The effect of 308 nm excimer laser on segmental vitiligo: a retrospective study of 80 patients with segmental vitiligo

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Summary

Background: Segmental vitiligo (SV), which frequently accompanies poliosis, indicating a poor prognosis that is likely resistant to treatments.

Objectives: In this study, we performed a retrospective analysis to evaluate the treatment response to 308 nm excimer laser in SV patients.

Methods: A retrospective chart and photographic review was performed on 80 SV patients who had been treated with 308 nm excimer laser for > 3 months.

Results: Eighty patients with SV (mean age: 24.0 years ± 15.3, males: 50%) were included in this study. The mean grade of repigmentation was 2.3 after 20.6 months of mean treatment duration; 23.8% of 80 patients showed grade 4, 20% showed grade 3, and 56.2% showed grade 1–2 repigmentation. However, none of them achieved complete repigmentation with excimer laser. The degree of repigmentation was positively correlated with treatment duration (r = 0.315, P = 0.004) and cumulative ultraviolet (UV) dosage (r = 0.366, P = 0.001), whereas it was negatively correlated with disease duration (r = −0.265, P = 0.017).

Conclusion: This study suggests that SV has a better repigmentation response when excimer laser is used at earlier stages of the disease and long-term use and high cumulative UV energy of the excimer laser elicit better responses. Additional treatments like surgical procedures in addition to excimer laser should be considered for complete repigmentation.

Vitiligo is an acquired disorder characterized by a progressive loss of melanocytes, and is traditionally categorized into non-segmental and segmental types. The clinical manifestations of segmental vitiligo (SV) are markedly different from those of non-segmental vitiligo (NSV) (1). SV usually occurs early in life, spreads rapidly in the affected dermatomal area, and has decreased association with autoimmune diseases. Leukotrichia is also common in SV. The presence of white hairs in a lesion of SV predicts a poor response to phototherapy, suggesting that SV with white hairs may require surgical treatments like epidermal grafting (2, 3). The therapeutic approaches for vitiligo include corticosteroids, topical immunomodulators, phototherapy, and surgical therapy (4). Previous reports on the response of vitiligo to narrowband ultraviolet B (NBUVB) therapy showed that, in the non-SV group, 48% of patients showed a marked response and 27% showed a moderate response. However, 92.3% in the SV group showed no more than a mild response to NBUVB regardless of the lesion site, and only 7.7% of SV patients showed a moderate response to treatment (5). Since the first reports in 2002, 308 nm excimer lasers have demonstrated efficacy in treating localized vitiligo (6). Although surgical treatment may be needed for many patients with SV, phototherapy still remains a first line treatment for early SV. However, knowledge regarding the long-term treatment response to 308 nm excimer laser in SV patients is limited. In this study, we performed a retrospective analysis of SV patients who were treated with 308 nm excimer laser in order to evaluate treatment response and to determine factors that affect treatment outcomes in SV patients.

Patients and methods

Patients were recruited from two dermatology clinics that had special clinics for vitiligo patients, Yonsei University Severance Hospital and Drs Woo & Hann’s Skin Clinic (Seoul, Korea). From January 2005 to July 2010, all patients with SV who had received 308 nm excimer laser therapy for > 3 months were included. SV was characterized by unilateral macules or a linear or flag-like pattern of mosaicism. One or more macules in one area (<2%), but not clearly in a segmental or zosteriform distribution, were categorized as the focal type of vitiligo and excluded from the study population. Patients who had been treated with other phototherapy or epidermal grafting during the evaluation period were also excluded. Patients were treated with a xenon
chloride laser, delivering monochromatic 308 nm UVB (PHAROS EX-308, Ra Medical Systems, Carlsbad, CA, USA), without treating surrounding normal skin. The initial doses were around 100–150 ml/cm². If erythema was not seen in 24 h, the dose was increased by 50 ml/cm². The treatment was administered twice a week on non-consecutive days. Other combined medical treatments, including systemic and topical corticosteroids and topical tacrolimus, were allowed during the study.

