Myocardial damage due to hypokalaemia and hypophosphataemia

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Summary

A case of severe hypokalaemia with stupor, skeletal muscle and heart muscle damage is reported.

An initial infusion of glucose-insulin and potassium (GIK) produced a temporary clinical improvement with reduction of creatine kinase (CKMB) and elevation of serum K⁺. On the 4th day of treatment, neuromuscular and cardiovascular deterioration occurred accompanied by a further rise of CKMB. This deterioration was coincident with a serum phosphate of 0.26 mmol/l. The impaired left ventricular (LV) function was measured using echocardiography and detecting the ejection fraction (EF).

GIK was stopped and a potassium phosphate infusion commenced. As the phosphate and potassium deficiencies were corrected, the neuromuscular and cardiac abnormalities resolved, CKMB fell to normal and LVEF rose from 40% to 72%.

We suggest that additional cardiac damage due to hypophosphataemia may have occurred in this patient, who already had cardiac impairment as a result of profound hypokalaemia. Possible mechanisms are discussed.

KEY WORDS: diuretic abuse, purgative abuse.

Introduction

In addition to the well-known electrophysiological effects of hypokalaemia, decreased myocardial contractility with congestive heart failure due to severe potassium depletion has been reported (Potts *et al.*, 1977).

Similarly reversible reduction of myocardial performance (O'Connor, Wheeler and Bethune, 1977) due to hypophosphataemia has been described.

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We report a case of heart muscle damage due to combination of hypokalaemia and hypophosphataemia.

Case report

A 46-year-old woman was admitted with stupor, tetraplegia, congestive heart failure and hypotension. For the last 5 years she had exhibited an extremely severe hypochondriacal neurosis. She had habitually abused laxatives and diuretics. She had had two previous admissions to hospital as a result of electrolyte imbalance. On this admission she was unconscious with motor responses only at the reflex level. She was dehydrated with basal lung rales. The heart rate was regular at 55 beats/min; the heart sounds were muffled with a third sound (S3) present; blood pressure (BP) was 80/60 mmHg.

Chest X-ray showed cardiomegaly with dilatation mainly of the left ventricle (LV) and pulmonary congestion of moderate severity. Electrocardiogram (ECG) showed sinus rhythm, rounded depression of ST segment more prominent in V1-V3, T wave inversion, prominent U wave with pseudo-lengthening (0.60 ms) of the QTc. The brain computerized assisted scan revealed no tomodensitometric abnormalities. The electroencephalogram revealed a slow wave (2.5 Hz) activity with overshadowing sharp waves and spikes on the left hemisphere. Laboratory studies revealed severe hypokalaemia (1.5 mmol/l normal—3.6–5) and moderately low levels of calcium, 1.95 mmol/l (normal 2.1–2.6), magnesium 0.8 mmol/l (normal 0.9–1.2) and phosphate (1.5 mg/dl; 0.48 mmol/l (normal 2.5–4.5 mg/dl 0.80–1.45 mmol/l). The creatine kinase (CK) activity was 2,660 mu/ml (normal <230) with increased MB (30%) fraction. Blood gases, pH, hepato-renal function and blood count were normal.

Infusional therapy was begun immediately with

potassium chloride (40 mmol every 8 hr) in a glucose-insulin solution (500 ml 10% glucose + 12 u of regular insulin/every 8 hr), magnesium sulphate 10% (4 vials 10 ml in 0.9 N NaCl 500 ml/24 hr), spironolactone 200 mg/daily orally.

We monitored cardiac rhythm and measured electrolyte values, CK and its MB fraction (Fig. 1) every 12–24 hr. Forty-eight hours after commencement of this treatment, the neurological status of the patient was markedly improved. She was conscious and manifested a right hemiparesis with aphasia and a moderate weakness in the limbs on her left side: electromyography of the right quadriceps muscle revealed moderate signs of myopathic damage. The cardiovascular condition also improved with an increase of blood pressure to 100/75 mmHg, the disappearance of chest rales and of S3. The heart rate stayed at 60–70/min without arrhythmias. On the ECG recordings the ST-T anomalies were progressively less pronounced, the U wave less prominent, CK activity decreased slowly to 660 mu/ml (MB 30%).

FIG. 1. The trend of biochemical values (potassium: K ■; phosphates: P ▲; CKMB ●) during glucose, insulin and potassium (GIK), and potassium phosphate infusion.

