Rise in serum calcium and magnesium concentrations after vitamin D administration in hypocalcaemic hypomagnesaemic magnesium deficiency

R. R. GHOSE
F.R.C.P.E., M.R.C.P.  
D. WYNFORD-THOMAS
M.B., B.Ch.

Singleton Hospital, Sketty, Swansea

Summary
A patient with hypocalcaemia and hypomagnesaemia secondary to small bowel resection and malabsorption was treated with synthetic vitamin D analogue, 1-α hydroxy vitamin D₃. A prompt rise in serum calcium concentration and some days later a smaller and transient rise in serum magnesium concentration was observed. These changes in extracellular fluid composition presumably resulted from enhanced calcium and magnesium absorption associated with vitamin D activity.

Introduction
Studies on patients with hypocalcaemia due to magnesium deficiency have shown that oral magnesium therapy alone is capable of restoring serum calcium concentration to the normal range over a period of 14 days (Heaton and Fourman, 1965). The basis of hypocalcaemia which accompanies magnesium deficiency is uncertain, but parathyroid hormone metabolism is deranged (Rude, Oldham and Singer, 1976). Serum immuno-reactive parathyroid hormone (PTH) ranged from undetectable to normal levels in the presence of hypocalcaemia and hypomagnesaemia. Intravenous magnesium administration immediately stimulated a rise in serum PTH, within one minute, indicating that the reduced serum PTH levels observed with magnesium depletion resulted from inhibited PTH secretion. PTH biosynthesis was apparently intact. In spite of serum PTH elevation, serum calcium concentration remained subnormal at 60 min, suggesting target organ resistance to PTH as well.

A case is now reported of hypocalcaemic hypomagnesaemic magnesium deficiency which responded to 1-α hydroxy vitamin D₃ (1-α OH D₃) by raising serum calcium and magnesium concentrations in the face of persisting magnesium depletion.

Case report
A 46-year-old married woman was sterilized through an abdominal incision twelve years previously. At the age of 40 years she presented with intestinal obstruction from gangrenous small bowel arising from abdominal adhesions, which necessitated extensive small bowel resection. Persistent ill health with fatty diarrhoea and weight loss followed this operation. Faecal fat excretion was 26 g/day. In spite of a low fat diet she remained thin, frail and depressed. Over the past year she had developed primary hypothyroidism which was adequately controlled by L-thyroxine sodium 0·2 mg daily.

One day after admission to hospital for fatigue, depression and weight loss, she developed frank tetany with generalized epileptiform convulsions. Serum biochemistry showed urea 3·0 mmol/l; potassium, 3·8 mmol/l; calcium, corrected for albumin, 1·66 mmol/l; magnesium, 0·2 mmol/l. Oral magnesium supplementation requires weeks to exert a slow and gradual restoration of serum calcium and magnesium concentration (Heaton and Fourman, 1965). Accordingly it was decided to treat the patient with oral calcium supplements, combined with 1-α OH D₃, in an attempt to raise serum calcium concentration quickly. Fig. 1 shows changes of serum calcium and magnesium concentrations after treatment. Biochemical improvement was associated with relief of tetany and convulsions, and amelioration of depression.

Results
Serum calcium concentration actually fell over the first few days when oral calcium supplements were given, but immediately 1-α OH D₃ was added there was a sharp curvilinear rise reaching a peak at the upper range of normal on day 20, when 1-α OH D₃ was stopped. After that, serum calcium concentration slowly declined to the lower range of normal.

A slight initial decline in serum magnesium concentration after commencing 1-α OH D₃ was followed by a subsequent rise to 0·6 mmol/l by day 20, after which there was a transient peak which
coincided with magnesium administration. Then a sharp fall in serum magnesium concentration was observed, and the level reached a plateau of 0.4 mmol/l by day 30.

Discussion

Calcium homoeostasis in man is regulated by PTH and 1,25-dehydroxycholecalciferol (1,25(OH)₂D₃), acting singly or in combination, on several target organs, namely bone, kidney and gut. Cholecalciferol, or vitamin D₃, undergoes 2 steps of hydroxylation, 25-hydroxylation in the liver, and 1-hydroxylation in the kidney, before conversion into the active vitamin D metabolite, 1,25(OH)₂D₃. PTH mediates renal 1-hydroxylation. Normal cellular and enzyme function is dependent on magnesium, and magnesium deficiency may conceivably affect the various enzymes involved in vitamin D metabolism, as well as inducing functional hypoparathyroidism. It is known that the synthesis of 25-OH D₃ is impaired by magnesium deficiency (Rosler and Rabinowitz, 1973).

In small bowel resection with malabsorption, hypomagnesaemia results from magnesium loss via the gastrointestinal tract. 1-α OH D₃ appeared to increase calcium and magnesium absorption in the present case. Metabolic balance studies in various metabolic bone disorders have shown that vitamin D and its hydroxylated derivatives such as 1-α OH D₃ increase calcium and magnesium absorption in patients with normal magnesium metabolism (Hodgkinson, Marshall and Nordin, 1979). The effect on magnesium absorption was relatively small compared with the effect on calcium absorption, and the molar ratio of the increase in magnesium absorption to the increase in calcium absorption was 0.114.

This is consistent with the rapid and considerable rise in serum calcium concentration in the present patient, compared with the relatively slow and transient rise in serum magnesium concentration. The prompt fall in serum magnesium concentration after discontinuing 1-α OH D₃ may be a reflection of intracellular magnesium depletion. Thyro-parathyroidectomized experimental animals quickly develop hypocalcaemic tetany and require the administration of 1,25(OH)₂D₃, in conjunction with PTH, to restore serum calcium concentration to normal (Garebedian et al., 1974).

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References


**Fig. 1.** The effect of oral calcium, magnesium and 1-α OH D₃ on the patient's serum calcium and serum magnesium concentrations.
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R. R. Ghose and D. Wynford-Thomas

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