

Shoshin Beri-Beri Precipitated by Intravenous Glucose

T. B. CORCORAN, B. O'HARE, D. PHELAN

Department of Anaesthesia and Intensive Care Medicine, Beaumont Hospital, Dublin, IRELAND

ABSTRACT

A thiamine deficient patient presented to the emergency department with an acute confusional state, becoming unconscious and hypotensive following the administration of 32 g of intravenous glucose over 4 hr. A dramatic clinical improvement in his cardiovascular and neurological status followed a single intravenous dose of 250 mg of thiamine. Profound thiamine deficiency was confirmed on biochemical testing.

A substantial proportion of hospital patients are thiamine deficient and intravenous dextrose may precipitate cardiovascular collapse and lactic acidosis due to the development of 'shoshin' beriberi. A rapid response to intravenous thiamine may confirm the diagnosis. All patients presenting with acute neurological dysfunction should receive thiamine before glucose-containing solutions are administered. (Critical Care and Resuscitation 2002; 4: 31-34)

Key words: Thiamine, sho-shin beri-beri, encephalopathy, metabolic acidosis

Acute thiamine deficiency is a life-threatening disorder requiring immediate treatment with intravenous thiamine. Thiamine deficiency is not rare, but unfortunately remains poorly recognised and underdiagnosed. Cruickshank *et al.*¹ recorded a 20 % prevalence in critically ill patients on admission to intensive care, which was associated with a higher mortality compared with non thiamine deficient patients.

In one study of trauma patients, all patients who had severe injuries (i.e. injury severity score greater than 12) developed thiamine deficiency during the first 7 days of their intensive care unit stay, despite a normal pre-morbid nutritional status and the routine use of enteral or parenteral feeding.²

Such apparently innocuous therapy as intravenous dextrose or the commencement of total parenteral nutrition,³ when administered to a patient with marginal or depleted thiamine stores, may precipitate acute 'beriberi', with fulminant haemodynamic and neurological disturbances. A high index of suspicion is required to correctly diagnose the disorder and to institute the simple but life-saving measure of intravenous thiamine administration.

CASE REPORT

A 30 year old chronic schizophrenic man was found semiconscious in his apartment, with extensive left sided decubitus ulceration. He was reported as being ataxic and stumbling into objects at home. On admission, his rectal temperature was 35.4°C, he had generalised hyperreflexia and hypertonicity and had a Glasgow coma score (GCS) of 12. No ocular palsy or nystagmus were noted. His regular medications included chlorpromazine, fluphenazine decanoate, diazepam, temazepam, clomipramine and bztropine. The laboratory investigations revealed a haemoglobin of 159 g/L and plasma sodium of 151 mmol/L, urea 48.8 mmol/L and creatinine 187 µmol/L.

Systemic sepsis with hypothermia, dehydration and prerenal uraemia was considered the most likely diagnosis. An intravenous infusion of 4% dextrose in 0.18% saline was commenced at 200 mL/hr. Blood cultures were taken and empirical intravenous antibiotic therapy with flucloxacillin and amoxycillin/clavulanic acid was commenced.

Four hours following admission his condition deter-

Correspondence to: Dr. T. B. Corcoran, Department of Anaesthesia and Intensive Care Medicine, Beaumont Hospital, Dublin 9, Ireland

iorated. He became unconscious with a GCS of 7, tachypnoeic with a respiratory rate of 32 breaths per minute, anuric and hypotensive with a systolic arterial blood pressure of 30 mmHg. Arterial blood gas analysis revealed a metabolic acidosis but otherwise the gas exchange was satisfactory. He was intubated and transferred to the intensive care unit where he was mechanically ventilated. Intravenous fluids and adrenaline were administered.

