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Vitamin A and E Blood Levels in Erythrodermic and Pustular Psoriasis Associated with Chronic Alcoholism

S. MARRAKCHI[1,2], I. KIM[2], E. DELAPORTE[3], G. BRIAND[2], P. DEGAND[2], H. I. MAIBACH[4] and P. THOMAS[1]

[1]*Department of Dermatology B,* [2]*Laboratory of Biochemistry and* [3]*Department of Dermatology A, C. Huriez Hospital, Lille, France and* [4]*Department of Dermatology, University of California, San Francisco, USA*

Vitamin A and E blood levels were determined, using a high-performance liquid chromatographic method, in 7 patients with erythrodermic psoriasis or psoriatic acral pustulosis associated or not associated with chronic alcoholism, during and after the acute episode. These vitamins were also studied in 5 patients with psoriasis vulgaris involving more than 80% of the surface body area and associated with chronic alcohol intake and in 17 patients with psoriasis vulgaris involving more than 50% of the skin but without chronic alcoholism. Vitamin A blood levels were reduced in all the patients in the group "erythrodermic psoriasis/psoriatic acral pustulosis", while vitamin E blood levels were below the normal range during the acute psoriatic episode only in the 5 patients having a history of chronic alcohol intake in this group. In the other groups – psoriasis vulgaris with chronic alcoholism and psoriasis vulgaris without heavy alcohol consumption – vitamin A and E blood levels were not reduced. The implication of vitamin E in psoriasis, probably by its antioxidant activity, and its relationship with selenium are discussed. We suggest that attention should be paid to the vitamin A deficiency in erythrodermic or pustular psoriasis and to the vitamin E deficiency when these inflammatory diseases are associated with chronic alcoholism. ***Key words: free radicals; lipid peroxides; selenium; antioxidants.***

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S. Marrakchi, Dermatologie B. Hospital C Huriez, 2 Place de Verdun, 59037, Lille Cedex, France.

Studies of vitamin A blood levels in psoriasis show conflicting results (1–4). Hoffmann et al. (1), comparing psoriatic and healthy women, reported an increase of plasma vitamin A in the psoriatic group, but the difference between the means was at the border of statistical significance. Mier & Van den Hurk (2) and Safavi (5) did not observe a statistically significant difference between patients with psoriasis vulgaris and normal controls. Recently, Majewski et al. (4) reported a correlation between the decrease of vitamin A blood levels in psoriasis and the severity of the disease.

Another liposoluble vitamin, vitamin E, has been studied in psoriasis; Jain et al. (6) demonstrated a diminution of vitamin E blood level correlated with the perentage of surface area involved.

We determined the vitamin A and E status during and after erythrodermic or pustular psoriasis episodes and compared these values with those found in psoriasis vulgaris associated or not associated with chronic alcoholism.

MATERIALS AND METHODS

Patients

Erythrodermic pustular psoriasis group (PE). Seven psoriatic patients (4 males and 3 females, 52.2 ± 10.8 years) with acropustulosis (2 patients), erythrodermic psoriasis (3 patients and generalized pustular psoriasis (2 patients) were studied. The length of time since the onset of psoriasis was 22 ± 7.8 years in this group. After their admission to the hospital 5 patients were treated with etretinate and psoralen plus Ultraviolet A (PUVA), and the 2 patients with acropustulosis were treated with oral etretinate. Among the 7 patients of the PE group, 5 had a history of chronic alcoholism.

Psoriasis vulgaris/alcoholics group (PVA). Five patients (2 males, 3 females, 43.8 ± 6.2 years of age) with psoriasis vulgaris involving more than 80% of the body surface and with a history of heavy alcohol intake were also studied. The duration of the disease since its onset was 10 ± 8.7 years.

Psoriasis vulgaris group (PV). Seventeen patients (9 males and 8 females, 49.5 ± 16.5 years) with psoriasis vulgaris involving more than 50% of the skin but without a history of heavy alcohol consumption were studied. The length of time since the onset of the disease was 24.5 ± 17.7 years.

Blood collection

Fasting venous blood samples were collected in Vacutainer® tubes, light-protected. After centrifugation, the serum was kept at −20°C until analysis. Blood collections were obtained within 2 days following hospital admission and before treatment. A second blood collection was made after the total clearing of lesions in the PE group.

