

## Case reports

# Acute Pernicious (sho-shin) Beri-beri: A Report of Three Cases

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### ABSTRACT

*Acute pernicious or sho-shin beri-beri is characterised by haemodynamic and biochemical features which include hypotension, high cardiac output, low peripheral vascular resistance, lactic acidosis and high mixed venous content. The disorder is a metabolic emergency and requires immediate treatment with intravenous thiamine. Three cases are described which were successfully treated with intravenous thiamine (500 mg intravenously, followed by 100 mg 8-hourly for 24 hours then 100 mg daily) without using catecholamines or sodium bicarbonate. Digoxin was used in two cases to manage cardiac dysfunction which was poorly responsive to thiamine. (Critical Care and Resuscitation 1998; 1: 69-73)*

**Key words:** Acute pernicious beri-beri, sho-shin beri-beri, thiamine deficiency, lactic acidosis

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The term beri-beri is derived from the Sinhalese word beri meaning 'I cannot', and refers to the symptom of profound fatigue associated with thiamine deficiency. Beri-beri is classically referred to as either 'dry' where features of peripheral neuropathy pre-dominant, or 'wet' where features of high output cardiac failure are the main findings.

An acute neurological form of thiamine deficiency known as Wernicke's encephalopathy consists of a triad of paralysis of eye movements, ataxia and confusion with apathy. Rarely, an acute cardiac form of thiamine deficiency known as acute pernicious beri-beri or shoshin beri-beri to the Japanese (sho = acute damage and shin = heart) may occur, which presents with shock, cyanosis, restlessness and dyspnoea. Both of these disorders are typically seen in the alcoholic patient due to their high carbohydrate low thiamine diet,<sup>1</sup> and increased destruction and impaired thiamine absorption caused by excess alcohol.<sup>2</sup>

The characteristic haemodynamic features of acute pernicious beri-beri are high cardiac output, depressed left ventricular function, high right atrial and left atrial

pressures, and low systemic vascular resistance.<sup>3,4</sup> The biochemical findings include lactic acidosis, high circulating catecholamine levels and high mixed venous oxygen saturations,<sup>5</sup> and the disorder is fatal unless thiamine deficiency is recognised and treated.<sup>6</sup>

However, a high cardiac output and low systemic vascular resistance with high mixed venous saturation and lactic acidosis may also be found in many other disorders including septic shock (particularly when high doses of adrenaline are administered).<sup>7</sup> Three cases of acute pernicious beri-beri are presented, highlighting the features of this disorder and some of the differences between this and other forms of high output cardiac failure in the critically ill patient.

### CASE REPORTS

#### *Patient 1*

A 34 year old man with a 14 year history of chronic alcohol abuse was admitted to the intensive care unit with a three day history of an excessive alcohol intake and a 24 hour history of dyspnoea, epigastric pain and vomiting. On examination, he was diaphoretic, cyan-

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osed, and restless with poor peripheral perfusion. The blood pressure was unable to be recorded manually, his respiratory rate was 34 per minute and temperature was 36.2°C. The jugular venous pressure was elevated to the angle of the jaw. On auscultation his chest was clinically clear, the heart sounds were faint and a third heart sound was heard at the apex. The liver was tender and enlarged to three fingers below the right costal margin and there was minimal pitting oedema of both ankles.

The ECG revealed sinus rhythm at a rate of 130 beats per minute, and generalised low voltage QRS complexes with non specific T wave flattening, The chest X-ray revealed cardiomegaly and early pulmonary venous congestion. An arterial catheter was inserted into the right femoral artery revealing a blood pressure of 85/50 mmHg. A right heart pulmonary flotation catheter was inserted into the right internal jugular vein and its position was confirmed by chest-Xray. The admission and 24 hour haemodynamic measurements and arterial and mixed venous blood gases, arterial lactate, plasma electrolytes, glucose and amylase levels are shown in Table 1. The complete blood picture showed a

haemoglobin of 132 g/l, white cell count of  $20.7 \times 10^9/l$  and platelet count of  $132 \times 10^9/l$ . The arterial blood lactate was 22.2 mmol/l. Blood and urine cultures were taken and subsequently found to be negative.

