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Exceptional case

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Lactate clearance and metabolic aspects of continuous high-volume hemofiltration

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Abstract

Lactic acidosis is associated with high morbidity and mortality in hospitalized patients. Treatment of lactic acidosis is targeted on correcting the underlying causes and optimizing adequate oxygen delivery to the tissues. Even though evidence is lacking, continuous renal replacement therapy (CRRT) and dialysis have been advocated as treatments for lactic acidosis. We report a 28-year-old Caucasian male with a history of hemophagocytic lymphohistiocytosis who presented with septic shock, severe lactic acidosis and multiple organ failure. Metabolic acidosis was corrected after bicarbonate therapy and CRRT with a hemofiltration rate of 7 L/h (58 mL/kg/h). Lactate clearance was calculated to be 79 mL/min. Compared with reported rates of lactate overproduction in septic shock, the rate of lactate clearance is quite small. Our case suggests that CRRT with high-volume hemofiltration is not effective for severe lactic acidosis. Lactic acidosis alone should not be considered as a nonrenal indication for CRRT.

Key words: continuous renal replacement therapy (CRRT), lactic acidosis, metabolic acidosis

Introduction

Lactic acidosis is the most common anion gap metabolic acidosis in hospitalized patients [1]. Tissue hypoperfusion in shock, leading to increased anaerobic metabolism, is responsible for the Type A lactic acidosis. Conversely, Type B lactic acidosis occurs without evidence of systemic hypoperfusion and may be seen in association with systemic diseases such as hepatic failure, or malignancies or occur as a result of certain classes of drugs such as biguanides [2, 3]. Increased plasma lactate level (hyperlactatemia) in critically ill patients is associated with high morbidity and mortality [4]. The effective treatment for lactic acidosis (Type A) is correcting the underlying cause and improving tissue oxygenation. Applicable measures include cardiopulmonary support and treatment of sepsis [5]. Even though supporting evidence is lacking, continuous renal replacement therapy (CRRT) is used commonly in the intensive care unit (ICU) to correct acidemia among patients with lactic acidosis and renal failure. We present a case of acute kidney injury (AKI) and severe lactic acidosis from septic shock requiring CRRT. Lactic acidosis improved significantly as the patient achieved more stable hemodynamics. A lactate clearance evaluation was performed to determine the effect of CRRT on lactate removal. We report our findings.

Case presentation

Clinical history

A 28-year-old Caucasian male police officer with a past medical history of hemophagocytic lymphohistiocytosis (HLH) was referred to our hospital from an outside facility for evaluation

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of a 1-week history of fever, acute diarrhea and poor oral intake. The patient was diagnosed with HLH 4 months prior to admission after presenting with fever, pancytopenia and splenomegaly. A bone marrow (BM) biopsy at the time confirmed the diagnosis of HLH which was in the setting of positive Epstein–Barr virus (EBV) titers. The patient was treated with dexamethasone, intravenous (IV) immunoglobulin and etoposide followed by cyclosporine. Surveillance imaging studies, including computerized tomography chest, abdomen, and pelvis and positron emission tomography scan revealed no evidence of malignancy and suggested a good response to therapy. The patient was doing well until his most recent presentation. His initial evaluation at the outside hospital revealed febrile neutropenia and the patient was empirically treated with IV vancomycin and cefepime and then transferred to our hospital for further management. On admission to our hospital, the temperature was 38.5°C, the blood pressure was 116/60 mmHg, the heart rate was 80 beats/min and the weight was 120 kg. The physical examination was normal except for a 2-cm left cervical lymph node that was noted on palpation.

Initial laboratory data and investigations

Laboratory testing, demonstrated in Table 1, revealed serum creatinine 2.6 mg/dL (creatinine was 0.9 mg/dL 3 months prior). Arterial blood gas (ABG) was pH 7.23, pCO_2 24 mmHg, pO_2 101 mmHg, HCO_3 10 mmol/L, indicating an anion gap metabolic acidosis with respiratory compensation (expected pCO_2 of 24–28). The urinalysis demonstrated granular casts and renal epithelial cells consistent with acute tubular necrosis. The patient underwent a cervical lymph node biopsy and a repeat BM biopsy which demonstrated a new diagnosis of peripheral T-cell lymphoma. The stool was positive for *Clostridium difficile*.