Vitamin A and E analysis

The extraction was performed according to the modified method described by MacCrehan & Shönberger (7). But during the extraction steps, no antioxidant was added, since this procedure seems unnecessary (8). To 250 µl of serum, 25 µl of tocol solution as an internal standard and 1 ml ethanol were added and vortex-mixed. Two ml hexane were added to the supernatant. The solution was shaken for 1 min and 1.5 ml of it evaporated under dry nitrogen. The residue was dissolved in 100 µl of ethanol/dichloromethane (4:1, v:v), and 50 µl were injected into the chromatograph and analysed with high-performance liquid chromatography (HPCL) (Kontron Instruments, Switzerland) with two model 420 pumps, a model 400 autosampler, a model 430 variable wavelength monitor and a model 450 data system. Guard-column: 2.3 cm × 0.39 cm I.D., packed with bondapack C18/corasil (35–50 µm, Waters). The stationary phase was a reverse phase C18 µ Bondapak column (10 µm, 15 cm × 0.39 cm I.D., Waters). Two solvents were used as the mobile phase: solvent A: water/acetonitrile/methanol (30:50:20, v:v:v); solvent B: acetonitrile/methanol/ethanol/dichloromethane (10:10:50:30, v:v:v:v).

Elution was performed at 1ml/min flow rate as follows: 10% solvent B: isocratic elution for 1.5 min, from 10% B to 50% B until 2.5 min, from 50% B to 95% B until 12.5 min, 95% B was maintained for 1 min, from 95% B to 10% B until 14.5 min, and 10% B was maintained until 20 min.

The detection wavelengths and retention times were to retinol: 325 nm; 5.8 min, tocol: 292 nm; 8.1 min, α-tocopherol: 292 nm; 9.4 min, β-carotene: 452 nm; 12.7 min.

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Table I. *Vitamin A and E blood levels in erythrodermic/pustular psoriasis group during and after the acute episode*

	Vitamin A (μmoles/l) Mean ± SD	Vitamin E (μmoles/l) Mean ± SD
During acute episode	1.09 ± 0.42	15.19 ± 9.03
After acute episode	1.80 ± 0.87	22.42 ± 12.82
p value	< 0.013*	< 0.005*

* Significance of difference between vitamin A and E values during and after the acute episode

Standard solutions of retinol, α-tocopherol and β-carotene were purchased from SIGMA (St Louis, MO), and the standard solution of tocol was a generous gift from Hoffman-La Roche (Basel, Switzerland). The concentrations of the standard solutions were determined using the specific absorbance of each compound: $A^{1\%}_{1cm}$: retinol: 1780 at 325 nm; α-tocopherol: 75.8 at 292 nm; β-carotene: 2620 at 452 nm.

The steps used in the serum extraction were also applied to the standard solutions.

Statistical analysis

The comparison between vitamin A and E blood levels in the PE group, during and after the acute episode, was performed using the two-tailed Student's *t*-test for paired data. To compare the vitamin A and E blood levels between the PE, PV and PVA group, the two-tailed Student's *t*-test for unpaired data was used.

RESULTS

Table I summarizes the vitamin A and E blood levels in the PE group during and after the acute episode. Statistical analysis showed significant changes in these values. During the erythrodermic episode, and in almost alle the PE group patients, vitamin A blood levels reached values below the normal range (N = 1.35–2.88 μmoles/l). These values increased significantly when the acute episode resolved.

The same trend was seen in the vitamin E blood levels, which were below the normal range (N = 11.36–35.10 μmoles/l) in 4 of the 5 alcoholic patients of the PE group but within the normal range in the 2 patients without history of chronic alcohol intake. When the acute episode resolved in the PE group, the vitamin E blood levels increased significantly. Table II presents the comparison of vitamin A and E blood levels determined during the acute episode in the PE group with those found in the PVA and PV groups. It shows a clear decrease of both vitamin A and E blood levels in the former group. Vitamin A was significantly ($p < 0.004$) lower than in the PVA group, even though more than 80% of the total body surface was involved in this group.

Vitamin E in the erythrodermic group was also significantly ($p < 0.013$) lower than in the PVA group.

