

The Comparison of Therapeutic Effectiveness Between Lesional and Whole Body Exposure on Oral PUVA for Generalized Vitiligo

Gi-Bong Ko, M.D., Ji-Hun Mun, M.D., Hong-Yong Kim, M.D.

Department of Dermatology, College of Medicine, Chonbuk National University, Chonju, Korea

Background : For the treatment of generalized vitiligo patients with oral PUVA, we can use two different methods; one is to treat the lesions while the whole body is exposed. Another one is to treat the lesions while only the lesions are exposed.

Purpose : This study was performed to determine whether lesional and whole body exposure in oral PUVA for generalized vitiligo show any therapeutic differences in effectiveness.

Methods : The vitiligo lesions were distributed over the whole body skin of the subjects and the lesion area was less than 6% of the whole skin area. PUVA was done to the subjects more than 20 times after oral administration of psoralen. The patients were classified into two different groups. One is the lesional exposure group in which the patient exposed only the vitiligo lesion. The other is the whole body exposure group in which the patient exposed almost their whole body.

Results : Our results show that there is no statistical difference of the therapeutic effectiveness between the two methods.

Conclusions : We recommend lesional treatment rather than whole body treatment to prevent the oral PUVA side effects. (*Ann Dermatol* 14(4) 200~203, 2002).

Key Words : Lesional exposure, Oral PUVA, Vitiligo, Whole body exposure.

Vitiligo shows white macules and patches caused by the loss of melanocytes¹. Although the vitiligo patients have been suffering great cosmetic and psychologic pressure, any perfect treatment method of the disease has not been developed yet. For the treatment of the disease, corticosteroids, PUVA (psoralen plus ultraviolet A), surgical techniques, and depigmenting agents are used. Among these methods, one of the most popular methods is oral ad-

ministration or topical application of psoralen followed by long-wave ultraviolet light exposure (oral or topical PUVA)^{2,3,4}. Topical PUVA is used for local or limited lesions⁵. Because topical application is difficult when there are many lesions, oral PUVA is usually used for the generalized vitiligo.

For the treatment of generalized vitiligo patients with oral PUVA, we can use two different methods; one is to treat the lesions while the whole body is exposed. Another one is to treat the lesions while only the lesions are exposed. However, it is not known whether the two methods show any therapeutic differences in effectiveness. If therapeutic efficacy of the lesional exposure is equal to whole body exposure, the lesional exposure should be recommended to reduce side effects of oral PUVA, such as skin cancer, cosmetic problems, etc.. Thus, we investigated the therapeutic effectiveness of the lesional and the whole body exposure treatment cases.

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Reprint request to : Hong-Yong Kim, M.D., Department of Dermatology, College of Medicine, Chonbuk National University, 634-18 Kuemam-Dong, Duckjin-Gu, Chonju, 561-712 Korea

Tel. (063)250-1978, Fax. (063)250-1970

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MATERIALS AND METHODS

Subjects were the vitiligo patients treated at the Department of Dermatology, Chonbuk National University Hospital, Korea, from September, 1992 to July, 2001. The vitiligo lesions were distributed over the whole body skin of the subjects, and thus they were all generalized type vitiligo patients. The lesion area of the subjects was less than 6% of the whole skin area. PUVA was done to the subjects more than 20 times after oral administration of psoralen and their treatment records were kept in detail. Any ultraviolet treatment was not done before our PUVA treatment. Young children under 10 years old and pregnant women were excluded. Also, the photosensitive disease patients, the cardiac disease patients, the cataract patients, and the patients accompanying precancerous lesions were excluded. Before PUVA treatment, we did routine complete blood cell count, urinalysis, liver function test, and antinuclear antibody test, which did not reveal any problems.

We examined and recorded the patients' sex, the age distribution, the duration of the disease, the size of the lesion area, the number of the treatment and the total accumulation dose of the UVA, the types of the exposure (whole body or lesional), the size of the exposed area, and the side effects.

Two hours before UVA exposure (the UVA source of the Ultralite 6809 Phototherapy, Ultralite Enterprises, Inc., USA), 0.3-0.5 mg/kg of 8-methoxypsoralen (8-MOP) was orally administered. We asked patients to wear dark-colored thick clothes for the PUVA treatment. And, we made holes on the clothes for the treatment of every lesional area. During the treatment, the patients were instructed to wear protective goggles, and when they went out after taking 8-MOP, they were asked to wear UVA protective goggles for 24 hours. We applied 2 J/cm² as the initial therapeutic dose and increased the treatment dose by 0.5 J/cm² every 2 treatments, and 2 times treatment per week were tried in principle. If there occurred a severe erythema on the lesion, the treatment was stopped temporarily and resumed with reduced dose when the erythema subsided.

The degree of the repigmentation percentile was recorded and classified as follows:

Grade 0(G0): 0-25% repigmentation

Grade 1(G1): 25-50% repigmentation

Grade 2(G2): 50-75% repigmentation

Grade 3(G3): 75-99% repigmentation

Grade 4(G4): 100% repigmentation

The differences between two groups were checked for significance using the Chi-square test with the SPSS 9.0 for Windows.

