

Serum Alkaline Phosphatase Activity in Acrodermatitis Enteropathica: An Index of the Serum Zinc Level

Kaare Weismann and Henrik Høyer

Department of Dermatology, University of Copenhagen, Rigshospital, Copenhagen, Denmark

Received August 12, 1978

Abstract. A significant positive correlation between serum zinc and serum alkaline phosphatase levels was demonstrated in four patients suffering from acrodermatitis enteropathica for which they received oral zinc sulphate therapy. In one of the male patients a significant inverse relation between serum zinc and serum copper was found.

Key words: Acrodermatitis enteropathica; Alkaline phosphatase; Copper; Zinc

Oral zinc therapy for acrodermatitis enteropathica (AEP) was introduced in 1973–74 (1, 3). Today, the beneficial effect of the therapy is well documented. Unfortunately, apart from zinc levels in serum, plasma and urine, no biochemical parameters of the patients' zinc nutrition have been available. In the present communication, evidence is presented that serum alkaline phosphatase is a useful index of AEP patients' serum zinc levels.

MATERIAL AND METHODS

Four patients receiving zinc sulphate for AEP (0.2–0.6 g daily) have been observed for 4 years (F. B. ♂ and D. H. ♀), 3 years (A. M. ♂) and 2 years (J. L. J. ♀). The zinc therapy was started at the age of 16 years (F. B. and D. H.), 10 years (A. M.) and 25 years (J. L. J.). Laboratory analyses included determination of serum zinc and copper by atomic absorption spectrophotometry (Medicinsk Laboratorium, Copenhagen), serum alkaline phosphatase activity and plasma albumin concentration. The blood tests were made at intervals of one to six months.

The association between the parameters studied was analysed by least squares linear regression and the correlation coefficient r .

RESULTS

A positive significant correlation between serum zinc and serum alkaline phosphatase levels was found in all patients (Fig. 1).

In patient A. M. a significant negative correlation between zinc and copper in serum was demon-

strated, $r = -0.59$, $P < 0.05$ ($n = 13$). The regression equation was $y = -0.35x + 25.21$, where y is the serum copper and x is the serum zinc concentration in $\mu\text{mol/l}$.

The plasma albumin concentrations were high within the normal range and, as expected during zinc supplementation, were not significantly correlated with the serum zinc levels ($P > 0.1$).

DISCUSSION

The slope of the regression lines was less in the females than in the males. This might be related to the fact that growth was activated in the 2 males after zinc therapy was started. The marked rise in serum alkaline phosphatase activity observed might thus be due to an increase in bone alkaline phosphatase (cf. patient F. B. in Fig. 1). Both females had closed epiphyseal lines of the long bones before zinc therapy was initiated, and, consequently, they showed no activation of linear growth. Clearly, determinations of alkaline phosphatase isoenzymes remain to be performed in AEP patients of both sexes before and after growth has stopped.

There seems to be a short lag between changes in serum zinc and serum alkaline phosphatase levels, suggesting that, like magnesium (2), zinc regulates the enzyme activity. However, no such effect could be demonstrated by adding zinc to serum from a patient with AEP (4). Similarly, addition of zinc to assay systems used for determination of intestinal alkaline phosphatase of zinc-deficient rats failed to normalize the enzyme activity (5). It is reasonable to believe that the synthesis of alkaline phosphatase, which contains four μatoms zinc per mole (2), is dependent on available zinc and that lack of zinc leads to a decreased synthesis or to qualitative changes of the enzyme.

The inversely directed changes in serum zinc and serum copper is probably of minor importance to the evaluation of the patients' zinc nutrition. The phenomenon is attributable to competition of the two elements for common binding sites on plasma albumin. A change in serum zinc can therefore be expected to be followed by a change in serum copper in the opposite direction.

