

ORAL ZINC THERAPY IN GERIATRIC PATIENTS WITH SELECTED SKIN MANIFESTATIONS AND A LOW PLASMA ZINC LEVEL

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Abstract. A geriatric population comprising 585 inhabitants of an institution for the aged was studied. Twenty-six persons with a mean age of 82 years were selected because of skin manifestations suggestive of chronic zinc deficiency. In 10 of the patients a subnormal plasma zinc level was found. This hypozincaemic group underwent a 4 week trial with zinc sulphate tablets, 0.6 g daily. The therapy failed to alleviate the skin condition in any of the patients, thus indicating that the changes were not caused by zinc deficiency. In the hypozincaemic group, plasma albumin was subnormal in all patients and significantly lower than in the normozincaemic subjects. The correlation between plasma zinc and plasma albumin levels in all 34 patients studied was highly significant ($r_s=0.69$, $p<0.001$). As plasma albumin tends to fall to subnormal concentrations with age, this explains why plasma zinc may be low in the elderly without indicating a state of zinc deficiency. After 2 and 4 weeks' zinc therapy, the mean plasma zinc concentration of the hypozincaemic group rose significantly from 9.5 to 17.6 and 23.4 $\mu\text{mol/l}$. This increase is higher than the rise observed in younger patients receiving an identical zinc sulphate dosage.

Key words: Eczema craquelé; Geriatric patients; Albumin; Plasma zinc; Xerosis; Zinc sulphate therapy

Over the last few years, characteristic skin changes have been recognized in humans suffering from congenital or acquired zinc deficiency disorders. Zinc deficiency was first described in acrodermatitis enteropathica (AE), which is an inborn defect of zinc metabolism (1, 11, 17, 19), and was recently recognized in the zinc depletion syndrome, an iatrogenic disorder due to an insufficient zinc supply during long-term intravenous feeding (7, 20). In the acute stage, both diseases are characterized by eruptions on the face, especially around the mouth, nose, and eyes, which in adult patients may

resemble seborrhoeic dermatitis. Bullae leaving erosive areas appear in the anogenital area, distally on feet and hands, and on elbows, knees, and heels.

Chronic or latent zinc deficiency is seen in AE patients being inadequately treated with zinc or oxyquinolines. The growth of hair and nails is poor and the skin is rough and scaly, especially on hands and feet. Well-defined red-brown patches may persist around the armpits, on the hands, elbows, knees, and feet, as well as in the major flexures of the extremities. The lesions often appear psoriasiform, paralleling the so-called parakeratosis of zinc-deficient animals (16). Identical changes were described in a patient who became depleted of zinc during penicillamine therapy for Wilson's disease (9). Another chronic zinc deficiency state occurs in alcoholics with malabsorption. The patients show chronic scaling acrodermatitis, diffuse hair loss and a pronounced, widespread eczema craquelé (21).

The skin changes typical of zinc deficiency might provide a useful diagnostic tool for the clinician in his search for zinc deficiency disorders in man. In the present study, we investigated the skin conditions of a geriatric population to ascertain if zinc deficiency could be identified by clinical criteria. A group of elderly people was chosen because skin changes are common in old age (18) and because zinc deficiency might occur as a consequence of general loss of appetite, altered digestive functions, and diets poor in proteins and zinc.

MATERIAL AND METHODS

Five hundred and eighty-five inhabitants of a municipal institution for the aged were studied. The mean age was 80 years, with a range from 55 to 106 years. The skin

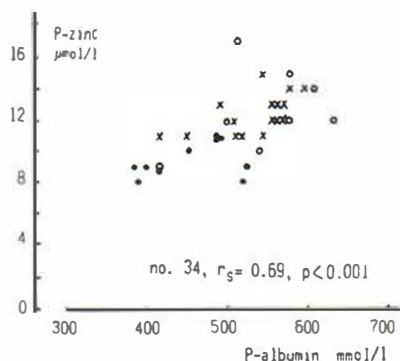


Fig. 1. Correlation between P-zinc and P-albumin in the hypozincaemic patients (●) normozincaemic patients (×) and of the controls (○). P-zinc reference limits: ♀, 10–19 µmol/l; ♂, 11–19 µmol/l. P-albumin reference limits: 540–800 µmol/l. r_s , Spearman's rank correlation coefficient.

