Comparison of PUVA and Retinoid-PUVA in the Treatment of Psoriasis in Korean Patients

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**Background**: Although treatment with PUVA or etretinate is effective for psoriasis, both treatment regimens have limitation because of the risk of long-term toxicity.

**Objective**: The present study was performed to compare the clinical effects of PUVA and retinoid-PUVA.

**Methods**: Twenty-five chronic plaque psoriasis patients with more than 20% involvement of the skin surface were included in this study. Sixteen patients were treated with the PUVA therapy and nine patients were treated with retinoid-PUVA.

**Results**: The number of phototherapy and cumulative UVA doses of retinoid-PUVA were significantly smaller than those of PUVA therapy.

**Conclusion**: Combining PUVA with etretinate in the treatment of psoriasis may lead to lowering of total number of PUVA treatments and the cumulative dosage and it may be possible to shorten the duration of using etretinate. (Ann Dermatol 7:(2)112-115, 1995)

**Key Words**: Psoriasis, PUVA, Retinoid-PUVA

Psoriasis is a disease of the skin that is characterized by chronic relapsing nature with epidermal cell proliferation of unknown etiology. The disease is most frequently treated with phototherapy and photochemot herapy. Photochemotherapy with 8-methoxypsoralen and UVA (PUVA) is a reliable and effective method of treating chronic plaque psoriasis. Etretinate, an oral aromatic retinoid, has shown to be effective for psoriasis treatment. But both treatment regimens have limitation because of the risk of long-term toxicity.

The present study was performed to compare the clinical effects of PUVA and retinoid-PUVA and assess the effects of adding retinoid to PUVA therapy in the treatment of psoriasis.

**PATIENTS AND METHODS**

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1. **Patients**

Twenty-five chronic plaque psoriasis patients with more than 20% involvement of the skin surface were included in our study. The PUVA group was sixteen and the retinoid-PUVA group was nine. The mean ages of PUVA and retinoid-PUVA group were 29.3 and 32.1 years respectively (Table 1).

2. **Treatment**

PUVA therapy was performed with our usual equipment, Waldman UV 8001K (Waldmann Co., Germany) which is a cabinet type UVA source of fluorescent lamp (Waldmann F80 100W PUVA lamp) with the peak emission at 340 to 365 nm. Twice a week 30 mg of 8-methoxypsoralen was given orally and two hours later UVA was given. The starting dose of UVA was 2.0 or 2.5 J/cm² and the dose was increased until clinical clearing was achieved. During the maintenance therapy the dose was not changed. In the retinoid-PUVA group, etretinate was given orally in a dose of 0.5 mg/kg from one week before starting PUVA therapy. After clinical clearing was achieved, the oral medication of etretinate was discontinued.

3. **Assessment**
Table 1. Subjects of PUVA and retinoid PUVA therapy

<table>
<thead>
<tr>
<th></th>
<th>Mean age</th>
<th>Male/female</th>
</tr>
</thead>
<tbody>
<tr>
<td>PUVA (n=16)</td>
<td>29.3 ±11.6</td>
<td>5/11</td>
</tr>
<tr>
<td>Re-PUVA (n=9)</td>
<td>32.1 ±12.8</td>
<td>7/2</td>
</tr>
</tbody>
</table>

therapy (p<0.05, Mann-Whitney U test). In clearing group with PUVA therapy, the mean number of phototherapy was 13.6 and the mean cumulative UVA doses of the trunk and extremities were 65.6 J/cm² and 68.5 J/cm² respectively. In clearing group with retinoid-PUVA therapy, the mean number of phototherapy was 8.1 and the cumulative doses of trunk and extremities were 32.6 J/cm². The mean duration

Table 2. Criteria of response to therapy

<table>
<thead>
<tr>
<th>Grade</th>
<th>Criteria</th>
<th>%improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>minimal improvement—slightly less scale and/or erythema</td>
<td>5–20%</td>
</tr>
<tr>
<td>2</td>
<td>definite improvement—partial flattening of all plaques—less scaling and less erythema</td>
<td>20–50%</td>
</tr>
<tr>
<td>3</td>
<td>considerable improvement—nearly complete flattening of all plaques, border of plaques still palpable</td>
<td>50–95%</td>
</tr>
<tr>
<td>4</td>
<td>clearing—complete flattening of plaques may be outlined by pigmentation</td>
<td>95%</td>
</tr>
</tbody>
</table>

Table 3. Results of therapy

<table>
<thead>
<tr>
<th></th>
<th>PUVA</th>
<th></th>
<th>PUVA</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of patients</td>
<td>%</td>
<td>No. of patients</td>
<td>%</td>
</tr>
<tr>
<td>Clearing</td>
<td>14</td>
<td>87.5</td>
<td>8</td>
<td>88.9</td>
</tr>
<tr>
<td>Improvement</td>
<td>1*</td>
<td>6.3</td>
<td>1*</td>
<td>11.1</td>
</tr>
<tr>
<td>Failure</td>
<td>1**</td>
<td>6.3</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
<td>100.0</td>
<td>9</td>
<td>100.0</td>
</tr>
</tbody>
</table>

