Treatment of Keratosis Pilaris With 810-nm Diode Laser: A Randomized Clinical Trial

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IMPORTANCE Keratosis pilaris (KP) is a common skin disorder of follicular prominence and erythema that typically affects the proximal extremities, can be disfiguring, and is often resistant to treatment. Shorter-wavelength vascular lasers have been used to reduce the associated erythema but not the textural irregularity.

OBJECTIVE To determine whether the longer-wavelength 810-nm diode laser may be effective for treatment of KP, particularly the associated skin roughness/bumpiness and textural irregularity.

DESIGN, SETTING, AND PARTICIPANTS We performed a split-body, rater-blinded, parallel-group, balanced (1:1), placebo-controlled randomized clinical trial at a dermatology outpatient practice of an urban academic medical center from March 1 to October 1, 2011. We included all patients diagnosed as having KP on both arms and Fitzpatrick skin types I through III. Of the 26 patients who underwent screening, 23 met our enrollment criteria. Of these, 18 patients completed the study, 3 were lost to or unavailable for follow-up, and 2 withdrew owing to inflammatory hyperpigmentation after the laser treatment.

INTERVENTIONS Patients were randomized to receive laser treatment on the right or left arm. Each patient received treatment with the 810-nm pulsed diode laser to the arm randomized to be the treatment site. Treatments were repeated twice, for a total of 3 treatment visits spaced 4 to 5 weeks apart.

MAIN OUTCOMES AND MEASURES The primary outcome measure was the difference in disease severity score, including redness and roughness/bumpiness, with each graded on a scale of 0 (least severe) to 3 (most severe), between the treated and control sites. Two blinded dermatologists rated the sites at 12 weeks after the initial visit.

RESULTS At follow-up, the median redness score reported by the 2 blinded raters for the treatment and control sides was 2.0 (interquartile range [IQR], 1-2; \(P = .11\)). The median roughness/bumpiness score was 1.0 (IQR, 1-2) for the treatment sides and 2.0 (IQR, 1-2) for the control sides, a difference of 1 (\(P = .004\)). The median overall score combining erythema and roughness/bumpiness was 3.0 (IQR, 2-4) for the treatment sides and 4.0 (IQR, 3-5) for the control sides, a difference of 1 (\(P = .005\)).

CONCLUSIONS AND RELEVANCE Three treatments with the 810-nm diode laser may induce significant improvements in skin texture and roughness/bumpiness in KP patients with Fitzpatrick skin types I through III, but baseline erythema is not improved. Complete treatment of erythema and texture in KP may require diode laser treatment combined with other laser or medical modalities that address redness.
Keratosis pilaris (KP) is a common hereditary, benign disorder of unknown etiology that is frequently seen in conjunction with atopy. The hereditary pattern of this skin disorder is thought to be autosomal dominant without a known predisposition based on race or sex. Keratinaceous plugging of follicles results in markedly visible papules, often involving the lateral and extensor aspects of the proximal extremities but sometimes also the face, buttocks, and trunk. Perifollicular erythema is routinely notable. Topical treatments for KP include emollients, exfoliants, and anti-inflammatory agents, such as urea, salicylic acid, lactic acid, topical corticosteroids, topical retinoids, and cholecalciferol. Because most patients obtain limited benefit from these treatments, less conventional treatments, including phototherapy and lasers, have been explored. Among lasers, the 532-, 585-, and 595-nm vascular devices have been used with modest success, particularly in reducing redness. Longer-wavelength lasers have not been studied for the treatment of KP, and lasers have not been shown to be successful for treating the textural components of KP. Our study investigates the effectiveness of the longer-wavelength 810-nm diode laser for color and texture of upper extremity KP.

Methods

Study Design
We performed a split-body, parallel-group, placebo-controlled randomized clinical trial with an allocation ratio of 1:1 and a block size of 2 at an urban academic medical center. The unit of randomization was the individual unilateral upper extremity. The study was approved by the institutional review board of Northwestern University. All participants provided written informed consent.

