CAROTENOID TREATMENT FOR LIGHT SENSITIVITY: A REAPPRAISAL AND SIX YEARS' EXPERIENCE

Göran Wennersten

Department of Dermatology, Karolinska sjukhuset, Stockholm, Sweden

Abstract. Long-term treatment with oral carotenoids in 57 patients suffering from a variety of photodermatoses and disorders associated with cutaneous light sensitivity was evaluated. All patients were treated for two or more 6-month periods in separate years. Best therapeutic results were seen in PMLE patients. a good to excellent therapeutic response was noted for 65% of all patients, increasing to 81% of those assigned to skin types III and IV, and decreasing to 47% of those with skin types I and II. The therapeutic effect observed in disorders characterized by other mechanisms than provocation by solar radiation per se was less conspicuous, viz. for light-sensitive psoriasis and lupus erythematosus. Even here, therapeutic failure seems to be more common in individuals with skin types I and II than for skin types III and IV. Photodermatoses such as persistent light reaction, actinic reticuloid and solar urticaria did not respond to any significant degree to carotenoid treatment. Our findings would appear to justify further treatment with oral carotenoids in selected cases of PMLE and a higher dosage level may be tried for non-responding individuals with light-sensitive psoriasis and DLE or SLE. Serious side effects have not been observed in spite of long-term therapy lasting several years.

The light-protective effect of carotenoid treatment of various photodermatoses, as reported by many investigators has shown such variations (1, 2, 5, 6, 7, 8, 9, 13, 16, 19, 20, 21, 22, 23) that the efficacy in general has been a matter of dispute (2, 5, 8, 13, 15, 17, 18, 20). The beneficial therapeutic effect of carotenoids for erythropoietic protoporphyria seems to be well documented (1, 3, 5, 6, 9, 10, 11, 12, 13, 23) although some objections have been raised (2, 23). Carotenoid treatment of polymorphous light eruptions (PMLE) was found effective in those investigated by us (19, 22) and the propitious effect was confirmed in another large study (7) but has been questioned by other investigators (4, 5, 13, 17).

In patients with PMLE and light-sensitive psoriasis earlier treated by us with carotenoids, the light protection factor varied between 4 and 8, with an average value of about 5 (22). In the PMLE patients described by Jansen (7) the therapeutic effect designated as an increase in threshold tolerance to sunlight ranged from 1 to 30 with a mean value of about 8.

The aim of the present study was to describe our 6-year experience of oral carotenoid treatment for different photodermatoses and to investigate the possible influence of skin type on the therapeutic response. Furthermore, in earlier studies (6, 19, 20, 22) the improvement was assessed by the use of a standardized light test procedure with estimation of changes in the minimal erythema dose, MED. In the present study clinical aspects were emphasized and improvement evaluated as the degree of reduction of specific clinical lesions and symptoms. Several patients included in the study have been on carotenoid therapy for 5 to 6 years during spring and summer periods and possible long-term side effects were observed.

MATERIAL AND METHODS

Patients

The investigation encompasses patients treated for photodermatoses or diseases associated with light sensitivity, viz. 31 cases of chronic polymorphous light eruptions (PMLE), 12 patients with light-sensitive psoriasis, 6 with discoid lupus erythematosus (DLE), 1 patient with systemic lupus erythematosus, 3 with erythropoietic protoporphyria (EPP), 1 patient with a persistent light reaction caused by tribromosalicylanilide, 1 patient with actinic reticuloid and 2 patients with solar urticaria. Results obtained for 12 patients with vitiligo were reported earlier (22) and the evaluation was not repeated.

The diagnosis was based on usual clinical and histological characteristics and the light sensitivity confirmed by light test provocations according to a procedure reported elsewhere (19, 22). Assessment with porphyrin analysis in blood, urine and faeces was carried out. Patients with atopic dermatitis or seborrhoeic dermatitis were not included in the study. In each patient photosensitivity had been present for more than 2 years and all had active cutaneous lesions at the time of evaluation.

Minimal erythema dose (MED) and possible UVA
sensitivity were estimated for all patients before therapy. Standardized light test provocations were performed only initially with multiples of MED to confirm the diagnoses but were not subsequently repeated, for ethical reasons.

Furthermore, light exposure to an extent sufficient to induce an increased degree of pigmentation or any hardening phenomenon was avoided by all patients during the period of investigation.