RESULTS

Fifty four patients (24 male and 30 female) were included in our study. The patients were classified into two different groups. One is the lesional exposure group in which the patient exposed only the vitiligo lesion. The other is the whole body exposure group in which the patient exposed almost their whole body. There were 27 patients in the lesional exposure group, and 27 patients in the whole body exposure group. For the lesional exposure patients, their average age was 35.7 years old (12-68 years old), the average vitiligo onset age was 32.4 years old (9-68 years old), the duration of the vitiligo was 3.3 years (0-10 years), the average size of the lesion area was 2.0% (0.2-6.0%), the average number of treatments was 38.4 times (20-162 times), the total amount of the UVA was 170.7 J/cm² (59-823.5 J/cm²), and the average exposure area ratio was 4.5% of the whole body (1-11%). For the whole body exposure patients, their average age was 34.2 years old (10-75 years old), the average vitiligo onset age was 31.3 years old (7-72 years old), the duration of the vitiligo was 3 years (0.2-10 years), the average size of the lesion area was 2.2% (1.0-6.0%), the average number of treatments was 53.1 times (20-129 times), the total amount of the UVA was 260.0 J/cm² (54.5-821 J/cm²), and the average exposure area was 80.7% of the whole body (57-99%) (Table 1).

Two out of 27 lesional exposure patients and 1 out of 27 whole body exposure patients showed no response, and the others showed response, even to a small extent. Sixteen (59.3%) out of 27 lesional exposure patients and 15 (55.6%) out of 27 whole body exposure patients achieved G2 or more. Six lesional exposure patients and 2 whole body exposure patients showed complete repigmentation. No statistically significant difference of the therapeutic effectiveness was shown between the two groups ($P>0.05$) (Table 2).

During the treatment period, 19 out of 54 pa-

Table 1. Characteristics of patients.

	Lesional exposure	Whole body exposure
Number of patients	27	27
Sex		
Male	10	14
Female	17	13
Age(years)*	35.7±18.3	34.2±19.8
Onset age(years)*	32.4±18.4	31.3±20.3
Duration(years)*	3.3±3.7	3.0±3.1
Size of the lesion(%)*	2.0±1.6	2.2±1.6
Number of treatments*	38.4±34.0	53.1±35.5
Total dose(J/cm2)*	170.7±169.0	260.0±212.3
Exposure area ratio(%)*	4.5±2.7	80.7±16.1

* Data expressed as mean ± standard deviation.

** There was no statistically significant difference between lesional and whole body exposure group in each parameter.

Table 2. Response to oral PUVA therapy in lesional and whole body exposure patients.

	Lesional exposure	Whole body exposure
G0*	6(22.2)**	4(14.8)
G1	5(18.5)	8(29.6)
G2	7(25.9)	8(29.6)
G3	3(11.1)	5(18.5)
G4	6(22.2)	2(7.4)
Total	27(100)	27(100)

*G0, G1, G2, G3, and G4 indicate 0-25%, 25-50%, 50-75%, 75-99%, and 100% repigmentation of the involved skin areas, respectively.

**Number of patients(%)

tients showed side effects. Among them, dizziness was observed in 8 patients, nausea (gastrointestinal trouble) in 7 patients, symptomatic erythema in 3 patients, and pruritus in 1 patient.

DISCUSSION

The pathogenesis of vitiligo is still unknown, but three major theories have been proposed: autoimmune, autocytoxic, and neural^{3,4}. If autoimmune mechanism is concerned in the vitiligo pathogenesis, it would be more effective to expose the whole body to UVA during PUVA. However, PUVA may imply a risk for development of lentigines, actinic keratosis, and squamous cell carcinoma. A large study in USA demonstrated a significant increase of skin cancer following PUVA therapy for 3 or more years^{6,7}. And it is reported

that squamous cell carcinoma and keratoses developed in vitiligo areas after a prolonged course of PUVA⁸. Thus, we investigated the therapeutic effectiveness of lesional and whole body exposure in the oral PUVA, and found that there was no statistically significant difference either.

We asked the patient to wear dark-colored thick clothes for the PUVA treatment. And, we made holes on the clothes for the treatment of every lesional area. Thus they did not complain about the treatment, even though the patients had many lesions.

The mechanism of repigmentation by the oral PUVA therapy has been explained in many ways^{3,9}. Some authors proposed that the local factors induce the repigmentation. Although the mechanism was not clear, PUVA caused a depletion of expression of epidermal growth factor receptor and

melanocyte surface antigens¹⁰. They also reported that PUVA induces local immune suppression, because PUVA decreased the number of Thy-1+ and Ia+ dendritic epidermal cells in the treated site and suppressed the induction of contact hypersensitivity to dinitrofluorobenzene¹¹. On the other hand, others proposed that the systemic factors induce the repigmentation. PUVA therapy induces keratinocyte to release soluble factors to suppress immune reaction¹², alters the distribution and function of T-lymphocytes⁹, and releases circulating growth factor(s) that stimulate(s) melanocyte proliferation^{13,14}.

Our results show that both the lesional and the whole body treatment achieved similar degrees of repigmentation (summarized in Table 2), with no statistically significant difference in therapeutic effectiveness. These results suggest that the repigmentation may be induced by local factors similar to systemic factors. Thus we recommend lesional exposure to UVA in oral PUVA to lessen side effects such as photoaging, hyperpigmentation, and skin cancers.

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