Using a 308-nm excimer laser to treat vitiligo in Asians

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ABSTRACT

Background: Current vitiligo therapies require many months of treatment and often result in disappointing outcomes. Treatment with a 308-nm excimer laser has shown promising results in patients with vitiligo.

Objective: This controlled prospective trial studied the effectiveness of the 308-nm excimer laser for treating vitiligo in Asians.

Methods: Thirty-four patients (14 males and 20 females) with localized vitiligo were enrolled in the study. Vitiligo patches were treated using a 308-nm excimer laser. Lesions were treated twice weekly for 13 weeks. The treatment was started with 50 to 100 mJ/cm² (according to site) and increased by 50 mJ/cm² in every session until erythema appeared. Patients were treated for 25 sessions, or until 100% repigmentation, whichever was achieved first. The overall response rate was assessed clinically and by comparison of photographs before and after treatment by two independent investigators.

Results: Twenty-nine patients (12 males and 17 females) completed the study. Lesions on the face responded better than elsewhere on the body. The least responsive areas were the hands and feet. The average number of treatment sessions prior to repigmentation was 11. Untreated control patches remained unchanged. In higher skin phototypes the response was more favorable. There was no significant correlation between the age of the patients and their response to treatment.

Conclusion: The use of the 308-nm excimer laser for the treatment of vitiligo is effective, relatively safe, and more convenient compared to other available modalities of treatment for stable vitiligo with small patches. However, similar to other modalities of treatment, the therapeutic effect is mainly dependent on the location of vitiligo lesions.

KEY WORDS

vitiligo, excimer, lasers, laser

Introduction

Vitiligo is an acquired idiopathic common skin disorder characterized by well-demarcated white patches of skin. It affects 1% to 3% of the general population with no age, sex, or racial predilection. Associations with other autoimmune diseases such as thyroid disease, Addison's disease, diabetes mellitus, alopecia areata, and

Table 1. Demographic data for patients with vitiligo

Subject no.	Sex	Age (years)	Skin type	Site*	Disease duration (months)	Max. dose (mj/cm²)	improvement %
1	F	15	3	k, df	120	600	15
2	F	19	3	k	132	1400	10
3	F	3	4	f, ax	13	100, 400	83
4	M	47	5	f, fi	64	200, 1400	50
5	M	68	4	f, ax, dh	144	150, 700	45
6	F	8	4	w, k, df	36	1000	30
7	F	26	4	fi	240	1600	10
8	F	11	3	dh, df	6	1100	5
9	F	12	4	f, k,	36	150, 1450	67
10	F	25	4	f	24	100	35
11	M	82	4	dh, df	84	200, 900	20
12	F	31	4	t, l	56	850	55
13	F	58	5	f, ax	58	250	90
14	F	19	4	f, l, df	84	100, 700	45
15	F	4	4	g	13	200	95
16	F	19	4	a, t	132	750	60
17	M	56	4	dh, a , l	24	1300	30
18	M	32	5	f, dh	9	500, 3300	89
19	M	21	4	f, t, fi	48	50, 800, 1100	51
20	M	5	4	e, w, k, l	3	1000	83
21	M	48	4	f	12	100	20
22	M	7	4	f, k	24	100, 1100	20
23	F	48	3	f	62	450	10
24	M	26	5	f, t	24	250, 800	48
25	M	33	4	f	44	1100	93
26	F	47	5	e, dh	276	1200	40
27	F	15	5	f, dh, e, k, df	12	150, 850	55
28	F	31	4	f	276	200	0
29	M	50	4	dh, df	24	800	20

**a = arm, ax = axilla, df = dorsum of feet, dh = dorsum of hands, e = elbow, f = face, fi = finger, g = genitalia, l = legs, k = knee, t = trunk, w = wrist*

pernicious anemia are documented.

Vitiliginous patches are often psychologically distressing and in some societies can lead to loss of social status. Conversely, it may be induced by any stressful event. Clinically, it may have localized, segmental, mucosal, or generalized distribution.

