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Thiamine responsive acute life threatening metabolic acidosis in exclusively breast-fed infants

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ABSTRACT

Background: Acute life threatening metabolic acidosis in exclusively breast fed infants due to thiamine deficiency is not described. Kashmir valley, a north Indian state has a population that largely consumes polished rice.
Methods: A six months prospective descriptive study of infants who presented with acute life threatening metabolic acidosis (Blood pH $\leq$ 7.0) due to thiamine deficiency.
Results: Twenty three infants (Eleven male; Twelve female) in the age range of 32 days to 4 months had a pH of $\leq$7 at admission. Onset of moaning was immediate (2–24 hours). Blood lactate levels were more than 15mmol/L. Blood thiamine levels of six infants in whom it was done ranged from 11–69 nmol/L (control 78–185 nmol/L). All infants were exclusively breast fed. Maternal staple diet consisted of polished rice. All mothers consumed rice after washing it thrice. Twelve lactating mothers were on customary dietary restrictions. Practice of straining rice after cooking was observed in thirteen. The commonest symptoms were irritability (82%) and reflux (56%). Commonest signs were tachycardia (100%) and moaning (73%). At presentation 52% were in cardiogenic shock. Response to thiamine was dramatic with moaning and irritability subsiding in two hours and tachycardia in four hours. Adequate perfusion was achieved in one hour. Eighteen patients seen at six months follow up had normal neurodevelopment.
Conclusions: Thiamine deficiency in an infant can present as sudden onset metabolic acidosis. If treated early, metabolic acidosis due to thiamine deficiency is associated with good immediate and long term prognosis even if pH is less than 7 at presentation.

Introduction

Thiamine deficiency has historically affected countries and populations consuming milled white cereal. Polished rice is a staple diet in Kashmir, a Northern Indian state. Infantile beri beri affects infants breast-fed by women having thiamine deficiency. It can present in three forms: cardiologic, aphonic, and pseudomeningitic [1]. A less common fulminant form characterized by lactic acidosis and cardiac failure called as Shoshin beri beri is described in adults. Different clinical phenotypes can be seen in a single geographic region. Infantile Wernickes encephalopathy has already been reported from our region [2].

We had been admitting a number of infants in the age group of 1 to 6 mo in our intensive care unit with unexplained severe metabolic acidosis of sudden onset. Clinical symptom complex was marked by nonspecific symptoms of reflux and irritability. A large proportion of these infants would succumb to the illness. Initially, an inherited metabolic disorder such as organic acidemias was thought of as a probable cause of illness. However, their blood biochemistry and urine gas chromatography mass spectrometry would only reveal lactic acidemia and lactic aciduria. Given this lactate buildup, the dietary practices of the region and clinical picture, thiamine deficiency was thought of

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and thiamine instituted as a first-line treatment in these infants. The response to thiamine was quick. The purpose of this study was to describe this rare fulminant presentation of infantile thiamine deficiency as lactic acidosis in a large series of infants.

Materials and methods

A prospective study of patients who were admitted in G. B. Pant Hospital, a tertiary care referral children's hospital, from March 2014 to August 2014 was conducted. Eligible patients were infants who presented with acute life-threatening metabolic acidosis due to thiamine deficiency. Life-threatening metabolic acidosis was defined as a blood pH of 7.0 or less. The diagnosis of thiamine deficiency was made by rapid response to parenteral thiamine. Samples for blood thiamine were processed in only six infants due to financial constraints. The levels were received later.

Patients were investigated as per standard protocol to look for causes of metabolic acidosis. This included complete blood count, blood culture, urine examination, cerebrospinal fluid examination, chest radiographs, serum biochemistry, electrolytes, blood sugar, lactate, blood gases, tandem mass spectrometry, urine gas chromatography mass spectrometry, and cranial ultrasonography.

Exclusion criteria included a history and examination suggestive of states associated with shock from hypovolemia and congestive heart failure, and laboratory confirmed diagnosis of sepsis, diabetic ketoacidosis, renal tubular acidosis, chronic kidney disease, and metabolic disease. Blood gases and lactate were measured by Arterial Blood Gas analyzer Gem Premier 3000 (Model 5700, Lexington, USA). The lower limit of detection of bicarbonate by this analyzer was 3 meq/L and upper limit of detection of lactate was 15 meq/L. Blood thiamine levels were measured by liquid chromatography/mass spectrometry.

We obtained epidemiologic, dietary, clinical, laboratory, and treatment data for these patients. Patients were called for neurodevelopmental follow-up at 3 and 6 mo. First head ultrasound was done within 24 h and follow up ultrasound was done at 1 mo. Five patients were lost to follow up.