was examined by two of us (K. W. and B. W.) to determine the prevalence of common skin diseases in old age (18), and with the purpose of selecting patients with skin manifestations suggestive of zinc deficiency. At least one of the following skin changes had to be present to ensure selection: 1) acute bullous or chronic scaly dermatitis distally on the extremities; 2) periorificial eczematoid lesions on the face and in the perianal area; 3) seborrhoeic dermatitis-like changes on the face, loss of hair, and perianal lesions; 4) widespread xerosis or eczema craquelé on the trunk and the extremities.

Twenty-six patients (13 females and 13 males; 4.4% of the population) were selected for this study. The average age was 80 years (range 65–100) in the males, and 84 years (range 55–106) in the females. In no case did we find skin changes suggestive of acute zinc deficiency, nor did we find skin lesions of the parakeratotic type. Briefly summarized, 14 patients showed seborrhoeic dermatitis-like changes on the face and the scalp, and 12 patients had dry scaling without erythema on the scalp and the face. Apart from this, the patients showed skin changes as follows: xerosis on the extremities (13 cases), widespread xerosis on the trunk and on the extremities (7 cases), widespread eczema craquelé (4 cases), perianal lesions (5 cases), and loose, sparse hair with alopecia (11 cases).

The type and severity of the skin manifestations were equally distributed between a group of 16 patients who were found to have normal plasma (P) zinc values (designated the normozincaemic group), and a group of 10 patients showing subnormal values (designated the hypozincaemic group). P-zinc was determined as fasting values and was measured by atomic absorption spectrophotometry. The laboratory's reference limits were 10–19 µmol/l, which was accepted for females. The lower limit for males was set to 11 µmol/l, because the lower reference limit of serum zinc was found to be about 1 µmol/l higher in males than in females (personal observation). In addition to P-zinc, the following quantities were

determined: haemoglobin concentration (Hgb), P-albumin, total serum (S) protein, S- α_1 -antitrypsin, S- α_1 -orosomucoid, S- α_2 -haptoglobin, S-IgG, S-IgA, S- α_1 -lipoprotein, S-pre- β -lipoprotein, S- β -lipoprotein, and S-thyroxine.

The hypozincaemic group underwent a 4 week trial on zinc in order to substantiate or reject our provisional diagnosis of chronic zinc deficiency. The patients received 0.2 g of zinc sulphate ($\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$) as effervescent tablets three times daily, to be taken immediately after the meals. Blood samples were drawn after 2 and 4 weeks' therapy, and the patients' skin condition was evaluated at weekly intervals.

One patient was excluded, as he refused to take the tablets, and 2 of the elderly patients expired during the study. The remaining 7 patients were treated for 4 weeks or more, according to the schedule. The trial was performed from September through December 1976.

Eight elderly controls without skin symptoms, closely matching the hypozincaemic group with regard to sex and age were selected for comparative studies on the biochemical parameters.

RESULTS

We were unable to observe any beneficial effect of the zinc supplementation on the skin condition of the hypozincaemic patients. In 3 of the patients the therapy was prolonged up to 7 weeks, which clearly showed us that the minor fluctuations that occurred were inconsistent and related to bathing, hair washing or local treatment with emollients.