Treatment of vitiligo is challenging. The use of camouflage products can be cosmetically acceptable. Common therapeutic options include potent topical corticosteroids (1), topical and oral psoralen with ultraviolet A radiation (PUVA) (2), and broadband and narrowband UVB phototherapy, which has fewer side effects (3, 4). The goal of phototherapy is to stimulate adjacent melanocytes in the outer root sheath of hair follicles and on the margins of lesions, or residual intralesional melanocytes, to migrate and repopulate the vitiliginous areas. Reported success rates for repigmentation varies from 50% to 60% after months to years of therapy. Topical application of pseudocatalase and calcium in combination with UVB has also been used (5). Various grafting methods that have been used effectively for treatment of vitiligo include full-thickness tissue graft (punch graft), split thickness graft, and suction blister graft (6–9). Cellular grafts consisting of cultured melanocytes/keratinocytes have shown promising results (10, 11). PUVA after autologous skin graft can enhance pigmentation. Tissue-engineered skin applied to dermabraded vitiligo skin followed by PUVA has been found highly effective in repigmenting vitiligo lesions (12). Despite the above potential treatments, a faster, easier, and more effective treatment is still needed.

While the age of onset, sex and associated diseases are not thought to correlate directly with the treatment outcome, the duration of vitiligo and the body site of vitiligo lesions seem to play an important role in the percentage of responders achievable with different treatment modalities (13).

Recently, XeCl excimer laser-generated 308-nm UVB radiation has been shown to be promising for the treatment of localized vitiligo (14–20). The first reports

Fig. 1. Vitiligo patches on the elbows of a 5-year-old male before treatment (subject 20)

gave evidence that this laser therapy could trigger follicular repigmentation within a few weeks of treatment and lead to cosmetically satisfactory results. Targeted phototherapy devices such as the XeCl excimer laser allow delivery of high-intensity radiation only to the affected skin, thus protecting unaffected skin from UV damage. In addition, body sites not accessible by common UV-sources can be treated with these targeted devices. The purpose of this study was to investigate the efficacy of excimer laser therapy in patients with vitiligo.

Fig. 2. After 25 treatments with a 308-nm excimer laser.

Methods

The study was a controlled prospective trial in which thirty-four patients (14 males and 20 females), each with multiple lesions at different body sites (face, trunk, axilla, arm, elbow, wrist, dorsum of the hand, knee, leg, and dorsum of the foot) were enrolled after taking their informed consent for the treatment and photographs. Five patients dropped out and 29 patients (12 males and 17 females) completed the study. Inclusion criteria were stable vitiligo patches in patients that had never had any treatment before or those that had stopped their previous treatment for at least 8 weeks. Exclusion criteria were active vitiligo or the use of systemic and/or topical immunosuppressive treatments within the last 8 weeks before study entry. The patients' ages ranged from 3 years to 82 years. Their skin phototypes ranged from III to V. The disease duration ranged from 3 months to 23 years. Our end-point was 25 treatments or 100% repigmentation, whichever was achieved first. All patients were treated at the Department of Dermatology at Adan Hospital, Kuwait, between January and June 2008.

Treatment with a monochromatic 308-nm XeCl excimer laser (Talos, WaveLight®, Germany) was administered twice weekly but never on 2 consecutive days, for an average of 13 weeks. The laser was operated with pulse repetition frequency of 200 Hz and impulse energy of 6.5 mJ. The pulse width was 60 nsec. Laser light was delivered through an articulated mirror arm to a handpiece with spot diameters of 15 mm, 20 mm, and 25 mm that was changed according to the size of the lesions. Treatment was started with 100 mJ/cm^2 for body lesions and 50 mJ/cm^2 for sensitive areas such as the eyes and genitalia. This was increased by 50 mJ/cm^2 until erythema appeared. If erythema remained less than 48 hours, the dose was kept the same. If erythema persisted more than 48 hours, the dose was reduced to the last well-tolerated one. Whenever burning or blistering developed a treatment was skipped. At least one vitiligo lesion per patient on a non–sun-exposed body site was left untreated for control purpose. The eyes were protected with UV-protective goggles. Only the application of emollients was allowed during the study. Assessment of the clinical response and recording of side effects was performed at every treatment session by at least one of the investigators. Photographs were taken before treatment and after 25 sessions of treatment. The overall response rate was assessed clinically and by comparison of photographs of before and after treatment, by two independent investigators. It was evaluated by calculating the mean of the improvement assigned by each investigator. The patients' overall satisfaction was assessed using a 3-point scale (poor, good, or excellent).