Statistical analysis

Since this was a descriptive study, the data was summarized and presented in the form of numbers and percentages. Mean and standard deviation was used to summarize continuous variables. The study was done after institutional ethical approval.

Results

A total of 23 infants (11 male, 12 female) in the age range of 32 d to 4 mo (mean age 1.7 mo) had a pH of $\leq$7 at admission. All the infants were exclusively breast-fed. 74% of mothers resided in rural areas and had low socioeconomic status. A sibling death due to similar illness was reported in two patients. There was temporal relation with vaccination (varying from 1 d to 1 wk) in three infants. Maternal staple diet consisted of polished rice which was washed three times before consumption. The practice of straining rice after cooking was observed in 13 (56%) infants and the practice of consuming restricted diet, as a part of cultural practice, based on rice and soup derived from boiled meat, was observed in 52% of infants. The mean blood thiamine levels of six infants were 41 nmol/L with a range of 11–69 nmol/L (control 78–185 nmol/L). Blood lactate levels in all patients were above detectable range (>15 mmol/L).

The clinical presentation was typical. Duration of reflux ranged from 6 h to since birth. Six patients reported increase in reflux episodes from the prior days. Fever preceded the illness in five patients. Eight infants had decreased feeding for 1 d. Seizure-like episodes occurred in six patients. They were reported 1 d before hospitalization in three and within 2 h of hospitalization in three. They were described or witnessed as uprolling or tonic posturing, respectively. No patient had epilepticus. Irritability was in the form of excessive crying and restlessness, with a mean duration of 2 d. Duration of moaning ranged from 2 to 24 h, except in one who developed moaning after hospitalization. All patients had tachycardia with a mean heart rate of 156. All patients had age-appropriate weight except one. The clinical features of the study population are given in Table 1.

Tachycardia was universal. Twelve (52%) patients had poor peripheral perfusion and weak pulses at presentation. Three patients were brought gasping into the emergency room. One developed gasping after cannulation.

Mean hemoglobin of 9.1 was consistent with physiological anemia of infancy. Leucocytosis (total leucocyte count >15,000/mm^3) was detected in five patients (lymphocytic 3, mixed 2). No patient had leucopenia. Mild thrombocytopenia was seen in one and thrombocytosis in two. Two patients had transaminitis with alanine transaminase elevation less than three times. No patient had hypoalbuminemia. Mean sodium and potassium levels were 137 meq/L and 4.3 meq/L, respectively. Eight patients had hyperglycemia and one had hypoglycemia at admission. Ionized calcium was low (<1 mmol/L) in fourteen, and in four of them, total calcium was also low. Vitamin D levels were low in infants with low total calcium and ionized calcium due to maternal hypovitaminosis D. Hematological and biochemical findings of patients are shown in Table 2. Bicarbonate ranged from below detectable limits to10 meq/L. Mean base excess was −23 (range −22 to −30 mmol/L). Mean PCO2 was 25 mmHG (range 17–38 mm Hg). No patient had hypoxemia.

C reactive protein was negative in all except one. Cerebrospinal fluid examination was done whenever meningitis was suspected (in 13 infants). There was no pleocytosis or cytoalbuminemic dissociation. Head ultrasonagram showed hyperechogenicity of putamen in eight. In these eight patients, hyperechogenicity was also witnessed in globus pallidus in four, caudate two and thalami two (Fig. 1). It was normal in 15.

Table 1
Clinical features of patients

Clinical features	n (%)
Systemic	
Reflux	13 (56)
Fever	5 (21)
Decreased feeding	8 (34)
Failure to thrive	1 (4)
GI	
Increased frequency of stools	3 (13)
Respiratory	
Hoarseness of voice	1 (4)
CNS	
Altered sensorium	
Irritability	19 (82)
Lethargy	2 (8)
Vacant stare	3 (13)
Ptosis	3 (13)
Seizure equivalents	6 (26)
Tonic posturing	3
Moaning	17 (73)
Gasping	4 (17)
CVS	
Poor perfusion. Weak thready pulses.	12 (52)
Tachycardia	23 (100)

Table 2
Hematological and biochemical findings of patients

Laboratory parameter	Mean ± SD (Range)
Hb (gm/dL)	9.1 ± 1.3.
TLC (/cmm)	13,500 ± 4,500.
Platelet count (lac/cmm)	4.05 ± 1.9
Sodium (meq/L)	137 ± 6.3 (126–146)
Potassium (meq/L)	4.3 ± 0.6 (3.8–5.9)
Blood sugar (mg/dL)	236 ± 116 (23–384)
Ionised Serum Calcium (mmol/L)	0.82 ± 0.2 (0.2–1.18)
Total Calcium (mg/dL)	8.7 (5–9.8)