Acta Dermatovener (Stockholm) 52: 462–466, 1972

# TREATMENT OF POLYMORPHOUS LIGHT ERUPTIONS WITH BETA-CAROTENE

Gunnar Swanbeck and Göran Wennersten

*From the Department of Dermatology, Karolinska sjukhuset, Stockholm, Sweden*

*Abstract.* Beta-carotene was used in the treatment of 5 patients with polymorphic light eruptions (PMLE). The therapeutic effect was evaluated by means of light tests with a Xenon lamp with respect to both minimal erythema dose (MED) and dose giving rise to papular reactions. After treatment with approx. 100 mg beta-carotene daily for approx. 2 weeks, the light tolerance of the patients increased by a factor of about five. Clinically, the status of the patients was markedly improved. During the treatment the beta-carotene content of the serum increased to 9–70 μmol litre and the patients got a slight yellow discoloration of the skin. The vitamin A content of the serum did not increase during the treatment.

Polymorphous light eruption (PMLE) is one of several diseases where the lesions can be induced by light. The entity of the disease and its relation to discoid lupus erythematosus has been discussed (2, 8, 17, 23).

The general opinion is that it is a separate disease belonging to the group of photodermatoses. The action spectrum of light for the induction of PMLE spans the sunburn range but also the long UV and visible spectrum (5, 11, 24, 27, 28, 29, 31). After the skin has received a certain dosage of UV light, the lesions appear within 24 to 36 hours (7, 11, 14, 16, 18, 19, 30).

The protection of the skin against light, especially the UV-part of the spectrum, is therefore an important therapeutical problem in PMLE. A commonly used agent against PMLE is chloroquin. It has some effect on the disease but its side-effects are such that it is not recommended for prolonged use (3, 4, 11, 17, 18, 26).

In erythropoietic protoporphyria and solar urticaria beta-carotene treatment has been reported to have a positive effect (9, 16, 21, 22). Since beta-carotene has a low toxicity it was tempting to investigate its effect on PMLE.

By exposing a small skin area of a PMLE patient with multiples of the minimal erythema dose (MED) the lesions could be reproduced (6, 7, 11, 18, 25).

As exposure of the patient to light in daily life and also during hospitalization may vary considerably, we decided to evaluate the therapeutical effect of beta-carotene on the experimentally induced lesions on a region of the skin normally protected by clothing. Possibilities of quantifying the therapeutic result might thus be effectuated.

## MATERIAL AND METHODS

The patients were phototested with an Osram High Pressure Xenon Arc Lamp (XBO 150 W). The skin of the back was irradiated with unfiltered light. The distance from the skin to the lamp was 15 cm.

First, the minimal erythema dose was established for each patient. The size of the irradiated areas was about 1.5 × 1.5 cm. Twelve areas were exposed from 6 to 28 sec with an increase of 2 sec each time. The reactions were read after 8 hr and the dose in seconds was noted for the slightest yet perceptible minimal erythema. When reactions were seen at 6 sec, other areas were irradiated for 2 and 4 sec.

In the control group consisting of patients without photodermatoses the MED had a mean of 13.5 seconds and standard deviation of 4.0 seconds. There was no significant heating of the skin, as shown by skin temperature measurements and the absence of heat sensation during clinical use. During the treatment with beta-carotene, repeated tests were made at intervals, with exposures from 1 to 10 multiples of the minimal erythema dose, to investigate the increasing protection against light.

Observations were made approximately 24 hours after the exposure. The degree of erythema and the presence of papules or vesicles were noted.

The patients were given beta-carotene in the form of oral capsules delivered by Roche, in doses from 50 to 150 mg daily. Blood samples were taken for analysis of the beta-carotene serum concentrations as well as the serum vitamin A values.

Vitamin A determinations were made according to the method of Kahan (15).

Beta-carotene determinations were made fluorospectrophotometrically by Dr E. Malmquist, Central Laboratory of Clinical Chemistry, Karolinska sjukhuset, Stockholm.

