Case Report

Reversal of severe lactic acidosis with thiamine in a renal allograft recipient

Nanda Kumar K., Veena R. Shah, Beena K. Parikh, Sumedha Sonde

Abstract

A 48-year-old female patient with end-stage renal failure developed unexplained severe lactic acidosis (LA) associated with hyperglycemia during robotic-assisted laparoscopic renal transplantation. Initial treatment with sodium bicarbonate and insulin infusion were ineffective in treating acidemia. Postoperatively, intravenous administration of thiamine resulted in rapid improvement of LA and blood sugar levels. Uremia and chronic hemodialysis might be the causes behind the quantitative/qualitative deficiency of thiamine unmasked during the surgical stress. Though a rare entity, acute thiamine deficiency should be considered in the differential diagnosis of unexplained severe LA in patients with chronic kidney disease and hemodialysis who undergo major surgery or admitted to critical illness care units.

Keywords: chronic hemodialysis, lactic acidosis, renal transplantation, thiamine deficiency

Access this article online

Website: www.ijccm.org

DOI: 10.4103/0972-5229.160293

Quick Response Code:

Introduction

Lactic acidosis (LA) is a high anion gap metabolic acidosis with serum lactate levels >5 mM/L and acidemia (pH < 7.35) caused by over-production or underutilization of lactic acid from the body. Thiamine deficiency is one of the causes[1] and cases of refractory LA treated successfully with thiamine were reported in the literature.[2] Though chronic kidney disease (CKD) and hemodialysis are proven risk factors for occult thiamine deficiency,[3] we are not aware of any case report describing reversal of acute refractory LA with intravenous (IV) thiamine in this patient population.

Case Report

A 48-year-old female with end-stage renal disease, hypertensive since past 7 years was electively posted for robotic assisted laparoscopic renal transplantation from a living related donor. She was on maintenance hemodialysis twice a week since 6 months, and her hypertension was well controlled with one antihypertensive agent. Her fasting, postprandial blood sugar and glycated hemoglobin levels were within normal limits in more than three examinations preoperatively. Preoperative hemodialysis was done within 24 h of the scheduled surgery.

On the day of surgery, standard monitoring was applied, and balanced general anesthesia was administered. Her baseline vitals were heart rate (HR) 94/min, mean arterial pressure (MAP) 103 mm of Hg, SpO_2 100%, central venous pressure (CVP) 12 cm of H_2O, and core temperature 98.6°F. Arterial blood gas (ABG) analysis after induction of anesthesia (10 AM) was unremarkable with a lactate of 1.9 mM/L [Table 1]. Volume controlled ventilation was adjusted to maintain $EtCO_2$ between 35 mm and 40 mm of Hg. Three hours after induction

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How to cite this article: Kumar KN, Shah VR, Parikh BK, Sonde S. Reversal of severe lactic acidosis with thiamine in a renal allograft recipient. I! ndian J Crit Care Med 2015;19:425-8.

Table 1: ABG analysis of the patient since the initiation of surgery till the next 22 h

	10 am	1 pm	2 pm	3 pm	4.30 pm	5.30 pm	7.30 pm	9.30 pm	11.30 pm	4.30 am	8.00 am
pH	7.496	7.342	7.289	7.206	7.145	7.225	7.216	7.337	7.409	7.458	7.431
PaO_2 (mm of Hg)	257.7	203.6	221.0	210.9	230.9	366.4	284.9	202.0	279.5	211.3	82.8
$PaCO_2$ (mm of Hg)	28.5	28.8	31.4	34.6	36.9	34	32.3	34.4	32.4	32.5	36.4
SaO_2 (%)	99.8	99.6	99.6	99.5	99.6	99.8	99.7	99.5	99.8	99.6	97.4
HCO_3 (mEq/L)	21.5	15.3	14.7	13.4	12.4	13.8	12.8	18	20.0	22.5	23.7
BE	−1.7	−9.4	−11.9	−13.5	−15.5	−12.8	−15.0	−6.9	−3.9	−1.4	−0.6
Na^+ (mEq/L)	140.8	142.1	139.8	139.4	140.8	143.2	142.9	141.1	142.7	140.5	139.3
K^+ (mEq/L)	3.65	3.26	3.4	3.29	3.48	2.99	3.38	4.21	4.04	4.57	4.83
Glucose (mg/dl)	134	295	322	357	330	293	264	216	187	160	184
Lactate (mMol/L)	1.9	5.2	6.3	8.9	12.6	13.1	14.0	10.2	8.6	2.6	2.0
Hb (g/dl)	12.6	8.5	6.4	9.4	11.1	12.1	11.5	12.2	9.9	9.3	9.1
Anion gap (mEq/L)	8.4	16.1	22.4	23.7	23.8	22.5	23.1	20.3	17.6	12.4	11.1

