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ORIGINAL ARTICLE

Comparison of the 308-nm excimer laser with the 308-nm excimer lamp in the treatment of vitiligo – a randomized bilateral comparison study

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ABSTRACT

Background
Vitiligo is an acquired pigment disorder characterized by areas of depigmented skin resulting from the loss of epidermal melanocytes. Recently, several investigations have documented the benefits of excimer phototherapy (e.g., using the 308-nm excimer laser or the 308-nm excimer lamp) for the treatment of vitiligo.

Aim
To compare the effectiveness of the 308-nm excimer laser with the 308-nm excimer lamp in the treatment of vitiligo patients.

Methods
This intervention study was designed as a randomized self-control trial. Fourteen subjects with 48 symmetrical vitiligo lesions were enrolled in this study. One lesion was treated with the 308-nm excimer laser, and its counterpart was treated with the 308-nm excimer lamp. Lesions were treated three times a week with the same dose on both sides for a total of 20 sessions.

Results
All of the patients completed the study, and 48 lesions were treated. The two treatments exhibited similar results in terms of repigmentation.

Conclusions
The 308-nm excimer lamp and the 308-nm excimer laser exhibited similar efficacies in treating vitiligo.

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Vitiligo is an acquired cutaneous disorder of pigmentation caused by the selective destruction of melanocytes. Vitiligo affects 1% to 2% of the world population with no predilection for age, sex or racial background (1). The depigmented patches may have a localized, segmental or generalized distribution. Vitiligo can be a psychologically devastating disease with a significant reduction in the quality of life and self-esteem of the affected patients (2). To date, the exact pathogenesis of vitiligo remains unknown. Oxidative stress, autoimmune, biochemical, autocytotoxic and neuronal mechanisms have been suspected (3–6).

Because the exact cause of vitiligo remains unclear, the treatment of vitiligo continues to present a challenge. Several nonsurgical treatments have been established, including the application of steroids and 311-nm narrowband ultraviolet B (NB-UVB) irradiation (7, 8). Skin atrophy has been a common side effect of treatment with topical steroids, while NB-UVB is currently used frequently with satisfactory results. However, NB-UVB therapy presents a number of problems. For example, lesions in hard-to-reach areas, such as skin folds, often do not receive adequate exposure. Moreover, the ability to deliver high doses is often limited by the phototoxicity to both lesional and nonlesional skin. Additionally, complete repigmentation cannot be achieved in all cases, and several months of treatment are required to obtain a therapeutic response.

Since the first report in 2002, targeted phototherapy systems (308-nm excimer) have recently proved their efficacy for the treatment of vitiligo. The new UV source emits wavelength effective for the treatment of vitiligo and presents some advantages over conventional NB-UVB phototherapy for delivering high-intensity light exclusively to depigmented areas and reduction of the cumulative UV dose (9, 10).

However, although the excimer lamp and laser share the same wavelength, they are different devices with distinct radiation properties. The number of head-to-head trial between the two devices was limited. On the basis of data that supports 308-nm excimer lamp and laser as efficacious and safe treatments modality for vitiligo, we embarked on a task of a randomized self control study to evaluate the efficacy of 308-nm excimer lamp vs. 308-nm excimer laser in vitiligo patients.

MATERIALS AND METHODS

Patients

Fourteen patients (seven men and seven women) with symmetrical vitiligo lesions evolving for at least 3 months and less than 10 cm^2, were included and all gave informed consent. Exclusion criteria included a history of photosensitive disorder, skin cancer, psychological disorders, pregnancy and breastfeeding. The Medical Ethics Committee of Xijing hospital, Fourth Military Medical University approved this study protocol.

The ages of the patients ranged from 2 to 39 years (median: 22.2 years). The disease durations ranged from 4 months to 240 months (median: 41.6 months). The patients were assessed for Fitzpatrick skin phototypes, overall disease duration and history of previous therapy. Patients' characteristics are tabulated in Table 1.

Treatment schedule

For each patient, two symmetrical target lesions were selected. The lesion to be treated with the 308 nm excimer lamp was selected according to a left–right randomization table. The contralateral lesion was irradiated with the 308-nm excimer laser. Treatments were given three times a week on non-consecutive days for a maximum of 20 treatments.

