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Rapid communication

Coronary artery bypass graft surgery depletes plasma thiamine levels

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Abstract

Objective: Thiamine is an essential component of cellular metabolism, and lack of this vitamin results in a potentially life-threatening biochemical lesion. The stress of surgery and critical disease depletes electrolytes, minerals, and essential biochemical substrates. We hypothesized that critical illness (represented by major surgery) would result in decreased thiamine levels over time.

Methods: We performed a prospective, observational study of serial thiamine levels of 15 patients who underwent non-emergent coronary artery bypass graft surgery. The primary endpoint was change in thiamine levels from before to immediately after surgery. Secondary endpoints included change in thiamine levels from presurgical to 6- and 24-h time points.

Results: Of the 15 study patients, 1 did not have a plasma thiamine measurement at time 0 because of laboratory error and could not be accounted for in paired comparisons over time. Plasma thiamine levels decreased significantly from before to after coronary artery bypass grafting ($P = 0.0004$). In addition, there was a statistically significant decrease in thiamine levels from before surgery to 24 h ($P = 0.003$).

Conclusion: Our data suggest that major surgery (as a surrogate for the stress of critical illness) depletes thiamine levels; further study is needed to determine whether routine replacement of thiamine in the critically ill is warranted.

Keywords: Thiamine deficiency; Critical illness; Coronary artery bypass graft surgery

Introduction

Thiamine is an essential component of cellular metabolism with a key role in mitochondrial machinery. Specifically, thiamine is a cofactor for pyruvate dehydrogenase, the enzyme responsible for the conversion of pyruvate into acetyl-coenzyme A. A deficiency of this vitamin results in a potentially life-threatening biochemical lesion, because pyruvate cannot enter the citric acid cycle and is instead converted to lactic acid [1–3]. Thiamine deficiency may result in neurologic dysfunction (Wernicke's encephalopathy), cardiac dysfunction (wet beriberi), peripheral polyneuropathy (dry beriberi), lactic acidosis, gastrointestinal beriberi, and death [1,3–10]. Moreover, lower levels of thiamine have been associated with increased mortality in the critically ill [11] and thiamine deficiency syndromes have been described in the intensive care setting [5,12–14].

Although electrolyte replacement therapy is routine for patients in a critical disease state or those undergoing the stress of surgery, little research or clinical consideration has been given to the potential loss of essential biochemical substrates or vitamins, specifically thiamine. As previously noted, the clinical consequences of thiamine deficiency may be severe and result in permanent neurologic dysfunction or death. We hypothesized that the stress of critical disease would result in decreased thiamine levels from increased metabolic demand. To test our hypothesis, we performed a prospective, observational study of serial thiamine levels of patients who underwent non-emergent coronary artery bypass grafting (CABG; major surgical stress).

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Materials and methods

Design

This prospective, observational study was conducted at an urban tertiary care center with 50 000 emergency department visits/year and intensive care units numbering a total of approximately 50 beds. This study was approved by the Beth Israel Deaconess Medical Center institutional review board and all patients provided informed written consent to participate.

Inclusion criteria

All outpatients older than 18 y who were undergoing elective CABG were eligible for inclusion. Data from all patients were included in the analysis. All patients were screened, consented, and enrolled before surgery.

Exclusion criteria

Exclusion criteria consisted of use of multivitamins, age younger than 18 y, or unwillingness to give consent.

Procedures

Plasma thiamine levels were measured before the operation, immediately after the operation, 6 h after the operation, and 24 h after the operation. The preoperation blood draw was performed in the preoperation area before the initiation of anesthesia. Blood was collected from patients by venipuncture or by a pre-existing arterial or venous catheter into two 5-mL tubes containing ethylenediaminetetra-acetic acid. Blood was centrifuged at $2000 \times g$ for 10 min after which 2 mL of this plasma was aliquoted into crytotubes and frozen. Blood was protected from light during the collection and freezing process. Frozen samples were sent to Quest Diagnostics (Chantilly, VA, USA). At Quest Diagnostics, plasma was deproteinized and then incubated with acid phosphatase to convert thiamine phosphate esters to free thiamine. The free thiamine was then oxidized to thiochrome by the addition of alkaline potassium ferricyanide. Depending on the age of the column and the temperature of the room, thiochrome retention time varied from 2.5 to 3.0 min. The mixture was injected to a Supelco (Bellefonte, PA, USA) high-performance liquid chromatographic column (7.5 cm × 4.6 mm, particle size 3 μm) connected to an high-performance liquid chromatographic system using a Hitachi (Pleasant, CA, USA) pump, autosampler, and fluorescent detector (excitation wavelength 365 nm, emission wavelength 440 nm). Seventy-five millimoles per liter of potassium phosphate at pH 7.5 with 25% methanol was used as the mobile phase for the high-performance liquid chromatographic system. The flow rate was set at 1.0 mL/min. Through this process, the thiochrome was then separated from other interfering substances and then measured fluorometrically. The amount of total thiamine in an unknown sample is proportional to the amount of thiochrome formed. Absolute thiamine deficiency was determined using a previously established standard laboratory reference range from Quest Diagnostics; specifically, absolute thiamine deficiency was defined as a level lower than or equal to 9 nmol/L.

Table 1
Baseline characteristics

Subjects	15
Age (y)	68.5 ± 6.7
Male/female	60/40
Ethnicity (%)	
White	100
African American	
Hispanic	
Asian	
Comorbidity (%)	
Hypertension	73.3
Coronary artery disease	40
Myocardial infarction	20
Chronic obstructive lung disease	13.3
Diabetes mellitus	40
Vital signs (baseline)	
Temperature (°F)	98.0 ± 0.9
Heart rate (beats/min)	77 ± 19.9
MAP (mmHg)	78.2 ± 25
Respiratory rate (breaths/min)	17.8 ± 2.6
Laboratory values	
WBC count (per mm^3)	11.4 ± 3.2
Hematocrit (g/dL)	36 ± 7.5
Sodium (mmol/L)	138 ± 3.1
Potassium (mmol/L)	4.3 ± 0.4
Bicarbonate (mmol/L)	26 ± 3.4
Creatinine (mg/dL)	2.1 ± 1.3
Total bilirubin (mg/dL)	0.5 ± 0.28
Alanine aminotransferase	24 ± 7
Aspartate aminotransferase	23 ± 1.4

MAP, mean arterial pressure; WBC, white blood cell

Statistical methods

Baseline characteristics were reported with simple descriptive statistics. We used a paired t test to compare thiamine levels before and after CABG over time. The primary endpoint was the difference in thiamine levels before to immediately after the operation. $P = 0.05$ was used to determine statistical significance. Secondary endpoints included 6- and 24-h thiamine levels. To account for multiple measurements, we used Bonferroni's correction factor to adjust the P value for significance such that $P = 0.025$ was considered statistically significant for time point differences between preoperative and 6- and 24-h postoperative thiamine levels.

Results

Twenty-five patients were screened, yielding a total of 15 study patients. The baseline characteristics of the study