ABG: Arterial blood gas

of anesthesia hemodynamic parameters deteriorated with HR of 122/min, MAP of 72 mm of Hg and CVP of 16 cm of H_2O. ABG analysis showed metabolic acidosis with elevated lactate levels, hyperglycemia, elevated anion gap and fall in hemoglobin [Table 1]. Blood sample for ketone bodies tested negative and it was repeated every fourth hourly to rule out diabetic ketoacidosis as a cause of the acidosis. Considering occult blood loss, IV fluids and two units of packed red blood cells were transfused. As vascular anastomosis of the graft kidney was being carried out, noradrenaline infusion [Figure 1] was started to maintain a MAP of 90 mm of Hg. Sodium bicarbonate and insulin infusion were started for treating acidosis and hyperglycemia respectively. The allograft was reperfused and urine output was established in 25 min after reperfusion.

The patient was shifted to Intensive Care Unit (ICU) 7 h after induction of anesthesia with noradrenaline infusion (0.12 μg/kg/min) for elective ventilation and possible need for continuous renal replacement therapy to correct acidosis. ABG analysis in the ICU revealed progressively increasing LA with hyperglycemia refractory to bicarbonate and insulin infusion [Figure 1]. However, she maintained an average urine output of 300 mL/h. Considering the possibility of sepsis, procalcitonin levels were obtained (14.6 ng/mL). Suspecting thiamine deficiency, empirical thiamine 300 mg was administered intravenously 3 h after surgery. ABG analysis 2 h after thiamine administration showed rapidly decreasing lactate and sugar levels with improvement in MAP. Bicarbonate, insulin and noradrenaline infusions were stopped. The patient was extubated 7 h after the completion of surgery. Thiamine injection 300 mg IV was repeated at the same time. ABG analysis, 8 h after the first dose of thiamine injection was within normal limits [Table 1]. The patient was shifted to posttransplant isolation ward 12 h after the surgery.

Discussion

Lactic acidosis is classified[1] into two types: Type A is caused by tissue hypoperfusion, hypoxia, etc., whereas Type B is caused by hereditary metabolic diseases, drugs, systemic disorders (thiamine deficiency, liver/kidney failure, malignancy etc.,) and release of endogenous catecholamines from stress response.

Among all the above-mentioned causes, thiamine deficiency leading to unexplained severe LA is generally overseen or ignored. Numerous case reports of unexplained LA in patients who were on parenteral nutrition without thiamine supplementation have been published in the past.[4] CKD, uremia and chronic hemodialysis have variable effects over thiamine activity and metabolism in the body: Diminished intestinal and mitochondrial thiamine transporters in spite of normal serum thiamine levels,[5] diminished transketolase (one of the enzymes requiring thiamine as a co-factor) activity,[6] chronic hemodialysis itself can lead to accelerated removal of thiamine from the body.[7,8] Thiamine requirement increases during stressful periods such as critical illness and major surgery etc., which can precipitate symptoms of thiamine deficiency in such individuals.[1]

Thiamine pyrophosphate is the cofactor for three important enzymes including pyruvate dehydrogenase (PDH). PDH catalyzes the oxidative decarboxylation of pyruvate to acetyl coenzyme A (CoA) which enters the Kreb's cycle. In thiamine deficiency, when pyruvate cannot undergo this conversion, it is then converted to lactate by the action of lactate dehydrogenase [Figure 2]. This conversion also results in the release of protons in equal number to the molecules of lactate produced leading to acidemia. Hyperglycemia can be an associated sign as excess lactate is metabolized by the liver into glucose through gluconeogenesis and thiamine deficiency *per se* can cause defective insulin secretion.[9]

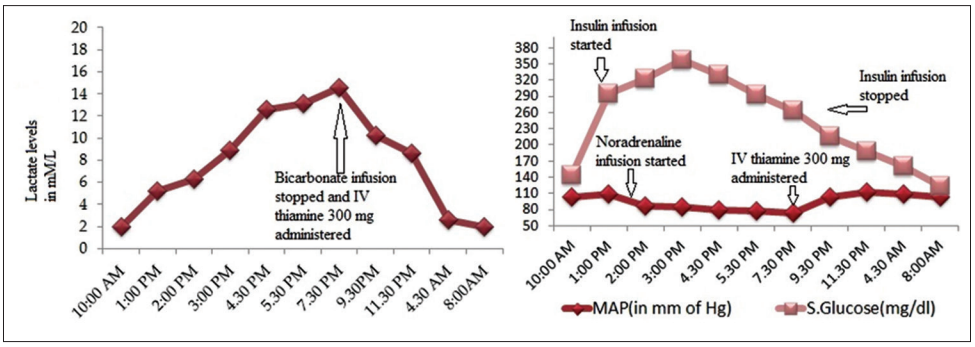

Figure 1: Trend of lactate/blood glucose levels/mean arterial pressure from the initiation of surgery till the next 22 h depicting various interventions