*Case 1*

The patient was a 13-year-old girl. There was no family history of photosensitivity, skin diseases or skin allergy. Since the age of two, she had "eczema" of the facial skin in early spring and summer. From 7 years old, she suffered from "eczema" all over the body, with severe itching. Most of the lesions were found on the face, arms and legs, with macules, papules, scaling, excoriations and crusts. After the autumn of 1969 she became worse, regardless of the season. When her skin was exposed to sunlight, she experienced severe itching and developed a papular response and scaling erythema and these lesions were very soon severely excoriated. Her dermatitis was reproduced by the phototesting procedure.

Before the treatment with beta-carotene she had developed a chronic pruritic dermatitis with severely excoriated lesions, particularly on the face, arms, hands and legs. Porphyrin levels in urine and faeces were normal and fluorescent investigations of erythrocytes was negative.

The histological picture of the "spontaneous" lesions and the papular test reactions were consistent with PMLE.

*Case 2*

The patient was an 8-year-old boy, with a short period of light asthmatic bronchitis at the age of $1\,^1/_2$ years. From 1968 he had "eczema" on his face, successively spreading to the body, but most pronounced on light-exposed areas such as face, hands and forearms. His dermatitis has been very resistant to usual local treatment, with red scaling small papular efflorescences, severely itching and excoriated and having no correlation to the season during the last 2 years. His dermatitis can be reproduced by photopatch testing procedures. Porphyrin levels in urine and faeces were normal, and fluorescent investigation of the erythrocytes proved negative.

The histological picture of the "spontaneous" lesions and the papular test reactions were consistent with PMLE.

*Case 3*

A 13-year-old girl whose family history was completely free from skin diseases or allergy. She was first seen in September 1970 with small papular eruptions on the face. On her face, especially on the forehead, cheeks and nose, there were red maculae and papules, some of which were confluent. She had erythematous areas even on the forearms, hands and fingers.

Treated locally with a steroid ointment, the lesions disappeared but in May 1971 after sunbathing she contracted an intense erythematous and confluent eruption with oedema on the face, arms and hands. Porphyrin estimations in urine and faeces were normal and her erythrocytes showed no fluorescence in UV-light.

The histological picture of the "spontaneous" lesions and the papular test reactions were consistent with PMLE.

*Case 4*

A 60-year-old woman with tuberculosis at the age of twenty, and hypertonia and auricular heart fibrillations for several years.

Hyperfunction of the thyroid was diagnosed 1969, and treated with antithyroid substances for 1.5 years, and in April 1971 with radioactive iodine. Since the age of 10, she had experienced a solar dermatitis every spring and summer, diagnosed as PMLE in 1965.

When seen, her facial skin was diffusely coarsened and unevenly infiltrated, particularly over the cheeks, nose and chin, with excoriations and easy-bleeding rhagades. Her hands were large and reddened with cracks and rhagades. There were several excoriations on the forearms and on the lower parts of the legs. Porphyrin levels in urine and faeces were normal, and erythrocytes and bone marrow showed no UV-light fluorescence.

The histological picture of the "spontaneous" lesions and the papular test reactions was consistent with PMLE.

*Case 5*

A 35-year-old woman; no instances of phototensitivity or allergic disease in her pedigree. For 3 years she had had recurrent erythematous, non-scaling maculopapulous skin eruptions on her face and forearms which grew worse every spring and summer. After a short time in the sun, July 1971, she experienced severe itching and eruptions on all light-exposed areas. Porphyrin levels in erythrocytes urine and faeces were normal.

The histological picture of the "spontaneous" lesions and the papular test reactions was consistens with PMLE.

None of the patients were receiving drug therapy at the time of the pretreatment test and subsequently only beta-carotene.

## RESULTS

The minimal erythema dose (MED) before, during and after beta-carotene treatment is given in Fig. 1 for all 5 patients. In Fig. 1 the MED of a control group with 2 standard deviations is indicated. Thus 3 of the 5 patients fell within this range. One patient had a higher, and one a lower MED. The effect of the beta-carotene treatment on the MED is also shown in Fig. 1. As is clearly seen, the beta-carotene treatment at dosages used in this investigation gave an appreciable increase in light-tolerance. The MED increased several times (3–60) after a few months' treatment. Even after 2 weeks' treatment a significant increase in light tolerance was found in the 4 patients who were tested after this period of treatment. Three of the 5 patients were light tested about 1 month after the beta-carotene treatment was discontinued. For these patients the MED dropped considerably (25–50 %) but not to the pre-treatment level.

