

BLOOD GLUTATHIONE-PEROXIDASE LEVELS IN SKIN DISEASES: EFFECT OF SELENIUM AND VITAMIN E TREATMENT

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Abstract. Blood glutathione-peroxidase (GSH-Px) was determined in 61 healthy subjects and 506 patients with various skin disorders. Depressed levels were observed in patients with psoriasis, eczema, atopic dermatitis, vasculitis, mycosis fungoides and dermatitis herpetiformis. Low values of GSH-Px were also found in some patients with pemphigoid, acne conglobata, polymyositis, rheumatoid arthritis, scleroderma and systemic lupus erythematoses. Vegetarian diet, malnutrition and alcohol abuse could possibly account for the low values in some patients. Fifty patients with low GSH-Px levels were treated with tablets containing 0.2 mg selenium as Na_2SeO_3 and 10 mg tocopheryl succinate. The GSH-Px levels increased slowly within 6-8 weeks of treatment. The clinical effect was encouraging and calls for controlled studies.

Key words: Glutathione-peroxidase; Blood; Skin diseases; Selenium treatment

The level of glutathione-peroxidase (GSH-Px; E.C. 1.11.1.9) in blood has been shown to be a sensitive index of its selenium content in animals and man (6). Analyses of blood GSH-Px have therefore been used to detect selenium deficiency. The enzyme has a molecular weight of about 81 000, with 4 atoms of selenium present as a selenocystein residue (5, 17).

In various parts of the world the amount of selenium in plants is below the minimum requirement for animals. Such a dietary deficiency of selenium causes various symptoms such as muscular dystrophy in sheep and cattle and pancreatic degeneration and exudative diathesis in poultry. These symptoms can be prevented by selenium treatment. Vitamin E is usually added, as it will spare the requirement of selenium and vice versa.

In man, thrombasthenia, hemolytic diseases, neuronal ceroid lipofuscinosis, internal malignancy and cardiomyopathy have been described in association with selenium and GSH-Px deficiency (7, 8, 12, 14, 16, 19). The Keshan disease in China with cardiomyopathy was related to selenium-deficient

areas and prophylactic treatment prevented the appearance of new cases (9).

A daily intake of 50-200 μg of selenium per day has been recommended (4). In Sweden, Borgström et al. (2) found that the daily intake was 9-96 μg selenium per day. Analyses of hospital diets have revealed selenium intakes of 23-200 μg per day (3, 15, 18). Foods rich in selenium are: liver, kidney, seafoods and mushrooms, but the main sources are meat and cereals, although their selenium content in certain areas can be low. A risk for selenium deficiency in certain populations is thus evident. We therefore thought it worthwhile to determine the GSH-Px level in blood of patients with various skin disorders and to find out if a deficiency might influence the clinical symptoms. The effect of treatment with selenium and vitamin E in patients with low GSH-Px levels has also been investigated.

PATIENTS

Patients treated on the dermatological wards as well as certain outpatients were included in the study. Their ages ranged from 16 up to 80 years. As a rule the blood was drawn in the morning, before breakfast. A total of 506 patients were examined. The most-studied disorders appear in Table I. The diseases listed under various skin disorders (Fig. 1) include the following diagnoses: acne (10), alopecia areata (9), aphtae (3), Darier's disease (5), Dercum's disease (1), drug reactions (6), erythema multiforme (2), hereditary angio-edema (3), herpes simplex (3), hirsutism (2), ichthyosiform dermatoses (5), impetigo (4), leg ulcers (5), lichen planus (6), lichen sclerosis et atrophicus (2), livedo reticularis (1), lupus erythematosus, discoid (5) and disseminated (1), mastocytosis (2), nail dystrophy (2), neurotic excoriations (3), pemphigoid (4), pityriasis versicolor (3), polymyositis (1), porphyria cutanea tarda (5), other photodermatoses (4), pruritus ani (4), purpura anaphylactica (2), pyoderma gangrenosum (5), rosacea (4), scleroderma (2), steatocystoma multiplex (1), tumours of the skin (10), vitiligo (5).

Sixty-one apparently healthy medical students and hospital personnel of various ages served as controls.

