JOURNAL OF COSMETIC AND LASER THERAPY
2016, VOL. 18, NO. 4, 208–212
http://dx.doi.org/10.3109/14764172.2015.1114648

Taylor & Francis
Taylor & Francis Group

ORIGINAL RESEARCH REPORT

Pulsed dye laser versus long-pulsed Nd:YAG laser in the treatment of hypertrophic scars and keloid: A comparative randomized split-scar trial

Abd El-Shakour Abd El-Hafiz Al-Mohamady, Shady Mahmoud Attia Ibrahim, and Muhammad Mohsen Muhammad

Dermatology and Venereology Department, Faculty of Medicine -Al-Azhar University, Cairo, Egypt

ABSTRACT

Introduction: Keloids and hypertrophic scars are benign fibrous growths that occur after trauma or wounding of the skin and present a major therapeutic problem. **Objective:** The purpose of this study is to evaluate and compare the effectiveness of pulsed dye laser (PDL) versus Nd:YAG laser in hypertrophic scar and keloid. **Methods:** Twenty patients with hypertrophic scars and keloid were included in this prospective, randomized, split-scar study. Half of each scar was randomized to treatment with a 595-nm PDL and the contralateral half with the 1064-nm Nd:YAG. Each patient received 6 laser treatment sessions at 1-month intervals. The scars were evaluated at baseline and one month after the last laser session using the Vancouver scar scale (VSS). **Results:** One month after the last laser treatment, final total VSS analysis of treated sites by PDL and long-pulsed Nd:YAG laser revealed significant improvements ($p < 0.001$), whereas the average percentage of improvement in the total VSS was 55.14% for PDL and 65.44% for Nd:YAG laser. However, there were no statistically significant differences between PDL- and long-pulsed Nd:YAG laser-treated sites for total VSS ($p = 0.074$). **Limitations:** This was a single-center non-controlled trial, which included a small number of patients and subjective outcome measures. **Conclusion:** PDL and long-pulsed Nd:YAG laser treatments for keloid and hypertrophic scar provide significant improvement with insignificant difference between both modalities.

ARTICLE HISTORY
Received 25 May 2015
Accepted 22 October 2015

KEYWORDS
PDL; Nd:YAG Laser; hypertrophic scar; keloid

Introduction

Wound healing is a complicated process, consisting of overlapping phases. These phases are: hemostasis, inflammation, granulation, and remodeling. Any alteration in the process would lead to a variety of sequelae, including chronic wound healing and scars (1).

There is a wide spectrum of cutaneous scarring ranging from mature linear scars to abnormal raised and widespread hypertrophic scars as well as major keloids (2). Keloids and hypertrophic scars are sequelae of abnormal wound-healing process. They are a common reason for dermatologic consultation owing to pruritus, pain, restriction in movement, and cosmetic disfigurement (3). The exact pathophysiology of scarring is unknown, but recent evidence implicates the importance of members of the TGF-β family in cutaneous scarring. Overproduction of TGF-β may result in excessive deposition of scar tissue and fibrosis. Abnormal levels of cytokines such as IL-6, IL-13, and IL-15 may also play a role in keloid formation (4). Hypertrophic scars and keloids differ clinically and histologically. Hypertrophic scars are fibrous tissue outgrowth with excessive scarring, which are confined to the original wound margins. These scars usually develop within a couple of months after initial wound development, grow rapidly for several months, and then gradually regress over the next few years. They are red or pink, rigid, and sometimes pruritic (5,6), whereas keloids extend beyond the borders of the original wound, invading into and around normal skin. Keloid usually appear as firm nodules, often pruritic and painful, and generally do not regress spontaneously (7).

Various treatment modalities are available; intralesional corticosteroids, topical applications, cryotherapy, surgery, laser therapy, pressure therapy, and silicone sheeting are options that have been extensively used (8). Also, the side effects of various treatment modalities such as dyspigmentation, atrophy, and high recurrence rate are considered a significant limitation (9). Currently, exciting new research on the minimization of postoperative and traumatic scarring is being conducted, and the use of existing laser technologies has proven beneficial in the treatment of established scars (10).

The therapeutic use of lasers with different wavelengths has been investigated. Nd:YAG laser (1064 nm), flash lamp pumped pulsed dye laser (PDL) (585–595 nm), CO_2 laser (wavelength 10,600 nm), and argon laser (488 nm) were frequently used in the treatment of raised scars (11,12).

