

Symptomatic zinc deficiency in experimental zinc deprivation

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Abstract

An evaluation of indices of poor zinc status was undertaken in five male subjects in whom dietary zinc intake was reduced from 85 $\mu\text{mol d}^{-1}$ in an initial phase of the study to 14 $\mu\text{mol d}^{-1}$. One of the subjects developed features consistent with zinc deficiency after receiving the low zinc diet for 12 days. These features included retroauricular acneform macullo-papular lesions on the face, neck, and shoulders and reductions in plasma zinc, red blood cell zinc, neutrophil zinc and plasma alkaline phosphatase activity. Alcohol induced hepatitis, which was suspected in this subject, may have caused a predisposition to altered zinc metabolism and possible zinc deficiency which was exacerbated by subsequent zinc deprivation. The report supports the value of neutrophil zinc concentration as an indicator of poor zinc status.

Case report

A 33 year old man took part in a study of zinc deprivation involving an initial 15 day baseline period followed by a very low daily zinc intake of 14 μmol .¹ The aim of the study, which involved a total of five subjects, was to investigate the mechanisms of zinc homeostasis in response to a low dietary zinc intake¹ and to undertake an evaluation of indices of poor zinc status including plasma, red blood cell and neutrophil zinc, and alkaline phosphatase activity in plasma and neutrophils. Ethical permission for the study was granted by the joint ethical committee of the Grampian Area Health Board and the University of Aberdeen. Written informed consent was obtained from the subject after the procedures, risks, and benefits of the study had been explained to him.

His dietary zinc intake, metabolic and biochemical data are summarised in the figure. He had an increased serum γ glutamyl transferase activity (286 IU/l) at the start of the baseline period, and this fell progressively over the subsequent six weeks to 36 IU/l. His blood film showed anisocytosis with a degree of macrocytosis and stomatocytosis. His previous dietary and alcohol intake are uncertain but on the basis of his previous occupation as a barman and evidence of resolving hepatitis and haematological abnormalities, it is suspected that he may have had an alcohol induced hepatitis.

After 12 days of zinc deprivation retroauricular acneform macullo-papular lesions

developed which spread during the next two days to his face, neck, and shoulders. He complained of headache, tiredness, and a sore throat. His plasma zinc was greatly reduced (2.7 $\mu\text{mol l}^{-1}$, local reference range 10.0–17.6 $\mu\text{mol l}^{-1}$). Neutrophil zinc fell from 0.96 nmol mg^{-1} protein to 0.56 nmol mg^{-1} protein (reference range 0.71–1.80 nmol mg^{-1} protein).² Plasma alkaline phosphatase activity (ALP) and red blood cell zinc also decreased, while neutrophil alkaline phosphatase increased. Plasma albumin concentration remained unchanged at 47 g l^{-1} throughout the study (figure).

Zinc repletion was begun by adding zinc sulphate to the semi-purified diet to provide 86 μmol zinc daily for five days and then 164 μmol a day for a further 18 days. During this period the skin lesions improved as did most of the biochemical variables. Plasma zinc concentration, however, remained below the reference range.

Comment

Symptomatic zinc deficiency is rare even in individuals at risk of specific or general malnutrition, although disturbances of zinc metabolism³⁻⁶ and zinc responsive clinical features^{6,7} have been described in alcoholic liver disease. We suspect that the subject had an alcohol induced hepatitis which may represent a predisposition to altered metabolism and possible deficiency of zinc. This was exacerbated by subsequent zinc deprivation while synthesising new tissue, as is suggested by his weight gain and nitrogen balance.

The study lends weight to the importance of tissue synthesis to the induction of zinc deficiency. Our subject achieved a positive zinc balance and had an overall net gain of zinc during the zinc deprivation period (74 μmol), whereas the subject who developed skin lesions in the study by Baer and King⁸ lost a total of 1120 μmol zinc. As our subject was anabolic during the deprivation period, gaining 1.5 kg in 15 days, it is possible that he was unable to fulfil his zinc requirement for anabolism. Assuming that nitrogen balance represents net synthesis of protein, 76 g of the total weight gain during zinc deprivation was protein. Synthesis of this protein would require 36–93 μmol zinc (assuming that muscle contains 0.47–1.22 $\mu\text{mol zinc/g wet weight}$ ⁹) which is close to the amount of zinc he retained. Had the subject's body weight been stable, his zinc requirements would have been reduced and symptomatic zinc deficiency may not have developed.