Table 1. The GSH-Px activity in some common dermatoses

	Mean \pm SEM (μ kat/l)	No. of pats.	P-value vs. controls
Controls	315 \pm 6.6	61	
Chronic urticaria	304 \pm 6.9	54	n.s.
Pustulosis palmo- plantaris	295 \pm 13.2	19	n.s.
Atopic dermatitis	275 \pm 8.6	40	<0.01
Eczema	270 \pm 6.2	68	<0.001
Psoriasis	270 \pm 5.6	95	<0.001
Vasculitis	265 \pm 16.3	16	<0.01
Mycosis fungoides	259 \pm 14.7	12	<0.01
Dermatitis herpeti- formis	249 \pm 7.7	72	<0.001
	249 \pm 7.7	72	<0.001

TREATMENT

Tablets containing 0.2 mg selenium (as Na_2SeO_3) and 10 mg tocopheryl succinate were taken twice daily with meals. Fifty patients with the following diagnoses were treated: psoriasis (8), palmoplantar pustulosis (7), seborrhoeic dermatitis (4), atopic dermatitis (6), alopecia areata (5), urticaria (3), eczema (3), mycosis fungoides (3), pemphigoid (2), vasculitis (2), various (7).

METHODS

Blood sampling: Blood was drawn into 10-ml Vacutainer glass tubes (Becton-Dickinson A 4716) containing 144 U of heparin; 0.5 ml of the blood was hemolysed in 2.5 ml of distilled water and frozen at -25°C . Samples were taken simultaneously for hematocrit determination.

GSH-Px determination: The method of Paglia & Valentine (13) was used, with slight modifications. Here GSH-Px oxidizes reduced glutathione with the aid of cumenehydroperoxide. The glutathione is then reduced as moles of oxidized NADPH per second by one litre of erythrocytes (μ kat/l). The activity determinations were performed on a LKB 8600 Reaction Rate Analyzer (LKB; Bromma, Sweden).

The intra- and interassay precisions for the range of activity measured in this study were 2.4 and 7.5%, respectively.

RESULTS

The distribution of GSH-Px in the control material shows values between 210 and 420 (with a mean of 314) μ kat/l. No correlation was found between the age of the control subjects or patients and the GSH-Px values. The distribution of values for some skin disorders is given in Fig. 1. Significantly depressed levels of GSH-Px were found in patients with psoriasis, eczema, atopic dermatitis, vasculitis, mycosis fungoides and dermatitis herpetiformis

(Table 1, Fig. 1). Patients with chronic urticaria had GSH-Px levels similar to the controls, with the exception of one patient who had had a severe chronic urticaria for 2 years with angioedema and wheals persisting for more than 24 h. Although his sedimentation rate was normal he should probably also be classified as suffering from vasculitis. He had also experimented with fasting and various types of diets. Of the 5 psoriatic patients with GSH-Px less than 200 μ kat/l, 2 also had arthritis and 3 had serious problems with alcohol abuse.

In the eczema group the eight lowest values were found in 3 alcoholics with severe seborrhoeic dermatitis and generalized eczema, 2 atopics who had been practising vegetarians for more than one year, 2 patients with exfoliative dermatitis and 1 patient with generalized contact dermatitis.

In the group of patients with various skin disorders, values below 200 μ kat/l were registered in 6 patients with severe acne conglobata, pemphigoid, polymyositis, rheumatoid arthritis, sclerodermia, and systemic lupus erythematosus (SLE) with arthritis. Values within the limits for the control

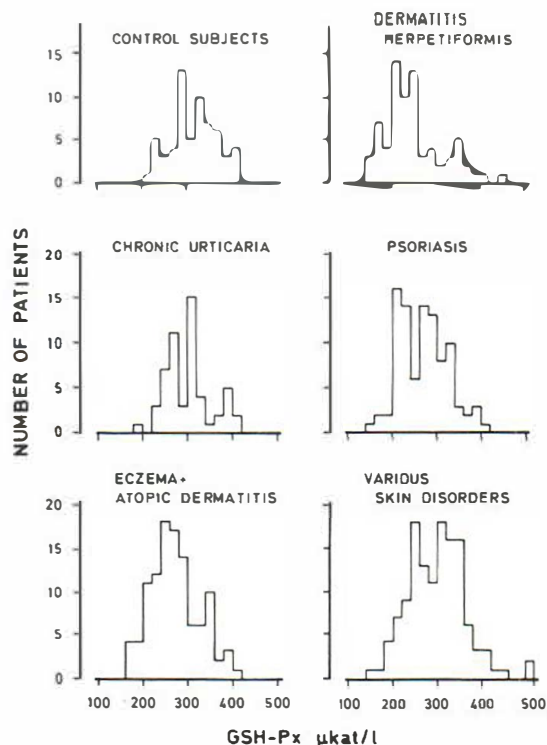


Fig. 1. The distribution of individual GSH-Px values for some of the skin disorders studied.