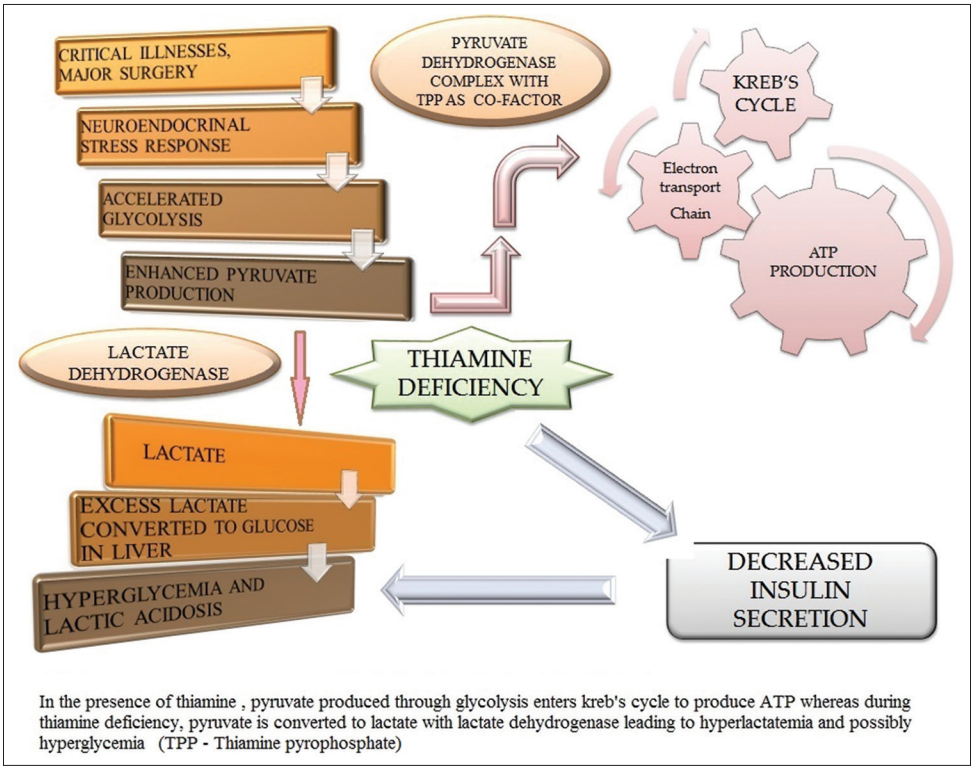

Figure 2: Lactate production and metabolism

Our patient was suffering from CKD and was on maintenance hemodialysis for 6 months, history and physical examination did not reveal the poor nutritional status or obvious signs and symptoms of thiamine deficiency. Septicemia was ruled out as a probable cause as the patient was afebrile, normal total leukocyte counts and she did not have significant hypotension when the LA was discovered. Although her postoperative pro-calcitonin level was high, it is not diagnostic as she received T-cell antibody anti-thymocyte globulin as induction therapy intraoperatively.[10] Other causes like hypoperfusion, hypoxia, drugs and liver failure were excluded. Hence, acute thiamine deficiency was suspected, which was supported by dramatic improvement in her clinical and biochemical parameters after IV thiamine supplementation. Probably, surgical stress stimulated accelerated glycolysis and enhanced pyruvate production, which increased her thiamine requirement unmasking occult thiamine deficiency and/or defective thiamine activity leading to severe LA with hyperglycemia.

Regardless of etiology, the treatment for LA is to correct the underlying cause.

Intramuscular/IV thiamine 100 mg once a day is the recommended dose in suspected thiamine deficiency. We administered 300 mg of IV thiamine as the excess dose has no proven adverse effects in humans.[1] Adequate thiamine favors rapid conversion of pyruvate to acetyl CoA. If thiamine deficiency is suspected, erythrocyte

transketolase activity and thiamine pyrophosphate effect can be measured for an objective documentation of the deficiency. We were not able to perform these biochemical tests as they were not available in local laboratories. However, the definitive test for Vitamin B_1 deficiency is an improvement of symptoms with thiamine administration.

Conclusion

Thiamine deficiency should be considered in the differential diagnosis of unexplained severe LA with hyperglycemia in patients with CKD. Physicians caring for these patients should maintain a low threshold for infusing a therapeutic dose of thiamine as treatment is safe, inexpensive, readily available and potentially life-saving.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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