On the basis of the patient's history of alcohol excess and nutritional insufficiency, and right cardiac catheter findings of high cardiac output, low peripheral resistance and high mixed venous oxygen content, a diagnosis of acute pernicious beri-beri was made. Blood for an erythrocyte transketolase activation by thiamine pyrophosphate (whole blood transketolase activity) was taken and subsequently found to be 33.5% (normal < 20%). The patient was treated with thiamine 500 mg intravenously, followed by 100 mg 8-hourly for 24 hours then 100 mg daily. Over the next 24 hours the blood pressure and urine output increased and the pulse, cardiac output, mixed venous oxygen content and pulmonary artery occlusion pressure decreased.

The patient's peripheral perfusion and urinary output improved, he became co-operative, and was discharged from the intensive care unit after three days, with a cardiac output of 5.6 l/min, pulmonary artery occlusion

**Table 1. Haemodynamic and arterial and venous biochemical values on admission (before) and 24 hours later (after)**

		Patient 1		Patient 2		Patient 3	
		Before	After	Before	After	Before	After
<i>Haemodynamic data (normal range)</i>							
Heart rate	(60 – 100 bpm)	124	104	68	106	104	114
MAP	(70 – 105 mmHg)	62	107	42	73	57	92
PaOP	(5 – 12 mmHg)	16	13	16	9	15	13
CO	(4 – 6 L/min)	11.9	10.6	5.74	11.4	10.3	8.85
CI	(2.5 – 3.5 l/min/m <sup>2</sup> )	6.88	6.13	3.07	6.07	5.59	4.8
LVSWI	(45 – 60 g/m/m <sup>2</sup> /beat)	36.8	79.8	16.9	52.7	32.5	47.9
SVRI	(1700 – 2400 dyne/sec/cm <sup>5</sup> /m <sup>2</sup> )	535	1290	573	791	629	1420
<i>Arterial blood (normal range)</i>							
pH	(7.35 – 7.45)	6.94	7.47	7.14	7.39	7.17	7.49
PaO <sub>2</sub>	(80 – 110 mmHg)	98	67	188	62	116	55
PaCO <sub>2</sub>	(35 – 45 mmHg)	15	44	12	33	34	42
Bicarbonate	(22 – 31 mmol/l)	3	32	5	20	12	32
Lactate	(< 2 mmol/l)	22.2	1.8	12.9	1.5	12.5	1.1
Sodium	(137 – 145 mmol/l)	134	133	133	133	137	140
Potassium	(3.1 – 4.2 mmol/l)	4.0	3.1	5.0	3.6	4.6	3.4
Chloride	(101 – 109 mmol/l)	89	90	97	94	94	94
Anion gap	(8 – 16 meq/l)	45	19	38	19	34.6	19.4
Magnesium	(0.7 – 0.9 mmol/l)	1.25	0.93	1.01	0.88	1.12	0.77
Amylase	(< 70 U/l)	110	-	80	-	53	-
Glucose	(3.0 – 6.0 mmol/l)	12.6	4.6	14.8	5.6	2.1	9.2
<i>Mixed venous blood (normal range)</i>							
pH	(7.33 – 7.42)	6.93	7.43	7.11	7.35	7.13	7.45
P $\bar{V}$ O <sub>2</sub>	(38 – 42 mmHg)	57	41	52	39	58	33
P $\bar{V}$ CO <sub>2</sub>	(41 – 51 mmHg)	20	48	16	35	38	45
Bicarbonate	(24 – 35 mmol/l)	4	31	5	19	12	31

MAP = Mean arterial pressure, PaOP = Pulmonary artery occlusion pressure, CO = Cardiac output, CI = Cardiac index, SVRI = Systemic vascular resistance index, LVSWI = Left ventricular stroke work index.

pressure of 8 mmHg, and a reduction in cardiac size on chest X-ray.

#### *Patient 2*

A 54 year old man with a long history of intermittent heavy alcohol intake, poor diet and one month history of lethargy, swelling of ankles and progressive dyspnoea, was admitted to the intensive care unit hypotensive and anuric. On examination he was cyanosed with poor peripheral perfusion and obtunded, responding purposefully to painful stimuli only.

His systolic blood pressure was 50 mmHg, the pulse was 68 beats per minute and irregular, respiratory rate was 30 per minute and his temperature was 30.8°C. His jugular venous pressure was elevated to 5 cmH<sub>2</sub>O and crepitations were heard at both lung bases on auscultation. The ECG revealed atrial fibrillation and generalised non-specific T wave flattening. The chest X-ray showed cardiomegaly, pulmonary venous congestion and generalised interstitial and alveolar oedema.