The papular reactions came between 50 and 90 seconds for all 5 patients (Table 1). On the aver-

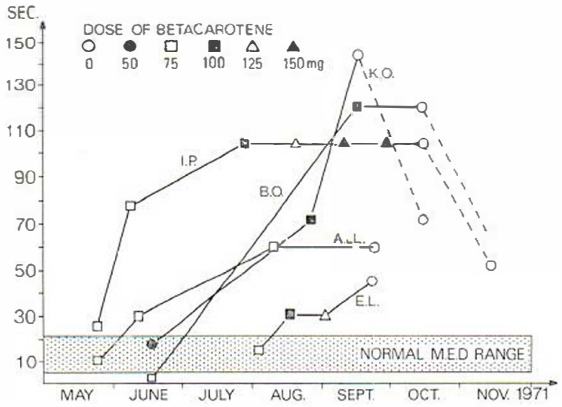


*Fig. 1.* Minimal erythema dose in seconds before, during and after beta-carotene treatment of the 5 patients with PMLE. Dotted lines indicate period without any treatment. The dark area shows the range of normal minimal erythema dose (MED) with 2 standard deviations.

age, this is approximately 5 times the MED, although this factor varied for the different patients.

The papular reaction appearing on PMLE patient was more persistent. For this reason we did not want to induce these reactions when the patients came for subsequent check-ups. Thus we can only cite the highest dose used in the test which did not cause papular reactions (see Table I), rather than the lowest dose that gave papular reactions after beta-carotene treatment, since the former (highest possible test doses) were not given during treatment.

The clinical effect was good in all patients. They were advised not to expose themselves more than usual to the sun. During the treatment, patient no. 4 was almost completely cured. Patient 3 had some remnant hyperkeratotic lesions on the nose, but was considerably improved. Patients 1, 2 and 5 became more pale on the face and hands but had some remaining papules. All patients regarded the beta-carotene treatment as a distinct improvement.

The beta-carotene content in the serum was, for 4 of the patients, within normal limits (2.6–5 $\mu$M/l) before the treatment and 1 patient had 11.0 $\mu$M/l. During the treatment, beta-carotene reached a serum concentration between 9.1 and 75.9 $\mu$M/l with no evident correlation to the clinical result. No increase in vitamin A content of the serum was found during the treatment period.

Table I

| Patient No. | MED sec | Papular reaction dose in seconds: Before treatment | Papular reaction dose in seconds: After 2 months' treatment | Minimal protection factor for papular reaction |
|---|---|---|---|---|
| 1 | 26 | 78 | >208 | 2.7 |
| 2 | 18 | 90 | >144 | 1.6 |
| 3 | 2 | 80 | >120 | 1.5 |
| 4 | 10 | 50 | >120 | 2.4 |
| 5 | 15 | 75 | >120 | 1.6 |

## DISCUSSION

Protection against sunlight with topical and parenteral remedies is of great importance for many light-sensitive patients. However, the treatment available today is not sufficiently effective for many patients. There are several topical preparations that give a certain degree of protection. Among the drugs for parenteral use the most commonly known is chloroquin. Yet it has serious side-effects which limit its value. The search for new drugs to supplement the topical preparations is therefore of importance. Beta-carotene has been used successfully in the treatment of erythropoietic protoporphyria and a few cases of solar urticaria (16, 22). In the present study we have investigated the effect of beta-carotene on polymorphous light eruptions. A purely clinical evaluation of the effect of a solar-protective agent is rather difficult. As the sunshine intensity and the time the patient spends out-doors varies considerably, it is very difficult to obtain reliable results without a standardization of the light exposure. In our opinion the best method is to light-test the patient with a Xenon lamp on a usually clothes-protected area of the skin during the treatment period. By using quartz optics in the lamp, a spectrum similar to sunlight is obtained although somewhat shorter wavelengths may be included.