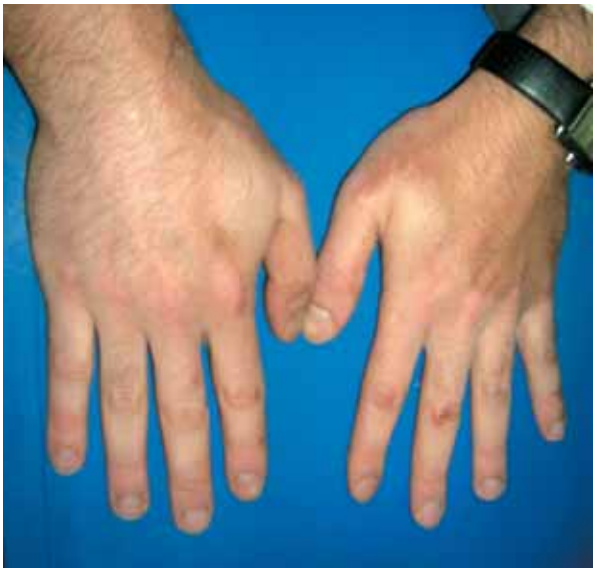

Fig. 3. Vitiligo of the hands of 9 months' duration before treatment (subject 18).

Data were analyzed using the Wilcoxon signed rank test and paired Student *t* test as appropriate. The correlation between disease duration and improvement as well as disease duration and age of the patients was evaluated by the Spearman rank correlation test. All statistical tests were two-sided with significance for *p*-values set at less than 0.05.

Results

There were five dropouts in our study. Three had difficulty in complying with the frequency of treatment sessions and two were found to have active vitiligo lesions. Twenty-nine patients with vitiligo completed the requested 25 treatments.

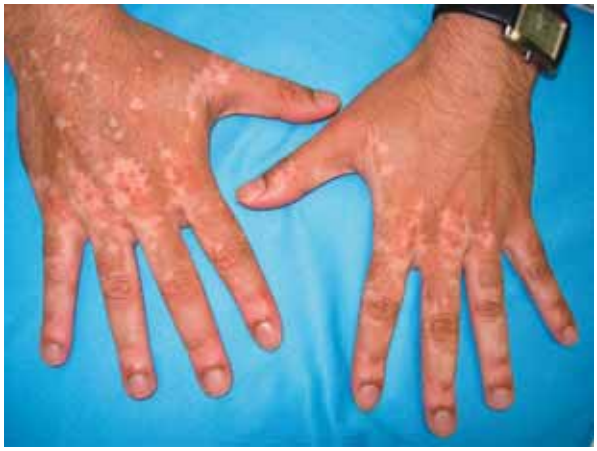

Fig. 4. Marked repigmentation after 25 sessions with a 308-nm excimer laser.

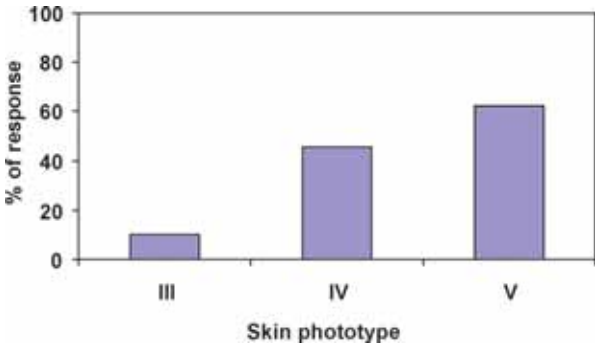

Fig. 5. Response to treatment according to skin phototype.