Patient Selection
Patients were recruited from a dermatology practice at Feinberg School of Medicine, Northwestern University, and the surrounding community. Inclusion criteria consisted of age 18 to 65 years, good health, Fitzpatrick skin types I to III, and a diagnosis of KP on both upper extremities. We excluded patients who had received any laser therapy to the arms in the 12 months before recruitment, with a concurrent diagnosis of another skin condition or malignant neoplasm, with a tan or sunburn over the upper arms in the month before recruitment, with open ulcers or infections at any skin site, or who were using topical or oral photosensitizing medications.

Study Procedures
When potential participants called or e-mailed the clinic for possible inclusion in the study, they underwent prescreening (performed by O.I.) over the telephone using the aforementioned inclusion and exclusion criteria. Once enrollment criteria were met, patients were scheduled for a total of 4 visits, 4 to 5 weeks apart, in the Department of Dermatology, Feinberg School of Medicine.

On the patient’s first visit, one of us (O.I.) reviewed the inclusion and exclusion criteria. After the patients provided written informed consent, they separately rated redness and roughness/bumpiness on each arm using a scale of 0 (least severe) to 3 (most severe) for a total maximum score of 6 per patient per arm. Next, patients were randomized into 2 groups as described below, and baseline standardized digital photographs were obtained. Each patient received treatment using the 810-nm pulsed diode laser to the arm randomized to be the treatment site. After laser treatment, both sides were treated with topical petrolatum. Treatments were repeated twice for a total of 3 treatment visits, with visits spaced 4 to 5 weeks apart. At the fourth and final visit, 12 to 15 weeks after the initial visit, the patients again rated disease severity as previously described. At this last visit, 2 blinded dermatologists (S.Y. and M.A.) also rated the roughness/bumpiness and redness of the treatment and control arms separately using the same scales, and digital photographs were again obtained.

Patient Randomization
Patient screening and enrollment were performed by one of us (M.D.), as were random sequence generation and concealment (R.K.), which were conducted by coin toss of the same fair coin, with the outcomes (1 or 2) recorded separately on individual paper cards then placed in sealed, opaque, consecutively numbered envelopes. Each patient was assigned to one of 2 groups (by W.D.). Patients in group 1 were designated to receive laser therapy on the right arm, and those in group 2 were assigned to receive laser therapy on the left arm. All study treatments were delivered by the same clinician (D.B.).

Laser Treatments
All study treatments used the 810-nm pulsed diode laser. A lidocaine and prilocaine–based cream was applied to the arms 30 to 60 minutes before treatment and washed off before treatment. Laser therapy was performed on the treatment side at a fluence of 45 to 60 J/cm² (to convert to gray, multiply by 1) (depending on Fitzpatrick skin type) and a pulse duration of 30 to 100 milliseconds, with precise settings selected to be just below the patient’s threshold for purpura. Each treatment session entailed 2 nonoverlapping passes separated by a 1-minute delay. The patient was then instructed to minimize sun exposure and apply sunscreen with a sun protection factor of 50 to the treatment area daily until the next visit.

Outcome Measures
The primary outcome measure was the difference in disease severity score, including redness and roughness/bumpiness, between the treated site and the control site as rated by the blinded dermatologists at 12 weeks after the initial visit. This scale was not validated because no relevant validated scale was available. However, raters were trained on the use of the study scale, and before the review of study images, they were asked to rate archival skin images on the same 4-point qualitative subscales used in the study. Raters reviewed and rated archival images separately and then reconciled their ratings through face-to-face forced agreement, with the pro-
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Results

Patient Baseline Demographic Characteristics

The study was conducted during a 7-month period from March 1 to October 1, 2011. A total of 26 patients underwent screening for our study, and 23 of those patients (46 arms) met our criteria and were enrolled in the study. Of these 23 patients, 18 (36 arms) completed the study and underwent analysis, 3 were lost to or unavailable for follow-up, and 2 voluntarily withdrew owing to inflammatory hyperpigmentation after the laser treatment. The demographic characteristics of our patients are presented in the Table. At baseline, patients rated the severity of the roughness/bumpiness in the texture of their arm test sites at a median score of 1.5 (interquartile range [IQR], 1-2) and the severity of the erythema of their arm test sites at a median score of 1.5 (IQR, 1-2). (The maximum score for both ratings was 3.0.)