For both modalities, the initial dose was 200 mJ (150 mJ for women and men under 16 years of age). The subsequent dose was determined as follows: dose increased 20% from treatment 1 to 10, 10% from treatment 11 to 13, 5% from treatment 14 to 16, and 2% from treatment 17 to 20. If symptomatic erythema or blistering developed, treatment was withheld (once or twice) until resolution; when the treatment was resumed, the dose was reduced to the last well-tolerated dose. During the treatment, unaffected skin inside the irradiation field was shielded to avoid double exposure.

The treatment of subjects who had undergone previous therapy was started after a washout period of 4 weeks for traditional Chinese drugs and psoralen and of 8 weeks for immunomodulating agents. All of the patients avoided any type of topical treatment during the study.

Phototherapy sources

The 308-nm excimer laser used was a self-contained gas system of Xe-Cl (Photomedex, Carlsbad, CA, USA). Laser light was delivered through a flexible fiber-optic cable to the hand piece and had a spot size of 20 × 20 mm. The laser is operated at 3 mJ per pulse with the pulse frequency up to 200 Hz and the pulse width of 30 μs. Additional pulses can be delivered by pressing the foot switch.

The 308-nm excimer lamp delivery system (USHIO, Tokyo, Japan) was used to irradiate skin with an average power density of 50 mW/cm^2 at a tube-to-skin distance of

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Table 1. Patients' characteristics

No.	Age (year)	Sex	Site	Type	Duration (month)	Clinical subtype	Previous therapy
1	19	F	Breast, perineum	Generalized	48	Stable	None
2	20	M	Face, neck	Generalized	48	Active	Traditional Chinese drug
3	17	M	Neck	Generalized	14	Active	Traditional Chinese drug Immunomodulator
4	2	M	Chest	Generalized	10	Active	None
5	30	F	Breast	Generalized	4	Active	None
6	27	F	Chest, back, ear	Generalized	240	Stable	None
7	21	F	Face, arm	Generalized	24	Stable	Traditional Chinese drug
8	38	F	Face	Generalized	24	Stable	Traditional Chinese drug
9	30	M	Abdomen	Generalized	48	Active	Traditional Chinese drug Transfer factor
10	21	M	Neck, wrist	Generalized	12	Stable	None
11	19	F	Neck, lip	Generalized	12	Active	Traditional Chinese drug, Psoralen
12	39	F	Breast	Generalized	48	Stable	None
13	8	F	Perineum	Generalized	6	Active	None
14	20	M	Chest, abdomen, neck, axilla	Generalized	8	Active	Traditional Chinese drug, Immunomodulator

15 cm and with a maximum rectangular irradiating area of 120 cm^2 (120 mm × 100 mm).

Assessment of treatment efficacy

This was an investigator-blinded study. The assessment of treatment efficacy was made based on a clinical examination and photography evaluation in a blinded manner at the baseline pretreatment visit and once a month thereafter until the end of the study. Assessment of repigmentation was performed by two physicians who did not follow the course of phototherapy.

Repigmentation was graded on a 5-point scale: score 0, no repigmentation; score 1, poor repigmentation (up to 25% of the affected area); score 2, moderate repigmentation (between 26% and 50%); score 3, good repigmentation (between 51% and 75%); and score 4, excellent repigmentation (between 76% and 100%).

The efficacy of treatment was assessed based on the following endpoints: average repigmentation scores at five-treatment intervals, the repigmentation rate of at least 50%, the repigmentation rate of at least 75%, the mean time to obtain the appearance of repigmentation, and the response rates of the vitiligo lesions at various sites. Any potential side effects were also noted.

Statistical analysis

Student's *t*-test for paired data was used to evaluate the difference in repigmentation between the areas treated with the 308-nm excimer laser and the excimer lamp. Statistical significance was defined by a P value of < 0.05.

RESULTS

Profile of patients

Fourteen patients (seven men, seven women) were included in the study. The ages of the patients ranged from 2 to 39 years (median: 22.2 years). The disease duration ranged from 4 months to 240 months (median: 41.6 months). All of the patients had skin phototype III and exhibited the generalized subtype. Six patients were in stable disease stages, and the rest were in the active stage of disease. Seven patients had received but failed to respond completely to previous therapy (Table 1).

