Comment

The maximum AFP concentration of 7.4 g/l recorded for our patient is, to our knowledge, the highest value ever reported. To appear as a separate band on routine electrophoresis, AFP must be present in a concentration exceeding 0.5 g/l.

¹ Kohn, J, *Nature*, 1957, **180**, 986.

² Kohn, J, in *Chromatographic and Electrophoretic Techniques*, ed Ivor Smith, 4th edn, ch 5, p 120. London, Heinemann, 1900 and 1976.

³ Ritchie, R F, and Smith, R, *Clinical Chemistry*, 1976, **22** (4), 497.

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Treatment of osteomalacia with oral 1-alpha-hydroxyvitamin D₃ in a patient with malabsorption

Vitamin D is now known to undergo 25-hydroxylation in the liver and subsequently 1 α -hydroxylation in the kidney to form 1,25-dihydroxyvitamin D, (1,25(OH)₂D), before exerting its biological effects.¹ This knowledge has stimulated investigation into possible therapeutic applications of vitamin D metabolites and their synthetic analogues in metabolic bone disease. 1 α -hydroxyvitamin D₃ (1 α OHD₃), an analogue of 1,25(OH)₂D, has been used to treat renal osteodystrophy² but there are no descriptions of its long-term use in osteomalacia due to malabsorption. This report describes the response to small oral doses of 1 α OHD₃ in a patient with severe osteomalacia after massive small intestinal resection.

Case history, methods, and results

The patient, a housewife now aged 33 years, underwent resection of all the small intestine excepting 30 centimetres of jejunum after a volvulus in 1971. Osteomalacia was diagnosed in January 1973, and details of treatment are shown in the figure. Renal and hepatic function were normal. Transiliac bone biopsies were performed in January 1973, March 1975, November 1975, and May 1976. Eight μ m undecalcified sections were assessed quantitatively using both a Quantimet 720 automated image analyser and an eye-piece graticule. Calcification fronts were demonstrated by tetracycline fluorescence on 10 μ m unstained sections following oral administration of demeclocycline (Ledermycin) 48 hours before the biopsy. Serum calcium, phosphate, and alkaline phosphatase concentrations were measured on an SMA 12/60 Autoanalyser.

Biochemical and histological data are shown in the figure. Serum calcium and phosphate concentrations were initially normal and remained so throughout the treatment period. The raised alkaline phosphatase returned to normal for the first time seven months after starting 1 α OHD₃. After two years of parenteral vitamin D₂ treatment calcification fronts had become normal and osteoid volume had decreased, although still abnormally raised. After six months of treatment with 1 α OHD₃ osteoid volume had become normal. Histological and biochemical improvement during 1 α OHD₃ treatment was accompanied by disappearance of bone pain which had been present for three years.

Discussion

Biochemical and histological improvement after short-term oral³ and intravenous⁴ treatment with 1 α OHD₃ has been shown in patients

with osteomalacia and malabsorption, but no long-term studies have been reported. In our patient a good biochemical, histological, and symptomatic response was obtained after 14 months' treatment with oral 1 α OHD₃, despite the presence of only 30 cm of jejunum. This indicates that sufficient intestinal absorption of the analogue occurred to produce therapeutic blood levels and promote bone healing, even though a comparatively small dose was given. Little information is available on intestinal absorption of 1 α OHD₃, although it seems likely that it is absorbed in a manner similar to that of the parent vitamin, and would thus be expected to be reduced in the presence of fat malabsorption.

Details of treatment and response of serum alkaline phosphatase concentration and bone histology. Dashed horizontal line indicates upper limit of normal for serum alkaline phosphatase.

The therapeutic use of this analogue has several theoretical and practical advantages over parenteral vitamin D treatment. Firstly, oral treatment is more acceptable than parenteral treatment to most patients. Secondly, even though some histological improvement was seen after almost two years of parenteral vitamin D treatment, a comparable further improvement was seen after only six months of 1 α OHD₃ treatment, suggesting a greater therapeutic effectiveness of 1 α OHD₃ compared with the parent vitamin, even though at the doses used the weight equivalent of the latter was 215 times greater. Thirdly, although hypercalcaemia may complicate either form of treatment, it can be much more rapidly reversed after 1 α OHD₃ treatment.⁵ Hypercalcaemia has not occurred in our patient, and possibly malabsorption may protect against this complication. We conclude that 1 α OHD₃, given orally, may prove to be of value in treating osteomalacia in patients with malabsorption.

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¹ Holick, M F, *et al*, *Biochemistry*, 1971, **10**, 2799.

² Coburn, J W, Hartenbower, D L, and Brickman, A S, *American Journal of Clinical Nutrition*, 1976, **29**, 1283.

³ Bordier, P J, *et al*, in *Vitamin D and Problems Related to Uraemic Bone Disease*, ed AW Norman, *et al*, p 133, Berlin, W de Gruyter, 1975.

⁴ Bordier, P J, *et al*, *New England Journal of Medicine*, 1974, **291**, 866.

⁵ Kanis, J A, and Russell, R G G, *British Medical Journal*, 1977, **1**, 78.

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