Suberythemic and erythemic doses of a 308-nm excimer laser treatment of stable vitiligo in combination with topical tacrolimus: A randomized controlled trial

To the Editor: The 308-nm excimer laser (EL) (EXL-440, Laser & Physics Co., Yong-in, Korea) has been widely used for targeted treatment of vitiligo; however, there is little evidence regarding the optimal dosimetric protocol.[1] EL treatment is often associated with hyperpigmentation, prolonged erythema, and accidental burning.[2] Recently, in a pilot study, Chiu et al[3] showed that low-dose phototherapy successfully treated vitiligo without causing erythema.

We conducted a randomized, controlled, split-body, noninferiority trial from April through December 2018 to compare the efficacy and safety of suberythemic doses (SEDs) and conventional erythemic doses (EDs) of EL treatment. Adult patients with stable vitiligo on the face and neck were recruited. Each side of the face or neck was randomly assigned to either SED or ED. The ED was defined as the dose producing pinkish erythema for at least 24 hours, and the SED was defined as half the ED. EL was performed twice weekly for 12 weeks on both sides. The subsequent SED and ED were escalated by 25 and 50 mJ/cm^2, respectively, if pinkish erythema did not persist for 24 hours or longer. Topical tacrolimus was applied twice daily in both groups. The primary outcome was the extent of repigmentation (percentage) from baseline, assessed on either side, in a blinded manner, using the Vitiligo Extent Score for a Target Area (VESTA). The secondary outcome was perilesional hyperpigmentation. All adverse events were recorded.

A total of 26 patients were screened; of these, 18 patients (12 women; median age, 48 years) with each side (36 sides) were randomly assigned to either group. All patients completed the study per the protocol. The extent of repigmentation was 86.1% ± 23.9% (mean ± SD) in the SED group and 86.9% ± 23.0% (mean ± SD) in the ED group (Table I). The mean difference between the 2 groups was −0.8% (95% confidence interval, −1.9 to 0.2), less than the noninferiority margin. In both groups, 15 patients (83.4%) achieved at least 75% repigmentation (Fig 1). Four patients (22.2%) complained of prolonged erythema lasting at least 3 days or pain on the ED side, but not the SED side.

We found that the therapeutic outcomes of EL treatment were equivalent between an SED and a conventional ED in combination with topical tacrolimus, but the cumulative dose of the SED was half that of the ED. This suggests that distinct factors could be responsible for the erythemic response and melanocyte induction after the treatment; the latter may be induced at lower energy of EL, whereas posttreatment erythema does not occur at this dose. Furthermore, the phototoxic changes in skin associated with long-term, high-dose EL treatment may be avoided with low-dose EL treatment. Repeated high-dose UV irradiation thickens the stratum corneum via photoadaptation, increasing the minimal ED of ultraviolet phototherapy and creating a need for higher-dose EL treatment.[4,5]

Our study is limited by small sample size, split-body study design, and concomitant use of topical tacrolimus. The study was restricted to the face and neck; the treatment responses of other body parts cannot be drawn in this study; however, our findings are meaningful because the face and neck are of great concern. This study was the first to show that stable vitiligo of the face and neck can be treated without the need for an erythemic response via a randomized controlled trial.

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Table I. Treatment parameters and results of enrolled patients

Results	SED side (ranges, min-max)	ED side (ranges, min-max)
Treatment parameter		
Maximum dose, mJ/cm^2, mean ± SD	154 ± 55.1 (50-300)	308 ± 110.2 (100-600)
Total cumulative dose, mJ/cm^2, mean ± SD	2593 ± 1397.8 (1000-6450)	5000 ± 2710.4 (2000-12,600)
Extent of repigmentation,* %, mean ± SD	86.1 ± 23.9	86.9 ± 23.0
≥75% repigmentation, n (%)	15 (83.4)	15 (83.4)
100% repigmentation, n (%)	6 (33.3)	6 (33.3)
Perilesional hyperpigmentation, n (%)	0	8 (44.4)
Prolonged erythema (≥3 days) or pain, n (%)	0	4 (22.2)
Patient overall dose preference, n (%)	6 (33.3)	1 (5.6)

ED, Erythemic dose; *SD,* standard deviation; *SED,* suberythemic dose.
*The repigmentation rate was assessed at 12 weeks.