No significant differences were found between the vitamin A and E blood levels after the acute episode in the PE group and the vitamin A and E blood levels in the PVA group. When compared to the PV group (without chronic alcohol intake), the PE group showed significantly lower vitamin A ($p < 0.001$) and vitamin E ($p < 0.001$) blood concentrations during the acute episode. Even after this episode, vitamin A ($p < 0.008$) and vitamin E ($p < 0.025$) remained significantly lower than in the PV group.

Although the mean value of vitamin A in the PVA group (2.77 ± 1.08 μmoles/l) was higher than the value in the PV group (2.64 ± 0.54) μmoles/l), it was not significantly different from the vitamin A in the PE group after the acute episode, whereas the vitamin A in the PV group was significantly different ($p < 0.008$). This is due to the high variance found in the vitamin A values in PVA and PE groups, probably related to the small size of these two groups.

No statistically significant differences were found in the vitamin A and E blood levels between the PVA and PV groups.

In the PE group, the 5 patients with a history of chronic alcoholism showed lower vitamin A and E levels, ranging from 0.55 to 1.47 μmoles/l for vitamin A (N = 1.35–2.88 μmoles/l) and from 6.76 to 13.84 μmoles/21 (N = 11.36–35.10) for vitamin E, than the 2 remaining patients with acropustulosis and erythrodermic psoriasis but without chronic alcohol consumption. In these 2 patients, the vitamin E blood levels during the acute episode were within the normal range: 28.30 and 27.69 μmoles/l, respectively. When the acute episode resolved, these values increased and ranged between 37.25 and 38.28 μmoles/l in the first patient and between 42.88 and 45.08 μmoles/l in the second. While the vitamin A blood levels were in the low normal range in the first patient – 1.39 μmoles/l – and below the normal range in the second patient – 1.25 μmoles/l – during the acute episode, they increased and reached normal values when the episode resolved: between 2.06 and 2.53 μmoles/l in the first patient and between 1.56 and 2.89 μmoles/l in the second patient.

DISCUSSION

Few studies report changes in vitamin A and E blood levels in psoriasis (1–6). The mechanism of these changes remains hypothetical. Majewski et al. (4) concluded that the hypovitaminosis A reflects the inflammatory process of the disease and might be one of the factors contributing to the disease process.

Our study clearly showed, in concordance with other studies (3,4), that during the acute episode of erythrodermic or pustular psoriasis, vitamin A blood levels decrease below the normal range. When the acute episode resolved, the vitamin A blood levels increased. However, a tendency to low vitamin A values after the acute episode remained when compared to the vitamin

Table II. *Vitamin A and E blood levels in erythrodermic/pustular psoriasis group (PE), psoriasis vulgaris/alcoholics group (PVA) and psoriasis vulgaris group (PV)*

	Vitamin A		Vitamin E	
	Mean ± SD (μmoles/l)	*p* value	Mean ± SD (μmoles/l)	*p* value
PE group (*n* = 7)	1.09 ± 0.42		15.19 ± 9.03	
PVA group (*n* = 5)	2.77 ± 1.08	< 0.004*	31.44 ± 9.61	< 0.013*
PV group (*n* = 17)	2.64 ± 0.54	< 0.001*	34.61 ± 10.65	< 0.001*

* Statistical significance of difference versus the PE group

A levels in PV and PVA groups. Although we cannot be certain, this tendency could be explained by the fact that vitamin A is bound to retinol binding protein (RBP), an acute-phase protein. In our study, the blood vitamin A was again investigatged in the PE group only 1 to 2 weeks after the acute episode. This interval is probably not sufficient for RBP to return to the normal level. Unfortunately, RBP was not investigated in our study.

In the alcoholic patients with pustular or erythrodermic psoriasis, vitamin E blood levels during the acute episode (6.76–13.84 μmoles/l) were below normal values or in the low normal range and increased to reach normal values when the condition improved. Nevertheless, in the same PE group, the vitamin E blood leves remained within the normal range in the two non-alcoholic patients with acropustulosis and erythrodermic psoriasis but increased significantly when the condition improved. The fact that the vitamin A and E blood levels are lower in the PE group than in the PVA group with more than 80% of the body area involved suggests that the vitamin A and E status is probably related to the type of psoriasis in addition to the role of the percentage of body involvement.