According to most investigators the MED is not decreased in PMLE but might vary somewhat more than in control group. The findings of the present study are in agreement with this concept. It is also known that by testing with a dose of 5–8 MED one initiates PMLE eruptions on the test site. In the present investigation the same finding was made and histological examinations of the lesions verified the PMLE nature of the induced

lesions. The administration of about 100 mg of beta-carotene per day gives, after a treatment period of 2–4 weeks, an approximately fivefold MED increase. When the administration of beta-carotene was discontinued, the light sensitivity slowly increased again (Fig. 1).

For the PMLE patient the liability to get solar erythema is no more pronounced than for other people. The problem for the patient is the papular lesions that the patient gets when exposed to sunlight. In the present study we have found that beta-carotene also gives partial protection against the induction of these lesions by Xenon light. We have not tested the patients so often with the higher doses needed to cause papular lesions since they persist for some time. But from the data we have, it is clear that the patients can stand at least two or perhaps three times as much sunlight before they get PMLE lesions, when they are on beta-carotene. There is no reason to believe that the protection against the PMLE lesions is not as good as against the erythema reaction, which would mean a four or fivefold better tolerance. Furthermore all patients reported that they could tolerate sunlight in daily life better when on beta-carotene. The full protective effect was not obtained however, until the patients had been on beta-carotene for 2 to 4 weeks. The experimental test and the clinical findings thus gave similar results. In our opinion beta-carotene is of great value in the treatment of PMLE.

In the patients we have studied there was no increase in the vitamin A content of the blood during the beta-carotene treatment, which agrees with the concept that beta-carotene is not converted to vitamin A in the human (1, 13, 20).

The beta-carotene content of the blood increased to a maximum of about 75 $\mu$M/l (normal values 2.6–5 $\mu$M/l). The only negative side-effect was a slight yellow or orange discoloration of the skin. After more than a month's treatment this discoloration was very weak but noticeable in all patients. As yet we do not know if beta-carotene acts merely as an absorbant of light, if it functions as fluorescence quencher (10, 12), or in some other way. Further studies to elucidate this problem are planned.

