arrival in the ED demonstrated a plasma glucose of 59.0 mmol/L, pH 6.57, partial pressure of carbon dioxide 3.3 kPa, bicarbonate 2.0 mmol/L, partial pressure of oxygen 51.9 kPa, lactate 13.3 mmol/L, sodium 149 mmol/L and potassium 3.9 mmol/L. Haemoglobin (Hb) was 7.5 mmol/L, leucocytes 41.6×10^9/L, C reactive protein 1 mg/L, urea 12.5 mmol/L and creatinine 165 µmol/L. The ECG was normal apart from sinus tachycardia.

TREATMENT

The patient was transferred to the intensive care unit (ICU), where he was mechanically ventilated, while the acidosis was treated by starting on a normal saline (and later glucose 5%) infusion with potassium suppletion, and intravenous (NovoRapid) insulin.

OUTCOME AND FOLLOW-UP

Metabolic derangements normalised within 36 h, after which the patient could be extubated making a full neurological recovery.

DISCUSSION

Lactate acidosis is a common finding in DKA. Several pathophysiological mechanisms are responsible for the extremely high lactate values sometimes found in patients with ketoacidotic. Originally, elevated lactate values in patients with DKA were thought to be the result of inadequate tissue perfusion and oxygenation (due to a contracted intravascular volume, aggravated by the presence of macrovascular disease and microangiopathies, an increased amount of glycosylated Hb, and an abnormal platelet function).[1–3] The resulting relative hypoxaemia stimulates the process of anaerobic glycolysis, where pyruvic acid is converted to L-lactate, yielding two ATP molecules.

More recently, however, it was demonstrated that the metabolic derangements itself present in DKA might contribute as well to the elevated lactate levels.[4] Various studies have reported the presence of a positive correlation between glucose levels and ketone (β-hydroxybutyrate) levels on the one hand, and lactate levels on the other hand.[4 5] This could be explained by various intracellular and extracellular mechanisms. First, an increased amount of D-lactate is formed in erythrocytes. Since erythrocytes do not require insulin for glucose uptake, intracellular glucose concentrations approach ambient extracellular levels during ketoacidosis. A substantial portion of the glucose in the erythrocyte is converted to pyruvate and finally L-lactate by aerobic glycolysis to produce ATP. The remainder is metabolised by the sorbitol pathway and the pentose-phosphate shunt to produce methylglyoxal, which is a toxic endogenous glucose metabolite, that is degraded by the glyoxalase system to produce D-lactate. Methylglyoxal (and thereby D-lactate) is also formed directly in the plasma via an interaction between glucose and proteins and via aminoacetone degradation directly in the plasma.[5 6] Lu *et al*[5] demonstrated that D-lactate levels could be as high as 10 mmol/L in DKA, significantly contributing to both acidosis and anion gap.

The D-lactate and L-lactate formed by these intracellular and extracellular mechanisms during DKA can be shunted to the liver as a substrate for gluconeogenesis (Cori cycle), or they can be utilised by the erythrocytes where they are formed. Alternatively, they can be shunted to anatomically

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Learning points

- Lactate acidosis is a common finding in diabetic ketoacidosis (DKA).
- Lactate acidosis in DKA is multifactorial in aetiology—anaerobic glycolysis due to inadequate tissue perfusion and oxygenation as well as the metabolic derangements itself present in DKA might contribute to the elevated lactate levels.
- The 'alternative fuel hypothesis' is a possible explanation why the outcome of lactic acidosis in DKA could be more favourable than would be anticipated based on the actual lactate levels.

distributed tissues (eg, heart and brain) for utilisation.[7] This latter mechanism provides vital tissues an alternative oxidisable substrate when glucose is unavailable as a result of the hypoinsulinaemic state of DKA. We hypothesise that, as in patients with isolated traumatic brain injury where cerebral hyperglycolysis is associated with a better neurological outcome,[8] patients with DKA might benefit from their hyperlactataemia. A recently published observational study from Cox *et al*,[4] where they could not demonstrate a relation between the degree of hyperlactataemia and ICU length of stay in patients with DKA, is not in contradiction with this hypothesis. However, neither in their study, nor in our case separate plasma concentrations of D-lactate (as a measure of metabolic derangements) and L-lactate (as a measure of tissue hypoxia) were determined, making it hard to draw causal relations between the hypothesised pathophysiological process and favourable outcome.

Although further research is warranted to explore this 'alternative fuel hypothesis', our case underscores that it is important for clinicians to realise that, although hyperlactataemia is generally related to a poor prognosis,[9 10] elevated lactate levels do not always (solely) result from hypoperfusion. Metabolic derangements (like those present in DKA) may play an (additional) role as well, and in such case, the outcome could be more favourable than would be anticipated based on the actual lactate levels.

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Competing interests None.

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