Treatment response

All of the patients completed the study, and 48 lesions were treated. Two pairs of lesions were located on difficult-to-treat areas (extremities), 5 pairs were located on the face (possibility of spontaneous repigmentation), and the remaining pairs of lesions were located on other parts of the body.

Photographic examples of the changes in repigmentation in patients are depicted in Fig. 1. Repigmentation scores at five-treatment intervals are presented in Table 2. We compared the average repigmentation scores of vitiligo

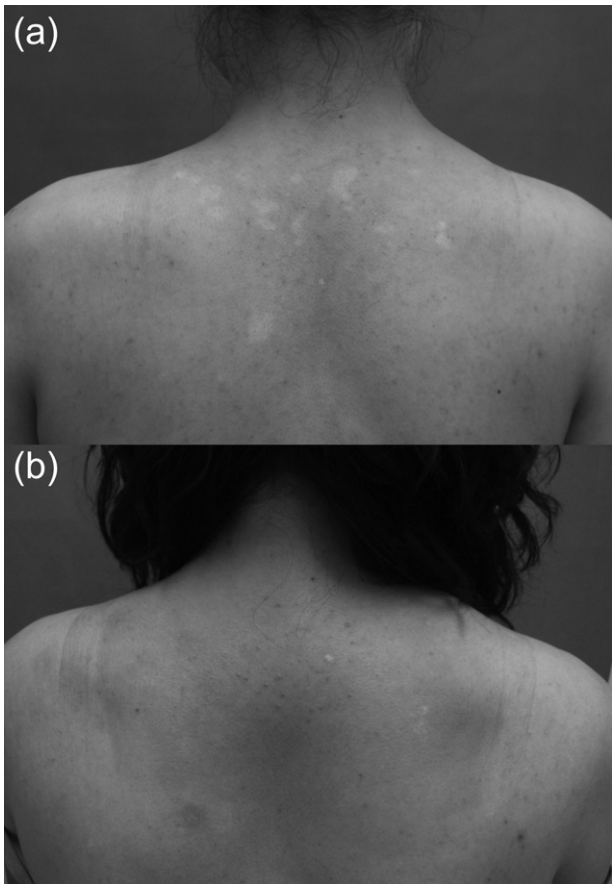

Fig. 1. Baseline (a) and post-treatment (b) photographs of symmetric vitiligo lesions located on the neck of one patient. The left side was treated with the 308-nm excimer laser, and the right side was treated with the excimer lamp.

patches that received the excimer lamp treatment with the 308-nm excimer laser-treated patches at five-treatment intervals. Improvements were observed with both modalities, but the difference was not statistically significant (Fig. 2). After five time treatments, the mean repigmentation scores were 1.292 for the laser and 1.250 for the lamp ($P > 0.05$). After 10 treatments, the mean repigmentation scores were 2.250 and 2.042 for the laser and lamp, respectively ($P > 0.05$). After 15 treatments, the laser-treated samples exhibited a mean repigmentation score of 2.792, and lamp-treated samples received a score of 2.833 ($P > 0.05$). At the end of the study, the mean repigmentation score was 3.0 for the laser and 3.2 for the lamp, respectively ($P > 0.05$).

At the end of the study, a repigmentation rate of at least 50% was achieved for 79% of the patches treated by laser and 87.5% of the patches treated by lamp. Fourteen lesions (58.3%) treated with the 308-nm excimer lamp and 11 lesion (45.8%) treated with the laser were assigned a repigmentation score of 4.

The difference in the mean repigmentation time between the two devices was not significant ($P > 0.05$).

The response rates of vitiligo lesions at various sites are presented in Table 3. The body site-dependent response rates of the two devices are consistent with each other.

The side effects of these therapies were notably mild. The majority of patients [12 patients (85.7%) with the lamp and 13 patients (92.9%) with the laser] had persistent erythema that was well tolerated. No blistering or bullous reactions occurred.

DISCUSSION

Since the first report in 2002, the 308-nm excimer lamp and laser have both demonstrated their efficacy for the treatment of vitiligo. We conducted this prospective monocentric randomized comparative study with the 308-nm excimer lamp and laser to test their efficacy. Our study revealed an equivalent repigmentation rate between the two devices.