Carotenoid administration

Carotenoids were administered to the patients in the form of oral capsules containing 25 mg active substance each (10 mg beta-carotene in combination with 15 mg canthaxanthin, Ro-8-8427 preparation) (18). 10 PMLE patients were one year given capsules containing pure canthaxanthin, 25 mg each, during the therapeutic period, Ro-1-9915. The capsules were kindly supplied by Roche-Produkter AB, Stockholm.

The administration was performed as an open study. Carotenoids were given 100 mg daily in divided doses, usually during the 6-month period April to September each year. Treatment commenced in 1972 and several patients have been followed yearly since then. Canthaxanthin-treated patients were earlier treated with Ro-8-8427 for another year and period and the therapeutic results compared between them.

Laboratory analysis

Porphyrin analysis was performed as described above. Laboratory evidence of side effects was assessed by the following parameters: sedimentation rate, haemoglobin, corpuscular values (MCV, MCHC), leukocyte count, platelet count, serum creatinine, blood glucose, liver function tests including bilirubin and transaminases, blood lipids and routine urinary analysis. Examinations were performed before, during and at the end of the therapy. Plasma concentrations of vitamin A were monitored.

Classification of skin type

The patients’ normal reactions to solar radiation as experienced in pre-disease conditions before the development of light sensitivity were evaluated. The criteria as stated by Melksi et al. (14) are based on the history of the usual reaction to the first hour of full sun exposure in early summer in Sweden with regard to the degree of erythema and pigmentation usually experienced by the patients and assessed according to the following types of reaction: skin type I—always burn, never tan; II—always burn, sometimes tan; III—sometimes burn, always tan; and IV—never burn, always tan.

The distribution of 66 normal, healthy, age-matched individuals without any sign of light sensitivity, within these different skin type groupings, was estimated for comparison. This control group comprised 20 men and 46 females, i.e. a proportion similar to that observed for the group of patients with light sensitivity investigated.

Evaluation of the therapeutic response

The therapeutic and clinically observed response was assessed according to an arbitrary four-point scale representing the degree of reduction of specific clinical lesions, also including the ability to return to a fairly normal pre-disease life. The clinical efficacy was recorded by both the patient and the doctor. All patients had been on therapy for at least two separate 6-month periods in different years. The clinical scores used were: 1. no or only slight improvement, less than 25% reduction of symptoms and clinical lesions; 2. moderate, 25-50% reduction; 3. good, 50-75% reduction; and 4. excellent, 75-100% reduction. Tolerance and any side effect observed was registered.

RESULTS

Skin types

Estimation of skin type for the major groups of patients treated, viz. PMLE, psoriasis and DLE/SLE, revealed a predominance of individuals always and easily burned, with poor tanning capacity prior to first appearance of their pathological light sensitivity (skin types I and II). This distribution is outlined in Table I. Of the PMLE patients, 48% belonged to skin types I and II; 42% of the psoriasis patients and 57% in the DLE/SLE group. Overall, 24% had skin type I and the same percentage had skin type II, total 48%. In the control group only skin type II was registered for the most sensitive individuals, comprising 11%.

For normal healthy individuals of Scandinavian extraction in the control group, skin type III was most frequently represented, being seen in 80% of those investigated, while only 9% belonged to skin type IV.

No relevant skin type could be determined for EPP patients because of the early appearance of

Table I. Distribution of skin types observed in different disease groups and for normal controls

<table>
<thead>
<tr>
<th>Skin type</th>
<th>PMLE</th>
<th>Psoriasis</th>
<th>DLE/SLE</th>
<th>Total</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>6</td>
<td>2</td>
<td>4</td>
<td>12</td>
<td>24%</td>
</tr>
<tr>
<td>II</td>
<td>9</td>
<td>3</td>
<td>3</td>
<td>12</td>
<td>24%</td>
</tr>
<tr>
<td>III</td>
<td>7</td>
<td>5</td>
<td>2</td>
<td>14</td>
<td>28%</td>
</tr>
<tr>
<td>IV</td>
<td>9</td>
<td>2</td>
<td>1</td>
<td>12</td>
<td>24%</td>
</tr>
<tr>
<td>Total</td>
<td>31</td>
<td>12</td>
<td>7</td>
<td>50</td>
<td>66%</td>
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</tbody>
</table>
Therapeutic response in diseases treated with carotenoids and related to skin type