Diagnosis

(i) Peripheral T-cell lymphoma; (ii) relapsing HLH; (iii) *C. difficile* colitis; (iv) acute kidney injury; (v) lactic acidosis.

Clinical follow-up

The patient was treated with oral vancomycin for his *C. difficile* colitis, as well as dexamethasone, etoposide, basiliximab, cyclosporin, alemtuzumab, nitrogen mustard and rituximab for relapsing HLH in the setting of concurrent EBV viremia (15 100 copies/mL) and T-cell lymphoma (Figure 1). On Day 2 of hospitalization, the patient developed septic shock and multiorgan system failure requiring multiple vasopressors. Continuous venovenous hemofiltration (CVVH) was started with a replacement fluid rate of 3.6 L/h (30 mL/kg/h), with 50% of the replacement fluid prefilter and 50% postfilter. Anticoagulant citrate dextrose solution A was administered at a rate of 300 mL/h prefilter for anticoagulation. Given the absence of improvement in his hyperkalemia and acid–base status after 8 h, the hemofiltration rate was increased to 7 L/h (58 mL/kg/h) with high bicarbonate (32 mEq/L) and low-potassium (2 meq/L) replacement fluid. Despite the increase in the hemofiltration rate, the patient continued to have persistent hyperkalemia (potassium 6.7 mmol/L) and severe lactic acidosis (pH 7.13 and plasma lactate 20.1 mmol/L). Intermittent hemodialysis (IHD) alternating with CVVH was performed to correct hyperkalemia and severe metabolic acidosis (Figure 1). However, the interruption of CVVH caused worsening volume overload and hypoxemia. The continuous venovenous hemodialysis (CVVHD) with a dialysate rate of 7 L/h and CVVH with replacement fluid at 5 L/h were initiated with the use of two machines (Figure 1). Twenty-four hours after initiating this hemofiltration rate, on Day 6 of hospitalization, the patient's volume status and hemodynamics stabilized with decreasing requirements for vasopressors and an improved serum lactate level of 11.4 mmol/L. We subsequently stopped CVVHD and continued only CVVH with the hemofiltration rate of 5 L/h using one machine. The plasma lactate level continued to decrease to 7.1 mmol/L at a relatively constant rate (Figure 1). Since the rate at which the serum lactate concentration decreased was not different between the lower and higher hemofiltration rates, further investigations were performed.

We measured lactate concentrations in samples of plasma and effluent from our patient to calculate the lactate clearance by the hemofiltration. The patient's calculated lactate clearance was 79 mL/min or 0.56 mmol/min calculated using *UV/P* [6]. The effluent fluid lactate (*U*) was 6.2 mmol/L, the CVVH output (total replacement fluid, citrate and additional volume removed)

Table 1. Laboratory data

Laboratory testing	At presentation	Reference range
Hb (g/dL)	10.7	13.5–17.5
WBC ($\times 10^3$/L)	0.6	3.5–10.5
Neutrophils ($\times 10^3$/L)	0.37	1.7–7.0
Platelet ($\times 10^9$/L)	65	150–450
Serum sodium (mmol/L)	138	135–145
Serum potassium (mmol/L)	4.6	3.6–5.2
Serum chloride (mmol/L)	103	100–108
Serum bicarbonate (mmol/L)	12	22–29
Serum creatinine (mg/dL)	2.6	0.8–1.3
BUN (mg/dL)	62	8–24
Serum albumin (g/dL)	2.3	3.5–5.0
Serum calcium (mg/dL)	8.9	8.9–10.1
Triglyceride (mg/dL)	644	<150
Fibrinogen (mg/dL)	60	200–375
Serum ferritin (μg/L)	91 400	24–336
Plasma lactate (mmol/L)	16.8	0.6–2.3

BUN, blood urea nitrogen; Hb, hemoglobin; WBC, white blood cell.