The admission and 24 hour haemodynamic measurements and arterial blood gases (receiving oxygen at 10 litres/minute via a face mask on admission) and mixed venous blood gases, arterial lactate, plasma electrolytes, glucose and amylase are shown in Table 1. The complete blood picture revealed a haemoglobin of 131 g/l, white cell count of 21.7 x10<sup>9</sup>/l and platelet count of 148 x10<sup>9</sup>/l. A right heart pulmonary flotation catheter was inserted into the right subclavian vein and its position was confirmed by chest X-ray. Blood and urine cultures were taken and subsequently found to be negative.

A diagnosis of acute pernicious beri-beri was made, and blood was taken for whole blood transketolase activity which was found to be 28.7% (normal < 20%). Intravenous thiamine 500 mg was administered. However, four hours later the patient remained anuric and the mean arterial pressure and cardiac output had not changed significantly, so digoxin 1 mg was administered intravenously. Within three hours the mean arterial pressure had increased to 70 mmHg and the patient's urine output for the third hour after digoxin was 180 ml. For the next 2 days, the patient was treated with thiamine 100 mg intravenously 8-hourly and digoxin 0.25 mg orally daily. The patient was discharged from the intensive care three days after admission, conscious and co-operative with a reduction in cardiac size and improvement in interstitial and alveolar oedema on chest X-ray.

#### *Patient 3*

A 46 year old man with a chronic history of alcohol abuse was admitted with a two day history of nausea, weakness and malaise following a heavy bout of

drinking over a three day period. An initial blood glucose of 2.1 mmol/l prompted one litre of an intravenous 10% glucose solution to be administered. Four hours later he was dyspnoeic, cyanosed and restless with a blood glucose of 8.2 mmol/l. On examination his blood pressure was 90/40 mmHg, the pulse was 104 beats per minute, respiratory rate 34 per minute, temperature 35.8°C and jugular venous pressure was elevated. On auscultation, crepitations were heard throughout both lung fields and the ECG revealed atrial fibrillation. The chest X-ray showed cardiomegaly and generalised pulmonary oedema. The admission and 24 hour haemodynamic measurements and arterial (receiving oxygen at 4 litres/minute via nasal cannulae on admission) and mixed venous blood gases, arterial lactate, plasma electrolytes, glucose and amylase are shown in Table 1. The complete blood picture revealed a haemoglobin of 146 g/l, white cell count of 24.0 x10<sup>9</sup>/l and platelet count of 151 x10<sup>9</sup>/l. A right heart pulmonary flotation catheter was inserted into the right internal jugular vein and its position was confirmed by chest-Xray.

From the clinical, haemodynamic and laboratory findings, a diagnosis of acute pernicious beri-beri was made and blood was taken for whole blood transketolase activity which was subsequently found to be 25.3% (normal < 20%). The patient was treated with thiamine 500 mg intravenously followed by 100 mg 8-hourly for 24 hours and 100 mg daily thereafter. However, during the first 6 hours the patient remained anuric, and the blood pressure, pulse and cardiac output did not alter significantly. The patient was then treated with intravenous digoxin 0.75 mg followed by a further 0.25 mg 2 hours later. Within the following 4 hours the patient became more co-operative and the urine output increased from 10 ml/hour to 220 ml/hour. The patient was discharged from the intensive care unit after three days.

#### DISCUSSION

Thiamine pyrophosphate has an important role in carbohydrate metabolism as it is required for the oxidative decarboxylation of pyruvate and alpha ketoglutarate, and for the transketolase reaction in the pentose phosphate pathway. In acute pernicious beri-beri, lactic acidosis is caused by the block to aerobic glycolysis and is exacerbated by high circulating catecholamine levels which increase glycogenolysis (a  $\beta_2$  adrenergic effect).<sup>8</sup> Activation of hormone-sensitive lipoprotein lipase (a  $\beta_3$  adrenergic effect) may also play a role by increasing lipolysis, acetylCoA and NADH production, which in turn inhibits pyruvate oxidation and causes an increase in the lactate pyruvate ratio.<sup>9</sup>

The clinical features of acute pernicious beri-beri include, breathlessness, agitation, cyanosis, absent upper arm pulses but moderately strong femoral pulses.<sup>10</sup> The cyanosis in the presence of a high cardiac output indicates regional perfusion abnormalities with high skeletal muscle blood flow and reduced skin blood flow. Difficulties in diagnosis occur in the alcoholic patient due to delirium tremens, pancreatitis and septicaemia, presenting similar clinical features.

