The 308-nm xenon chloride excimer laser in combination with topical calcipotriol in the treatment of vitiligo

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Background: Treatment of vitiligo remains an attractive topic and several therapies with varying degrees of success have been used. The aim of this study was to find out whether the combination of topical calcipotriol and excimer laser increases the efficacy of therapy compared to excimer laser alone.

Methods: Twenty eight patients in two groups were treated with 308nm excimer laser alone (14 patients) and the combination of excimer laser–calcipotriol (14 patients). After 16 sessions, response rate, side-effects and compliance were assessed.

Results: Repigmentation rate more than 50% was significantly higher in the laser- calcipotriol group. No differences were seen in complication rate between the two groups.

Conclusion: Combination of calcipotriol and 308nm excimer laser might enhance the response rate without increasing treatment complications.

Keywords: excimer, calcipotriol, laser, phototherapy, NBUVB, vitiligo

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INTRODUCTION

Vitiligo is an acquired depigmentation disorder of the skin in which there is loss of epidermal melanocytes. The prevalence of vitiligo is approximately 0.1-2% worldwide. The precise pathogenesis of vitiligo remains subtle and is probably multifactorial [1]. Treatment of vitiligo remains an interesting topic and many centers have been reported as having varying degrees of success. Medical therapies such as corticostroids, phototherapy such as PUVA, UVB and excimer laser, vitamin D3 analogs, new topical immunosuppressors such as tacrolimus and pimecrolimus and more aggressive treatment such as cultured and noncultured melanocyte transplantation have been used for treatment. It has been proved in several studies that 308 nm excimer laser and topical calcipotriol are both effective in repigmentation of vitiligo as monotherapy [2,3,4].

Vitamin D [3] compounds are known to influence melanocyte maturation and differentiation and also up-regulate melanogenesis through pathways activated by specific ligand receptors, such as endothelin receptor and c-kit. Therefore, they could affect melanogenesis and be useful in vitiligo treatment [5].

The excimer lasers are a group of lasers that have found extensive application in various medical fields including dermatology. These lasers function in the ultraviolet range, and examples include the 193 nm argon-fluroide, 248 nm krypton-fluoride, 351 nm xenon-fluoride, and of particular interest to dermatology, the 308 nm xenon-chloride. They were first used in medicine for their capacity to generate cold tissue ablation, but more lately

have been used in dermatology as a means of non-ablative phototherapy. They also seem to be an effective method for the treatment of vitiligo even with results similar to older treatment options such as narrow band UVB [6,7,8].

The aim of this study was to find out whether the combination of topical calcipotriol and excimer laser increased the efficacy of therapy compared to excimer laser alone.

PATIENT AND METHOD

Thirty patients with vitiligo were enrolled in the study. They were all older than 16 years, had experienced no change in the lesions in the previous 6 months, and had at least 2 lesions with a diameter of 1-10cm. Our exclusion criteria were pregnancy, lactation, use of steroid or PUVA therapy in last 6 month, use of photosensitizer and immunosuppressor drugs, history of photosensitivity or skin cancer. We enrolled 30 patients with vitiligo in this study with regard to previous assays and our limitation in laser facilities and resources.

All patients signed a detailed informed consent form and were then randomly divided into 2 equal groups, one received excimer laser alone and the other received topical calcipotriol twice daily in addition to excimer laser. For each patient in each group, one lesion was regarded as control. Excimer laser was done for 16 sessions with weekly intervals. The starting dose was determined as 50mj/cm^2 with increments of 50mj/cm^2 every two sessions. The patients were visited at the end of the 8th, 12th and 16th week for the evaluation of the response rate. We chose the 16-week treatment period with regard to similar reports in the literature [9]. Photographs were taken at the beginning of the study and during each visit and were assessed by two independent blinded dermatologists to evaluate the degree of repigmentation. Then, the two groups were compared for improvement rate, improvement pattern, and complications. The improvement or response to treatment was defined as the rate of repigmentation of the lesions and repigmentation less than 10% was regarded as minimal or no response (Table1).

All patients were informed about the study, and signed informed consent forms. This study was approved by the Ethics Committee of our center. The study was performed according to the Declaration of Helsinki Principles.

Table 1. Repigmentation rate in the two groups

Repigmentation rate	Laser	Laser-calcipotriol
No response	3 (21.4%)	0 (0%)
<25%	5 (35.7%)	3 (21.4%)
25%-50%	4 (28.5%)	2 (14.2%)
50%-75%	1 (7.1%)	5 (35.7%)
75%-100%	1 (7.1%)	4 (28.5%)

Data were finally analyzed with software SPSS-11.5 using independent t-tests and paired t-test. Values were expressed as average and standard deviation. A P-value <0.05 was considered as statistically significant.