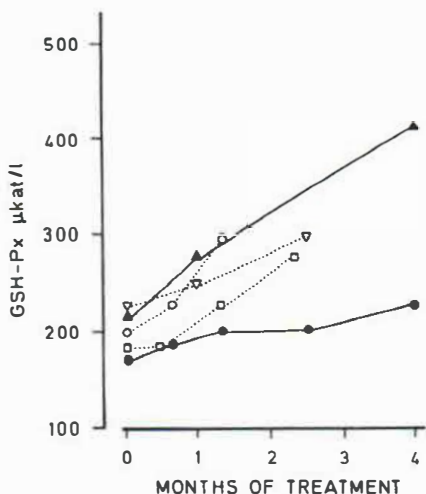


Fig. 2. GSH-Px levels in 5 patients treated daily with an oral dose of 0.2 mg selenium (as Na_2SeO_3) + vitamin E.

group were found in the other patients investigated. Patients with pemphigoid had values below 250 $\mu\text{kat/l}$. Two patients with alopecia areata had GSH-Px values below 220. Values over 500 $\mu\text{kat/l}$ were recorded in a boy with alopecia areata and a man with anaphylactoid purpura.

Treatment with selenium and vitamin E for 6–8 weeks raised the GSH-Px level slowly (Fig. 2). Two subjects who had supplemented their diet for a year showed the highest values (423–475 $\mu\text{kat/l}$). No side effects were noted except in 2 patients who noted gastric irritation and nausea immediately after ingestion. The best and most remarkable effect of the treatment was seen in 2 patients with protracted severe seborrhoeic dermatitis who improved within 4 weeks. One patient with cold urticaria and periodic depressions found no effect on her urticaria but the usual spring depression was absent. The patient with chronic urticaria and low GSH-Px level also improved. Two patients with pemphigoid could stop their intake of corticosteroids which they had needed for a long time. Patients with psoriasis had a very positive attitude to the treatment, but the effect on the skin lesions was difficult to evaluate, since other treatments were also given. No certain effect was seen in patients with alopecia areata. Here the patients had GSH-Px values between 210–280 $\mu\text{kat/l}$ before treatment. In palmoplantar pustulosis the effect was difficult to assess but not impressive, although 3 of them reported a lower incidence of common colds.

DISCUSSION

Low levels of GSH-Px have been found in patients with certain skin disorders. In some cases of eczema and psoriasis they can possibly be explained by malnutrition, alcohol abuse and vegetarian diet. Decreased serum concentrations of zinc are known to occur in alcoholics, which can in part be due to a reduction of the zinc-binding albumin. Markedly depressed levels of selenium have recently been described in alcoholic cirrhosis (1). A likely reason here is a selenium-deficient diet, although an increased excretion cannot be excluded. Malabsorption might also be the reason for the low values in patients with dermatitis herpetiformis. Further studies in these patients are under way. In other patients with psoriatic or rheumatoid arthritis, mycosis fungoides, pemphigoid and SLE, the low GSH-Px level could not be explained by alcohol abuse and in most cases there was no obvious malnutrition. Here a change in selenium metabolism seems more probable. In patients with widespread eczema and psoriasis, increased desquamation of skin with loss of selenium could be a possible cause of the low GSH-Px values. Molin & Wester (11) found by neutron activation analysis in epidermis from both normal and psoriatic lesions 1.2 μg selenium per g dry weight. They calculated that 7 μg per day can be lost via desquamation. Since sweat contains about 1.4 $\mu\text{g/l}$ (10), increased sweating could be another factor contributing to low selenium levels. The GSH-Px levels increased slowly under treatment with selenium and vitamin E for 6–8 weeks. The clinical effects were encouraging in the patients treated and call for carefully controlled studies with placebo to rule out other factors possibly responsible for the improvement. In cases of severe psoriasis, eczema, dermatitis herpetiformis pemphigoid, vasculitis, arthritis, polymyositis, SLE and liver disease, checking of GSH-Px levels would seem justified and selenium and vitamin E supplementation should be considered.

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