PDL treatment of scars was first described by Alster et al. (13), after which it rapidly became a mainstream form of laser

CONTACT Shady Mahmoud Attia Ibrahim Drshadyaly@yahoo.com; Drshadyaly@azhar.edu.eg Dermatology and Venereology Department, Faculty of Medicine, Al-Azhar University, Cairo, Egypt.

Color versions of one or more of the figures in the article can be found online at http://www.tandfonline.com/ijcl

treatment for scars. Long-pulsed, 1064-nm Nd:YAG laser had been used with low fluences to treat keloids and hypertrophic scars with satisfactory results (14).

Patients and methods

Patients

This study was a prospective randomized blinded comparative split-scar trial. Twenty-eight patients of both sexes with either keloids or hypertrophic scars were recruited from the laser clinic of Al-Azhar University Hospitals. Twenty patients successfully completed the study and only eight patients were missed during follow-up.

Patients with the following criteria were excluded: pregnancy, history of malignancy or radiation therapy, infections or viral skin diseases, immunosuppression, and history of any topical or intralesional treatment for the scar in the past 4 weeks prior to the initiation of therapy. Informed consent was obtained from all patients before treatment.

Treatment protocol

The treatment areas were cleaned using a mild cleanser. A topical anesthetic cream (eutectic mixture of 2.5% lidocaine hydrochloride and 2.5% prilocaine; EMLA; AstraZeneca AB, Sodertalje, Sweden) was applied on the skin for 60 minutes before the laser treatment. Each scar was divided into 2 equal parts. One part was randomized to treatment with 595-nm PDL (Synchro VasQ, Deka, Florence, Italy) using fluence of 7–9 J/cm^2, pulse duration of 1.5 ms, and spot size of 10 mm; and the second part was treated using 1064-nm long-pulsed Nd:YAG laser (Synchro Repla:y Excellium HP, Deka, Florence, Italy) using fluence of 30–35 J/cm^2, pulse duration of 20 ms, and spot size of 14 mm. The type of treatment administered to each of the two scar segments was randomly assigned, based on a research randomization program available on the Internet (www.randomizer.org), to ensure that segment location did not influence outcome. All patients received 6 treatment sessions with 4-week intervals.

Assessment

Standardized photographs were obtained using the same digital camera set at a fixed distance from the patient's lesion without using flash light of the camera (CyberShot digital, DSCH50, Sony, Tokyo, Japan) and were taken before every session and one month after the final session. Two blinded dermatologists who were not aware of therapeutic modalities physically assessed the effectiveness and safety of the treatments by using the Vancouver scar scale (VSS). The VSS includes assessment of pigmentation, height, pliability, and vascularity of the scar. Each of the four parameters was assigned numbers according to the previously mentioned characteristics. Scores from all parameters are added together to attain a final VSS score. Side effects and complications were also recorded at each session.

Statistical analysis

Clinical data was coded and securely stored. Analysis was performed using statistical software (SPSS version 15, SPSS Inc., Chicago, IL, USA).

Results

The present study was designed to compare safety and efficacy of PDL (595 nm) versus Nd:YAG (1064 nm) on treatment of hypertrophic scar and keloid using VSS assessment.

The age of the patients ranged from 5 to 35 (22.6 ± 8.1) years. Eleven patients (55%) were female and nine patients (45%) were male. Regarding Fitzpatrick skin type, 11 patients (55%) had skin type III while 9 patients (45%) had skin type IV. According to type of scar, 11 patients (55%) had hypertrophic scar and 9 patients (45%) had keloid. Meanwhile, the age of the scar ranged from 2 to 10 months with a mean of 7 ± 2.1 months. Regarding the possible cause, 6 patients attributed their scar to burn (30%), 10 to trauma (50%), 1 to surgery (5%), and 3 patients (15%) were not certain of cause of their scars.

At the end of the study, there was a significant improvement in VSS total score of both types of laser modalities in comparing the scores before and after treatment ($p < 0.001$),whereas the average percentage of the VSS was 55.1% for PDL and 65.4% for Nd:YAG laser (Table 1) (Figures 1,2).

There was a non-significant difference between VSS total score of lesions treated by PDL and Nd:YAG laser after six sessions ($p = 0.074$); however, Nd:YAG laser showed better results than PDL in hypertrophic scar and PDL showed better results than Nd:YAG laser in keloid after six sessions (Figure 3).