Patients suffering from zinc depletion during long-term parenteral nutrition show a decrease in serum alkaline phosphatase activity and a rise following repletion with zinc (8). A rise in the serum

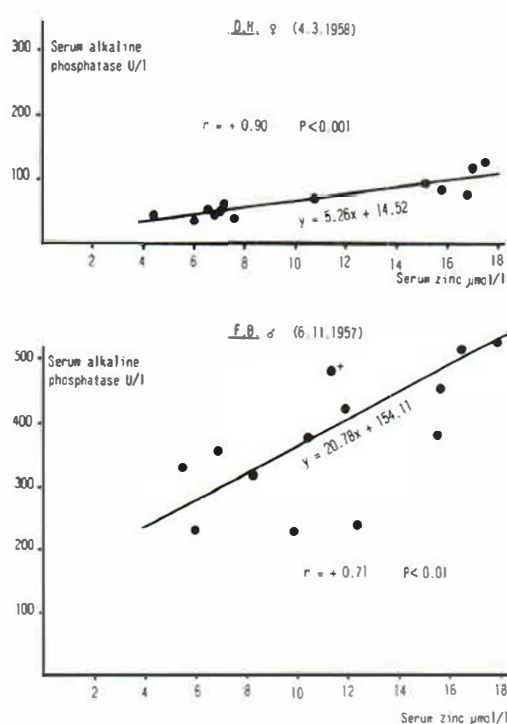


Fig. 1. Scatter diagrams showing serum alkaline phosphatase activities with varying serum zinc concentrations in 4 patients with acrodermatitis enteropathica. In the diagram for F. B., + indicates determination of al-

kaine phosphatase isoenzymes: bone-type 87% and liver-type 13% of total activity. Reference limits: serum zinc 10.6–17.7 μmol/l (♀), 11.4–18.9 μmol/l (♂); serum alkaline phosphatase 50–250 U/l.

alkaline phosphatase level has been observed in patients who received oral zinc for rheumatoid arthritis (6) and for post-alcoholic cirrhosis (9). Both diseases are believed to be connected with zinc deficiency. Geriatric patients with low plasma zinc levels due to a physiological decrease in the plasma albumin level showed no increase in serum alkaline phosphatase level during oral zinc therapy (7). These facts suggest an association between zinc and alkaline phosphatase which is not only confined to AEP, but apparent in disease states causing disturbances of the zinc metabolism.

REFERENCES

1. Barnes, P. M. & Moynahan, E. J.: Zinc deficiency in acrodermatitis enteropathica: multiple dietary intolerance treated with synthetic diet. *Proc R Soc Med* 66: 327, 1973.
2. Bosron, W. F., Anderson, R. A., Falk, M. C., Kennedy, F. S. & Vallee, B. L.: Effect of magnesium on the properties of zinc alkaline phosphatase. *Biochemistry* 16: 610, 1977.
3. Michaëlsson, G.: Zinc therapy in acrodermatitis enteropathica. *Acta Dermatovener (Stockholm)* 54: 377, 1974.
4. Neldner, K. H. & Hambidge, K. M.: Zinc therapy of acrodermatitis enteropathica. *N Engl J Med* 292: 879, 1975.
5. Reinhold, J. G. & Kfoury, G. A.: Zinc-dependent enzymes in zinc-depleted rats: intestinal alkaline phosphatase. *Am J Clin Nutr* 22: 1250, 1969.
6. Simkin, P. A.: Oral zinc sulphate in rheumatoid arthritis. *Lancet* ii: 539, 1976.
7. Weismann, K., Wanscher, B. & Krakauer, R.: Oral zinc therapy in geriatric patients with selected skin manifestations and a low plasma zinc level. *Acta Dermatovener (Stockholm)* 58: 157, 1978.
8. Weismann, K.: Intravenous zinc sulfate therapy in zinc depleted patients. *Dermatologica* (in press).
9. Weismann, K., Christensen, E. & Dreyer, V.: Zinc supplementation in alcoholic liver cirrhosis. *Acta Med Scand* (in press).