Data collected from medical records included: patient characteristics (age, sex, age of onset of vitiligo, and location of lesion), medical and family histories, duration of excimer laser treatment, maximum and cumulative UV dosages, and combined treatment modalities. Clinical outcomes were evaluated using photographic estimation by comparing the initial pre-treatment and final follow-up photographs. These photographs were evaluated by two independent dermatologists. Repigmentation was graded as: grade 0, no repigmentation; grade 1, 1–24% repigmentation; grade 2, 25–49% repigmentation; grade 3, 50–74% repigmentation; grade 4, 75–99% repigmentation; grade 5, complete repigmentation of the treated area. Any side effects during the treatment were also recorded.

Descriptive statistics were performed using mean, range, and proportions. Student’s t-test was used to determine significance in differences between patient data. Correlations between various factors and repigmentation grades were determined by Pearson’s correlation test. Multiple linear regression analysis was used to evaluate the contribution of factors to grade of repigmentation. A two-sided P-value of 0.05 indicated statistical significance.

Results

Clinical characteristics of the patients

The clinical characteristics of SV patients are summarized in Table 1. During the study period, 80 patients (40 males and 40 females) were followed. Age of patients at inclusion was 24.0 years ± 15.3 (mean ± SD; range 4–55 years). Mean age of disease onset was 22.5 ± 15.1 years (range 3–54 years), and mean disease duration was 21.0 ± 48.0 months (range 0.3–360 months).

Sixty-five patients (81.3%) demonstrated facial segmental involvement. The most common sites of facial involvement were the periorbital areas (35.0%), cheek (28.8%), forehead (26.3%), and perioral areas (18.8%). Other involved areas were the neck (12.5%) and the trunk (6.3%). There were no patients with SV of the extremities. Thirty-three patients (41.3%) showed extensive involvement, extending >2 contiguous dermatomes. Many patients received other treatments in addition to the excimer laser during the study period; 36 patients (37.5%) were treated with oral corticosteroids, 28 patients (35%) with topical steroids, and 50 patients (62.5%) with topical tacrolimus ointment.

Clinical efficacy assessment

Mean grade of repigmentation was 2.33, and mean duration of treatment needed to achieve this was 20.6 months. Maximum and cumulative dosages were 700.3 and 36857.6 ml/cm², respectively. Thirty-five patients (43.8%) demonstrated more than grade 3 (>50% repigmentation of treated area) repigmentation (Fig 1), and 27 patients (33.8%) demonstrated less than grade 1 (<25% repigmentation of treated area). No patients reported complete repigmentation. Response varied at different sites of involvement; facial lesions responded better than lesions located elsewhere. Even among facial lesions, the nose (grade 3.0) and perioral areas (grade 2.8) were sites that had good responses, while the perioral areas (grade 2.1), chin (grade 1.8) and neck (grade 1.8) showed lower response rates (Table 2).

When patients were divided into two age groups, younger than 15 (2.47) and older than 15 (2.26), degree of repigmentation was not influenced by age group. Maximum and cumulative UV doses were not significantly different between the two groups.

With multivariate analysis to determine factors influencing repigmentation, disease duration was a significant negative factor (β = −0.239, P = 0.028), and treatment duration (β = 0.312, P = 0.041) and maximum doses (β = 0.299, P = 0.022) were significant positive factors (Table 3).

Discussion

Phototherapy is one of the most reliable treatments for vitiligo. NB-UVB is currently the most efficient and probably safest treatment for vitiligo in both children and adults. NB-UVB has an immunomodulating effect on cellular and humoral immunity and can stimulate residual melanocytes located in the outer root sheath of the hair follicle (7). A 308 nm excimer laser induces photobiological effects similar to NB-UVB. Previous studies indicated that the mechanisms contributing to the greater clinical efficacy of the excimer laser were its direct cytotoxic
Fig. 1. A 15-year-old segmental vitiligo (SV) patient showing grade 4 repigmentation in the perioral area before (a) and after 8 months of excimer laser treatment (b). A 54-year-old SV patient showing grade 4 repigmentation in the periorbital area before (c) and after 36 months of excimer laser treatment (d).