The major mechanism of action of UVB light (including the laser and lamp) in the treatment of inflammatory dermatosis is the cytotoxic effect on infiltrating T cells, where the mechanism of cell death is probably apoptosis. Recently, the mechanism of the excimer laser's high efficacy in psoriasis treatment has been investigated. Novak *et al.* (11) demonstrated that the irradiation of T cells with the excimer laser in vitro induced a higher number of apoptotic cells than did irradiation with NB-UVB light at the same dosage. Bianchi *et al.* (12) investigated the immunohistochemical evaluation of T cells and the expression of various apoptosis-related molecules in psoriatic hyperproliferative skin before and after treatment with 308-nm monochromatic excimer light. The authors proposed that psoriatic skin after monochromatic excimer light therapy is associated with significant T cell depletion and alterations of apoptosis-related molecules accompanied by a decreased proliferation index and clinical remission.

Phototherapy of vitiligo may be explained not only by the action on cytotoxic T lymphocytes but also by the stimulation of melanocyte proliferation and the migration of melanocytes to the epidermis from the hair follicle (13–15). In addition, UVB can activate the pseudocatalase complex, which is capable of degrading H_2O_2 and is associated with the successful repigmentation of vitiligo (16).

Based on these studies, several uncontrolled trials have been performed to evaluate the efficacy of the excimer laser and lamp in the treatment of vitiligo (9, 10, 17–24). Baltas *et al.* (9) determined that the excimer laser exhibited a high repigmentation efficacy. Indeed, three of the four patients (75%) that were treated by the excimer laser over 48 treat-

Table 2. Treatment response

		Repigmentation grade							
		308-nm excimer laser				308-nm excimer lamp			
ID	Site	×5	×10	×15	×20	×5	×10	×15	×20
001	Breast	3	4	4	4	1	2	3	4
001	Perineum	1	2	3	4	0	2	3	4
002	Face	1	1	3	4	1	2	3	4
002	Neck	1	2	2	3	1	1	3	4
003	Neck	3	3	4	4	1	2	3	4
004	Chest	0	1	2	3	1	1	3	4
005	Breast	1	1	2	2	1	1	3	4
006	Chest	4	4	4	4	2	4	4	4
006	Back	1	4	4	4	4	4	4	4
006	Ear	2	4	4	4	2	2	3	3
007	Face	1	2	2	2	1	1	2	2
007	Arm	1	2	2	3	1	2	2	3
008	Face	1	2	4	4	1	2	4	4
009	Abdomen	1	2	3	3	1	2	3	4
010	Neck	1	2	2	3	1	2	2	3
010	Wrist	0	1	1	1	0	1	1	1
011	Neck	1	4	4	4	2	3	4	4
011	Lip	1	2	2	2	1	2	2	2
012	Breast	1	4	4	4	1	4	4	4
013	Perineum	2	3	3	4	3	4	4	4
014	Chest	1	1	2	2	1	1	2	3
014	Neck	1	1	2	3	1	1	2	3
014	Abdomen	1	1	2	3	1	2	2	3
014	Axilla	1	1	2	3	1	1	2	3

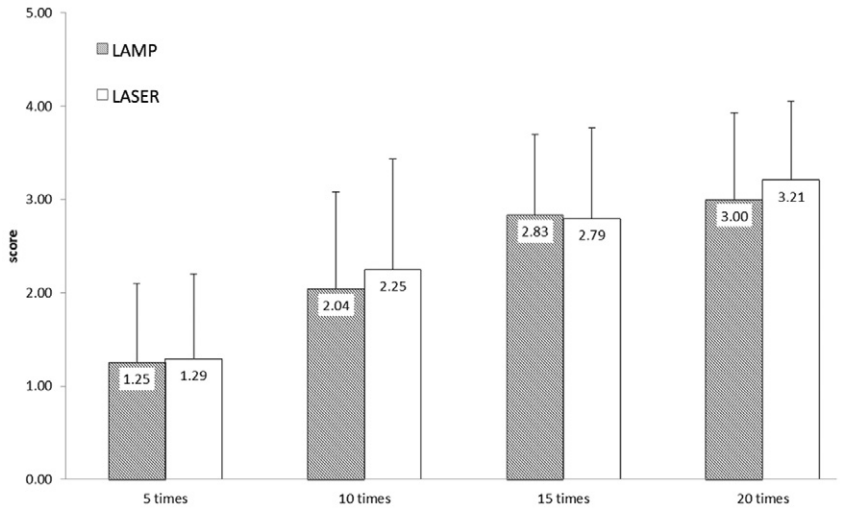

Fig. 2. Average repigmentation scores at five-treatment intervals.

ments obtained a score of 4 (repigmentation between 76% and 100%). However, this study was performed with a small number of patients. In addition, our results are more satisfactory than those reported by Taneja *et al.* (17) In their study, a repigmentation rate of at least 50% was achieved in 38.5% of the patches treated by the laser.

