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Selenium in Whole Blood and Plasma Is Decreased in Patients with Moderate and Severe Psoriasis

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Concentrations of selenium in whole blood and plasma in 113 patients with moderate to severe psoriasis were compared with those in 104 healthy reference subjects. Most of the patients (85%) had had their psoriasis for at least 10 years and all had previously been treated with PUVA baths. Selenium concentrations both in whole blood and plasma were decreased both in male and female psoriasis patients. Male psoriatics 20–49 years old and women with disease of long duration (>20 years) had particularly low selenium concentrations in whole blood. The lowest whole blood values were found in a subgroup of male patients with widespread disease of long duration who had also required treatment with methotrexate and/or retinoids to control their disease. The blood selenium in patients who also had psoriatic arthritis or arthralgia did not differ from those without such symptoms.
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Psoriasis is an inflammatory disease. Little is known about what factors may influence the inflammation. It has been proposed that, for example, the trace elements zinc (1) and selenium (2), and also long chain fatty acids (3), may have modulating effects on inflammatory reactions.

The concentration of selenium as determined by neutron activation analysis has been reported to be 0.5–1.1 μg/g dry weight in normal epidermis and 0.4 μg/g in the dermis (4). The function of selenium in the skin is not known, but it has been assumed to be of importance for normal keratinization and particularly for the S-S linkage. The concentration of selenium in the blood has been found to be highest in areas where the soil is rich in this element (5). The levels in whole blood usually vary between 1 and 2 μmol/l. Erythrocytes and, particularly, neutrophils and thrombocytes are rich in selenium (6).

The known biological function of selenium is associated with the activity of glutathione peroxidase (GSH-Px), as selenium is an integral part of this enzyme. GSH-Px catalyzes the reaction glutathione–glutathione disulphide, which is considered essential in the protection of cells and tissues from damage induced by hydrogen peroxide and lipid peroxide. Glutathione and GSH-Px are also involved in the production of leukotrienes (2). This is another reason why the role of selenium in inflammatory disease has attracted much interest in recent years.

There is indirect evidence that patients with psoriasis may have low selenium levels in their blood, as they have been reported to have significantly lower values of blood GSH-Px than healthy controls (7). The activity of this enzyme has previously been utilized to estimate blood selenium levels. However, non-selenium-dependent GSH-Px activity has also been reported, and in humans has recently been found to be as high as 80% of the total activity (8). Also, the activity of this enzyme is influenced by hormonal factors and

oral contraceptives (9). Against this background, direct determination of selenium in whole blood and plasma was undertaken in a large group of psoriasis patients.

PATIENTS AND METHODS

Patients

The study comprised 113 patients with psoriasis from the province of Uppland without previous supplementation with selenium. The group consisted of 57 women and 56 men of ages 20–75 years; 68% of the patients were 20–49 years old. They were all seen during a 2-week period in 1982, when a follow-up study of long-term effects of PUVA-baths was carried out (10). The PUVA treatment had been commenced between 1974 and 1978. At the follow-up the patients answered a detailed questionnaire. The following anamnestic and clinical parameters were considered to be of particular interest in relation to selenium: age, sex, duration of disease, a history of arthropathy, the location and extent of the psoriasis through the years, and treatment with methotrexate and/or retinoids in addition to PUVA baths.

Eighty-five percent of the patients had had psoriasis for more than 10 years and 48% for more than 20 years. The majority of the patients had moderate psoriasis, but in 31% there was a history of widespread disease often involving more than one third of the skin surface and also a duration of more than 20 years. At the time of examination the degree of erythema, scaling and infiltration was estimated on a 1–4-grade scale, the percentage of skin involved was recorded and a PASI score was calculated (11). The mean score was 4.7, with a range 0–25. Twenty of the patients had a score of <2, i.e. had few or no lesions, while 10 had a score 10–25.

Controls

The majority of the 104 reference subjects (61 women and 43 men, 20–69 years old) were healthy blood donors without previous supplementation with selenium. The female and male controls were well matched to the female and male patients with regard to age, with a similar percentage distribution of controls and patients in each of the four decades from 20–59 years. However, for male patients (n=18) older than 60 years the number of age-matched controls was too low (see, however, results concerning lack of relationship between selenium and age).

Determination of selenium

Venous blood was collected in heparinized tubes. From each patient both whole blood and plasma were analyzed. All samples were prepared and counted in duplicate. The analyses were performed by an energy dispersive X-ray fluorescence technique (EDXRF). The system used was a Kevex 0600 ultratrace described in detail by Sky-Peck and Joseph (12). Briefly, an X-ray tube (Ag-anode, 35 kV, 40 mA) excites the atoms and the secondary X-rays from the sample are measured by a Si(Li) detector. One milliliter of whole blood or plasma is spiked with 10 ppm Cr and Y as internal standards. Twenty microliters of the spiked sample is dried (50°C) overnight and then put into a low temperature plasma asher (Nanotech 100) for 14 h, the temperature not exceeding 150°C. No loss of selenium has been reported to occur at this temperature (13). Thus when 10 aliquots from the same batch of Seronorm Trace Element Standard (batch 105) with a selenium concentration of 1.13 μmol/l were analyzed, the mean SD was 1.12±0.074 μmol/l. For five samples taken from the standard batch at different times and analyzed in duplicate, the mean ± SD was 1.09±0.047 μmol/l. The coefficients of variation were 6.6% and 4.5%, respectively.

