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Evaluation of Efficacy and Safety of Low-Fluence Q-Switched 1064-nm Laser in Infra-orbital Hyperpigmentation Based on Biometric Parameters



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Abstract

Introduction: Dark circles and wrinkles under the eyes are common cosmetic problems, caused by various conditions, especially aging and overproduction of melanin in the epidermis or dermis of the skin. Iin addition to the application of topical lightening agents, different types of lasers, especially the Q-Switched ND:YAG laser, have been used for the treatment of cutaneous hyperpigmentation. Because of a high prevalence of idiopathic eye dark circles (EDCs) or periorbital melanosis and a poor response to available therapies, we decided to evaluate the efficacy and safety of the Fractional QS 1064 nm ND:YAG Laser through a before-after trial.

Methods: 18-65-year-old patients with skin Fitzpatrick phototype of I-V and without any usage of a topical or systemic therapeutic regimen (2-4 weeks before the trial) were enrolled in the study. Each patient was treated with 6 sessions of the Fractional QS 1064 nm ND:YAG Laser at 2-week intervals and assessed for response and possible side effects or recurrences through 4 outcome measures, including Visoface-based color and erythema, melanin index and lightness (Before the fourth and sixth sessions of the therapy; also 1 week and 3 months after finishing the trial).

Results: The changes of Visoface-based color and erythema, the melanin pigment amount by the Mexameter (melanin index) and the degree of lightness by the Colorimeter of patients after 6 months of intervention were statistically significant (P < 0.001).

Conclusion: The fractional QS 1,064 nm ND:YAG Laser is an effective and safe therapy in EDCs since objective outcomes like the reduction of the melanin index and improving lightness and subjective ones like the reduction of darkness and erythema were confirmed.

Keywords: Eyelids dark circle; Periorbital hypermelanosis; Q-switched 1064-nm laser; Hyperpigmentation; Hypermelanosis.

Introduction

Dark circles and wrinkles under the eyes are common and annoying cosmetic problems caused by various conditions, especially aging and overproduction of melanin in the epidermis or dermis of the skin.¹ Pigment and vascular structures may play important roles in developing eye dark circles (EDCs), but usually there is not an accurate classification of etiological and structural changes in EDCs. This classification could help dermatologists with better management of EDCs.² In dermatology, Pigmentation-related disorders are the third cause of disease with significant social and psychosocial problems which usually have a natural resistance to therapy. Skin lightening agents are used to target hyperactive and hyperplastic melanocytes or inhibit various stages of melanin synthesis.^{3,4}

Checking the history of inflammatory disorders and skin phototype is the most important role for treating

post-inflammatory hyperpigmentation in patients.⁵⁻⁸ In addition to using topical lightening agents, different types of lasers, especially the Q-Switched ND: YAG laser, have been used for treating cutaneous hyperpigmentation. The Q-Switched ND: YAG laser is known as a selective photothermolysis system with a therapeutic effect on epidermal and dermal pigmentation and also vascular structures that can facilitate the migration of melanophages.^{6,9-18} post-inflammatory Therapeutic methods for hyperpigmentation, melasma and nevic lesions through the Q-Switched ND: YAG laser have been shown to have a proper efficacy with minimum tissue-damage and side effects.¹⁸⁻²² Because of a high prevalence of idiopathic EDCs or periorbital melanosis and its cosmetic importance and poor response to available therapies,19-22 in this study, we decided to evaluate the efficacy, safety and satisfaction of Fractional QS 1,064 nm Nd:YAG laser treatment through a before-after trial.

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Materials and Methods

The assessor, analyst and data processor were blinded in this trial, while the two other assessors, the physician and the patients knew the type of treatment. This before-after study included patients with EDCs, that were referred to dermatology clinic of Skin and Stem Cells Research Center in Tehran University of Medical Sciences (SSRC).

According to previous studies, the assessors estimated the efficacy of topical modalities in hyperpigmentation at about 10% and for the laser at about 40%. Considering 30% improvement in hyperpigmentation, power=90% and α =0.05, the number of patients needed to treat was calculated about 27. Finally, given the probable failure of the patients to follow up, thirty-seven patients were enrolled in the study.

Eligibility Criteria

This clinical trial included patients with EDC, who were confirmed in terms of mental health by an expert psychologist, and they also met the inclusion criteria, including ages between 18 to 65 years, skin Fitzpatrick phototype of I-V and no usage of topical or systemic therapeutic regimen (from 2 and 4 weeks before the trial). These patients were enrolled in the study by using a simple convincing method.