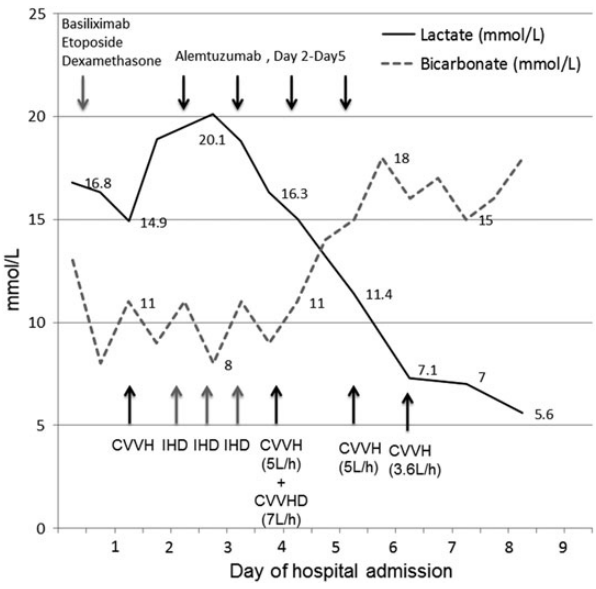

Fig. 1. Demonstrated serum lactate and bicarbonate levels during hospitalization; CVVH, continuous venovenous hemofiltration; CVVHD, continuous venovenous hemodialysis; IHD, intermittent hemodialysis.

(V) was 91 mL/min and the plasma lactate (P) was 7.1 mmol/L. The patient's calculation of lactate clearance and plasma $\text{lactate}_{\text{filter}}$ were demonstrated as following [7]:

$$\begin{aligned}\text{Plasma lactate}_{\text{filter}} = [&(\text{plasma lactate} \times \text{plasma flow rate})\\ &+ (\text{replacement lactate} \times \text{replacement flow rate})\\ &+ (\text{citrate lactate} \times \text{citrate flow rate})]/\ (\text{plasma flow rate}\\ &+ \text{replacement flow rate} + \text{citrate flow rate})\end{aligned}$$

$$\begin{aligned}\text{Plasma lactate}_{\text{filter}} &= [(7.1 \times 153) + (3 \times 42) + (0 \times 1)]/(153 + 42 + 1)\\ &= 6.2\,\text{mmol/L}\end{aligned}$$

$$\begin{aligned}\text{Lactate clearance} &= \text{effluent lactate}\\ &\quad \times \text{effluent rate}/\,\text{plasma lactate}\\ &= 6.2 \times (83 + 1 + 7)/7.1 = 79\,\text{mL/min}\end{aligned}$$

Despite a further reduction in the total CVVH replacement fluid rate from 5 L/h to 3.6 L/min (30 mL/kg/h), the plasma lactic acid level continued to decrease to 5.6 mmol/L with improvement in the metabolic acidosis (ABG, pH of 7.35, pCO_2 of 35 mmHg and HCO_3 of 18 mmol/L). The patient was able to be weaned off of vasopressors with improvement in his mental status to the point that he was able to communicate with his family. Unfortunately, the patient developed massive lower gastrointestinal bleeding from severe thrombocytopenia and ischemic colitis. Clinically, he continued to deteriorate. After discussion with his family, the patient received palliative treatment and passed away peacefully on Day 24 of hospitalization.

Discussion

Lactic acidosis can be classified into Type A which occurs as the result of tissue hypoperfusion and Type B seen in the absence of hypoperfusion and associated with toxin-induced impairment of cellular metabolism as could be seen with certain medications or malignancies (Table 2). In this case presentation, the lactic acidosis is likely due to a combination of Type A (from tissue hypoperfusion in the setting of septic shock) and Type B (from underlying malignancy). We presented this case report showing that severe lactic acidosis alone should not be considered as a nonrenal indication for CRRT.

Table 2. Causes of lactic acidosis

Causes of lactic acidosis
Type A
• Acute hypoxia
• Anemia
• Carbon monoxide poisoning
• Cardiogenic shock
• Hemorrhagic shock
• Septic shock
Type B
• Systemic disease
Liver failure
Malignancy
• Drugs or toxins
Metformin
Cyanide
Salicylate, ethylene glycol, methanol, propylene glycol
Linezolid
Propofol
Stavudine, didanosine
Isoniazid
• Hereditary enzyme deficiency

Treatment of lactic acidosis is directed toward correcting the underlying cause and optimizing adequate oxygen delivery to the tissues [5]. There have been many efforts to study the treatment of lactic acidosis. Proposed treatments include bicarbonate therapy [8, 9], alternatives to bicarbonate therapy such as tromethamine [10], carbicarb [11] and dichloroacetate [12], IHD and CRRT [13–16]. The role of bicarbonate in patients with lactic acidosis is controversial [8, 9, 17]. Several studies have suggested that bicarbonate use may in fact cause harm by increasing the arterial and tissue capillary PCO_2 and worsening intracellular acidosis [18, 19]. Moreover, bicarbonate therapy may lead to electrolyte disturbances, such as hypokalemia and hypocalcemia. Alternative agents to bicarbonate thus far have not shown any clinical benefit in treatment of patients with lactic acidosis [10, 11].