Analysis of the VSS subscales (erythema, pliability, height, and pigmentation) after six sessions showed a significant improvement in scar erythema, height, and pliability (Figure 4A–C), while a non-significant change occurred for pigmentation (Figure 4d). However, there was a significant difference in improvement between PDL and Nd:YAG laser in pliability for Nd:YAG after six sessions (Figure 4c).

Side effects were limited to mild-to-moderate treatment pain in 100% of the treatment sites with significant higher pain score with Nd:YAG laser (6.2 ± 2.2) versus PDL (4.7 ± 2.3); 7 patients reported purpura on the PDL treatment (35%); hyperpigmentation occurred in two patients who had skin type IV after PD treatment (10%); also bullae occurred in two others after one day of treatment with Nd:YAG laser (10%).

Table 1. Comparison between PDL and Nd:YAG laser according to total VSS before and after treatment ($n = 20$).

VSS	Before	PDL After	Nd:YAG After	P1
Range	3–11	0–6	0–6	0.074
Mean ± SD	6.80 ± 1.96	3.05 ± 1.70	2.35 ± 2.06	
Change %	0%	55.14%	65.44%	
Median (IQR)	7 (6–8)	3 (2–4)	2 (1–4)	
P2		< 0.05*	< 0.05*	

$P > 0.05$: NS.
$P \leq 0.05$: S.
P1: Comparison between PDL and Nd:YAG laser after treatment sessions.
P2: Comparison between VSS before and after laser treatment.

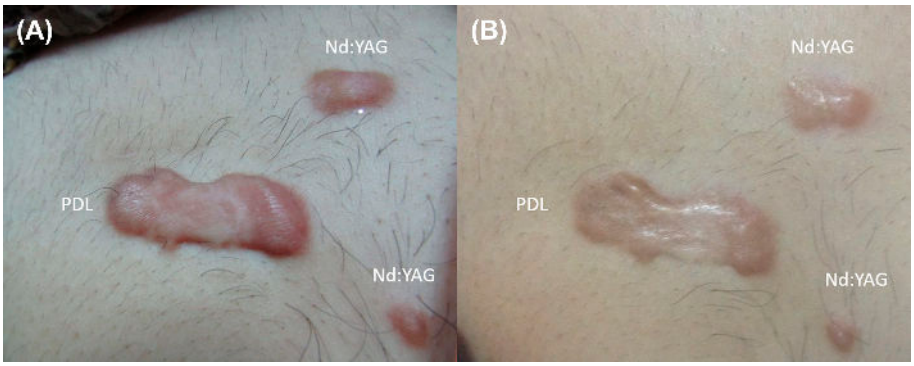

Figure 1. A twenty-four year old female with keloid on chest, at (A) baseline and (B) one month after last session by PDL and Nd:YAG laser treatments. The left lesion was treated by PDL and the right two lesions were treated by Nd:YAG laser.

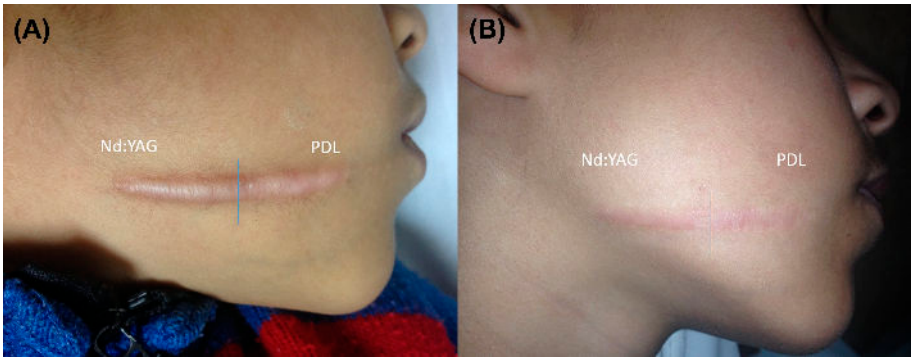

Figure 2. A thirteen year old boy with hypertrophic scar on the right side of the face, at (A) baseline and (B) one month after last session by PDL and Nd:YAG laser treatments. The anterior segment was treated by PDL and the posterior segment was treated by Nd:YAG laser.

Discussion

Prevention and treatment of hypertrophic scar and keloid have been reviewed by a wide variety of articles (15); however, no methodology has been emerged as the "gold standard" of clinical care (16). Once medical lasers were proven to be effective for scars, researches have been proceeded mainly on the basis of two premises: the comparative effectiveness among lasers, and laser therapy as a preventive measure (17).