Statistics

For the comparisons referred to in the text and table, two-sample t tests were used to compute p values and as a basis of conclusions (14).

RESULTS

The results for the whole group of psoriasis patients and for the reference group are summarized in Fig. 1*a*, *b* and in Table I, where data are also given for some subgroups. Generally the concentrations of selenium in the blood and plasma were significantly lower among the psoriatic patients than in the controls.

There was no correlation either in the reference group or in the patient group between age and whole blood or plasma selenium.

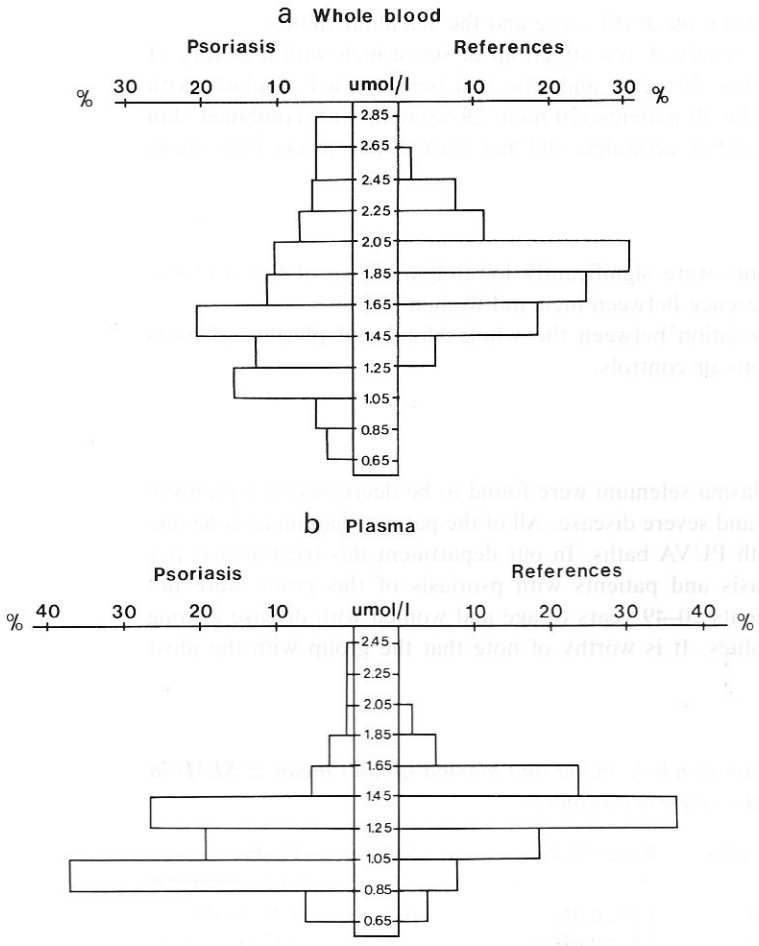

Fig. 1. Percentage distribution of patients and reference subjects with regard to the concentration of selenium in whole blood (*a*) and in plasma (*b*).

Whole blood

As shown in Table I, the female controls had higher values ($p<0.01$) than the male controls.

As seen in Fig. 1*a*, 10% of the psoriatics (7 women, 5 men)—but only 2% of the controls—had whole blood values of >2.45 μmol/l. All these patients had moderate or mild psoriasis. Both the male and female patients had significantly lower values than the male and female controls. Within the whole group of psoriatic patients, the difference between the mean values for males and females was not statistically significant. However, when data from male and female patients 20–49 years of age were compared, the difference was highly significant ($p<0.005$). This was mainly due to the low mean selenium values in the male patients of this age group, although the women in this age group also had significantly lower values ($p<0.05$) than their age-matched controls. However, the subgroup of 26 women with psoriasis of more than 20 years' duration (mean age 43 years and all except one in the range 29–55 years) had nearly as low values as the male psoriasis group 20–49 years old.

The selenium values in male and female patients who had suffered from psoriasis for more than 20 years and who also had a history of widespread psoriasis were not lower than in those with a history of more moderate psoriasis of the same duration (data not shown).

There was no relationship between the PASI score and the selenium values.