None reached 100% repigmentation at this stage. Six patients (20.7%) achieved repigmentation of 75% or more, and 12 patients (41.4%) achieved 50% or more repigmentation. Lesions on the face responded better than lesions elsewhere on the body. Seven of the 16 (43.75%) patients with facial lesions developed 75% or greater pigmentation.

Two of the six patients (33.4%) with trunk lesions had 75% or above pigmentation. Five of the 19 patients (26.31%) with lesions on the extremities had 75% or more pigmentation and the rest showed some degree of repigmentation.

The least responsive lesions were on the hands and feet. No more than 25% improvement was observed in any of the nine patients with foot lesions. Only one of the 11 patients with hand lesions had more than 75% repigmentation whereas the other 10 had less than 50% pigmentation (Figures 1-4).

Only one patient had genital and perianal vitiligo. She responded highly satisfactorily, with 95% repigmentation. The average number of treatment sessions prior to repigmentation was 11. The control patches did not show repigmentation in any patient during this study.

Skin phototype seemed to play a role in patient response to the therapy. Four patients (13.8%) with skin phototype III developed 10% repigmentation. Nineteen (65.5%) were skin phototype IV, in whom the average repigmentation was 45.4%. Six (20.7%) were skin phototype V, in whom the average repigmentation was 62% (Figure 5).

Disease duration seemed to play some role in response to treatment. The shorter the duration of disease, the more favorable was the result (Figures 6 and 7). However, the correlation was not statistically significant as evaluated by the Spearman rank correlation test (p = 0.08).

In our study, there was no significant correlation between the age of the patients and their response to treatment (p = 0.392; Spearman rank correlation test).

Overall, the patients were satisfied with laser treatment even though the objective improvement was not as remarkable.

Conclusions

Vitiligo is a distressing disease to treat. Response rates for the various modalities of treatment are highly variable. The best results are achieved with surgical methods, in which repigmentation rates of 87% to 95% are reported with different methods. These include split-thickness skin grafts and epidermal blister grafting, melanocyte transplantation, and tissue-engineered skin, especially if followed by PUVA radiation (1, 12). Among the nonsurgical methods, narrowband UVB therapy with a response rate of 63% is most promising. This is followed by 57% for broadband UVB, 56% for topical class 3 and 4 corticosteroids, and 51% for PUVA therapy (1, 4). Although narrowband UVB has been shown to give the best results, it requires 6 to 12 months of treatment before optimal results are evident (4). The same is true of other modalities of phototherapy, which take months to years for significant improvement and are associated with side effects such as nausea, vomiting, and phototoxicity with PUVA. In addition, conventional phototherapy delivers UV radiation to affected and unaffected skin over a long period of time, which may increase the risk of skin cancer. Skin atrophy, striae, and telangiectasia are seen with corticosteroids.

Recently, the 308-nm excimer laser has been shown to be highly efficacious in treating vitiliginous patches in a small number of treatment sessions over a relatively short period of time. Moreover, it delivers UV radiation only to affected areas with uninvolved areas of skin being unexposed. This reduces the risk of skin aging and carcinogenesis. Targeted phototherapy with the 308-nm excimer laser can also reach areas inaccessible to conventional phototherapeutic modalities. The benefit of providing focused phototherapy with a 308-nm excimer laser is also its drawback. The maximum spot size we could use was 25 mm in diameter. It is time-consuming and inefficient to treat larger patches (15–20).

This prospective study confirms that the 308-nm excimer laser is effective for treatment of localized vitiligo. Sixty-six percent of our patients showed some degree of repigmentation (more than 25%) after 25 sessions. Hofer et al. reported some degree of repigmentation in 67% of their patients after 30 sessions and Westerhof et al. found the same percentage of vitiligo patients (67%) achieving some repigmentation after 4 months of UVB 311-nm therapy (21, 22). Our study indicates good therapeutic results on the face and trunk. In the extremities, the results were more favorable on the arm and leg than the elbow and knee. Lesions on hands and feet had the least favorable results, which is comparable to other studies. The reasons for this body-site variation are unknown, although it has been hypothesized that in body sites with lower hair-growth density there are fewer melanocytes to proliferate and spread into the perifollicular epidermis (21).