In view of his abrupt deterioration following intravenous dextrose therapy, a diagnosis of thiamine deficiency was considered and thiamine 250 mg was administered intravenously. Fluid therapy was changed to bolus colloid administration, for haemodynamic support, and 0.45% saline at 150 mL/hr. This was followed by a rapid improvement in the patient's haemodynamic parameters and conscious level (Table 1), allowing the inotropic and ventilatory support to be rapidly weaned and the patient to be extubated 24 hr after admission to hospital.

Blood, urine, faeces and sputum cultures were negative and plasma toxicology screening failed to detect significant levels of tricyclic antidepressants, benzodiazepines, ethanol or barbiturates. Enteral nutrition was commenced with vitamin supplementation. Four days after his admission his renal function returned to normal, although he had persistent hyperreflexia and hypertonicity in his lower limbs. His plasma biochemistry revealed a deficient nutritional status with an albumin level of 19 g/L (reference range 35 - 53 g/L), folate 1.1 µg/L (reference range 2 - 14 µg/L), ferritin 36 µg/L (reference range 20 - 330 µg/L) and vitamin B₁₂ 160 ng/L (reference range 220 - 950 ng/L). Thiamine assays performed before thiamine administration revealed a profound deficiency state, which normalised after one month of treatment (Table 2).

DISCUSSION

Thiamine is a water soluble vitamin, requiring hepa-

tic conversion to the active form of thiamine pyrophosphate. It plays a crucial co-enzymatic role in carbohydrate metabolism, as both of the enzymes pyruvate dehydrogenase and alpha ketoglutarate dehydrogenase depend on it to permit entry of pyruvate into the tricarboxylic acid cycle. Both of these reactions are required to permit the efficient utilisation of glucose as an energy source. A deficiency will cause pyruvate to accumulate, which is then converted to lactate to regenerate NAD⁺ from NADH, permitting glycolysis to continue.

Thiamine is also required as a cofactor for the pentose phosphate pathway transketolase reaction. This reaction is essential for the regeneration of NADPH, to facilitate extramitochondrial reductive processes to generate fatty acids, and to provide ribose for nucleotide and nucleic acid synthesis. Thiamine is also involved in the synthesis of acetylcholine, and a non-enzymatic role in the function of neuronal chloride channels has also been postulated.⁴

The recommended daily intake is 0.5 mg per 1000 Joules of caloric intake, with a minimum thiamine amount of 1 mg per day, irrespective of caloric intake. Total body stores last from 18 to 60 days in states of absolute depletion, equivalent to a total storage amount of 30 mg.

Clinical syndromes of thiamine deficiency are classically described in three forms: "dry beri-beri", where peripheral neuropathy is the cardinal feature; "wet beri-beri", where cardiac failure predominates; and Wernicke's encephalopathy, which comprises a triad of altered consciousness, ocular signs, and ataxia. However, only 10 % of patients have Wernicke's clinical triad, with the majority of patients (82 %) presenting with confusion only.^{5,6} Wernicke's encephalopathy often progresses to Korsakoff's psychosis, which is characterised by retrograde amnesia and confabulation.

A new form of acute thiamine deficiency or "shoshin"beriberi is being increasingly described.⁷⁻⁹

Table 1. Haemodynamic and arterial biochemical values on admission (0 hr) and during treatment (5 - 17 hr)

