Excimer light phototherapy of segmental and non-segmental vitiligo: experience in Taiwan

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Abstract

Purpose: To determine the efficacy of excimer light in the treatment of vitiligo and to assess parameters affecting therapeutic results.

Methods: This retrospective study analyzed 227 patches of vitiligo in 142 patients. Treatment was performed twice weekly and treatment efficacy was assessed by two independent dermatologists. Patients who received less than 24 treatment sessions were excluded from the analysis of predictive factors for response.

Results: Sixty-eight (30.0%) patches achieved more than 50% repigmentation, and 42 (18.5%) achieved more than 75% repigmentation. The mean treatment numbers to achieve any repigmentation and more than 50% repigmentation were 19.41 and 34.93, respectively. Fewer treatment sessions number, segmental lesions and absence of melasma were significant predictors for poor treatment response in multivariate analysis. Lesions on the hands/feet needed the highest dose and scalp lesions needed the highest number of treatment sessions to produce initial repigmentation.

Conclusions: Excimer light is a valuable treatment modality for both segmental and non-segmental vitiligo even in patients who have failed previous treatments. The number of treatment sessions needed to produce initial pigmentation may be higher than 30 for scalp lesions. There is a need to find other combination methods, both medical and surgical, to enhance its therapeutic efficacy.

Vitiligo is a clinical conundrum that affects 0.1% to 1% of the general population among different ethnic groups (1). Phototherapy is the mainstay in the treatment of generalized vitiligo and both 308 nm xenon chloride excimer laser (2) and light (3) are efficient tools as targeted vitiligo treatment in Caucasians. The therapeutic efficacy of excimer laser was also good in Chinese vitiligo patients (4, 5). However, the effectiveness and the predictive factors for the outcome of excimer light therapy in vitiligo are less well studied, which are the aims of our study.

Patients and methods

Patients

We retrospectively reviewed the medical and photographic records of 241 Chinese patients with vitiligo who underwent excimer light treatment in our phototherapy center, a tertiary referral hospital in northern Taiwan, between December 2008 and July 2010. Patients were excluded from the analysis if they were lost to follow-up (had less than six sessions, did not take photography or had photographs with bad quality), were in active phase (had significant progression before the treatment), had concurrent surgical treatment for vitiligo, had treatment interruption for more than 1 month and/or were receiving concurrent systemic immunosuppressants including corticosteroids. Patients who received less than 24 treatment sessions were also excluded in the analysis of predictive factors for response (Fig. 1).

Methods

A 308 nm xenon chloride excimer light machine (Excilite-μ™, DEKA, Florence, Italy) was used in the study. Excilite-μ produces 50 mW/cm² power density and targets 30 cm² treatment area in each spot. Treatment was performed by dermatologists and scheduled twice a week on non-consecutive days. Except for hands and feet, which has a higher minimal erythema dose (6–10), the initial dose was 150 mJ/cm² and increased by 50–100 mJ/cm² in each subsequent session until minimal erythema dose was reached. Maintenance dose was chosen as the dose providing asymptomatic delayed erythema that lasted between 1 and 3 days. The dose was further increased if no more erythema occurred or erythema faded within 24 h during the subsequent treatment. If erythema lasted for more than 3 days or
painful erythema occurred, the treatment was held and the subsequent dose was reduced to the previous dose. For hands and feet, the initial dose was 500 mJ/cm² and the incremental dose was 250 mJ/cm². The lesions were photographed with digital single-lens reflex camera (D70, Nikon Corporation, Tokyo, Japan) with lens 18–50 mm EX 2.8, Sigma (Sigma Corporation, Tokyo, Japan) every eight treatments.

Clinical efficacy evaluations

Repigmentation was evaluated with a 5-point scale: 4 = 76%, 3 = 51–75%, 2 = 26–50%, 1 = 1–25% and 0 = no repigmentation (Fig. 2). Two dermatologists independently reviewed the photographs for degree of repigmentation.

Statistical analysis

The response rates were expressed by percentage; the treatment sessions numbers and maintenance doses were presented by mean ± SD. ANOVA test was used to compare the mean maintenance doses among different treated sites. A logistic regression model was used to assess the associations between each possible predictor factor and the response to excimer light therapy. The response to excimer therapy was defined as repigmentation ≥ 50% (5, 11). In the multivariate analysis, we retained and adjusted for possible confounding factors, including age, genders, sites, duration, size, segmental/non-segmental, previous treatment, treatment frequency, peripheral hyperpigmentation, total treatment number, pigmented disorders and maintenance and loading dose. Statistical analyses were
performed using the Statistical Package for the Social Sciences (SPSS for Windows version 17.0; SPSS, Inc., Chicago, IL, USA). P < 0.05 was considered to be statistically significant.

