SHORT REPORTS

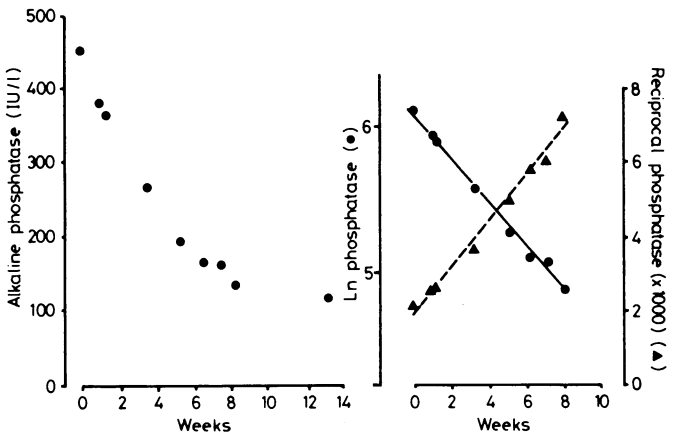
Linear decline in serum alkaline phosphatase activity during treatment of renal osteodystrophy

Raised serum alkaline phosphatase activity is important in the diagnosis of renal osteodystrophy, particularly as an indicator of secondary hyperparathyroidism. The response to treatment with vitamin D derivatives or parathyroidectomy or both is shown by declining alkaline phosphatase activity after a variable latent period.[1] The rate of decline is a convenient index of skeletal response to treatment. In addition, clinical experience has shown that hypercalcaemia tends to occur as the phosphatase activity falls to within normal limits, which necessitates frequent biochemical review in the first weeks of treatment. We describe here the use of transformed values of serum alkaline phosphatase activity to characterise these events.

Methods and results

We reviewed the records of 17 consecutive adult patients treated for renal osteodystrophy with vitamin D derivatives or subtotal parathyroidectomy or both. Details of these patients are available on request. Renal osteodystrophy was established by *x*-ray findings of hyperparathyroidism (periosteal erosions) or bone biopsy. Total serum alkaline phosphatase activity was assayed using a commercial kit (Boehringer), with a 95th centile value of 190 IU/l.[2] Phosphatase activity was plotted against time and transformed as a logarithm or reciprocal, and coefficients of linear correlation were calculated.[3]

Initial phosphatase activity lay between 723 and 165 IU/l; when the raw data were plotted against time the declining values gave a curvilinear relation (figure (left)). In 11 cases the logarithm and the reciprocal of



Left: Serum alkaline phosphatase activity plotted against time from onset of response to 1-α-hydroxycholecalciferol. Right: Linear decline in log transformed phosphatase activity compared with linear increase in reciprocal values.

phosphatase activity showed rectilinear relations in time, with correlation coefficients above 0·95 for both transforms (figure (right)). The latent period before the first decline in phosphatase activity during treatment with 1-α-hydroxycholecalciferol varied from one to seven weeks (mean 3·2 weeks). Phosphatase activity fell in each patient to a characteristic plateau value, from 0·46 to 0·96 of the upper limit.

The range of declining phosphatase activity from peak to plateau values may be regarded as the pathological increase, with a nominal value of 100%. Intermediate phosphatase values were recalculated as a percentage of this using the formula

$$\frac{\text{Alkaline phosphatase (t)} - \text{final (plateau) phosphatase}}{\text{Initial (peak) phosphatase} - \text{final (plateau) phosphatase}} \times 100$$

and the logarithm plotted against time. Standardised curves for each individual were compared in terms of the half time and showed a range of 1·7-9·3 weeks (mean 3·3 weeks) (n=10). The shortest value occurred after parathyroidectomy. There was no correlation between initial phosphatase activity and half time.

Five patients became hypercalcaemic at phosphatase activities between 0·55 and 1·10 of the upper limit. In four of these five hypercalcaemia occurred as the phosphatase activity fell into the normal range but at a value well above the final "plateau." The time required for the upper limit of normal to be reached could not be predicted from the starting values or the half time. Both variables were necessary for the prediction.

Comment

After an observation made during routine clinical work 17 unselected patients with renal osteodystrophy were studied; in 11 transformed alkaline phosphatase activity showed a rectilinear relation with time. This group all had evidence of secondary hyperparathyroidism. The half time shown by some patients was surprisingly short, and the maximal half time (1·7 weeks) may represent a physiological limit to the response of an osteoblast population.[4] The half time is potentially useful in indicating an optimum dose of vitamin D derivatives, with three weeks used as a model half time for treatment. The most desirable rate of response to treatment is not yet known.

The rectilinear behaviour of phosphatase activity permitted a prediction of the time at which it dropped to the upper limit of the normal range; in four instances this coincided with, or just preceded, the development of hypercalcaemia (no dose adjustments were made during this study). Hypercalcaemia may therefore be predictable, and a review of blood variables can potentially be timed to coincide with the period of greatest risk.

We thank Dr R P Burden, some of whose patients were included in this study, and Mrs J Hayes and Mrs L Hodgson for typing the manuscript.

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(*Accepted 4 October 1982*)

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Albendazole in hydatid disease

Surgery is usually successful in the removal of uncomplicated primary cysts, but the management of disseminated or recurrent hydatid disease is a much greater problem.[1] The first report of the clinical use of mebendazole was encouraging,[2] and good experimental evidence of its potency exists. Some subsequent workers found many patients resistant to treatment. The reason for this is probably the very poor absorption of mebedanzole.[3] Albendazole is another benzimidazole compound which at least in animals has much better absorption properties.[4]

Patients, treatment, and results

Four patients in whom surgery was decided against owing to multiple cysts, advanced age, or outright refusal of surgery were treated with albendazole 10 mg/kg/day in two divided doses. The first patient presented with chest and abdominal pain due to multiple recurrent mediastinal, pleural, pulmonary, pancreatic, and retroperitoneal hydatid cysts clearly shown by CT scan, and the second patient ruptured her large hepatic cyst into the pleural cavity as a result of an injury. The third patient's hepatic cysts were detected by an antenatal ultrasound scan, but in retrospect she had suffered back and loin pain for several years. The final patient suffered