RESULT

Twenty eight out of 30 patients finished the treatment course. The mean age of the patients in the laser group was 37.7+/-12.6 [6 (43%) males and 8 (57%) females] and patients in the laser plus calcipotriol group had a mean age of 33.1 +/- 8.7 [8 (57%) males and 6 (43%) females]. One patient due to travel and another due to accident left the study. Except for 3 patients who achieved to more than 75% improvement after 12 sessions, all patients finished the whole 16 sessions. Table 1 shows repigmentation rate in the two groups. There was no overall significant difference between groups. We compared the groups for repigmentation rate >50% and the difference was statistically significant. In other words, the repigmentation rate more than 50% was significantly higher in the laser-calcipotriol group (p=0.018). Improvement pattern was also different between groups. Perifollicular repigmentation was seen in 64% and 21% of the patients in the laser group and the calcipotriol-laser group, respectively. Peripheral improvement was seen in 36% and 78% of the patients in the laser group and the laser-calcipotriol group respectively with a significant difference (p<0.05). We also investigated the difference of the response rate in UV sensitive (face, neck, trunk and limb except the extremities and bony prominences) and UV resistant areas. In the laser-calcipotriol group, repigmentation rate more than 50% was seen in 44.4% of the UV resistant and 100% of the UV sensitive areas. In the laser group, however, repigmentation rate more than 50% was seen 12.5% (1 patient) of the

Table 2. Side effects of treatment in two groups.

	Laser	Laser+ Calcipotriol
None	8 (57.2%)	12 (85.7%)
Photosensitivity	1 (7.1%)	0 (0%)
Erythema	4 (28.6%)	2 (14.3%)
Vesicle	1 (7.1%)	0 (0%)
Bullae	0 (0%)	0 (0%)

UV resistant and 16.6% of the UV sensitive areas. There was no difference in the complication rate (photosensitivity, erythema, vesicle or bulla) between the two groups (Table 2).

DISCUSSION

Current treatments for vitiligo are mostly disappointing and vary widely between cultures and within health systems. Variations in the study design and different outcome measures limit the evidence for the different therapeutic methods. The best evidence from individual trials have shown temporary advantages of topical steroids and various forms of UV light with topical preparations. There is a vital need for high quality randomised trials using standardised measures of repigmentation which attend to relevant clinical outcomes together with the quality of life [10,11].

To accomplish better therapeutic outcomes, combination therapy including both systemic and targeted ones could be considered. Targeted combination therapies in vitiligo seem to be more effective than single treatments [12].

Topical steroids, especially with high potency, are the most common approach all over the world. Their efficacy is highest on the face and neck, where the complications (atrophy, telangectasia) are more common and restrict their use. A long list of drug types, such as various systemic and topical immunomedulators including vitamine D analouges and recently application of some enzymes (such as pseudocatalase) or some enzyme inhibitors (such as phenylalanine hydroxylase inhibitor) have been used with different response rates. There are lots of reports about the synergistic effects of calcipotriol with PUVA and UVB [9,13,14]. But some debate exists upon the additional effect of topical calcipotriol on NBUVB therapy [15-17].

Recently, PUVA therapy is replaced with narrow band UVB and 308nm xenon chloride excimer laser because of their superior effect in repigmentation and lower risk of subsequent skin malignancies [9]. Narrow band UVB and excimer laser are very similar and probably have the same mechanism of action in inflammatory diseases, which is inducing apoptosis in T cells. But it has been shown that in equal dosages, 308nm excimer laser can induce more apoptosis and more clinical improvement than NBUVB. Combination of excimer laser with vitamin D3 analogues has been considered in two important studies. Through the Study of Lu Yan, combination therapy with excimer laser and Tacalcitol was evaluated in 35 patients. Repigmentation rate more than 75% was seen in 5.7% of patches treated with laser and in 25.7% of those treated with laser and tacalcitol [9]. A similar study was conducted by Goldinger on the combination of excimer laser and cacipotriol. Unlike our study, no difference was seen between groups [14] which may be due to the short course of their treatment (8 weeks) and small sample size (10 cases).

In our study, repigmentation rate more than 50% was significantly higher in the laser-calcipotriol group. According to the results of this study, it could be suggested that combination of calcipotriol and 308nm excimer laser might enhance the response rate. Interestingly, this combination seems to promote the response rate of UV resistant and peripheral parts such as extremities where the most resistant vitiligo patches exist. However, future structured study with larger sample sizes should be performed to elucidate the additional effect of excimer laser and calcipotriol combination in the treatment of vitiligo, especially the resistant sites including hands and feet.

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