In our study, a good overall cosmetic result (more than 75% repigmentation) was observed in 21% of the patients within 25 treatment sessions compared to 13% in the Hofer et al. study. When lesions on UV-sensitive areas (the face and trunk) only were taken into account,

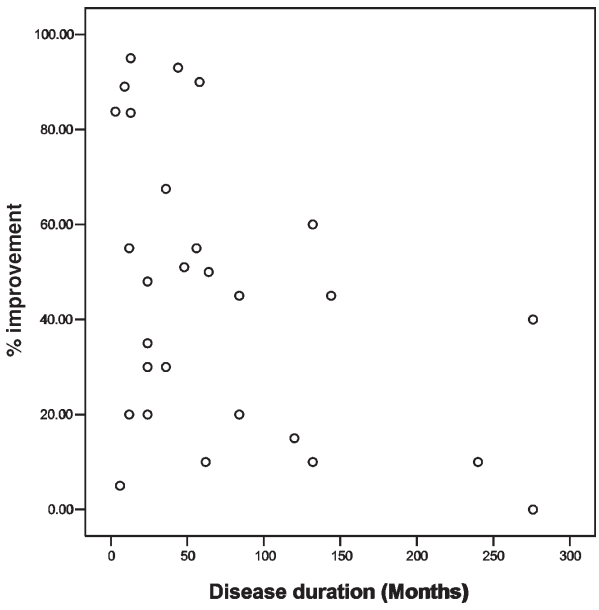

Fig. 6. Percentage of improvement plotted against the duration of vitiligo.

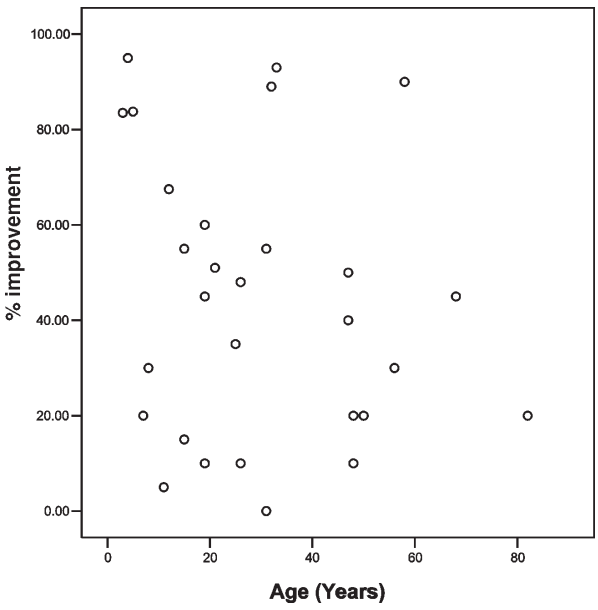

Fig. 7. Percentage of improvement plotted against patient age.

a 75% repigmentation rate in 41% of patients was seen in our study. This was 40% in the study by Hofer et al. and 57% in the study by Westerhof et al. (21, 22). In contrast, with UVB 311-nm therapy, Westerhof et al. reported repigmentation of more than 75% in only 8% of patients after 3 months of treatment (22). These data indicate that more satisfactory results with the 308-nm excimer laser can be achieved within 25 to 30 treatment sessions (12–15 weeks) compared to UVB 311-nm therapy, which takes much longer for optimal results to be seen.

The adverse effects noted were minor. Mild erythema was more evident in areas of overlap. Blistering developed in one patient and burning in two patients in whom treatment was subsequently skipped.

Our results show that the use of the 308-nm excimer laser for the treatment of vitiligo is effective, relatively safe, and more convenient compared to other available modalities of treatment for stable vitiligo with small patches. Larger prospective studies of this new therapeutic intervention are recommended to answer questions such as the mean excimer laser treatment duration necessary to achieve repigmentation above 75% over different body sites, the safe average cumulative dose a patient may receive, why some body sites are more resistant to treatment, and why some patients respond more favorably than others.

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