Effect of 1-alpha-hydroxycholecalciferol on magnesium metabolism in chronic renal failure

Vitamin D derivatives and analogues are increasingly being used to treat bone disease in chronic renal failure but their effects on magnesium metabolism have not been fully documented. The use of 1- α -hydroxycholecalciferol (1- α -OHD₃) in chronic renal failure, however, may be associated with a special risk of magnesium intoxication.¹ This prompted us to review our own data.

Methods and results

We studied the external balances of calcium and magnesium² in two patients with chronic renal failure and renal bone disease (cases 1 and 2; plasma creatinine 480 μ mol/l (5.4 mg/100 ml) and 640 μ mol/l (7.2 mg/100 ml) respectively) before and during treatment with 1- α -OHD₃ 2 μ g/daily by mouth (see figure). Considerable increases in calcium retention during the first four days of treatment in case 1, and after 18 months in case 2 (a renal dwarf who ate little calcium), were unaccompanied by significant changes in magnesium balance.

Urinary (white areas) and faecal (black areas) excretion of calcium and magnesium in cases 1 and 2 before and during treatment with 1- α -OHD₃ (hatched areas). Case 2 was restudied after 18 months of continuous treatment.

Conversion: SI to traditional units—Calcium: 1 mmol/24 h $\approx$ 40 mg/24 h. Magnesium: 1 mmol/24 h $\approx$ 24.3 mg/24 h.

In 13 other patients with chronic renal failure, nine of whom were being treated with haemodialysis, there was no significant difference between the mean predialysis plasma magnesium concentrations before (mean 1.14 ± 0.06 mmol/l; 2.77 ± 0.15 mg/100 ml) and after nine months' treatment with 1- α -OHD₃ (1.23 ± 0.04 mmol/l; 2.99 ± 0.97 mg/100 ml). During long-term treatment hypercalcaemia occurred in 10 of these patients (range 2.65–3.38 mmol/l; 10.60–13.52 mg/100 ml) but there was no significant change in the mean plasma magnesium concentration (1.32 ± 0.08 mmol/l; 3.21 ± 0.19 mg/100 ml). In some patients, however, the plasma magnesium concentration increased by up to 0.53 mmol/l (1.28 mg/100 ml) during hypercalcaemia, but no measurements of possible variations in the dietary intake of magnesium were made and the increases did not correlate with those of calcium.

Comment

Changes in intestinal absorption of magnesium might be expected to resemble those of calcium, but several observations suggest that this may not be so. Firstly, animal studies and our observations in uraemic patients suggest that magnesium absorption is not increased by doses of 1- α -OHD₃ sufficient to increase greatly the retention of calcium, although vitamin-D-induced magnesium absorption may become apparent only when the magnesium intake is increased. Secondly, like

others,^{3,4} we have observed no consistent changes in plasma magnesium after long-term treatment with 1- α -OHD₃, even after accidental overdose. Finally, in chronic renal failure plasma magnesium concentrations rise when the dietary intake of magnesium is moderately increased,⁵ whereas plasma calcium is affected only by large increases in oral calcium intake.

Our evidence suggests that 1- α -OHD₃ may have little effect on magnesium absorption in chronic renal failure and that increased plasma magnesium concentrations associated with the administration of 1- α -OHD₃¹ may independently reflect changes in the dietary intake of magnesium. This conclusion cannot necessarily be extended to other vitamin D metabolites or to patients without renal failure.

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² Smith, R, *et al*, *Quarterly Journal of Medicine*, 1973, **42**, 235.

³ Tougaard, L, *et al*, *Lancet*, 1976, **1**, 1044.

⁴ Nielsen, S P, *et al*, *Vitamin D and Problems Related to Uraemic Bone Disease*, p 623. Berlin, De Gruyter, 1975.

⁵ Randall, R E, *et al*, *Annals of Internal Medicine*, 1964, **61**, 73.

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Metabolic Unit, Nuffield Orthopaedic Centre, Oxford

J A KANIS, MRCP, Wellcome senior clinical research fellow

R SMITH, PHD, FRCP, first assistant and honorary consultant physician

R J WALTON, MRCP, Goodger scholar

M BARTLETT, technician

Acute ileus in myxoedema

Acute ileus mimicking a surgical emergency is a rare complication of severe hypothyroidism. Bastenie¹ concluded that it was caused by myxoedematous deposits separating muscle fibres in the bowel wall from their ganglia. We report a typical case, which throws new light on the pathology of this condition.

Case report

A 68-year-old woman was admitted with a history of increasing confusion. She was myxoedematous, and the abdomen was grossly distended, with scant bowel sounds. Her temperature was 35.4°C and blood pressure 60/40 mm Hg. Myxoedematous precoma with concurrent bowel obstruction was diagnosed. Treatment with triiodothyronine 200 μ g 8 hourly for 48 hours and thyroxine 0.25 mg/day was started, and the obstruction was treated conservatively with fluid and electrolyte replacement. On admission potassium concentration was 2.4 mmol (mEq)/l, protein-bound iodine 130 nmol/l (1.6 μ g/100 ml), and thyroxine 10 nmol/l (0.8 μ g/100 ml). The hypokalaemia was attributed to preadmission diuretic treatment. A folate deficiency megaloblastic anaemia (haemoglobin 5.4 g/dl; folate 1.0 mg/l), which was thought to be dietary, was treated with vitamin B₁₂ and folate. Blood pressure and temperature quickly returned to normal. Abdominal radiographs indicated a paralytic type of ileus, and conservative treatment was continued. After 10 days the hypothyroidism was much improved, and the ileus had become the dominant problem. Potassium values were consistently normal at this stage, and although the initial hypokalaemia may have aggravated the ileus, it became clear that the likely cause of the continuing ileus was myxoedema. The abdominal signs showed no improvement, and the patient died after 20 days.

Pathological findings—At necropsy the thyroid was shown to be replaced by fibrous tissue. The heart was normal and there was moderate pulmonary oedema. The colon was slightly dilated but otherwise macroscopically normal. Paraffin sections of mucosa, muscle coats, and the myenteric plexus were normal, and special stains showed no mucopolysaccharide deposits in the bowel wall. Frozen sections through the myenteric plexus stained with silver showed a few round clear areas, devoid of stainable material, and the neurones and processes were distorted around them. Some axons were grossly abnormal, showing ellipsoids, axon swellings, and fragmentation. These changes were present in the plexus itself, but more prominently in the trunks entering the bowel from outside.

Comment

Previous reports of acute ileus in myxoedema emphasise the inadvisability of surgical intervention. A broad spectrum of reduced