Results

Patients

This study included 227 patches of vitiligo in 142 patients with a mean age of 37 years (range 3–83). All patients were Chinese Han with Fitzpatrick skin phototype III and IV. The female : male ratio was 1.41 : 1. The mean age was 37 years (range 3–83). The duration of the disease was less than 1 year in 38 (26.8%), between 1 and 2 years in 19 (13.4%) and more than 2 years in 85 patients (59.9%). All the patients had been treated with topical agents, and 88 patients (61.0%) had been treated with phototherapy with inadequate response. One hundred and sixty-six (73%) patches were less than 25 cm², 43 (18%) were 25 to 100 cm² and 18 (8%) were more than 100 cm². The mean number of total treatment sessions was 46 (range 6–157). The mean of total treatment duration was 33 weeks (range 3.6–83 weeks) and the mean of treatment frequency was 1.5 times per week (range 0.2–3.6 times per week). The locations of lesions were face and neck (67%), trunk (12%), hand/feet (11.5%), extremities (7%) and scalp (2.6%). One-third of the lesions belonged to the segmental type. Fifteen patients (10.6%) had melasma and contributed 25 (11.5%) patches.

Clinical efficacy evaluations

Sixty-eight (30.0%) patches achieved more than 50% repigmentation, and 42 (18.5%) achieved more than 75% repigmentation. After excluding the patients with less than 24 treatment sessions, 51 (33%) patches achieved more than 50% repigmentation and 33 (21%) achieved more than 75% repigmentation. Sixteen and nine patients, respectively, showed more than 50% and 75% repigmentation with less than 24 treatment sessions. Twelve (16.9%) patches of the segmental type and 56 (35.9%) patches of the non-segmental type achieved more than 50% repigmentation. Seventeen (65.3%) patches of the patients with melasma and 51 (25.4%) patches of those without melasma achieved more than 50% repigmentation.

Among the 19 patients (25 patches) who failed previous He-Ne laser treatment, 9 of 19 patients (47.4%) still showed > 25% repigmentation in 13 patches (52%), and 6 of 19 patients (31.6%) achieved > 50% repigmentation in eight patches (32%). A total of 48 and 13 patients underwent examination of thyroid function and anti-thyroid antibodies (e.g. anti-thyroid peroxidase antibody and anti-thyroglobulin antibody), respectively. In the examined patients, two of them (n = 48) had hypothyroidism and three of them (n = 13) had anti-thyroid antibodies. The positive rates for hypothyroidism and anti-thyroid antibodies were 4.2% and 23.1%, respectively. However, all the patients with hypothyroidism and anti-thyroid antibodies underwent less than 24 treatment sessions and were not included in the univariate and multivariate analyses.

The mean treatment sessions numbers to achieve any repigmentation and more than 50% repigmentation were 19.41 and 34.93, respectively, for all subjects, and 22.97 and 42.43 after excluding the patients receiving less than 24 treatment sessions. Lesions of the scalp and trunk needed more treatment sessions (38.0 and 54.5 sessions, respectively) to achieve 50% repigmentation. Lesions of the hands/feet were most resistant to treatment, and only 11.5% of the patches achieved 50% repigmentation. The mean maintenance dose (± SD) was 441.29 ± 274.6 mJ/cm². The mean maintenance doses (± SD) on different areas were, in increasing orders, 330.39 ± 110.67 mJ/cm² (face and neck), 358.33 ± 106.84 mJ/cm² (scalp), 444.44 ± 250.90 mJ/cm² (trunk), 513.33 ± 166.33 mJ/cm² (extremities), and 1044.23 ± 582.98 mJ/cm² (hands/feet).

Genders, age and duration of the disease did not affect the results of repigmentation significantly, although odds ratio (OR) showed favorable results in young, female patients, and in vitiliginous patches with short duration. Location of vitiliginous patches also did not influence the result of treatment, although the odd ratio between head/neck and hands/feet was significant in univariate analysis (OR = 9.31, P = 0.034). Predictors for better response were non-segmental vitiligo (OR = 2.37, P = 0.029), presence of melasma (OR = 4.59, P = 0.003) and phototherapy naïvety (OR = 2.34, P = 0.018).