To our knowledge, our study was the first to compare the clinical efficacy of PDL and Nd:YAG laser keloid and hypertrophic scar patients as no previous studies had compared the efficacy of both types of laser on hypertrophic scar and keloid.

Assessment of the erythema, height, pliability, and pigmentation was done using the VSS which was originally designed to assess subjective parameters in an objective way. Regarding total VSS, there was a significant improvement in VSS for

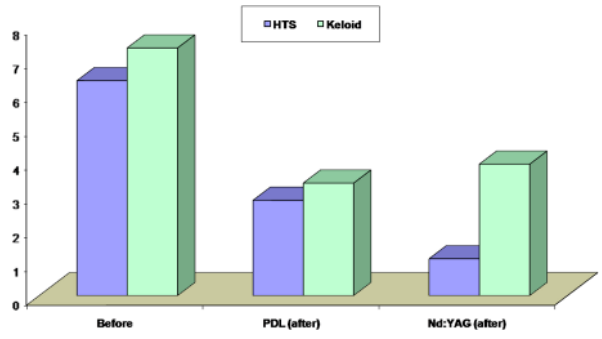

Figure 3. Comparison between PDL and Nd:YAG laser according to total VSS in keloid and hypertrophic scar before and after treatment.

sites treated by PDL and by Nd:YAG laser after six sessions. This result was consistent with that of Akaishi et al. (18), who reported that Nd:YAG laser treatment is highly effective for both keloids and hypertrophic scars. This response may be due to heat generation by Nd:YAG laser, which initiates inflammation and in turn elevates vascular permeability, matrix metalloproteinase (MMP) production, and collagen fiber fascicle decomposition. Also, the same findings were reported by Alster et al. (13) and Manuskiatti et al. (19) regarding the efficacy of PDL in keloid and hypertrophic scar. PDL selectively targets hemoglobin and coagulates microvasculature in the papillary and reticular dermis and inhibits nutrient supply to the scar (20).

Regarding hypertrophic scars, the result showed a non-significant difference between PDL and Nd:YAG laser. However, it showed better results with Nd:YAG laser. This response may be because Nd:YAG laser has more pronounced effect as it achieves greater penetration than PDL. This result was in agreement with that of Koike et al. (21), who showed that hypertrophic scars responded significantly better to 1064-nm Nd:YAG laser treatment than keloids.

On the other hand, the result of keloid showed non-significant difference with respect to PDL and Nd:YAG laser. However, it showed better results with PDL. This response may be due to occlusion of abnormal vascular structure in keloid as the target chromophore for PDL is the hemoglobin. In addition, the PDL can regulate cellular activity, such as inhibition of growth factors—TGF-β and PDGF—and stimulation of MMP and IL-6 for matrix degradation. This result was in agreement with that of Paquet et al. (22), who explained that PDL improves