Modifications of vitamin E psoriasis could be explained by its major role as antioxidant. In psoriasis, important lipid changes have been demonstrated: arachidonic acid, a polyunsaturated fatty acid, is increased in psoriatic epidermis (9, 10). Arachidonic acid is a target for free radicals (10), which are generated by polymorphonuclear cells (PMN). Sera from patients with psoriasis activate PMN (11, 12), which are a major cellular infiltrate of psoriatic skin. Release of free radicals generated by PMN into the extracellular space will result in an attack on organic molecules and in particular the polyunsaturated fatty acids, moieties of membrane phospholipids. This reaction will produce lipid peroxyl radicals (13), toxic components which will generate a chain reaction unless a peroxyl radical-trapping agent like vitamin E is present in the vicinity. Vitamin E is a major lipid-soluble chain-breaking antioxidant in plasma (14).

The increase of free radicals (15) and lipid peroxidation (16) in alcoholics might explain the reduced vitamin E blood concentrations found in alcoholic patients even without liver disease (17, 18).

Selenium is a widely studied antioxidant in dermatology. Its relationship with vitamin E has been investigated. Hækstra (19) hypothesized that vitamin E prevents the formation of hydroperoxides, while glutathione peroxidase, which is the major enzyme containing selenium, metabolizes them whenever they form.

However, the relationship between vitamin E and selenium is complex. The antioxidant role of glutathione peroxidase has been questioned, and new antioxidant selenium-dependent proteins have been identified and are now under investigation (20). The level of glutathione peroxidase in blood is considered as a sensitive index of its selenium content in man. In fibroblasts, in vitro, glutathione peroxidase is protected by vitamin E supplementation (21). The mechanism was attributed to the powerful antioxidant effects of vitamin E, which is preferentially oxidized, thus sparing the glutathione peroxidase.

However, no relationship between vitamin E and glutathione peroxidase was detected in hepatocytes (22), where the enzyme is considered as at storage form of selenium in addition to its enzymatic function.

Studies of the relationship between selenium and vitamin E in psoriasis and other dermatoses have produced conflicting results. Juhlin et al. (23) reported a glutathione peroxidase deficiency in psoriatic patients and noticed encouraging clinical responses after vitamin E and selenium supplementation.

Another therapeutic study examining the effect of selenium and vitamin E supplementation on psoriasis, demonstrated a lack of significant clinical improvement of the disease (24). These clinical results might be explained by the normal vitamin E levels in the patients investigated.

In our study, the 5 patients with erythrodermic or pustular psoriasis associated with chronic alcoholism had very low vitamin E blood levels, leading to values below the normal range during the acute episode. These findings, associated with the fact that the 2 patients with erythrodermic psoriasis and acropustulosis but without 9 history of heavy alcohol intake had normal vitamin E blood levels during the acute episode, and the fact that in the PVA group, vitamin E blood concentrations were within the normal range, raise the hypothesis that two associated conditions (chronic alcoholism and erythrodermic or pustular psoriasis) are needed to induce a vitamin E deficiency during the acute phase of the psoriatic disease. We suspect that in this particular group of patients, vitamin E supplementation during the acute episode might be utilized in association with a classical therapy to examine the beneficial effect of such supplementation.

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REFERENCES

1. Hoffman R, Schneider A, Quamo Y. The sex difference in vitamin A metabolism. J Invest Dermatol 1950; 15: 409–419.
2. Mier PD, Van Den Hurk JJMA. Plasma vitamin A levels in the common dermatoses. Br J Dermatol 1974; 91: 155–159.
3. Rollman O, Vahlquist A. Psoriasis and vitamin A: plasma transport and skin content of retinol, dehydroretinol and carotenoids in adult patients versus healthy controls. Arch Dermatol Res 1985; 278: 17–24.
4. Majewski S. Janik P, Langner A, Glinska-Ferenz M, Swietochowska B, Sawicki I. Decreased levels of vitamin A in serum of patients with psoriasis. Arch Dermatol Res 1989; 280: 499–501.
5. Safavi K. Serum vitamin A levels in psoriasis: results from the first national health and nutrition examination survey. Arch Dermatol 1992; 128: 1130–1131.
6. Janin VK, Bansal RK, Aggarwal SK, Chaudhary SD, Saini AS. Erythrocyte glutathione peroxidase activity and plasma vitamin E status in patients with psoriasis. J Dermatol 1988; 15: 487–490.
7. MacCrehan WA, Shönberger E. Determination of retinol, α-tocopherol, and β-carotene in serum by liquid chromatography with absorbance and electrochemical detection. Clin Chem 1987; 33: 1585–1592.
8. Arnaud J, Fortis I, Blaichier S, Kia D, Favier A. Simultaneous determination of retinol, α-tocopherol and β-carotene in serum by isocratic high-perofrmance liquid chromatography. J Chromatogr 1991; 572: 103–116.
9. Hammarström S, Hamberg M, Samuelsson B, Duell EA, Stawiski M, Voorhees JJ. Increased concentrations of nonesterified arachidonic acid, 12L-hydroxy-5, 8, 10, 14-eicosatetraenoic acid, prosta-