Discussion

Vitiligo is an enigmatic condition and the response to treatment is often frustrating. Two types of vitiligo exist, i.e. segmental and non-segmental, each with distinct clinical features and therapeutic responses (12). Non-segmental vitiligo is often autoimmune based, and is usually treated with topical corticosteroids or phototherapy (13). Segmental vitiligo is often managed by surgical treatment, either alone (14, 15) or in combination with other modalities (16) because of poor response to medical treatment (17) although potent topical corticosteroid has been reported to produce more than 50% repigmentation in 34.2% of patients (18). Standard phototherapy produced no more than mild response irrespective of the sites of involvement (19). He-Ne laser has been reported to produce better effect with marked repigmentation (> 50%) in 60% of 30 patients after an average of 137 treatment sessions (20). In recent years, 308 nm excimer laser and light have been introduced to target the vitiliginous lesions more accurately with better efficacy compared to conventional phototherapy (21). Although excimer laser is more efficient in inducing T-cell apoptosis than excimer light (22), clinical studies show a similar efficacy between the two light sources in the treatment of vitiligo (23) and psoriasis in Caucasians (24).

The psychosocial impact of vitiligo is higher in the pigmented races due to greater visibility of the lesions and social stigmata (25–28). However, reports on the use of excimer laser/light in the treatment of Asian patients with vitiligo are still few. One study of excimer laser showed that 27/44 patches (61.4%) achieved more than 75% repigmentation and 4/44 lesions...
(9.1%) showed 51–75% repigmentation in Chinese patients after 30 treatments (4). In another study, 21 subjects with symmetrical vitiligo lesions were treated twice weekly for 6 months with excimer light on one side and narrow-band UVB on the opposite side. At the end of the study, six lesions (37.5%) treated with excimer light achieved an excellent repigmentation (≥76%) (3, 29). In another study in Korean patients with vitiligo, 51 patients treated with narrow-band UVB were compared with 52 patients treated with excimer laser regarding the pattern of repigmentation. In their study, the most frequent repigmentation pattern was the perifollicular type, followed by marginal, diffuse and combined, in both modalities. However, factors affecting the repigmentation rates were not analyzed (30). In another study done in Kuwait, 34 patients (14 males and 20 females) with localized vitiligo were enrolled. Twenty-nine patients (12 males and 17 females) completed the study. Lesions were treated twice weekly for 13 weeks. Facial lesions responded better than lesions elsewhere. The least responsive areas were the hands and feet. The average number of treatment sessions to induce repigmentation was 11 (31).

In our study, the percentage of patients who achieved more than 50% repigmentation was only 33%. In previous studies, age, site, disease duration and previous treatment had been shown to affect the treatment efficacy (4, 5, 11, 31, 32). In Taiwan, traditional phototherapy, photochemotherapy and He-Ne laser were all reimbursed for vitiligo treatment, and excimer light treatment is self-paid. Thus, the less satisfactory treatment response to excimer light in our patients might be because all the patients had been treated with topical agents and only 38% of lesions were naïve to phototherapy, and 60% of patients had disease duration more than 2 years.

In our study, type of vitiligo (segmental vs. non-segmental), previous treatment and the numbers of treatment sessions influenced the efficacy. Although younger patients with vitiligo responded better to excimer light treatment, the result was not statistically significant. Location showed significant difference between face/neck and acral skin in univariate analysis, although the significance disappeared in the multivariate analysis.

Some current recommendation suggests that for vitiligo lesions which do not respond to excimer laser after 20 to 30 treatment sessions, a different treatment modality should be considered (5). In our study, although most lesions (81.9%) showed initial repigmentation within 30 treatment sessions, lesions on the scalp required a higher mean number. A selection bias may be present because only six lesions were on the scalp. Another possibility is the deeper localization of the putative reserved melanocytes (or melanocyte stem cells) in the scalp hairs at the bulge areas (33), and the hair cycling time is longer in terminal hairs compared to vellus hairs. Thus, it takes longer for melanocytes on the scalp to migrate to the surface epidermis. The scattering effect of scalp hairs might be unimportant because the maintenance dose needed to produce the repigmentation was not higher on the scalp compared to the trunk. Whatever the reasons, the optimal treatment number to consider excimer light treatment failure may exceed 30 times, especially for the scalp.