Table 2. Differences in treatment response according to site of involvement

<table>
<thead>
<tr>
<th>Site</th>
<th>Number of patients (%)</th>
<th>Involvement</th>
<th>Non-involvement</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nose</td>
<td>6 (7.5)</td>
<td>3.00 ± 0.89</td>
<td>2.28 ± 1.19</td>
<td>NS</td>
</tr>
<tr>
<td>Periorbital</td>
<td>28 (35.0)</td>
<td>2.75 ± 1.08</td>
<td>2.11 ± 1.18</td>
<td>0.011</td>
</tr>
<tr>
<td>Cheek</td>
<td>23 (28.7)</td>
<td>2.42 ± 1.22</td>
<td>2.31 ± 1.18</td>
<td>NS</td>
</tr>
<tr>
<td>Forehead</td>
<td>21 (26.3)</td>
<td>2.33 ± 1.11</td>
<td>2.34 ± 1.21</td>
<td>NS</td>
</tr>
<tr>
<td>Trunk</td>
<td>5 (6.3)</td>
<td>2.20 ± 1.30</td>
<td>2.34 ± 1.18</td>
<td>NS</td>
</tr>
<tr>
<td>Perioral</td>
<td>15 (18.7)</td>
<td>2.08 ± 1.31</td>
<td>2.38 ± 1.16</td>
<td>NS</td>
</tr>
<tr>
<td>Neck</td>
<td>10 (12.5)</td>
<td>1.80 ± 1.14</td>
<td>2.41 ± 1.17</td>
<td>NS</td>
</tr>
<tr>
<td>Chin</td>
<td>8 (10)</td>
<td>1.75 ± 1.16</td>
<td>2.40 ± 1.17</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS, difference between groups is not statistically significant.

Table 3. Pearson’s correlation coefficient and multiple linear regression analysis for the grade of repigmentation with various factors in segmental vitiligo patients

<table>
<thead>
<tr>
<th>Pearson’s correlation coefficient γ (P-value)</th>
<th>Multivariate linear regression analysis β (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of onset</td>
<td>-0.084 (0.461)</td>
</tr>
<tr>
<td>Duration of disease</td>
<td>-0.265 (0.017)*</td>
</tr>
<tr>
<td>Duration of treatment</td>
<td>0.315 (0.004)*</td>
</tr>
<tr>
<td>Maximum UV dosage</td>
<td>0.200 (0.077)</td>
</tr>
<tr>
<td>Cumulative UV dosage</td>
<td>0.366 (0.001)*</td>
</tr>
</tbody>
</table>

*Correlation is significant at the 0.05 level (two-tailed).
†Correlation is significant at the 0.01 level (two-tailed).

Effect on the T cells infiltrating the skin, its effect on the induction of T cell apoptosis, and a greater capacity for stimulation of melanocyte migration and proliferation from the niche located in hair follicles. Because of these effects, the excimer laser is known to have the advantage of providing a more rapid repigmentation response, especially in the limited form of vitiligo, when compared with NBUVB (8, 9).

The segmental type of vitiligo is usually localized to one dermatome, shows relatively stable disease activity after an initial rapid spreading phase, and is associated with a significantly lower rate of autoimmune diseases than the non-segmental type. The etiopathogenesis of SV remains unclear, but several hypotheses have been put forward, including mainly neuronal mechanisms. SV is usually associated with psoriasis, which indicates complete loss of melanocytes in the vitiligo lesion and low possibility of repigmentation with medical treatment only (2, 3). A previous study utilizing portable digital microscopy reported that surgical treatment should be considered in all patients with SV who have psoriasis in the vitiligo lesions because psoriasis indicates no hope for repigmentation (3). However, a recent preliminary study reported that melanocytes still exist in the white hairs, though white hairs have fewer melanocytes than black hair and tyrosinase-positive melanocytes were only observed in black hair follicles. In addition, the expression of SCF in the dermis of areas with white hair was weaker than in areas of black hair (10). These findings suggest that the melanocyte reservoir is not completely depleted in vitiligo lesions with psoriasis. Thus, we wanted to examine the effects of excimer laser in SV with psoriasis and to determine if it could induce complete repigmentation in SV. There have been no reports to our knowledge of the effects of excimer laser exclusively in patients with SV.

