Lesson of the Week

Refeeding hypophosphataemia in anorexia nervosa and alcoholism

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Phosphate is important for cellular metabolism. Body phosphate stores may become depleted during inadequate nutrition, and severe hypophosphataemia may ensue when metabolic demand for phosphate is subsequently increased acutely; this condition is termed the nutritional recovery syndrome. We describe two such cases associated with anorexia nervosa and with severe alcoholism. Narrow suppression, anaemia, thrombocytopenia, neuroencephalopathy, convulsions, and cardiac effects occurred associated with acute hypophosphataemia.

Case 1

An 18 year old man with anorexia nervosa was admitted, having collapsed after alcohol ingestion. He weighed 29 kg. Pulse rate was 40/min, and blood pressure 100/70 mm Hg. Plasma glucose concentration was <1 mmol/l (normal 3-6-5-8), plasma phosphate concentration 1-34 mmol/l (normal 0-8-1-4), haemoglobin concentration 124 g/l, white cell count 15·4×10⁹/l, and platelet count 316×10⁹/l. He responded to intravenous dextrose, and a ward diet was instituted. After two days the plasma phosphate concentration fell to 0·45 mmol/l and after four days to 0·20 mmol/l. Haemoglobin concentration fell to 98 g/l, white cell count to 2·8×10⁹/l, and platelet count to 41×10⁹/l. Bone marrow was severely hypoplastic. No cause for the marrow suppression was found other than hypophosphataemia. Over two weeks of normal diet the plasma phosphate value rose to 0·64 mmol/l and full blood count returned to normal with a 5-7% reticulocytosis.

Three months later the patient relapsed and was readmitted weighing 27 kg. He was given a normal diet and gained 4 kg. After 10 days grand mal convulsions began, recurring over three days despite anticonvulsants. There were no focal neurological signs; conscious level remained depressed between convulsions. Plasma phosphate concentration was 0·07 mmol/l. Plasma glucose, calcium, and potassium concentrations and arterial oxygen tension were normal; plasma magnesium was 0·6 mmol/l (normal 0·7-1·3). Computed tomography showed some brain shrinkage only. Results of lumbar puncture were normal. An electroencephalogram was diffusely abnormal without epileptiform activity. Bone marrow was hypoplastic, haemoglobin concentration 84 g/l, white cell count 2·3×10⁹/l, and platelet count 139×10⁹/l with no identifiable cause other than hypophosphataemia.

After treatment with phenytoin and a ward diet the plasma phosphate concentration rose to 1·25 mmol/l and he recovered over 10 days. At follow-up all haematological and biochemical analytes were normal.

Case 2

A 60 year old woman with longstanding alcohol dependency was admitted having collapsed. She lived alone and derived virtually all of her intake of energy from gin and wine. She was emaciated and jaundiced; pulse was 110/min and blood pressure 140/70 mm Hg and the liver was palpable four finger breadths below the costal margin. She was rational, orientated, and had no neurological abnormalities. Bilirubin concentration was 86 µmol/l, alkaline phosphatase activity 255 IU/l, and γ-glutamyltransferase activity 1504 IU/l. Sodium, potassium, and total carbon dioxide values were reduced at 131, 3-2, and 14·0 mmol/l respectively; glucose concentration was 6·1 mmol/l, and calcium 2·3 mmol/l. Plasma phosphate concentration was 0·30 mmol/l and magnesium 0·36 mmol/l. Liver biopsy showed cirrhosis, fatty change, and alcoholic hepatitis. She began a normal diet. Twenty four hours later the plasma phosphate concentration fell to 0·1 mmol/l, remaining so for 48 hours. She became progressively less well, with confusion, tachycardia, and widespread T wave inversion. She could not tolerate treatment by mouth and was given 100 mmol mixed phosphate solution (Polyfusor) intravenously over 48 hours by infusion pump, which raised the plasma phosphate concentration to normal (1·2 mmol/l). Plasma calcium and magnesium concentrations fell, necessitating separate infusions of calcium.

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magnesium, and potassium. Within 24 hours her mental state, pulse rate, and electrocardiogram were normal and her general condition greatly improved. No psychotropic drugs were used.