| Hours post presentation | | 0 | 5 | 6 | 7 | 8 | 9 | 10 | 13 | 17 |
|-------------------------|----------|------|-------|-------|-------|------|-------|-----|------|------|
| Heart rate | (bpm) | 60 | 50 | 100 | 100 | 100 | 110 | 110 | 110 | 100 |
| Central venous pressure | (mmHg) | | - 2 | 4 | 8 | 0 | 1 | 1 | - 3 | 0 |
| Systolic blood pressure | (mmHg) | 110 | 30 | 100 | 110 | 100 | 130 | 120 | 110 | 120 |
| Urinary output | (mL/hr) | | 0 | 6 | 30 | 190 | 200 | 270 | 300 | 450 |
| Adrenaline | (µg/min) | 0 | 20 | 20 | 20 | 20 | 18 | 12 | 0 | 0 |
| Lactate | (mmol/L) | 0.88 | | | 7.26 | 5.84 | | 1.3 | 0.7 | |
| Glasgow coma score | | 12 | 7 | 3 | 3 | 3 | 3 | 3 | 6 | 12 |
| pH | | | 7.29 | 7.16 | 7.22 | 7.25 | 7.30 | | 7.40 | 7.45 |
| BE | (mmol/L) | | - 4.8 | - 9.5 | - 9.9 | - 11 | - 8.6 | | - 2 | 0 |
| PaO ₂ | (mmHg) | | 75 | 144 | 118 | 95 | 113 | | 153 | 126 |
| PaCO ₂ | (mmHg) | | 45 | 53 | 41 | 34 | 33.5 | | 36 | 34 |

BE = arterial blood base excess, PaO₂ = arterial blood partial pressure of oxygen, PaCO₂ = arterial blood partial pressure of carbon dioxide

Table 2. Biochemical and thiamine status before and after treatment

| | <i>Normal</i> | <i>On admission</i> | <i>At 28 days</i> |
|-----------------------------------|---------------|---------------------|-------------------|
| Thiamine pyrophosphate effect (%) | < 25 | 39 | 4.2 |
| Red cell transketolase IU/L | > 50 | 16.6 | 74.5 |

Shoshin beriberi is characterised by an acute cardiovascular presentation with cyanosis and hypotension being the predominant features, although it is usually accompanied by obtundation. Patients become anuric and develop a severe lactic acidosis, often aggravated by conventional inotropic support attributed to adrenergic-receptor driven glycogenolysis, and an increased lactate/pyruvate ratio.¹⁰ While they usually have a hyperdynamic circulation, both high and low cardiac output states have been reported, although a low systemic vascular resistance is characteristic of both forms. Most authors maintain that intravenous dextrose can precipitate acute thiamine deficiency in these patients,¹¹⁻¹³ although some contend that such a phenomenon has not been clearly described.¹⁴

As with the third case in Motherway's series,¹⁰ our case demonstrated shoshin beriberi precipitated by intravenous dextrose. The precise biochemical mechanisms underlying the acute deterioration are not clear, although the provision of glucose may have diverted marginal neuronal thiamine stores, causing a "thiamine steal", and precipitating an acute neuronal dysfunction with altered consciousness. Shoshin beriberi was considered in our case because of the abrupt neurological and cardiovascular deterioration following the administration of intravenous glucose. Extrapyramidal crisis or neuroleptic malignant syndrome were considered unlikely in view of poor drug compliance and the absence of tricyclic antidepressants in the toxicology screen. The negative septic screen ruled out sepsis as the cause of his condition. Moreover, the rapid response to definitive therapy established thiamine deficiency as the cause of his condition which was subsequently confirmed biochemically.

There is a high prevalence of thiamine deficiency in the community, with one report indicating an incidence of 1.5%.¹⁵ There is also an increased incidence of thiamine deficiency in patients admitted to the Accident and Emergency department,¹⁶ in critically ill patients,^{1,2} and in patients on total parenteral nutrition, even those who have thiamine supplementation.³ In the emergent setting of shoshin beriberi, a response to treatment is diagnostic and an improvement in the haemodynamic

disturbances should be observed within 90 minutes.¹⁷ The neurological features often take longer to improve, and doses up to one gram may be required.¹⁸

We believe that intravenous glucose, even in modest amounts, can precipitate shoshin beriberi in susceptible individuals. Thiamine therapy should be commenced at the same time as intravenous carbohydrate in all patients with a disrupted or deteriorating conscious level of unknown cause, particularly if the patient falls into an 'at risk' category. We would endorse the use of thiamine in the 'coma cocktail' recommended in the first five minutes of management of all patients with an altered consciousness in Emergency or Intensive Care departments.¹⁹

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