Dialysis and hemofiltration may be required in ICU patients with severe AKI. Even though evidence is lacking, their use is still advocated as treatment modalities for lactic acidosis [5]. Prolonged hemodialysis was reported as a possible treatment option for metformin-induced lactic acidosis [20]. In addition, Schetz [16] included lactic acidosis as one of the nonrenal indications for CRRT. It was believed that extracorporeal elimination with high-volume hemofiltration or dialysis might result in clinically significant reduction of lactate level by increasing the clearance of lactate. However, in this case presentation, we showed that lactate removal by high-volume hemofiltration (58 mL/kg/h in our case) was ineffective in comparison to rate of lactate production in septic shock. Our patient's calculated lactate clearance by CVVH was 79 mL/min (0.56 mmol/min or 4.67 μmmol/kg/min) which was significantly lower than the rate of lactate production in the setting of septic shock (54 μmol/kg/min [21] or 6.4 mmol/min for 120 kg body weight).

The lactate clearance by CVVH in our case presentation was higher than a reported result in a previous study by Levraut *et al.* [14] which found a lactate clearance with continuous venovenous hemofiltration with dialysis (CVVHDF) range of 7–36 mL/min a median filter lactate clearance of 24.2 mL/min. This discrepancy could be explained by much lower flow rates of CVVHDF in their study (blood flow rate was 100 mL/min, dialysate 1000 mL/h, median effluent 714 mL/h) than used in our patient as shown in Figure 1. The findings of an ongoing prospective observational study on effects of CVVH on plasma lactate in critically ill patients by Liu *et al.* (ClinicalTrials.gov identifier, NCT01824771) will elucidate if the dose of CVVH affects lactate clearance.

Although lactate clearance by CRRT cannot meet lactate overproduction, our patient's metabolic acidosis did improve with the use of bicarbonate therapy in CRRT as evidenced by the improvement in serum pH (from 7.10 to 7.35) and bicarbonate (from 11 to 18 mmol/L) levels.

No study has shown that correcting acidosis improves survival especially when the serum pH is higher than 7.1 [8, 9]. The reduction of lactate level during hemofiltration reflects an improvement in patients' hemodynamic status leading to enhanced lactate metabolism [14]. In this case presentation, CRRT helped improve the volume status and optimize the metabolic derangements in the setting of AKI until the effect of treatment for the septic shock and malignancy occurred. The lactic acidosis subsequently improved with the increased lactate metabolism.

In our case presentation, citrate was used as an anticoagulant for CRRT. Since citrate toxicity is an important cause of high anion gap metabolic acidosis in patients with decreased hepatic

blood flow (e.g. in sepsis or other shock states) [22] and studies have demonstrated that lactic acidosis is a risk factor for citrate toxicity [23, 24], patients on CRRT given citrate-based replacement solution need careful monitoring of total calcium concentration along with ionized calcium concentration. In our case report, the patient was found to have lactic acidosis prior to the initiation of CRRT, and there was no evidence of citrate toxicity during CRRT treatment.

CRRT or IHD should only be considered in treatment of patients with severe lactic acidosis if the patient has other indications for initiation of dialysis such as volume overload, metabolic disturbances [25]. Filtered lactate clearance by high-volume CRRT is small compared with overproduction of lactic acid in septic shock. Therefore, lactic acidosis alone should not be the sole indication for initiation of CRRT.

Conclusion

In summary, although metabolic acidosis is corrected by CRRT, high-volume hemofiltration is not effective for severe lactic acidosis, and this suggests that lactic acidosis may not be an indication for CRRT alone.

Authors' contributions

All authors were involved and approved the final manuscript. All authors had access to the data and a role in writing the manuscript.

Conflicts of interest statement

None declared.

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