The lowest concentration was observed in a subgroup of seven men with a history of widespread psoriasis for more than 20 years and who had been treated regularly with methotrexate and/or retinoids. The 49 patients (20 men, 29 women) with combined skin disease and psoriatic arthritis and/or arthralgia did not have lower levels than those without joint symptoms.

Plasma

The plasma values of the patients were significantly lower than those of the controls. There was no tendency to a difference between men and women.

There was no significant correlation between the whole blood and plasma selenium concentration either in the patients or controls.

DISCUSSION

In this study whole blood and plasma selenium were found to be decreased in a group of psoriatic patients with moderate and severe disease. All of the patients had undergone one or more series of treatments with PUVA baths. In our department this treatment is not used for milder types of psoriasis and patients with psoriasis of this grade were not included in the study. Male patients 20–49 years of age and women with disease of long duration had particularly low values. It is worthy of note that the group with the most

Table I. *Concentration of selenium in whole blood and plasma (μmol/l mean ± SEM) in patients with psoriasis and healthy reference subjects*

	Number	Whole blood	Number	Plasma
All reference subjects	104	1.87±0.026	104	1.34±0.023
All psoriasis patients	113	1.67±0.047***	113	1.17±0.027***
All reference women	61	1.93±0.036	61	1.33±0.031
All women with psoriasis	57	1.74±0.069**	58	1.12±0.031***
All reference men	43	1.80±0.035	43	1.35±0.034
All men with psoriasis	56	1.61±0.064**	55	1.21±0.043**
Reference women 20–49 years	53	1.93±0.039	53	1.34±0.035
Psoriasis women 20–49 years	43	1.78±0.082*	44	1.12±0.037***
Reference men 20–49 years	37	1.80±0.039	37	1.36±0.037
Psoriasis men 20–49 years	31	1.53±0.085**(*)	30	1.18±0.54**(*)
Duration of psoriasis >20 years				
Women	26	1.59±0.083***[a]	26	1.12±0.052***[a]
Men	24	1.63±0.089*[a]	24	1.25±0.060
Psoriasis >20 years, widespread disease, retinoids and/or methotrexate				
Men	7	1.46±0.167**[a]		1.17±0.092*[a]

Comparisons marked with *, **, *** have been made between whole blood or plasma values of references and the corresponding group of psoriatics and denote p-values <0.05, 0.01, 0.005 and 0.001, respectively.

[a] Compared to the whole group of male or female references.

severe psoriasis, namely those requiring treatment with retinoids or methotrexate, had the lowest whole blood value.

Decreased whole blood, plasma and leucocyte selenium levels were recently reported in a group of 23 British patients with psoriasis of seemingly moderate severity (15). However, patients with eczema also had low blood selenium. If the blood GSH-Px activity is related to the selenium blood levels, low selenium levels may be expected in several other skin diseases, as low activity of this enzyme has also been reported in, for example, atopic dermatitis, dermatitis herpetiformis (7) and severe acne (9).

The decreased selenium levels in psoriasis may reflect a marginal selenium deficiency due to too low intake and/or decreased absorption of selenium, and/or increased losses from the skin. Sweden has low contents of selenium in the soil and the daily intake has often been found to be below the recommended amount (16). Fortification of animal fodder with selenium has therefore been allowed since 1981. In recent years there has also been an increase in selenium supplementation in Sweden. This study was undertaken, however, before this trend began. Women seem to have a lower intake of selenium than men (16), which may explain the low values in women with longstanding psoriasis. The reason for the low values in the male patients is not known, however.

There are also some reports indicating that mucosal changes and a certain degree of malabsorption (17) may occur in psoriasis. The losses of selenium from normal skin have been calculated to be 0.5–1 μg/24 h (18). In widespread psoriasis, the losses are likely to be higher, especially as the epidermal transit time is much higher in the lesional skin.

A redistribution of selenium associated with the inflammatory process—as described, for example, for zinc and iron (19), may be another explanation for the low values. No studies on the influence of inflammatory processes on blood selenium appear to have been published so far, however. Whole blood selenium is low in smokers and in persons with high alcohol consumption, but there was no evidence in our study that the patient and reference groups differed in this respect.

The relevance of reduced blood selenium for the activity and severity of psoriasis is unknown. Although the reduction was moderate, it might be of importance in the regulation of the inflammatory process. It is known, for instance, that neutrophils from selenium-deficient animals have a decreased capacity to induce chemotaxis and luminol-dependent chemiluminescence (20). In recent years the role of low selenium intake in relation to hyperlipidemia has been discussed. In this context it is noteworthy that the long chain fatty acid spectrum in the lipid esters of blood and adipose tissue (21), as well as the lipoprotein pattern, show abnormal tendencies in men with psoriasis, particularly in those whose disease is widespread and severe (22).

Controlled double-blind studies will be needed to elucidate the question whether selenium supplementation can modulate the activity of psoriasis and other skin diseases in which the circulating selenium levels are decreased.

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