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Patients with Dermatitis Herpetiformis, Acne, Psoriasis and Darier's Disease have Low Epidermal Zinc Concentrations

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Zinc concentration was determined in epidermis, papillary dermis and serum in patients with dermatitis herpetiformis, acne or psoriasis and in two small groups of patients with ichthyosis vulgaris and Darier's disease. Except in ichthyosis vulgaris the zinc level in epidermis was decreased in all these disorders.

The mean serum zinc concentration was, however, significantly decreased only in men with dermatitis herpetiformis. There was no correlation between the concentration of zinc in epidermis or dermis and that in serum. The decreased epidermal zinc concentration indicates that many of the patients have a zinc deficiency in spite of a "normal" serum zinc value. Supplementation of zinc might therefore be of value in patients with these disorders. ***Key words: Papillary dermis; Serum.***

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There is increasing awareness of the essential role of zinc in the function of many enzymes and also in the modulation of immune and inflammatory reactions. In patients with severe zinc deficiency, the clinical picture is characteristic and the serum zinc level is very low.

A marginal zinc deficiency – without any characteristic clinical signs – may be common in a number of clinical conditions associated with decreased absorption or increased losses of zinc. The best way to reveal moderate but relevant deficiency is still under debate (1, 2, 3 for ref). The zinc concentration in the serum is claimed to decrease at a late stage in long-standing deficiency and it may be influenced by non-specific factors such as inflammatory reactions, food intake and oral contraceptives, for example.

To obtain information about the zinc status in patients with dermatitis herpetiformis (DH), psoriasis, acne, Darier's disease and ichthyosis vulgaris we have measured the zinc concentrations in the serum and in epidermis and dermis obtained from small shave biopsies (4).

PATIENTS

Dermatitis herpetiformis

Fifty patients with dermatitis herpetiformis (33 men, 17 women) were investigated. They were 20–78 years old (mean age 52 years for both men and women). Three of the men and three of the women were 70–78 years old. The duration of their DH varied between 6 months and 53 years. All patients had IgA in a granular pattern in the dermal papillae and in all of them the skin symptoms had been successfully treated with dapsone (5). In most patients the biopsies were taken before glutenfree diet was started.

Acne vulgaris

Forty-five young men (mean age 22 years, range 17–28 years) and 28 young women not using oral contraceptives (mean age 24 years, range 15–28 years), with inflammatory acne, grades II–IV according to Pillsbury's classification (6), were included. Sixty-six per cent of the male and 25% of the female patients had acne grades III and IV. The duration of their acne varied between 1 and 10 years. None of them were using topical or oral zinc preparations.

Psoriasis

Twenty-six men (mean age 42 years, range 20–59 years) and 13 women (mean age 41 years, range 27–61 years) with psoriasis were included. The majority had a nummular and/or plaque type psoriasis involving 20–40% of the skin. Two were nearly erythrodermic and one had had erythroderma for several years, but this cleared on treatment with methotrexate. None of the patients had psoriasis comprising less than 5% of the skin surface. Most of the patients had had their psoriasis for more than 10 years. Six of them also had a history of psoriatic arthritis. None were receiving topical treatment containing zinc compounds.

Darier's disease

This group comprised six men and one woman, aged 21–39 years, and two boys aged 13 and 17 years. Two of the male patients had widespread lesions, three had lesions mainly in

Table I. *Zinc concentrations in the epidermis, dermis and serum (mean ± SD) in patients with dermatitis herpetiformis, acne, psoriasis and Darier's disease*

Diagnosis	No./M,F	Zinc μg/g dry weight		Zinc in serum μmol/l
		Epidermis	Dermis	
Dermatitis herpetiformis	33/M	48±11***	37±12	12.1±1.8**
Dermatitis herpetiformis	17/F	46±11**	34±9	11.9±1.7
Dermatitis herpetiformis	50/M,F	47±11***	36±18	
Acne	45/M	55±9	35±8**	13.1±0.6
Acne	28/F	53±9*	35±9	13.1±0.5
Acne	73/M,F	54±9**	35±8**	
Psoriasis	26/M	48±12**	36±11	13.6±0.9
Psoriasis	13/F	50±9*	37±9	13.5±0.9
Psoriasis	39/M,F	49±11***	36±10	
Darier's disease	9/M,F	48±9*	34±9	12.9±0.4
Ichthyosis vulgaris	8/M,F	55±10	36±11	13.0±0.4
Healthy men	18/M	59±12	41±10	13.6±2.0
Healthy women	15/F	61±17	40±10	12.2±1.6
Healthy men and women	33/M,F	60±14	40±10	

*, **, *** denote $p < 0.05$, $p < 0.01$ and $p < 0.001$ compared with the values of the controls. F = female, M = male.

the seborrhoeic regions and one had only a mild papular type of the disease.