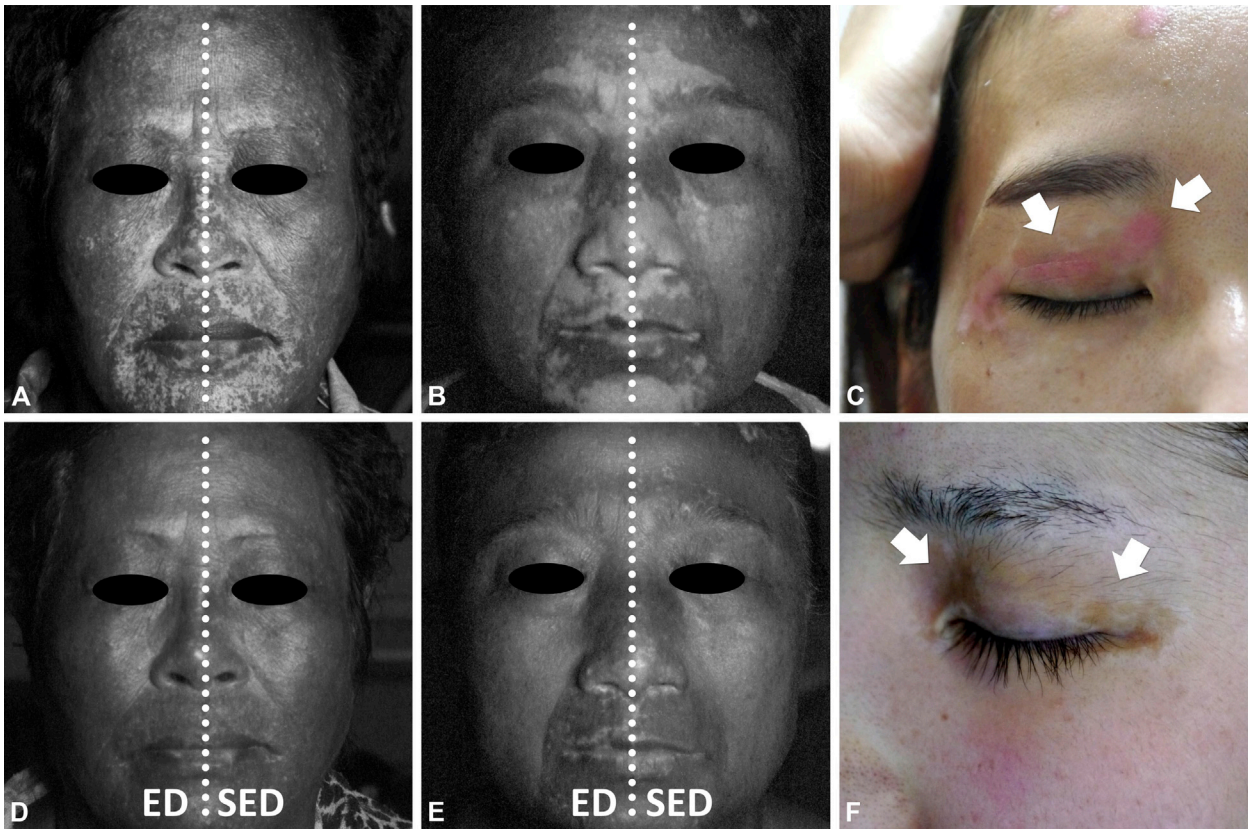

Fig 1. Repigmentation of vitiligo after delivery of suberythemic or conventional erythemic irradiation doses by an excimer laser. Patient 17 with facial vitiligo exhibited repigmentation rates of 96.5% and 97% after EL treatment on the (**A**) SED and (**D**) ED sides, respectively, at the end of the 12-week trial. The respective rates in patient 4, who had symmetric vitiliginous facial patches, were (**B**) 98% and (**E**) 98%. Prolonged painful erythema and hyperpigmentation developed at the ED EL treatment site in patients (**C**) 5 and (**F**) 14. *ED,* Erythemic dose; *EL,* excimer laser; *SED,* suberythemic dose.

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