The exclusion criteria in this study were patients who do not attend regular intervention and follow-up sessions, patients with any ulcer or infection in the intervention area and photosensitive dermatoses like lupus erythematosus, patients who have excessive caffeine intake (>6 glass per 1 day), and patients with the recent low sleep period (less than which was routine in their lifestyle) and anemia.

Patient recruitment

All of the patients involved in this study were justified about the design and aim of the study and also probable side effects. The patients could leave the study for any reason whenever they desired. Informed consent was obtained from the patients.

Intervention and Follow-up

Each patient received 6 sessions of the Fractional QS 1064 nm Nd:YAG laser at 2-week intervals, and they were assessed for response and possible side effects or recurrences through 4 outcome measures including Visoface-based color and erythema, melanin index and lightness (Before fourth and sixth sessions of the therapy, also 1 week and 3 months after the last treatment session). All patients were photographed and objectively examined by Mexameter MX 18 and Colorimeter CL 400 systems at baseline and at the special times during the trial. For the reduction of pain before each therapeutic session, xylocaine-P cream was applied peri-orbitally. The HELIOS Fractional QS 1064 nm Nd:YAG laser was used with the frequency of 5 Hz, energy of 1000 J/cm², and Pass

of 2-3. Given the fact that most Iranian people have skin type 3 and 4, the least invasive protocol was utilized for all patients, using the minimum effective setting of the laser device. Based on patient compliance and not having any complications, energy increased by 50 J/cm² in each consequent session up to maximum of 1200 J/cm². An eyeshield was utilized for all patients, as Mid-IR laser radiation can cause ocular injuries.²³ If moderate to severe erythema, ulcer, post-inflammatory hyper-pigmentation (PIH) or worsening of EDC occurred during the use of the laser, the primary investigator stopped the procedure and proper treatment like hydroquinone (HQ) based agents were applied.²⁴ Moreover, after each therapeutic session, it was proposed to use an ice pack for 10 minutes and then apply betamethasone ointment twice daily (for the reduction of inflammation) and zinc oxide ointment 3-4 times daily (for repairing) that continued for 2-3 days until the relief of erythema. Close adherence to the use of anti-solar creams was extremely recommended. In each session, patient satisfaction and probable side effects like erythema, bulla, ulcer, pain, burn, darkness and PIH were recorded as no, mild, moderate and severe.

In this clinical trial study, efficacy evaluation of the laser in pigmentary changes of EDC was performed using many methods. Lightness was assessed by Colorimeter CL 400 of the Multi Probe Adaptor System (MPA) and the Melanin index was assessed by Mexameter MX 18 of the MPA as objective outcome measures. Darkness degree and erythema, based on the photographs of Visoface, were assessed as subjective outcome measures and scored via the VAS (visual analogue scale) from 0 to 100.

Statistics and Data Analysis

Statistical analysis was performed by SPSS software (version 20.0). The one-way analysis of variance and Tukey HSD test were used to compare the data between the groups. P value less than 0.05 was considered statistically significant for all tests.

Results

The total number of the patients participating in this study was 37, out of whom 28 (4 male and 24 female) patients finished the trial, and their response, therapeutic side effects, and satisfaction with this treatment method were assessed. The average age of the patients in the intervention group was 38.40 ± 11.94 years (min: 19; max: 59). All patients had skin types 3 and 4, except 4 patients (10.8%) who exhibited skin type 2. Changes of Visioface-based color and erythema, the melanin pigment amount by the Mexameter (melanin index) and the degree of lightness by the Colorimeter of patients after 6 months of the trial were statistically significant (P < 0.001) (Table 1). Changes of Visioface-based color and erythema, the melanin pigment amount by the Mexameter (melanin index) and the degree of lightness by the Colorimeter of patients after 6 months of the trial were statistically significant (P < 0.001) (Table 1). Changes of Visioface-based color and erythema, the melanin pigment amount by the Mexameter (melanin index) and the degree of lightness by the Colorimeter of patients after 6 months of the trial were statistically significant (P < 0.001) (Table 1). Changes of Visioface-based color and erythema, the melanin pigment amount by the Mexameter (melanin index) and the degree of lightness by the Colorimeter of patients after 6 months of the degree of lightness by the Colorimeter (melanin index) and the degree of lightness by the Colorimeter (melanin index) and the degree of lightness by the Colorimeter of patients after 6 months of the degree of lightness by the Colorimeter (melanin index) and the degree of lightness by the Colorimeter (melanin index) and the degree of lightness by the Colorimeter of patients after 6 months of the degree of lightness by the Colorimeter of patients after 6 months of the degree of lightness by the Colorimeter of patients after 6 months of the degree of lightness by the Colorimeter of patients after 6 months of the degree of lightness by the Colorimeter of patients afte