Ichtyosis vulgaris

Five men and three women aged 20–45 years with mild to moderate ichthyosis affecting mainly the extensor aspects of the legs and arms were also included. In the shoulder region where the biopsies were taken no scaling was visible.

Reference subjects

Fifteen women of ages 18–61 years (mean age 32 years) and 18 men of ages 20–53 years (mean age 30 years) served as a reference group. Six of the women were 41–61 years old and three of the men were 41–53 years. Their values have been reported earlier (4).

The biopsies from the patients in this report were taken and analyzed during the same period as those from the reference subjects.

METHODS

The method for zinc assay has been described in detail previously (4). Avoidance of zinc contamination throughout the procedure is essential. From each patient two (in some cases three) tangential shavings were taken from the upper, lateral area of the buttock and/or the upper lateral area of the shoulder with a platinum razor blade after cleansing the skin with 70% alcohol and intradermal lidocaine 1%. In healthy subjects there is no significant difference in the zinc content of gluteal and that of shoulder skin (4).

Epidermis was separated from the thin papillary layer of the dermis. The epidermal and dermal specimens were dried and weighed, and thereafter kept in deionized water for 24 hours and then digested in 65% nitric acid for 96 hours. Zinc was measured by atomic absorption spectrophotometry (AAS) at 214 nm. The zinc concentration in serum was assayed by AAS at the Department of clinical chemistry. The blood samples were drawn in the morning when the patients were fasting.

Statistics

For the comparisons referred to in the text and Table I, two-sample *t*-tests were used to compute *t*-values (7).

RESULTS

The results are summarized in Table I. With the exception for ichthyosis vulgaris the mean epidermal zinc concentration was significantly decreased in all the disorders studied as compared with the values for the healthy reference group.

Ten of the patients with DH had values between 20 and 40 μg/g dry weight epidermis. None of the ten, however, had lower serum zinc concentrations than 10.5 μmol/l.

Three of the acne patients had epidermal values between 20 and 40 μg/g dry weight epidermis. The mean dermal zinc concentration was low in all the disorders studied, but the decrease compared with the healthy subjects was only significant in the male acne patients.

In the psoriasis group, eight of the patients had epidermal zinc values of < 40 μg and five of the eight had values of < 30 μg/g dry weight. Out of these

eight only one patient had a low serum zinc concentration (7 μmol/l), whereas the other seven had serum zinc values of >10 μmol/l. In scales collected from six patients with psoriasis, the mean zinc concentration was 65 μg/g (range 55–73 μg/g dry weight).

In none of the disorders was there any correlation between the concentration of zinc in the serum and that in the epidermis or dermis.

DISCUSSION

When evaluating the results, we have assumed that the zinc concentrations per dry weight epidermis and dermis in non-involved skin in the patient groups are comparable with the values obtained in the reference group, as the biopsies were taken in the same areas in all subjects, namely the shoulder and/or buttock region.

Both men and women with dermatitis herpetiformis showed a marked decrease in epidermal zinc, although the serum zinc level was significantly decreased only in the male patients with this disease. The mean age of the reference groups and particularly of the male reference subjects, was lower than that of the patients. There are no data for epidermal and dermal zinc in healthy persons older than 60 years and it is therefore not known whether age has an influence on tissue zinc. However, we found no significant difference between the values on the zinc contents in these tissues of the six healthy women above 40 years of age and those of the healthy women below 40. Nor was there any evidence that the epidermal or dermal zinc level in the DH group was related to the age of the patients.

A decrease in the epidermal zinc content seems to occur at a late stage in moderate, long-standing zinc deficiency (8). To what extent and after how long a period the tissue zinc is restored during treatment with a gluten-free diet is not known although zinc absorption tends to improve on a strict diet (9). During the first year on a gluten-free diet supplementation of zinc may be needed for quicker repletion of the zinc stores in these patients.

