Sustained low-efficiency dialysis as a treatment modality in a patient with lymphoma-associated lactic acidosis

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Introduction

Lactic acidosis is a potentially life-threatening metabolic disorder, initiated by an imbalance between lactic acid production and utilization. The only effective treatment is reversal of the cause of the disordered lactic acid metabolism [1]. Intravenous bicarbonate (HCO₃⁻) administration is often used as an interim treatment to attempt to ameliorate the effects of the acidosis, particularly ventilatory fatigue and haemodynamic instability [2,3], even though this treatment has not been shown to improve either haemodynamic stability or overall survival [4]. The ability of bicarbonate to correct the metabolic acidosis is limited by complications from rapid administration of hypertonic fluid and by alkali-induced stimulation of lactic acid production [1]. Lactic acidosis associated with haematological malignancies is a rare condition, where the latter effect is best illustrated [5]. To avoid the problem of hypertonic fluid administration, continuous renal replacement therapy has been used to try to correct metformin-associated lactic acidosis [6]. In this report, we describe a patient with undiagnosed B-cell lymphoma who presented with severe lactic acidosis requiring intubation and ventilatory support. The acidosis was corrected by delivering large amounts of alkali, using sustained low efficiency dialysis (SLED), despite evidence of continuous or even increased lactic acid production. This treatment stabilized the patient until chemotherapy was initiated and halted the abnormal lactic acid metabolism.

Case

A 65-year-old man, with a history significant only for cardiac bypass surgery 10 years earlier, presented with myalgias, severe fatigue, abdominal pain with distention, confusion for a week and loss of appetite, with about 20 pounds weight loss. He was initially admitted to another hospital with hypoglycaemia and metabolic acidosis (pH 7.13, pCO₂ 25 mmHg, calculated [HCO₃⁻] 8 mmol/l), and serum lactate level of 17 mmol/l (0.7–2.1). The serum anion gap was 28 mmol/l. His renal function was normal [serum creatinine 1.3 mg/dl (0.7–1.5)]. Intravenous HCO₃⁻ failed to correct the acidosis. He was intubated due to respiratory fatigue and transferred to our hospital for further management. On admission, the patient was afebrile, normotensive (blood pressure 118/70 mmHg) but tachypneic (respiratory rate 20 breaths/min). Physical examination was otherwise unremarkable. Arterial blood gases revealed pH 7.23, pCO₂ 33 mmHg and calculated [HCO₃⁻] 13.5 mmol/l, and serum lactate level of 17 mmol/l (0.7–2.1). The serum anion gap was 28 mmol/l. His renal function was normal [serum creatinine 1.3 mg/dl (0.7–1.5)]. Intravenous HCO₃⁻ failed to correct the acidosis. He was intubated due to respiratory fatigue and transferred to our hospital for further management. On admission, the patient was afebrile, normotensive (blood pressure 118/70 mmHg) but tachypneic (respiratory rate 20 breaths/min). Physical examination was otherwise unremarkable. Arterial blood gases revealed pH 7.23, pCO₂ 33 mmHg and calculated [HCO₃⁻] 13.5 mmol/l. Arterial pO₂ ranged from 90 to 120 mmHg on 0.35 fractional inspired oxygen concentration. Other pertinent laboratory findings included serum glucose 86 mg/dl, aspartate aminotransferase 271 IU/l (<50 IU/l), alanine aminotransferase 159 IU/l (15–75), alkaline phosphatase 146 IU/L (<126 IU/l), and total bilirubin 2.2 mg/dl. Complete blood count revealed leucocytosis (WBC 17 000/mm³) and thrombocytopenia (platelets 39 000/mm³). Despite additional intravenous bicarbonate administration and maximal ventilatory support, his serum pH dropped further below 7.15. Sustained low-efficiency dialysis (SLED) was then initiated with an F5 dialysis membrane (Fresenius, polysulphone) and a blood flow rate of 200 ml/min, with the dialysate [HCO₃⁻] 26 mmol/l,
at a flow rate of 200 ml/min. Sodium phosphate (70.5 mmols/gallon) was also added to the dialysate to manage serum phosphorus. Twelve hours later, the serum [HCO₃⁻] was 17 mmol/l and the dialysate [HCO₃⁻] was increased to 36 mmol/L. At this time, the blood was simultaneously sampled from the ‘arterial’ and ‘venous’ ports of the extracorporeal circuit for [lactate] and [HCO₃⁻]. ‘Arterial’ lactate and HCO₃⁻ concentrations were 11.8 and 22 mmol/l respectively, while ‘venous’ lactate and HCO₃⁻ concentrations were 4.3 and 33 mmol/l respectively (Figure 1). The patient’s haematocrit at the time of these measurements was 27%. The increase in his serum [HCO₃⁻] resulted in no change in his blood pressure. Minute ventilation was maintained high at 161/min for the first four treatment days. It was reduced on the fifth day for 24 h prior to extubation as the pH increased. A bone-marrow biopsy showed a large B-cell type (non-Hodgkin’s) lymphoma and liver biopsy verified lymphoid infiltration. Chemotherapy was started on day five. By day 6 his serum (lactate) decreased abruptly, the serum [HCO₃⁻] rose to the normal range and SLED was discontinued. Acidosis did not recur during his hospitalization, which was prolonged because of severe peripheral neuropathy most likely secondary to vincristine use. He was finally discharged to a rehabilitation facility.