The high initial cardiac output and mixed venous oxygen tension and low peripheral vascular resistance and left ventricular stroke work index were found in all patients which were indicative of acute thiamine deficiency. For septic shock patients to have all these features, resuscitation with fluid and adrenaline is usually required first. Moreover, normothermia (present in the first and second patient) and hypoglycaemia (present in the third patient) are unusual in patients with septic shock.

The plasma amylase levels were normal in all patients and while restlessness was a feature in two patients, none were delirious, making acute pancreatitis and delirium tremens, respectively, unlikely. Finally, a low erythrocyte transketolase activity which when activated in vitro by thiamine pyrophosphate indicates thiamine deficiency. While the latter is a specific effect in patients who have thiamine deficiency, it not a sensitive test as it may not occur in patients with gross thiamine deficiency.<sup>11</sup> All patients demonstrated erythrocyte transketolase activation by thiamine pyrophosphate.

The body's thiamine reserve is limited and deficiency may appear within 14 days with a thiamine free diet.<sup>6</sup> The recommended daily allowance for thiamine is 0.5 mg/1000 Kcal<sup>12</sup> and 3 mg/day will maintain normal levels of thiamine in the normal postoperative patient,<sup>13</sup> although, up to 250 mg a day of thiamine has been recommended in critically ill patients.<sup>14</sup> While acute pernicious beri beri usually responds to 500mg of thiamine intravenously followed by 100 mg 8-hourly for 24 h, and thereafter 100 mg daily for 14 days (although up to 1000 mg i.v. 12-hourly has been recommended<sup>15</sup>) two patients in our report responded poorly to thiamine alone.

Normally a return towards a normal systemic vascular resistance occurs within 30-90 minutes after administering intravenous thiamine and the blood pressure and clinical symptoms may be normal after 24 hours, although a normal haemodynamic status may not occur until 1-2 weeks of treatment.<sup>3</sup> The haemodynamic response usually begins with an increase in peripheral resistance followed by an increase in blood pressure and stroke work index and a reduction in cardiac output and

mixed venous oxygen saturation.<sup>16</sup> However as alcohol has a direct cardiotoxic effect<sup>17</sup> the myocardial defect in chronic alcoholics may be caused by both chronic alcohol toxicity and thiamine deficiency. Correction of peripheral vascular resistance may therefore unmask myocardial insufficiency to explain the development of cardiac insufficiency noted in two of the patients reported in our study, and which has also been reported after treatment of high cardiac output with thiamine.<sup>18,19</sup> Digoxin was of benefit in the two patients who had a poor response to thiamine and has also been reported previously in the management of low cardiac output state following thiamine.<sup>18</sup>

While the lactic acidosis associated with acute pernicious beri-beri has been treated with thiamine alone,<sup>1</sup> sodium bicarbonate (up to 300 mmol) is usually also recommended.<sup>6</sup> However, sodium bicarbonate increases lactate production,<sup>20</sup> and should be used with caution in thiamine deficient patients with lactic acidosis<sup>21</sup>. The three cases reported here indicate that bicarbonate is not required to achieve a successful outcome. The return of a normal metabolic and haemodynamic status reduced lactate production and allowed metabolism of the excess lactate to provide a normal acid-base status.

Magnesium depletion in the alcoholic patient may occur (despite normal plasma magnesium levels, requiring a magnesium infusion test for its diagnosis<sup>22</sup>) and may account for a poor response to thiamine in thiamine depleted states.<sup>23</sup> In the three patients reported, the plasma magnesium and potassium levels decreased during the first 24 hours of therapy, indicating that these electrolytes should be closely monitored and replaced during management.

Acute pernicious beri-beri is a disease that requires immediate intravenous thiamine and close haemodynamic and biochemical monitoring, reviewing the change in peripheral resistance, cardiac output, mixed venous oxygen content and acid base status, during treatment. Digoxin (unlike adrenaline) improves myocardial contractility without exacerbating lactic acidosis and is useful in the management of myocardial insufficiency unresponsive to thiamine. Sodium bicarbonate may exacerbate lactate production, worsen pulmonary oedema and is not required in the management of this disorder.

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