Leone *et al.* (18) demonstrated that phototherapy with the 308-nm excimer light resulted in an acceptable degree of repigmentation in 33 patients (89%) after 3 months. Twenty-one (57%) of these patients achieved 'good repigmentation', and 12 (32%) achieved 'excellent repigmentation'. These results are comparable with our

Table 3. Repigmentation by treatment area (after 20 treatments)

	No. of vitiligo patches							
	Face		Neck		Trunk		Extremity	
Repigmentation grade	Lamp	Laser	Lamp	Laser	Lamp	Laser	Lamp	Laser
0	–	–	–	–	–	–	–	–
1	–	–	1	–	–	–	1	1
2	2	2	–	–	–	2	–	–
3	1	–	1	3	3	4	1	1
4	2	3	3	2	9	6	–	–
Sum of grade score	15	16	16	17	45	40	4	4

results; in our study, a repigmentation rate of at least 50% was achieved in 87.5% of the patches treated by the lamp.

Casacci *et al.* (22) conducted a study aimed at comparing the effectiveness of 308-nm MEL and NB-UVB phototherapy in vitiligo patients. At the end of the study, 10 lesions (62.5%) treated with 308-nm MEL achieved a repigmentation rate of at least 50%.

The latest study performed by Le Duff *et al.* (24) demonstrated that a repigmentation rate of at least 50% was achieved in 15% of the patches treated by either device. The limited number of sessions, the location of several patches in difficult-to-treat areas and the history of previous therapy failure may explain these relatively low repigmentation rates. The authors have demonstrated that the 308-nm excimer lamp and laser exhibited similar efficacy in treating vitiligo, and their results are comparable with our own.

In our study, a repigmentation rate of at least 50% was achieved in 79% of the patches treated by the laser and 87.5% of the patches treated by the lamp. The mean repigmentation score was 3.0 for the laser and 3.2 for the lamp. This rate is surprisingly high and more promising compared with the previously reported data. Many prognostic factors of good response to therapy could explain these relatively high rates of repigmentation. All of the patients are Chinese and had skin phototype III, which is more sensitive to phototherapy compared with other skin phototypes. In addition, several patches were located in easy-to-treat areas, and the patients' diseases were of relatively short duration and mild severity. All of these factors could contribute to the relatively high rates of repigmentation but would not affect the comparison of the two devices.

The excimer lamp emits polychromatic (spectrum between 295 nm and 315 nm with a peak at 308 nm), continuous, incoherent light, whereas the excimer laser emits coherent, monochromatic, UVB light in short pulses. This permits the variation of some important phototherapeutic parameters, such as impulse frequency and intensity, which might result in differences between the lamp and laser in clinical practice. Thus, we investigated the mean time to obtain appearance of repigmentation and the body site-dependent response rates of the two devices in our comparative study. To date, we have not found any differences between them.

In conclusion, the results of this study strongly support the similar efficacy of the 308–nm excimer lamp and 308-nm excimer laser in treating vitiligo. We have also demonstrated the advantages of targeted phototherapy with the 308-nm excimer, including the rapid onset of repigmentation and the decreased number of treatments needed to achieve repigmentation compared with traditional phototherapy. Further studies using larger series are needed to confirm our findings.

Our experience demonstrate that in practical use, the 308-nm excimer lamp may present some advantages over the 308-nm excimer laser – specifically, a larger irradiation area – thus contributing to a shorter treatment duration and decreased cost. All these advantages would allow the 308-nm excimer lamp to become more accessible in the treatment of vitiligo.

CONCLUSIONS

We have demonstrated that the 308-nm excimer lamp and the 308-nm excimer laser exhibit similar efficacy in treating vitiligo.

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