**Comment**

The dangers of refeeding after periods of starvation are well recognised. Many factors contribute to this morbidity and mortality, but acute severe hypophosphataemia may be the most important. During starvation body stores of phosphate become depleted, but plasma phosphate is usually only modestly depressed. On refeeding a sudden shift of phosphate into cells occurs, primarily for phosphorylation of glycerol and protein synthesis. Profound hypophosphataemia may ensue (<0.3 mmol/l) and be associated with anaemia, thrombocytopenia, liver damage, myocardial dysfunction, muscle weakness and rhabdomyolysis, and a neuroencephalopathic syndrome which may include convulsions. Though other metabolic abnormalities—for example, hypokalaemia, hypomagnesaemia, and acid-base disturbance—may contribute to this syndrome, the rapid response to phosphate supplementation, as in case 2 and animal studies, suggests a central role for hypophosphataemia. This syndrome is relevant to patients with anorexia nervosa; alcoholic patients surviving on wine, which contains little phosphate, and spirits, which contain none, also have reduced body phosphate stores and are at risk after a sudden increase in carbohydrate intake. Hypophosphataemia is best treated by oral supplements; if intravenous treatment is required the infusion rate should be controlled and plasma calcium and magnesium concentrations monitored. A plasma phosphate concentration below 0.3 mmol/l represents a lifethreatening medical emergency. Plasma phosphate should be monitored over several days in patients being fed after a period of inadequate nutrition.

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**References**


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**A young man in his 30s with diabetic retinopathy who is well controlled on biphasic insulin has refractory hypertension—blood pressure 170/120 to 180/125 mm Hg—which has not responded to treatment with nifedipine. What treatment is advised?**

The choice of a suitable antihypertensive drug in diabetic patients depends not only on efficacy and safety but also on possible adverse effects on glycaemic control and plasma lipids that may occur when these patients take β blockers and thiazide diuretics. As this patient has moderately severe hypertension not controlled with nifedipine the use of an angiotensin converting enzyme inhibitor (captopril, enalapril) given alone or combined with a diuretic could be considered. Although further studies are still needed, reports to date suggest that angiotensin converting enzyme inhibitors are safe in insulin dependent diabetics and do not affect blood glucose. Captopril when combined with a diuretic attenuated the effect of the latter on plasma glucose and cholesterol. In insulin dependent diabetics with nephropathy captopril treatment reduced microalbuminuria and over a two year period reduced the deterioration in glomerular filtration rate. Provided that dosage is adequately adjusted renal impairment should not therefore be a contraindication.—BASIL F CLARKE, consultant physician in diabetes, Edinburgh.

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**What is the postviral syndrome?**

The postviral syndrome is a poorly defined illness for which there are no clearly accepted diagnostic criteria. The main clinical characteristic is excessive fatigue, which may be associated with one or more of several other symptoms, such as myalgia, palpitations, headaches, anxiety, and depression. These symptoms often date from a minor viral like illness and may persist for many years. Both sporadic and epidemic forms have been recognised, with probably the most famous outbreak being that described at the Royal Free Hospital in 1955. Royal Free disease is just one of the alternative terms used for this syndrome; others include Iceland disease, epidemic neuromyasthenia, and myalgic encephalomyelitis. There has been discussion whether this syndrome is hysterical in origin, but many would consider it to have an organic basis. Diagnosis can be difficult, but various abnormalities have been described in several patients. For example, in one study most patients in the chronic phase of the illness had abnormal histological findings in muscle, a reduction in helper T cells, and a reduction in the helper:suppressor T cell ratio. A small group of patients underwent nuclear magnetic resonance studies of muscle. This technique showed an abnormally early and excessive intracellular acidosis that was considered to be due possibly to the formation of excessive lactic acid as a consequence of disordered metabolic regulation. In the United Kingdom most attention has been focused on coxsackievirus B as the possible responsible agent. This is based on a higher frequency of raised coxsackievirus B neutralisation titres in patients than in controls. In the United States more attention has been paid to Epstein-Barr virus being the possible culprit. Probably the sporadic cases follow any one of several viral infections, but this does not explain the epidemic form of the disease—perhaps yet another “new” virus awaits discovery.—F MORGAN-CAPNER, consultant virologist, Preston.

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**A 66 year old man’s father died of secondary prostatic cancer diagnosed too late for any treatment at the age of 75. Should this patient be offered any regular testing apart from an annual check up and rectal examination? Would the advice change had he already had a transurethral resection for benign hyper trophy?**

There is a significant increased incidence of carcinoma of the prostate in relatives of patients with the disease. It would be reassuring for the patient to undergo regular check ups. Apart from digital assessment of the prostate, blood should be taken for serum acid phosphatase determination and certainly prostatic specific antigen measurement. Prostatic specific antigen has been shown to be the most sensitive tumour marker for prostatic cancer. A positive test for transurethral resection for benign hyper trophy does not in any way influence the subsequent development of prostatic cancer, as the latter occurs in the peripheral part of the gland, particularly the posterior lobe inferior to the ejaculatory ducts. Rectal evaluation of the prostate after transurethral resection is always difficult, but it should not be difficult to document change if the rectal findings are periodically recorded. When suspicions are aroused then fine needle aspiration of the prostate for cytology, or Tru-Cut biopsy for histology, may be done. The detection of prostatic cancer confined to the prostate gives the clinician the opportunity to give deep x ray treatment and hence to reserve for a later date hormone manipulation if treatment is unsuccessful.—J C GINGELL, consultant urologist, and D GILLATT, research registrar, Bristol.