Blinded Raters’ Scores

At follow-up, the median redness score assigned by the blinded raters for the treatment and control sides was 2.0 (IQR, 1-2), a null difference (Figure 1). The median roughness/bumpiness score was 1.0 (IQR, 1-2) for the treatment sides and 2.0 (IQR, 1-2) for the control sides, a difference of 1 (P = .004) (Figure 1). The median overall score combining erythema and roughness/bumpiness was 3.0 (IQR, 2-4) for the treatment sides and 4.0 (IQR, 3-5) for the control sides, a difference of 1 (P = .005) (Figure 1).

Patient Self-assessment Scores

At follow-up, patients’ self-reported median erythema rating for the control sides did not change from the baseline score of 2.0 (IQR, 1-2), but the self-reported median erythema score for the treatment side decreased from 2.0 to 1.5 (IQR, 1-2), a nominal difference that was not statistically significant (P = .13) (Figure 2). The median roughness/bumpiness score for the control sides increased from 1.5 to 2.0 (IQR, 1-2) and for the treatment sides decreased from 1.5 to 1.0 (IQR, 1-2). The 1-point decrease in roughness/bumpiness in the treatment arm compared with the control arm was significant (P = .008) (Figure 2). The overall score (erythema and roughness/bumpiness) for the control sides increased from 3.5 to 4.0 (IQR, 3-4), and for the treatment arm decreased from 3.5 to 2.5 (IQR, 2-4), with the cumulative difference of 1.5 points being significant (P = .005) (Figure 2).

Adverse Events

We found no unexpected adverse events associated with laser treatment. Two participants developed inflammatory hyperpigmentation after laser treatment and chose to withdraw...
from the study. These patients were instructed to continue sunprotective measures to their affected extremities, and in both cases hyperpigmentation completely resolved within 3 months.

Discussion

We investigated the effectiveness of the 810-nm diode laser in the treatment of KP. After 3 treatments spaced 4 to 5 weeks apart, blinded dermatologist ratings and patient self-report indicated significant improvements in skin texture and roughness/bumpiness when compared with baseline (Figure 3). However, neither raters nor patients detected a significant change in erythema.

Most topical treatments for KP, including emollients, corticosteroids, and retinoids, are of limited effectiveness.9 Light-based treatments have typically entailed use of vascular lasers, like the application of a 532-nm potassium titanyl phosphate laser to treat a case of resistant facial KP by Dawn et al.9 Repeated treatments resulted in a marked improvement in erythema and some clearance of papules. A study of 12 patients using the 585-nm pulsed-dye laser6 found improvement in erythema but not in roughness/bumpiness. A similar report7 described a case in which multiple treatments with a 595-nm pulsed-dye laser induced marked improvements in facial erythema, patient satisfaction, and quality of life. A study of 10 patients treated with a 595-nm pulsed-dye laser8 confirmed these results.

To our knowledge, our study is the first of its kind to investigate the use of a longer-wavelength laser, the diode laser, in the treatment of KP. More important, our results are the first from a clinical trial that demonstrate the effectiveness of laser treatment of the textural abnormality and roughness/bumpiness associated with KP. The data from our investigation suggest that the 810-nm diode laser is a particularly promising and effective treatment for the nonerythematous variants of KP. The variant of KP known as keratosis pilaris alba, which presents mostly as follicular papules, may be highly responsive to this laser modality.10 The variant that includes perifollicular erythema with follicular papules, keratosis pilaris rubra,9,10 may best respond to joint treatment with diode and vascular lasers, with the former improving texture and the latter addressing erythema.