A highly statistically significant correlation was demonstrated between P-zinc and P-albumin in all 34 patients studied (Fig. 1). Accordingly, the mean P-albumin of the hypozincaemic group was significantly lower than the mean values of the normozincaemic group and of the controls (Fig. 2). P-

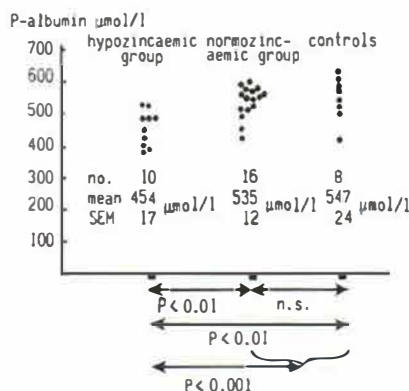


Fig. 2. P-albumin in the hypozincaemic group (before treatment), the normozincaemic, and the control groups. The statistical significance of the group differences (indicated with arrows) was tested by means of Wilcoxon's rank sum test. n.s.: $p > 0.05$.

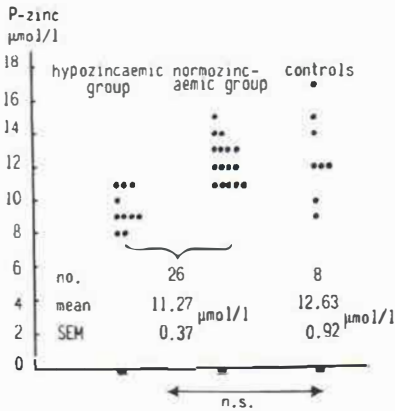


Fig. 3. P-zinc in the hypozincaemic group (before treatment), the normozincaemic group, and control group. The difference between the hypo- and normozincaemic patients and the controls was tested by means of Wilcoxon's rank sum test. n.s.: $p > 0.05$.

zinc of the patients with skin changes did not differ significantly from P-zinc of the controls (Fig. 3). The females showed lower mean P-zinc values than the males in all three groups, but the sex difference in this limited study did not reach statistical significance (Wilcoxon's rank sum test, $p > 0.05$). The P-zinc levels of 8 patients receiving thiazides or frusemide (which was reported to increase serum zinc (23)) did not differ significantly from the values of the remaining 26 patients who did not take diuretics (Wilcoxon's rank sum test, $p > 0.05$).

During zinc therapy, the P-zinc level of the hypozincaemic group rose significantly—beyond the upper reference limit in all but 2 patients (Fig. 4). The levels of Hgb and S-alkaline phosphatase of the hypozincaemic group did not differ significantly from those of the normozincaemic group (Wilcoxon's rank sum test, $p > 0.05$).

In one of the hypozincaemic patients S-alkaline phosphatase was elevated before and during zinc therapy, probably caused by a metastatic mammary cancer. In the remaining treated patients, S-alkaline phosphatase remained practically unaltered within the reference limits.

Minor fluctuations were noted in Hgb, P-albumin, total S-protein, and S-alkaline phosphatase, but they were statistically insignificant (Wilcoxon's rank sum test, $p > 0.05$) and were not correlated to the alterations in P-zinc (Spearman's rank correlation coefficients statistically insignificant, $p > 0.05$).