On the 4th day there was a sudden worsening of the neurological and cardiovascular conditions, the patient became confused, and the blood pressure dropped to 80/60 mmHg. Rales became audible again in the basal region of lung fields and S3 reappeared. The ECG recording was nearly normal with sinus rhythm 70/min. There was a resurgence of CK to 1250 mu/ml with MB fraction 40%. A two-

dimensional echocardiographic study was carried out with an Irex phased array real time imaging system. The videotape recording was analyzed in slow motion, frame-by-frame, by a Cardio 80 microprocessor computer, digitizing LV end-diastolic and end-systolic frames to obtain, by a systo-diastolic superposition, the percentual analysis of the LV wall's motion and LV ejection traction (LVEF). The apical four-chamber view showed on the fourth day septal akinesis and lateral wall hypokinesis of LV. The LVEF was 40% (Fig. 2).

Electrolyte analysis revealed net improvement of serum K⁺ (3 mmol/l), but the serum phosphate concentration was further lowered to critical levels (0.8 mg/dl; 0.2 mmol/l) (Fig. 1); Mg²⁺ and Ca²⁺ were in the normal range. Blood cell count revealed a mild anaemia with haemoglobin 11.8 g/dl.

The infusional therapy was modified, the glucose, insulin and potassium chloride was stopped and a solution of potassium monohydrogen and dihydrogen phosphate salts was made up in 0.9 N NaCl (40 mmol of KH₂PO₄-K₂HPO₄ in 500 ml 0.9 NaCl/every 8 hr). Neither digitalis nor other inotropic agents were administered. Following the phosphate infusion the serum phosphate, K⁺ and CKMB returned to normal; the patient became conscious, the shortness of breath, chest rales and S3 disappeared; the BP rose to 120/70 mmHg. After 6 days of potassium phosphate administration a second echocardiographic study (Fig. 2) was undertaken with the same procedure: at this examination, on the apical four-chamber view we observed a recovery of the LV wall kinesis, with mild septal hypokinesis and moderate hyperkinesis of the LV lateral wall; the EF had risen to 72%. The patient was discharged 5 days later in good health.

Discussion

It is known that carbohydrate-rich total parenteral nutrition can induce hypophosphataemia, if there is not an adequate phosphorus intake (Knochel, 1977). In general, significant clinical manifestations are absent because the basal values of serum phosphate are normal, hypophosphataemia is not at a critical level (0.323 mmol/l) or there coexists a metabolic acidosis which, due to the Bohr effect, prevents tissue hypoxia. The phosphate consumption is due to phosphorylation of carbohydrates induced by the insulin that promotes the passage of phosphorus and carbohydrates through the cellular membranes.

In our patient the cardiac and neuromuscular abnormalities were attributed to hypokalaemia and there was an initial clinical response to a potassium infusion. However she was also deficient in phosphate (0.49 mmol/l) as a result of chronic laxative

FIG. 2. Segmental analysis of LV kinesis and ejection fraction (EF) by a two-dimensional echocardiographic study in apical four-chamber view, before (a) and after (b) potassium phosphate infusion.

and diuretic abuse. Correction of the hypokalaemia by glucose, insulin and potassium resulted in further depletion of available phosphate to 0.26 mmol/l with deterioration in her clinical condition and elevation of CKMB. The echocardiographic recording then undertaken (Fig. 2) revealed a marked decrease of myocardial contractility with LVEF of 40%. The administration of potassium phosphate in place of glucose-insulin-potassium produced a normalization of enzyme values and a large improvement in myocardial contractility with LVEF of 72% (Fig. 2). The second peak in CKMB cannot be attributed to hypokalaemia which was undoubtedly responsible for the first peak, as it was only moderate (3 mmol/l) at the time.

We would like to suggest that the profound hypophosphataemia induced this second peak indicating myocardial damage and the second episode of functional impairment. These latter changes resolved with phosphate replacement.

Others have described reduction of myocardial performance (O'Connor *et al.*, 1977) as a result of hypophosphataemia. Myocardial damage with elevation of CKMB has not previously been described. In this case the temporal relationship between the plasma phosphate and CKMB changes would suggest such an effect.

At the moment we know little about the pathogenetic mechanism. However a reduced availability of cellular ATP and a reduction of red cell 2,3 diphos-

phoglycerate content with impaired release of oxygen from oxyhaemoglobin and tissue hypoxia has been attributed to severe hypophosphataemia (Knochel, 1977; O'Connor *et al.*, 1977).

Therefore we suggest that before use of glucose-insulin-potassium solutions, which as noted (Mantle *et al.*, 1981) improves left ventricular function in patients with acute myocardial infarction, account must be taken of the basal value of phosphataemia, especially in patients under total parenteral nutrition and patients whose hypokalaemia is the result of drug abuse, in order to avoid cardiovascular side effects.

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