We have theoretical reasons for selecting the 810-nm diode laser and the settings used in this study. Specifically, KP is an inflammatory condition of vellus hair follicles. Compared with terminal hair, vellus hair is relatively deficient in melanin (ie, has less chromophore) and smaller in diameter (ie, has shorter thermal relaxation time). Based on the theory of selective photothermolysis, these features would be consistent with a thermal relaxation time of approximately 50 milliseconds, which means that a pulse duration of less than 50 milliseconds, such as the 30 milliseconds used in this study, would be appropriate for treatment. Because of a substantial lack of chromophore, the fluence required for photothermal destruction of a vellus hair follicle is 40 to 45 J/cm², greater than that for a terminal hair. Ideally a highly absorbing wavelength such as 695 nm would be the best to treat vellus follicles, but this wavelength is absorbed by epidermal pigment in darker skinned individuals before it can reach deeper targets, such as the stem cells in the bulge region of the follicles. Similarly, 1064 nm is not highly selective for melanin, and we know that the vellus follicle has little melanin to begin with. As a consequence, the 810-nm wavelength appears to be the best choice because its depth of penetration is sufficient, it has selectivity for melanin, and it is compatible with a pulse duration of 30 milliseconds.

In terms of adverse events, our study found that treatment with the 810-nm diode laser was safe and not associated with any serious or unexpected adverse events. Although 2 patients (9%) developed bothersome inflammatory hyperpigmentation after laser treatment, resulting in their withdrawal from the study, these sequelae resolved completely in the medium term. Further counseling about the need for sun protection and avoidance of tanning during the period of laser treatment may mitigate the risk for posttreatment inflammatory hyperpigmentation in the future.
A limitation of our study is that enrollment was restricted to participants with Fitzpatrick skin types I to III. The exclusion of darker skin types was not incidental but rather designed to minimize the risk for posttreatment inflammatory hyperpigmentation, which is more common after laser procedures in patients with Fitzpatrick skin types IV to VI. That posttreatment inflammatory hyperpigmentation was observed in this study despite careful patient selection suggests that this precaution was appropriate. Regardless, patients with darker skin types can indeed be treated safely with the diode laser if gentle settings are used. Once this treatment paradigm is optimized, such broader application will likely be appropriate and feasible. One protective benefit of the current treatment settings was that they were deliberately below the threshold for purpura and thus designed to avoid bruising, which can resolve with tan pigmentation, particularly in darker skin. To the extent that the 810-nm diode laser has hair-removing activity, this treatment may be inappropriate for patients who do not want hair loss at the site of their KP. Finally, although incidental reports from some participants previously in this study have indicated that they have maintained textural benefits for more than a year, it remains to be seen to what extent these improvements are maintained over the longer term. To the extent that laser treatment may significantly modify hair growth in abnormal vellus hair follicles initially induced by genetic predisposition, improvement may be long lasting. This result would then be parallel to the case of traditional hair removal, in which posttreatment long-term remission of coarse terminal hairs and the corresponding pseudofolliculitis is often observed. However, this study was not designed to assess long-term improvement, and additional studies would need to be performed to systematically measure the duration and likelihood of persistent benefits. The present study only provides proof of concept and indicates that improvement of the textural abnormalities associated with KP is possible after treatment with an 810-nm diode laser.

Conclusions

By objective and subjective measures, we found that, among lighter-skinned persons, serial treatment with a long-pulsed 810-nm diode laser at subpurpuric levels provided medium-term improvement in KP, particularly for the associated roughness/bumpiness and textural irregularity. Combined with pre-existing data about the utility of vascular lasers for the reduction of KP-associated erythema, this finding suggests that laser treatment may comprehensively address the clinical manifestations of KP in selected patients. Future studies may assess the durability of these responses and the comparative effectiveness of different long-wavelength lasers.