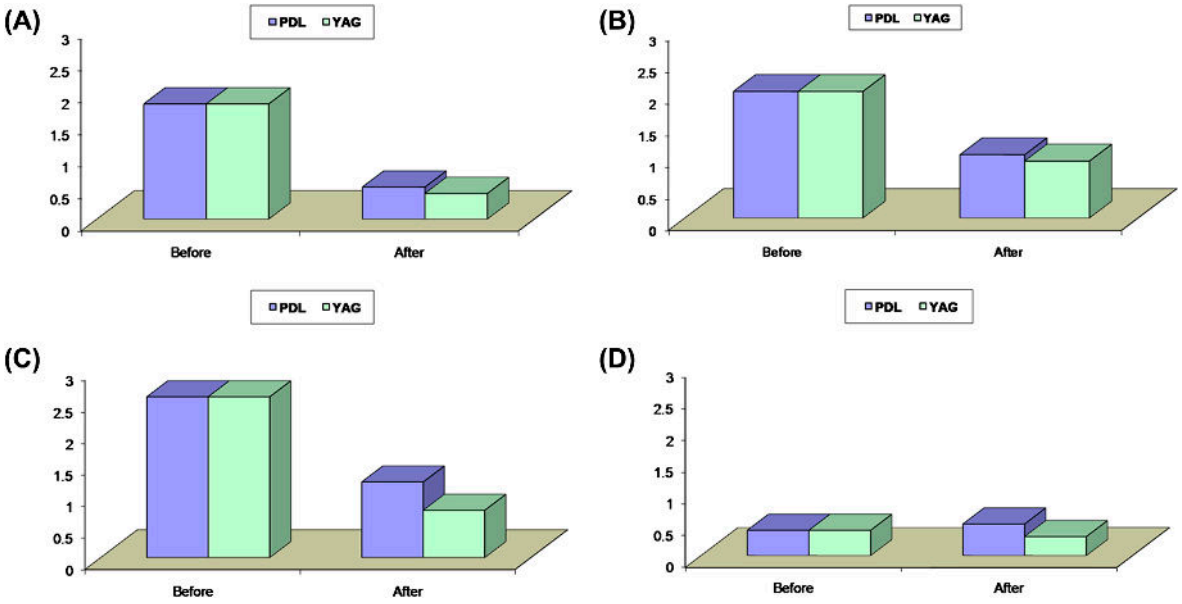

Figure 4. Comparison between PDL and Nd:YAG laser according to (A) vascularity, (B) height, (C) pliability, and (D) pigmentation before and after treatment.

keloids by inducing occlusion of abnormal vascular structure, which generates hypoxemia and in turn alters the local collagen production.

There was significant fading of erythema, a decrease in thickness, and improvement in pliability for sites treated both by PDL and Nd:YAG laser after six sessions. However, there were non-significant differences between PDL and Nd:YAG laser regarding erythema and height. Whereas for pliability, there was a significant difference regarding Nd:YAG laser, which showed better response than PDL which may be due to high penetration depth for Nd:YAG laser. This result was inconsistent with that of Mutalik (23), who reported that PDL has been tried successfully for softening the lesions but this study did not compare the results of PDL with those of Nd:YAG laser as in our study.

Statistical analysis for pigmentation score showed non-significant changes for area treated by PDL or by Nd:YAG laser after six sessions. Also, there was a non-significant difference between PDL and Nd:YAG laser. However, hypertrophic scars showed worsening in pigmentation after six sessions in area treated by PDL, although this result was not significant. Pigmentation is expected to be related to thermal injury of the epidermis from high melanin absorption at short wavelengths especially in dark skin type. This result was in agreement with that of Oliaei et al. (24), who reported that pigmentation may occur with PDL due to competitive absorption by melanin.

Assessment of pain score showed that pain was higher with Nd:YAG laser than PDL. This result was in contrast to that of Alam et al. (25), who reported that Nd:YAG laser was less painful when compared to 595-nm PDL in treatment of facial erythema. This difference may be due to the use of relatively higher fluences and longer pulse duration with Nd:YAG laser in our study.

The present study showed that there was a strong negative correlation between the total improvement of scar score and age of scar, which may occur as a response to inhibition of abnormal blood vessels formation. Also, there was a negative correlation between skin type and the total improvement in the score, which may be due to competitive absorption by melanin chromophore.

Limitations

There were some limitations in our study, such as being single center in nature, small number of the patients, EMLA cream as a topical anesthesia with vasoconstrictive effect on vessels, and, in addition, our primary outcome measure, although validated, is largely subjective.

Conclusion

Both the PDL and the Nd:YAG laser are effective and safe therapeutic modalities for the hypertrophic scars and keloids. There is no significant difference in the effectiveness between both laser types. However, the Nd:YAG laser showed a significant improvement in pliability of the scar over the PDL.

Declaration of interest

The authors report no declarations of interest. The authors alone are responsible for the content and writing of the paper.

References

1. Bian D, Zhang J, Wu X, Dou Y, Yang Y, Tan Q, et al. Asiatic acid isolated from centella asiatica inhibits TGF-β1-induced collagen expression in human keloid fibroblasts via PPAR-γ activation. Int J Biol Sci. 2013;9:1032–1042.
2. Monstrey S, Middelkoop E, Vranckx JJ, Bassetto F, Ziegler UE, Meaume S, Téot L. Updated scar management practical guidelines: non-invasive and invasive measures. J Plast Reconstr Aesthet Surg. 2014;67:1017–1025.
3. Nouri K, Elsaie ML, Vejjabhinanta V, Stevens M, Patel SS, Caperton C, Elgart G. Comparison of the effects of short- and long-pulse durations when using a 585-nm pulsed dye laser in the treatment of new surgical scars. Lasers Med Sci. 2010;25:121–126.