glandin E_2, and prostaglandin $F_{2\alpha}$ in epidermis of psoriasis. Proc Natl Acad Sci USA 1975; 72: 5130–5134.
10. Corrocher R, Ferrari S, de Gironocoli M, Bassi A, Olivieri O, Guarini P, et al. Effect of fish oil supplementation on erythrocyte lipid pattern, malondialdehyde production and glutathione-peroxidase activity in psoriasis. Clin Chim Acta 1989; 179: 121–132.
11. Sedgwick JB, Bergstresser PR, Hurd E. Increased superoxide generation by normal granulocytes incubated in sera from patients with psoriasis. J Invest Dermatol 1981; 76: 158–163.
12. Das UN, Vijaykumar K, Madhavi N, Suryaprabha P, Sravankumar G, Ramesh G, et al. Psoriasis: current concepts and new approaches to therapy. Med Hypotheses 1992; 38: 56–62.
13. Diplock AT. Antioxidant nutrients and disease prevention: an overview. Am J Clin Nutr 1991; 53: 189S–193S.
14. Ingold KU, Webb AC, Witter D, Burton GW, Metcalfe TA, Muller DPR. Vitamin E remains the major lipid-soluble, chain-breaking antioxidant in human plasma even in individuals suffering severe vitamin E deficiency. Arch Biochem Biophys 1987; 259: 224–225.
15. Fink R, Clemens MR, Marjot DH, Patsalos P, Cawood P, Norden AG, et al. Increased free-radical activity in alcoholics. Lancet 1985; II: 291–294.
16. Suematsu T, Matsumura T, Sato N, Miyamoto T, Ooka T, Kamada T et al. peroxidation in alcoholic liver disease in humans. Alcohol Clin Exp Res 1981; 5: 427–430.
17. Drevon CA. Absorption, transport and metabolism of vitamin E. Free Radic Res Commun 1991; 14: 229–246.
18. Bjørneboe GEA, Johnsen J, Bjørneboe A, Marklund SL, Skylv N, Høiseth A, et al. Some aspects of antioxidant status in blood from alcoholics. Alcohol Clin Exp Res 1988; 12: 806–810.
19. Hækstra WG. Biochemical function of selenium and its relation to vitamin E. Fed Proc 1975; 34: 2083–2089.
20. Levander OA. Selenium and sulfur in antioxidant protective systems: relationships with vitamin E and malaria. Proc Soc Exp Biol Med 1992; 200: 255–259.
21. Hu WL, Goldring CEP, Rao NR, Rice-Evans C, Burdon RH, Diplock AT. Variable α-tocopherol stimulation and protection of glutathione peroxidase activity in established and malignant fibroblasts. Biofactors 1992; 4: 47–49.
22. Burk RF. Recent developments in trace element metabolism and function: newer roles of selenium in nutrition. J Nutr 1989; 119: 1051–1054.
23. Juhlin L, Edqvist LE, Ekman LG, Ljunghall K, Olsson M. Blood glutathioneperoxidase levels in skin diseases: effect of selenium and vitamin E treatment. Acta Derm Venereol (Stockh) 1982; 62: 211–214.
24. Fairris GM, Lloyd B, Hinks L, Perkins PJ, Clayton BE. The effect of supplementation with selenium and vitamin E in psoriasis. Ann Clin Biochem 1989; 26: 83–88.