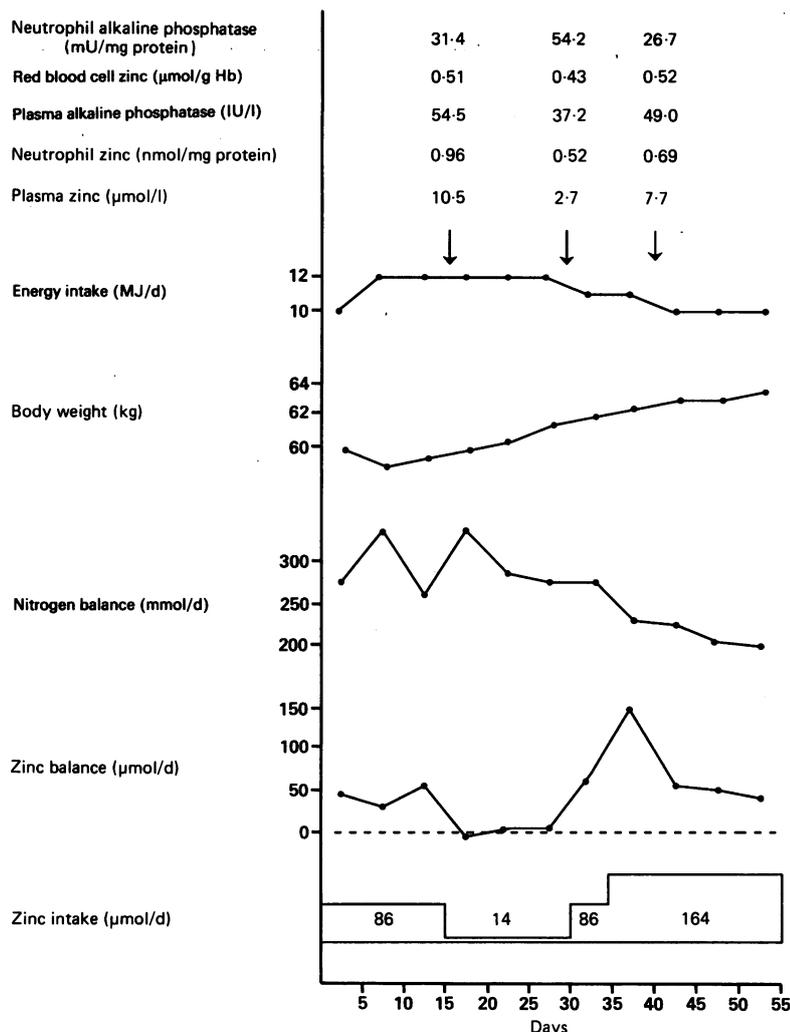
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Dietary zinc and energy intake and biochemical data from a subject receiving a low zinc diet.

Skin changes of varying degrees have been described in other zinc deprivation studies^{8 10} despite only marginal depressions of plasma zinc. The most characteristic clinical symptom of zinc deprivation, skin lesions, affect a tissue whose total zinc content is probably little changed by zinc deprivation.¹¹ Skin constitutes about 16% of total body weight and contains up to 10% of total body zinc (1.0–3.4 mmol/70 kg)⁹ but has a slow turnover rate and could not act as a source of readily available zinc in the short term.

Our data support the suggestion that neutrophil zinc is an indicator of zinc deficiency^{10 12} as neutrophil zinc decreased by 50% when the subject was deprived of this mineral. Although decreased leucocyte zinc concentrations have been reported in some patients with liver

damage,⁴ neutrophil zinc concentration is low only in more severe liver disease.¹³ This suggests that changes in neutrophil zinc concentrations in this subject were unlikely to have been due to suspected alcoholic hepatitis. A decrease in alkaline phosphatase in the plasma or serum has been reported in man,^{10 14} but increases in the neutrophils of rats.¹⁵ Decreased red blood cell zinc has also been observed in experimental zinc deprivation,^{10 16} although other workers have not seen these changes.^{17 18}

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