The patients were examined at 2-week interval for 16 weeks. The response of the therapies were evaluated by means of the grading system suggested by the PUVA cooperative study group of United States in 1979 (Table 2). The grade 4 before 16 weeks of PUVA therapy was assessed as clearing. The grade 3 at 16 weeks of PUVA therapy was considered improvement and grade 1, 2 or aggravation of lesion were considered failure of the treatments. Clinical adverse reactions were monitored at each visit. Laboratory examinations consisted of blood count, blood chemistry and urinalysis.

RESULTS

Fourteen patients of the PUVA group (87.5%) and eight patients of the retinoid-PUVA group (88.8%) showed clearing (Table 3). The number of phototherapy and cumulative UVA doses of retinoid-PUVA for clearing were significantly smaller than those of PUVA and final UVA dose of retinoid-PUVA therapy was smaller than those of PUVA therapy but this results are not statistically significant (Table 4). There were some adverse reactions such as nausea, pruritus, and mild degree of erythema in both groups. In the retinoid-PUVA group, transient cheilitis and peeling of palms were additionally noted.

DISCUSSION

PUVA is a therapeutic modality utilizing a photosensitizing chemical compound, psoralen and UVA to induce a beneficial result not produced by either method alone. In a multicenter study in eighteen European cities, 3175 patients with severe psoriasis were treated with oral PUVA and the data obtained over a period of 39 months were analyzed. This was an aggressive protocol designed to induce and maintain minimal erythema phototoxic responses and to try and clear the psoriatic lesions before tanning.
developed, which might require higher PUVA doses. A marked improvement was obtained in 88.8% of the patients. An average of twenty exposures and a cumulative UVA dose of 96J/cm² were required for clearing. In the United States Cooperative Clinical Trial (sixteen-center study) reported in 1979, 1308 patients with extensive psoriasis were treated at 16 centers over 18 months. Psoriasis cleared up in 88% of patients. This protocol used suberythematous and minimally phototoxic doses of PUVA designed to minimize acute phototoxicity. The duration of treatment was twice as long in the United States Clinical Trial as in the European PUVA study, although the number of treatments needed for clearing was approximately the same using the two protocols. Total UVA requirements were 249J/cm² compared to 96J/cm² in the European study. In our study we used the protocol of PUVA designed to minimize acute phototoxicity. The clearance rate of PUVA therapy in our study was the same as those of the European multicenter study and the United States Cooperative Clinical Trial, but the cumulative UVA dose for grade 4 was 65.6J/cm² which is smaller than those of the two studies.

Etretinate, the aromatic retinoid, has been shown to be effective in the treatment of severe chronic plaque, exfoliative, palmoplantar, and generalized pustular psoriasis. Although both PUVA and etretinate therapies are effective in the treatment of psoriasis, side effects may occur in long term therapy which sets limitations for both therapies.

To minimize the side effects of long term use, the combined therapy of PUVA and etretinate was tried in many previous studies. In Korea, Park et al. reported the effects of retinoid-PUVA in the treatment of psoriasis and a cumulative UVA dose was 67.5J/cm² which is larger than that of our study. The different results between the two studies may be due to the different methods of using the etretinate. In most studies retinoid-PUVA appears to speed up the treatment by reducing the number of UVA exposure required to achieve remission and it might diminish potential long term hazards of PUVA therapy such as actinic degeneration and cancers of the skin. Additionally, because etretinate therapy prevents the development of skin cancers in patients at risk, for example, in the basal cell nevus syndrome and in xeroderma pigmentosum, etretinate can be expected to show an anticancer effect in retinoid-PUVA therapy. But two double-blind controlled studies showed no statistically significant difference between etretinate-PUVA and place-PUVA for the number of PUVA exposures and the cumulative dose of UVA required for clearance of psoriasis.

The results of our study show a significant difference in clinical response between PUVA and retinoid-PUVA. Especially the cumulative UVA dose was markedly decreased by adding retinoid to PUVA therapy. In the retinoid-PUVA group transient cheilitis and peeling of palms were noted due to etretinate but these side effects were not so significant as to change the treatment schedules.

The advantage of combining PUVA with retinoid can be summarized as follows: (1) it may lead to a lowering of the total number of PUVA treatments and the cumulative UVA dosage, (2) it may be possible to use lower doses of retinoid and (3) when lower doses of retinoids are prescribed, their side effects may be decreased.

In conclusion from the results of this study, combining PUVA with etretinate in the treatment of psoriasis may lead to a lowering of the total number of PUVA treatment and the cumulative dosage and it may be possible to shorten the duration of using etretinate.

REFERENCES

2. Gupta AK, ANderson TF : Psoralen photo-