4. Elsaie ML, Choudhary S, McLeod M, Nouri K. Scars. Curr. Probl. Dermatol. 2011;42:131–139.
5. Seo BF, Lee JY, Jung SN. Models of abnormal scarring. Biomed Res Int. 2013;2013:423147.
6. Bouzari N, Davis SC, Nouri K. Laser treatment of keloids and hypertrophic scars. Int J Dermatol. 2007;46:80–88.
7. Hunasgi S, Koneru A, Vanishree M, Shamala R. Keloid: A case report and review of pathophysiology and differences between keloid and hypertrophic scars. J Oral Maxillofac Pathol. 2013;17:116–120.
8. Berman B, Viera MH, Amini S, Huo R, Jones IS. Prevention and management of hypertrophic scars and keloids after burns in children. J Craniofac Surg. 2008;19:989–1006.
9. Niwa ABN, Mello APF, Torezan LA, Osório N. Fractional photothermolysis for the treatment of hypertrophic scars: clinical experience of eight cases. Dermatol Surg. 2009;35:773–778.
10. Khatri K, Mahoney DL, McCartney MJ. Laser scar revision: a review. J Cosmet Laser Ther. 2011;13:54–62.
11. Mrowietz U, Seifert O. Keloid scarring: new treatments ahead. Actas Dermosifiliogr. 2009;100:75–83.
12. Yang Q, Ma Y, Zhu R, Huang G, Guan M, Avram MM, Lu Z. The effect of flashlamp pulsed dye laser on the expression of connective tissue growth factor in keloids. Lasers Surg Med. 2012;44:377–383.
13. Alster TS, Kurban AK, Grove GL, Grove MJ, Tan OT. Alteration of argon laser-induced scars by the pulsed dye laser. Lasers Surg Med. 1993;13:368–373.
14. Huang C, Murphy GF, Akaishi S, Ogawa R. Keloids and hypertrophic scars: update and future directions. Plast Reconstr Surg Glob Open. 2013;1:e25.
15. Sharma M, Wakure A. Scar revision. Indian J Plast Surg. 2013;46: 408–418.
16. Gold MH, McGuire M, Mustoe TA, Pusic A, Sachdev M, Waibel J, et al. International Advisory Panel on Scar Management: Updated International Clinical Recommendations on Scar Management: Part 2—Algorithms for Scar Prevention and Treatment. Dermatol Surg. 2014;40:825–831.
17. Ha JM, Kim HS, Cho EB, Park GH, Park EJ, Kim KH, et al. Comparison of the effectiveness of nonablative fractional laser versus pulsed-dye laser in thyroidectomy scar prevention. Ann Dermatol. 2014;26:615–620.
18. Akaishi S, Koike S, Dohi T, Kobe K, Hyakusoku H, Ogawa R. Nd:YAG laser treatment of keloids and hypertrophic scars. Eplasty. 2012;12:e1.
19. Manuskiatti W, Wanitphakdeedecha R, Fitzpatrick RE. Effect of pulse width of a 595-nm flashlamp-pumped pulsed dye laser on the treatment response of keloidal and hypertrophic sternotomy scars. Dermatol Surg. 2007;33:152–161.
20. Hultman CS, Edkins RE, Lee CN, Calvert CT, Cairns BA. Shine on: Review of laser- and light-based therapies for the treatment of burn scars. Dermatol Res Pract. 2012;51:24–36.
21. Koike S, Akaishi S, Nagashima Y, Dohi T, Hyakusoku H, Ogawa R. Nd:YAG laser treatment for keloids and hypertrophic scars: an analysis of 102 cases. Plast reconstr surg Glob open. 2015;2:e272.
22. Paquet P, Hermanns JF, Piérard GE. Effect of the 585 nm flashlamp-pumped pulsed dye laser for the treatment of keloids. Dermatol Surg. 2001;27:171–174.
23. Mutalik S. Treatment of keloids and hypertrophic scars. Indian J Dermatol Venereol Leprol. 2005;71:3–8.
24. Oliaei S, Nelson JS, Fitzpatrick R, Wong BJ. Use of lasers in acute management of surgical and traumatic incisions on the face. Facial Plast Surg Clin North Am. 2011;19:543–550.
25. Alam M, Voravutinon N, Warycha M, Whiting D, Nodzenski M, Yoo S, et al. Comparative effectiveness of non-purpuragenic 595-nm pulsed dye laser and microsecond 1064-nm neodymium:yttrium-aluminum-garnet laser for treatment of diffuse facial erythema: A double-blind randomized controlled trial. J Am Acad Dermatol. 2013;69:438–443.