## REFERENCES


1. Almond, S. & Logan, R. F. L.: Carotinaemia. Brit Med J *2:* 239, 1942.
2. Cahn, M. M., Levy, E. J., Shaffer, B. & Beerman, H. J.: Lupus erythematosus and polymorphous light eruptions. An experimental study on their possible relationship. J Invest Derm *21:* 375, 1953.
3. Cahn, M. M., Levy, E. J. & Shaffer, B.: The use of chloroquine diphosphate (Aralen) quinacrine (Atabrine) hydrochloride in the prevention of polymorphous light eruptions. J Invest Derm *22:* 93, 1954.
4. — Polymorphous light eruption. The effect of chloroquine phosphate in modifying reactions to ultraviolet light. J Invest Derm *26:* 201, 1956.
5. Epstein, J. H.: Polymorphous light eruptions. Wavelength dependency and energy studies. Arch Derm (Chicago) *85:* 82, 1962.
6. — Polymorphous light eruptions. Phototest technique studies. Arch Derm (Chicago) *85:* 502, 1962.
7. — Polymorphous light eruptions. Ann Allerg *24:* 397, 1966.
8. Fisher, D. A., Epstein, J. H., Kay, D. & Tuffanelli, D. L.: Polymorphous light eruption and lupus erythematosus: differential diagnosis by fluorescent microscopy. Arch Derm (Chicago) *101:* 458, 1970.
9. Fitzpatrick, T. B., Pathak, M. A., Parrish, J. A. & Mathews-Roth, M.: Topical and systemic approaches to photoprotection. Proc Roy Soc Med *64:* 861, 1971.
10. Foote, C. S. & Denny, R. W.: Chemistry of Singlet Oxygen. VII. Quenching by beta-carotene. J Amer Chem Soc *90:* 6233, 1968.
11. Frain-Bell, W., Mackenzie, L. A. & Witham, E.: Chronic polymorphic light eruptions. A study of 25 cases. Brit J Derm *81:* 885, 1969.
12. Fujimori, E. & Tavla, M.: Light-induced electron transfer between chlorophyll and hydroquinone and the effect of oxygen and beta-carotene. Photochem Photobiol *5:* 877, 1966.
13. Greenberg, R., Cornbleet, T. & Jeffay, A. I.: Accumulation and excretion of vitamin-A-like fluorescent material by sebaceous glands after oral feeding of various carotenoids. J. Invest Derm *32:* 599, 1959.
14. Jillson, O. F.: *In* The Biologic Effects of Ultraviolet Radiation: Testing for phototoxicity and photoallergy (ed. F. Urbach), pp. 533–540. Pergamon Press, Oxford, 1969.
15. Kahan, J.: A method for the fluorimetric determination of vitamin A. Scand J Clin Lab Invest *18:* 679, 1966.
16. Kesten, B. M.: Urticaria solare. Arch Derm (Chicago) *65:* 221, 1951.
17. Lester, R. S., Burnham, T. K., Fine, G. & Murray, K.: Immunologic concepts of light reactions in lupus erythematosus and polymorphous light eruptions. I. The mechanism of action of hydroxychloroquine. Arch Derm (Chicago) *96:* 1, 1967.
18. Levy, E. J., Cahn, M. M. & Shaffer, B. J.: Polymorphic light eruption: some unusual reactions in ultraviolet-light test sites. J Invest Derm *28:* 147, 1957.
19. Magnus, I. A.: Studies with a monochromator in the common idiopathic photodermatoses. Brit J Derm *76:* 245, 1964.
20. Mandel, G. H. & Weiss, W. P.: *In* The Pharmacological Basis of Therapeutics. Vitamin A and Vitamin

D. (ed. L. S. Goodman and A. Gilman), 3rd ed. pp. 1681–1696. Macmillan Co, New York, 1966.

21. Mathews, M. M.: Protective effect of beta-carotene against lethal photosensitization by haematoporphyrin. Nature *203:* 1092, 1964.
22. Mathews-Roth, M. M., Pathak, M. A., Fitzpatrick, T. B., Harber, L. C. & Kass, E. H.: Beta-carotene as a photoprotective agent in erytropoetic protoporphyria. New Engl J Med *282:* 1231, 1970.
23. Pohle, E. L. & Tuffanelli, D. L.: Study of cutaneous lupus erythematosus. By immunohistochemical methods. Arch Derm (Chicago) *97:* 520, 1968.
24. Scott, F. P. & Molhuysen-v. d. Walle S. M. C.: Light dermatoses. Dermatologica *116:* 96, 1958.
25. Schorr, W. F. & Monash, S.: Positive papular phototests in normal subjects. Arch Derm (Chicago) *87:* 560, 1963.
26. Shaffter, B., Cahn, M. M. & Levy, E. J.: Polymorphic light eruption. A discussion of its pathogenesis and the therapeutic action of the antimalarials in this disease. J Invest Derm *32:* 363, 1959.
27. Stevanovic, D. V.: Polymorphic light eruption. Brit J Derm *72:* 261, 1960.
28. Verhagen, A. R. H. B.: Contralum and the pathogenic wavelengths in chronic polymorphous light dermatoses. Dermatologica *129:* 292, 1963.
29. — Light tests and pathogenic wavelengths in chronic polymorphous light dermatoses. Dermatologica *133:* 302, 1966.
30. Wiskeman, A.: Zur Diagnose des chronisch polymorphen Lichtexanthems. Hautarzt *7:* 162, 1956.
31. Wiskeman, A. & Wulf, K.: Untersuchungen über den auslösenden Spektralbereich und die direkte Lichtpigmentierung bei chronischen und akuten Lichtausschlägen. Arch Klin Exp Derm *209:* 443, 1959.

*Received March 2, 1972*

G. Swanbeck, M.D.
Department of Dermatology
Karolinska sjukhuset
S-104 01 Stockholm 60
Sweden