Van Geel et al. (11) described the early clinical and immunological sequence of SV appearing in a patient with halo nevi. The findings provided evidence that a cell-mediated immune response, including melanocyte-specific CD8+ T lymphocytes, is involved in the early phases of SV and suggested that in some cases, SV and NSV are not two completely separate.
entities but could represent variants of the same disease spectrum.

Lotti et al. (12) tried UVB microphototherapy for eight SV patients by focusing a beam of UVB on vitiligo patches only. After 6 months of microphototherapy, five of the eight subjects (62.5%) achieved normal pigmentation on > 75% of the treated areas. In particular, three of the subjects became totally repigmented. Although the number of patients in that study was small, and the researchers did not report on treatment response in relation to clinical variables like disease onset and involved sites, UVB microphototherapy was suggested to be a treatment of choice in the limited form (segmental type) of vitiligo. In our study, 43.8% of 80 patients showed > 50% repigmentation with 308 nm excimer laser treatment after 20.6 months of mean treatment duration. In contrast to the previous study (12), there were no patients who achieved complete repigmentation in our study. This may be because only SV patients with definite segmental and zosteriform distributions were enrolled, which excluded focal types of vitiligo. Some variables like extent and distribution of lesions and duration of disease in recruited SV patients may also have affected the treatment outcome of excimer laser.

Clinical variables including age at disease onset, sex, family history, and associated diseases were not thought to correlate directly with the treatment outcome. However, duration of SV was one of the important factors that influenced treatment outcome. In this study, the degree of repigmentation was inversely correlated with disease duration (r = −0.265, P = 0.017). This finding indicated that early SV could have a high probability of considerable repigmentation if treated as early as possible. A study on the effect of topical steroids in SV lesions found that there was > 50% repigmentation if the patients presented within the first year of the disease (13).

The most commonly involved sites of SV were the face, trunk, neck, extremities, and scalp, in descending order of frequency (14). Because the face, which is the most commonly involved site, is the area that has the greatest psychological impact, most patients are willing to undergo intensive treatment. We compared treatment response in the various sites of the face. The nose (grade 3.0) and periorbital areas (grade 2.8) were sites that had good responses, while the perioral areas (grade 2.1), chin (grade 1.8), and neck (grade 1.8) showed less response. Anbar et al. (5) evaluated the treatment response of SV and NSV to NBUVB and compared the responses of different body sites to therapy in the NSV group. They noted that the face was the area that was fastest to respond with the least dose of NBUVB, and that the resistant areas of the face were the pre- and post-auricular areas, the lips, and the angles of the mouth because these areas are less hairy than the rest of the face. Although the correlation between treatment response and sites of vitiligo was examined only in NSV group, the result was in agreement with our study, which investigated treatment response to excimer laser only in SV patients.

According to one comparative study in NSV between 308 nm excimer laser and excimer light, the two treatments showed similar results in terms of efficacy for a repigmentation of at least 50% (15). Another randomized, investigator-blinded and half-side comparison study targeting symmetrical vitiligo appeared that 308 nm excimer laser was more effective than NBUVB, because the repigmentation was more rapid in the excimer laser treatment (16). In this study, there was no additional evaluation with regard to limited type of vitiligo only, even if NSV was divided into extensive and limited types. However, to our knowledge, there is no known study regarding the effect of 308 nm excimer laser on SV only compared with other treatments including 308 nm non-laser excimer light and NBUVB. Therefore, further clinical study to compare the effect of various types of phototherapy on SV only is also required. The study would be helpful to establish appropriate treatment option and provide optimal dosages and treatment duration of each treatment.

The limitation of this study was that this was a retrospective chart and photograph review study of 80 SV patients and it is difficult to say that the effect of excimer laser only on SV was examined because other medical treatments were allowed to be used together with excimer laser. In this study, thirty-five of 80 patients (43.8%) showed > 50% repigmentation after 20.6 months of mean treatment duration, but none of them achieved complete repigmentation. Although the 308 nm excimer laser is a relatively effective and safe modality for treating SV, it requires long-term use and high cumulative UV energy at earlier disease stages for better outcomes. Furthermore, combination therapy or additional treatments like surgical procedures in addition to excimer laser should be considered for complete repigmentation because SV usually involves the hair follicle as a source of repigmentation soon after onset.

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References

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