In a previous study patients with pustular acne improved when treated with oral zinc (10). Baer & King (11) found that acne-prone men had an exacerbation of their acne during a 4–9 weeks' zinc depletion study, although their erythrocyte, hair and salivary zinc did not decrease (11). This is in accordance with our findings in acrodermatitis enteropathica, that the epidermal zinc did not decrease until after 4–6 months of a reduced zinc dosage (8) but that acne pustules tended to reappear within 1–2 months.

The cause of the zinc reduction in the epidermis in acne and its relevance for the inflammatory acne process are unknown. It cannot be excluded, however, that acne-prone patients with a decreased epidermal zinc content – perhaps merely reflecting the increased demand for zinc in the adolescence – may develop a more pustular acne than acne-prone patients with normal tissue contents of zinc.

A relative decrease in the proportion of linoleic acid in some sebum fractions has been observed in acne (12 for ref). In this context it is of interest that there is a marked decrease in the proportion of linoleic acid both in the plasma lipid esters and in adipose tissue in zinc deficiency (13). Normalisation takes place during zinc supplementation. In young men with acne, similar trends were observed after 12 weeks of treatment with oral zinc (Michaëlsson et al., unpubl. data). However, it is not yet known whether there is any relation between the fatty acid pattern in the plasma lipid esters and adipose tissue and that in sebum. Nor is it known whether a decreased epidermal zinc content is associated with a change in the fatty acid composition in the sebocytes and sebum.

The low epidermal zinc levels in patients with psoriasis are worthy of note and indicate that these patients may have an inadequate zinc intake in relation to their losses, resulting in decreased tissue stores. In fact the mean epidermal value was about the same in psoriasis as in dermatitis herpetiformis and some of the patients with psoriasis had the lowest epidermal zinc observed in this study. Our results differ from those of the few previous studies on zinc in this tissue, but they comprised only a small number of patients (14) or the biopsies were taken in the vicinity of the plaques and seemed to include both involved and non-involved skin (15). The results may therefore not be comparable with those of our study. Our data on the zinc content of scales, however, are in agreement with the findings of Molokhia et al. (15) and may indicate that the zinc content is higher in lesional than in non-involved skin. One possible explanation for this might be that lesional skin is usually rich in granulocytes, which have a high content of zinc.

It should also be noted that the mean serum zinc concentration in the patients with psoriasis did not differ from that of the control group and that there

was no correlation between the individual serum zinc and epidermal or dermal zinc values. A similar lack of a significant difference in serum zinc between psoriasis patients and healthy subjects has been reported both by Wasik et al. (16), and by Mc Millan & Rowe (17). The latter, however, found that psoriasis patients with skin surface involvement of less than 10% had significantly higher plasma zinc values than those with more widespread lesions, whereas Wasik et al., in their large group, found no such difference. Wasik et al. also determined the zinc content in leukocytes (without differentiation between lymphocytes and granulocytes) and found a reduction of the zinc content by 39% in patients with psoriasis comprising less than 30% of the skin surface and by as much as 72% in those with more than 30% of the skin surface involved.

The relevance of the low epidermal zinc found in this study, and of the decreased leucocyte zinc reported by Wasik et al. (16), for the activity of the psoriasis is not known. A depletion of tissue zinc may be of importance, for example, for the observed disturbance in the long-chain fatty acid pattern in the plasma lipid esters and adipose tissue (18) and for the abnormality in granuolcyte function (19). In general the loss of zinc, as well as of other minerals, e.g. selenium and iron, from the psoriatic skin has been a neglected field. One explanation with regard to zinc might be the contradictory results obtained when only serum zinc is mesured, and another reason might be the technical difficulties in all zinc studies caused by the risks of contamination.

Although the group of patients with Darier's disease was small, their epidermal zinc value was significantly lower than that of the controls. The reason for this is not known. Increased losses from the skin seem a less likely explanation, as several of the patients had only mild disease. The finding may be of interest with regard to the immune disturbance reported in this disease (21).

This study has shown significant decreases in epidermal and/or dermal zinc contents in four of the five disorders studied, namely dermatitis herpetiformis, acne, psoriasis and Darier's disease, whereas the serum zinc level was significantly decreased only in male patients with dermatitis herpetiformis. The results indicate that these patients may have a moderate but chronic zinc deficiency, which may influence the clinical course in a negative way.

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