<table>
<thead>
<tr>
<th>Disease</th>
<th>Skin type</th>
<th>Therapeutic response</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>PMLE</td>
<td>I</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>I</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>III</td>
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<td>3</td>
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<td>IV</td>
<td>1</td>
<td>1</td>
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<tr>
<td>Total</td>
<td></td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>DLE/SLE*</td>
<td>I</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>1</td>
<td></td>
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<tr>
<td>Total</td>
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<td>3</td>
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</tr>
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</table>
patients described by Jansén (7) when the patients who subjectively registered a higher threshold tolerance to sunlight exposure were evaluated. The light protection factor was found to be increased by a mean factor of about 8, though variations ranging from 1 to 30 were seen. In still other investigations carotenoid treatment for PMLE has been considered ineffective and discarded (4, 13, 17, 20). These contradictory findings may imply some differences, for example in the selection of patients, and warrant further exploration. The present study summarizes our 6-year experience with carotenoid treatment for various photodermatoses and diseases associated with light sensitivity, and provides an increased insight into some mechanisms which may partly explain the discrepancies observed.

The previously reported beneficial light-protective effect of oral carotenoids for PMLE (5, 6, 7, 19, 21, 22) was confirmed in this study when a large number of patients were investigated, but also when the therapeutic effect was evaluated by another method, i.e. the degree of reduction of specific clinical lesions and ability to return to a fairly normal pre-disease life. Furthermore, significant variations in the therapeutic response were observed amongst PMLE patients according to skin type, i.e. degree of sensitivity to solar radiation observed before the pathological light sensitivity had appeared. In general, a good to excellent therapeutic response was reported by 65% of the PMLE patients, but the proportion increased to 81% when only those patients with skin types III and IV were considered, and decreased to 47% for patients with skin types I and II. Strict therapeutic failure was observed in 32% of the group as a whole and of these patients 70% were classified as having skin type I or II. No correlation between the type of PMLE lesion—plaque, papular, or eczematous—and therapeutic response to carotenoids was noted.

The therapeutic effect observed in disorders characterized by mechanisms of disease activity other than provocation by solar radiation per se was less conspicuous, i.e. light-sensitive psoriasis and lupus erythematosus. A complete reduction of clinical lesions could not be anticipated, yet in light-sensitive psoriasis 42% experienced a moderate and 16% a good therapeutic response. Even here, therapeutic failure seems to be more common for skin types I and II (60%) than for skin types III and IV (29%) (Table II). Similar findings were observed for the DLE/SLE patients and the favoura-

ble response described by others (6, 16) was not confirmed. However, best results were displayed by the SLE patient included who, interestingly enough, had skin type I.

Improved light tolerance has not been observed in normal individuals (11), nor in patients with vitiliginous skin (22).

The exact site and mechanism of oral carotenoid action in human skin is unknown. Specific photochemical effects do occur, i.e. quenching of singlet state excited oxygen and/or free radicals—mechanisms thoroughly discussed earlier (1, 2, 3, 4, 6, 13, 15, 17, 18, 19, 20, 22). Carotenoid absorption is seen within the longwave ultraviolet (UVA) and visible region. Erythropoietic protoporphyria induced by porphyrins with an absorption and action spectrum around 400 nm usually responds favourably to carotenoid treatment (1, 2, 3, 5, 6, 9, 10, 12, 13, 23), but photochemical mechanisms seem to be more important than any possible filtering effect. Interestingly enough, UVA-sensitive patients in the present study demonstrated a disappointing therapeutic response. Other photodermatoses usually provoked by UVA radiation, such as persistent light reaction, actinic reticuloid and solar urticaria, were earlier proved not to respond in any significant degree to carotenoid treatment (8, 13), and this was confirmed by those cases included in the present investigation.

In conclusion, best therapeutic response was experienced by PMLE patients, particularly those assigned to skin types III and IV. These findings appear to justify further treatment with oral carotenoids for selected cases of PMLE. Less beneficial results should be expected for patients with light-sensitive psoriasis and DLE/SLE, but a considerably higher dosage level may be tried for non-responding individuals. The laboratory parameters assessed were normal and no serious side effects were observed, even in patients undergoing repeated therapy for several years.

REFERENCES
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G. Wennersten, M.D.
Department of Dermatology
Karolinska Sjukhuset S-104 01 Stockholm 60 Sweden