Discussion

In this case, SLED was used to correct acidemia in lactic acidosis without untoward complications, despite continued production of lactic acid by the tumour cells and/or decreased utilization by the liver. Using SLED the serum [HCO₃⁻] was increased in a stepwise fashion with incremental increases in the dialysate [HCO₃⁻], without causing any major changes in the patient’s extra-cellular fluid (ECF) volume. Serum [HCO₃⁻] increased from 12 to 17 mmol/l and serum pH increased from 7.15 to 7.28 during dialysis treatment with a dialysate [HCO₃⁻] of 26 mmol/l. An increase in dialysate [HCO₃⁻] to 36 mmol/l was followed by an increase in serum [HCO₃⁻] to 22 mmol/l and serum pH to 7.38 until the chemotherapy treatment was initiated. At the same time, other electrolytes such as sodium, phosphorus and potassium were easily controlled in normal range. Note that the change in serum [HCO₃⁻] during dialysis occurred in the absence of a significant fall in serum lactate concentration, indicating continuous lactic acid production and/or decreased utilization (Figure 1).

Measurement of pre- and post-dialysis membrane serum lactate concentration in this case allowed us to estimate the rate of lactate removal by SLED. Based on the inflow and outflow concentration differences, blood flow rate and haematocrit, plasma lactate clearance was 92 ml/min. Assuming no lactate was removed from red blood cells and that serum lactate was stable for 24 h (as shown by our data), at least 1 l mmol/min, or 1577 mmol/day of lactate was removed. Despite the additional route for removal, serum lactate level remained stable at 12–13 mmol/l until chemotherapy was begun. This finding suggests that net lactate production must have increased. Although our observations do not allow us to separate changes in lactate production from changes in lactate utilization, studies in human forearm muscle metabolism indicate that alkali administration increases muscle lactic acid production [7]. It is very likely that in our case, the hepatic utilization of lactate was impaired as well, as indicated by the elevated serum transaminases and by the biopsy findings of lymphoma infiltration of the liver.

Numerous arguments have been made for withholding HCO₃⁻ supplementation in patients with lactic acidosis [2–8]. A major concern is that bicarbonate therapy in lactic acidosis will increase lactic acid production [7]. This remains a problem regardless of whether bicarbonate is given by dialysis or intravenously. In addition to this potentially negative effect, it is difficult to document that increasing the plasma [HCO₃⁻] and pH will improve the vasoconstrictor and inotropic effects of catecholamines [9]. Despite these considerations and although we cannot conclude that our intervention was beneficial in this case, it certainly facilitated our management by removing the issue of acidemia while awaiting diagnosis of the cause and initiation of treatment. Furthermore, we suggest that timely initiation of SLED and correction of the acidemia may obviate the need for intubation and help avoid the complications associated with it. The best therapy for lactic acidosis remains reversal of the cause for increased lactic acid production. If concerns about acidemia arise in the interim, SLED offers a reliable way to raise body alkali stores without the complications that occur in intravenous bicarbonate therapy.

Conflict of interest statement. None declared.
References


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