The effectiveness rates to excimer light were, in decreasing orders, head and neck, trunk, extremities and hands/feet. However, the effect of location did not show statistical significance in the univariate and multivariate analysis in our study. It might be due to the small sample size in non-facial locations. Besides, most of our patients had vitiliginous patches which had failed previous treatments. Therefore, there is a selection bias for more resistant lesions.

Segmental vitiligo is the single most important parameter affecting therapeutic efficacy in our study population. Segmental vitiligo has been shown to respond less well to traditional phototherapy and various medical treatment modalities (11, 19, 34, 35). In our study, if only non-segmental vitiligo on face and neck was considered, 42% patients achieve 50% repigmentation. The result was similar to a previous study in Asians (31). However, 61.4% of more than 75% repigmentation rate was reported in the other report (4). Short disease duration, treatment naïveness, disease instability and possible concomitant treatment in the previous study might be the reasons. In unstable vitiligo, vitiligo was reported to respond better to excimer laser because of the presence of residual melanocytes within and around the vitiliginous lesions (5). Because we included only patients with stable disease, the treatment response may thus be less favorable.

Segmental vitiligo showed poor response in our study despite a high percentage of initial repigmentation (73%), and only 20% of patients achieved 50% repigmentation with a mean treatment sessions number of 42.75 sessions. The result is compatible with another Asian study, in which 66.2% of the patients demonstrated repigmentation >25%, but only 43.8% of them reached 50% repigmentation and none of them achieved complete repigmentation after 20.6 months of mean treatment duration (32). Although the percentage of repigmentation >50% was higher in the study, the mean number of treatment sessions was as high as 164.8 sessions according to the twice a week treatment frequency (32). Our result is much worse than the 60% repigmentation rate by He-Ne laser (36). However, the mean number of treatment sessions of He-Ne laser was as high as 137 sessions. Besides, in our study, the patients who failed previous He-Ne laser treatment still showed >25% repigmentation in more than half of the vitiligo patches. Therefore, excimer light still remains a valuable choice in patients who have failed previous He-Ne laser treatment in segmental vitiligo. In particular, because of the more rapid onset of repigmentation and a different mode of action of excimer light treatment compared to He-Ne laser, it is intriguing to speculate the additive or synergistic value of combining these two treatment modalities in segmental vitiligo. Although the patients with segmental vitiligo who had failed previous treatments showed a poorer response rate, more than 10% of them still achieved >50% repigmentation.

The presence of facial melasma is an important parameter to predict the response of vitiligo treatment. In a study of narrow-band UVB treatment in India, vitiligo patients with melasma achieved repigmentation earlier and with better response than patients without melasma (37). In our study, patient with melasma also had better response to excimer light in both
univariate and multivariate analysis. Melasma represents a state of hyperactive melanocytes affected by both intrinsic and extrinsic factors. The intrinsic hyperactivity of melanocytes might explain the good treatment response of vitiligo treatment. However, the presence of nevus zygomaticus did not affect the treatment response.

This retrospective study had some limitations. First, patients in the study self-paid for excimer treatment and most had failed other previous treatments. Thus, the less favorable treatment results should not be generalized to vitiligo patients in general. Second, to enhance the efficacy of excimer treatment, we encouraged our patients to apply topical corticosteroids or tacrolimus concomitantly. However, the amount and frequency of drugs applied were not controlled. Thus, a bias toward better results might be present compared to excimer light treatment alone. However, in the assessment of predictive factors for treatment response, the influences might be negligible since the bias was likely present equally in different subgroups of our patients. Third, our patient number is still limited, especially for nonfacial lesions, although our patient numbers are already the largest among reports of excimer light for vitiligo. All in all, we think the result of this study is valuable because it reflects the practical experience of excimer light in non-reimbursed patients with vitiligo in Asians.

In conclusion, excimer light is a valuable treatment modality in patients with both segmental and non-segmental vitiligo even in patients who have failed previous treatment. Our treatment parameters may serve as a reference for the treatment of Chinese patients with vitiligo using excimer light. However, a larger cohort study is needed to find out and confirm the parameters affecting the treatment response. There is also a need to find other combination methods, both medical and surgical, to enhance the therapeutic efficacy of excimer light treatment.

References