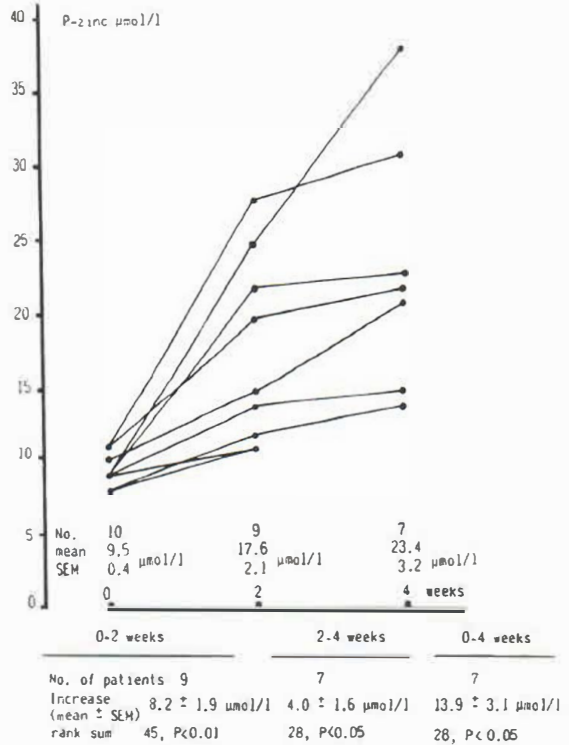


Fig. 4. Increases in P-zinc during treatment of the hypozincaemic group. The increases from 0-2, 2-4 and 0-4 weeks of treatment were tested by means of Wilcoxon's signed rank sum test.

S-thyroxine was normal in all hypozincaemic patients prior to the zinc therapy. S-lipoproteins remained normal in all, whereas minor, inconsistent changes occurred in the fractionated S-proteins.

DISCUSSION

The fact that more than half of the selected elderly patients with skin changes, which we found suggestive of chronic zinc deficiency, showed normal P-zinc values suggested that lack of zinc was not the causative agent of these changes. A negative response to zinc supplementation for 4 weeks, and the fact that parameters reflecting the zinc status such as S-alkaline phosphatase (8, 19, 20), Hgb and P-albumin (21) remained unaffected, substantiate this. Consequently, we found no reason to include the normozincaemic group in further clinical trials on zinc.

Other factors than zinc deficiency were probably causing the low P-zinc levels. First of all, the

significant correlation between P-zinc and P-albumin should be considered. Albumin is the major zinc-binding protein of plasma (6), and as the P-albumin level falls to subnormal levels with increasing age (2, 13, 14), a concomitant lowering of the P-zinc concentration should be expected. This provides a simple explanation for the fact that the P-zinc level was found to be depressed in our elderly patients without indicating a state of zinc deficiency. Ignorance of this fact no doubt accounts for some of the still existing controversy regarding the possible effect of zinc on the healing of leg ulcers. Unless zinc possesses some unknown pharmacological property, it should only be expected to work in zinc-deficient states. Yet such a state cannot be identified by isolated S-zinc determinations, especially not if the patients belong to the elderly age groups.

The cause of the age-dependent fall in P-albumin level remains unexplained. We found no evidence that zinc deficiency was involved, as the P-albumin level did not rise following 4 weeks' zinc supplementation. Our results confirm the age-dependence of the P-albumin concentration and, furthermore, explain the decrease in P-zinc with age, reported by Chooi et al. (3) and Lindeman et al. (10), who did not determine the P-albumin levels in their patient groups.

About 80% of the P-zinc is loosely bound to P-albumin (6) which has a large unsaturated binding capacity for zinc. The metal-free part of the albumin molecule, and transferrin, is believed to mediate the intestinal zinc absorption and transport of zinc to the tissues (4, 5). This might explain why the patients absorbed zinc well and achieved high P-zinc levels despite having low P-albumin levels. The increase in P-zinc reported in this study is remarkably high when compared with the rise observed in young adults receiving an identical zinc dosage for acne (22). The pretreatment mean serum zinc value of these patients was $13.05 \mu\text{mol/l}$, and after 4 weeks' therapy it was $17.75 \mu\text{mol/l}$. The difference between these results and those reported here might be explained by a physiologically lower renal function in old age causing a reduced renal clearance of P-zinc. Or, as food is known to impair the gastro-intestinal zinc uptake (15), the difference might also be explained by a lower food consumption in the elderly patients prior to ingestion of the tablets.

Xerotic skin is commonly found in the elderly

and was present in the majority of the patients selected for this study. Skin dryness is often exacerbated during the cold season when central heating and a low air humidity provide a desert-like indoor climate. Furthermore, eczema craquelé might develop due to scratching and to contact with soap, shampoo, and water, and with woollen or synthetic fabrics (12). We believe that such external factors, combined with a physiological senile atrophy of the skin, constituted the main cause of the dystrophic skin changes in these elderly patients.

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