Treatment of osteomalacia associated with primary biliary cirrhosis with oral 1-alpha-hydroxy vitamin D_3

Osteomalacia sometimes occurs in chronic cholestatic liver disease and is usually treated with large doses of parenteral vitamin D, although oral treatment is also effective.[1] Treatment with oral 1α-hydroxy vitamin D_3 (1α-OHD_3), a synthetic analogue of 1,25-dihydroxy vitamin D_3, is of particular interest in liver disease since a therapeutic effect depends on its intestinal absorption and hepatic 25-hydroxylation,[2] both of which may be impaired in severe chronic cholestasis. We report the biochemical and histological responses to six months' treatment with oral 1α-OHD_3 in a patient with primary biliary cirrhosis (PBC) and severe osteomalacia.

Case history

In 1976 a 65-year-old woman presented with pruritus and jaundice. Liver biopsy showed changes consistent with late PBC, and antimitochondrial antibodies were present. Subsequently the serum bilirubin concentration remained between 50 and 103 μmol/l (2·9 and 6·0 mg/100 ml) (normal 3-20 μmol/l; 0·2-1·2 mg/100 ml) and oesophageal varices developed. In April 1978 transiliac biopsy showed severe osteomalacia, and in June treatment began with oral 1α-OHD_3 2 μg daily. Serum calcium concentration was measured monthly and a repeat bone biopsy was performed in December 1978. Renal function was normal throughout. She was also receiving frusemide 80 mg twice daily, potassium supplements, diphenoxylate, and parenteral vitamins A and K.

Fasting serum alkaline phosphatase activity and calcium, albumin, phosphate, and bilirubin concentrations were measured on an autoanalyser (SMA 12/60), the serum calcium concentration being corrected for serum albumin value.[3] Plasma immunoreactive parathyroid hormone (PTH) values were measured by radioimmunoassay[4] (MRC antiserum code BW 211/41). Undecalcified sections of transiliac biopsy specimens (8 μm) were quantified with a Zeiss 25-point eyepiece graticule. Calcification fronts were shown both by 1% toluidine-blue staining and by fluorescence microscopy of unstained sections after giving 900 mg demethylchlortetracycline by mouth 48 hours before biopsy. Hyperparathyroidism was assessed qualitatively. Control values were obtained in biopsy specimens from seven women aged 54-73 years (mean 61·8); three were from healthy women and four from women who had died suddenly with no previous immobilisation or history of metabolic bone disease.

After treatment with 1α-OHD_3 the serum calcium and phosphate concentrations increased and the serum alkaline phosphatase activity lessened (see table). The plasma PTH concentration, which was high before treatment, was normal six months later. Liver function, as judged from serum bilirubin and albumin concentrations, remained stable during treatment. Hypercalcaemia was never encountered at monthly monitoring. The first bone biopsy showed severe osteomalacia with evidence of secondary hyperparathyroidism; after treatment with 1α-OHD_3 for six months the histological appearances had returned to normal.

Serum biochemical values and quantitative bone histology before and after treatment with 1α-OHD_3. (Normal values for bone histology expressed as means ± SD)

	Before treatment	After treatment	Normal value
Corrected serum calcium concentration (mmol/l)	2·29	2·41	2·3-2·6
Serum phosphate concentration (mmol/l)	0·92	1·1	0·8-1·4
Serum alkaline phosphatase activity (IU/l)	1390	910	30-85
Plasma parathyroid hormone concentration (μg/l)	2·3	0·44	0-0·9
Cancellous bone volume (% total sectional volume)	29·7	10·7	24·9 ± 18·8
Osteoid volume (% total cancellous volume)	25·8	4·7	1·7 ± 3·4
Osteoid surface (% total cancellous surface)	86·5	18·1	22·3 ± 29·5
Calcification fronts (% total osteoid surface)	5·4	67·5	70·1 ± 3·5

Conversion: SI to traditional units—Serum calcium: 1 mmol/l ≈ 4·0 mg/100 ml. Serum phosphate: 1 mmol/l ≈ 3·0 mg/100 ml.

Comment

This case shows that oral 1α-OHD_3 may be rapidly effective in healing severe osteomalacia associated with chronic cholestasis and suggests that even in severe liver disease adequate intestinal absorption and hepatic 25-hydroxylation of the vitamin may occur to produce a therapeutic effect, provided that a large enough dose is given. These findings accord with the report that either oral 25-OHD_3 or parenteral vitamin D_2 may heal osteomalacia associated with PBC.[1]

There is no evidence that 1α-OHD_3 is more effective than other forms of vitamin D in healing hepatic osteomalacia but it has important practical advantages; its short biological half life and comparatively narrow therapeutic dose range enables the correct dose to be established more quickly, and hypercalcaemia associated with overdosage may be more rapidly reversed than with the parent vitamin.[5] Hypercalcaemia did not occur in our patient but is a potential hazard of any vitamin D treatment and may appear only after bone healing has occurred. We conclude that oral 1α-OHD_3 is safe and effective in healing osteomalacia associated with PBC.

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An unusual case of respiratory obstruction due to inhalation of the epiglottis with an unusual attempt at self-treatment

We report an unusual cause of respiratory obstruction, in which the diagnosis was originally missed because of the anaesthetic technique used.

Case report

After suffering with a sore throat for seven days a 36-year-old man experienced rapidly increasing difficulty in breathing. He had read in a newspaper that laryngotomy could be a life-saving operation and had attempted to perform this on himself unsuccessfully. Fortunately he was found by a friend in time to bring him to hospital.

On admission there was obvious upper airway obstruction with lacerations in the neck skin. He was seen by a junior anaesthetist, who, not realising the potential dangers of this procedure in a patient with severe airway obstruction, induced anaesthesia with Althesin and suxamethonium and intubated an apparently normal larynx. The larynx was examined in theatre three hours later under anaesthesia with muscular paralysis, but apart from slight inflammation of the mucosa no abnormality was seen. The superficial skin lacerations were sutured. After extubation the patient's airway became progressively and rapidly obstructed. Anaesthesia was re-established, and examination under deep anaesthesia without muscular paralysis showed that the epiglottis was flaccid and flopped backwards with each inspiration to obstruct the laryngeal inlet completely. This was noted to give rise to a cogwheel pattern of inspiratory obstruction, with unobstructed expiration.

The patient was reintubated for 48 hours and then re-examined in theatre. There was no visible abnormality. After extubation, however, on return of spontaneous breathing the epiglottis appeared no longer flaccid, and after 12 months the patient has suffered no further airway obstruction after upper respiratory tract infections.