Variables	N	Mea	n±SD	Man Devent Change	<i>P</i> Value
		Before the Intervention Initiation	After 3 Months of the Last Intervention Session	Mean Percent Change (%)±SD	
Visioface color	28	-6.052 ± 2.62	-3.79 ± 1.94	-38.03 ± 24.01	< 0.001
Visioface erythema	28	405.57 ± 72.24	361.54 ± 66.18	-10.01 ± 11.53	< 0.001
Melanin index	28	260.85 ± 76.85	202.53 ± 66.46	-22.15 ± 10.60	< 0.001
Colorimeter (lightness)	28	-11.22 ± 11.01	3.07 ± 10.95	160.13 ± 303.13	< 0.001

 Table 1. Efficacy of Fractional QS 1,064 nm Nd:YAG Laser for Treating Eye Dark Circles in a 6-Month Period (a 2.5-Month Period of Therapy and a 3-Month Period of Follow-up After the Last Treatment Session)

A P value less than < 0.001 was considered statistically significant in the intervention group of patients.

female patients after 3 months of the last intervention session were statistically significant (P < 0.001), but in men, only the melanin pigment amount and the degree of erythema showed statistically significant difference before and after 3 months of the last intervention session of the trial (P < 0.03) (Figures 1, 2; Table 2). None of the patients reported any severe side effects during the treatment and follow-up period; only mild erythema or irritation was reported in few patients, which did not last more than few days. Also, most of the patients (86%) were highly satisfied with the treatment results.

Discussion

Periorbital hyperpigmentation has different causes such as genetics, post-inflammatory hyperpigmentation due to atopic dermatitis, periorbital edema, excessive vascularity and aging.²⁵ Also, it has been mentioned that dermal melanization or post-inflammatory hemodynamic congestion with a prominent role of melanin and hemoglobin is very important in this context.²⁶ However, histologic evaluations have exhibited that there is a poor relation between melanosis reduction in the skin and improvement of EDCs.^{27,28} Thus, it can be claimed that the mechanism of improvement in periorbital hyperpigmentation is not quite well known and more histologic studies integrated with clinical trials are needed.

There are different topical treatment agents for this problem, such as hydroquinone, kojic acid, azelaic acid and retinoic acid, and chemical peeling and laser therapy are the most common treatment modalities.²⁹⁻³¹ Various lasers are used such as Q-switched ruby laser (694 nm) for Fitzpatrick skin type 1-3, Q-switched Alexandrite (skin types 4 and 5), Nd:YAG laser (1064) for skin types 5 and 6 and ablative laser resurfacing.^{3,16} Other lasers including Pulsed Dye laser, Diode laser, 1320 Nd-YAG and intense pulsed light fractional lasers such as CO₂ and Erb:YAG lasers act by controlled tissue injury. In a study by Momosawa et al, 3 sessions of the ruby laser with tretinoin and hydroquinone were used for 6 weeks, and 15 out of 18 patients got satisfying results.²⁴ In another study in Japanese people, the efficacy of the ruby laser was approved.27

The Lutronic dual pulsed Q-switched Nd: YAG laser was the first and only FDA-approved Q-switched laser



Figure 1. Infra-orbital Hyperpigmentation Treatment Process on the Right and Left Sides Based on Visioface Results (A,C) Before the Treatment Initiation on Day (0) and (B,D) 3 Months After the last Treatment Session.



Figure 2. Closed-up Focusing in the Infra-orbital Hyperpigmentation (A) Before the Treatment Initiation and (B) 3 Months After the Last Treatment Session.

for the treatment of melasma.²⁰⁻²² However, this approach requires multiple sessions in each week during the treatment period, and also it shows a higher recurrence rate in comparison to other treatment modalities (64-81%).³² Combining this approach with the long-pulsed Nd: YAG laser or Intense pulsed light might be beneficial for decreasing the recurrence rate.^{33,34} Also, Ustuner et al combined the Q-switched Nd: YAG laser with microneedling for the treatment of recalcitrant melasma and observed promising results.³⁵ However, in the present study, the Fractional QS 1064 nm Nd:YAG Laser was applied alone, along with supportive ointments to decrease erythema after laser therapy.

In a study by Xu et al, 30 women were treated with a lowfluence Q-switched 1064-nm laser at 4.2 J/cm² with 3.5 mm spot size and pulse duration of 8 ns at 3-4-day intervals. The melanin deposition was assessed by reflectance confocal microscopy in vivo, a narrow-band reflectance spectrophotometer, and a skin hydration measurement instrument. A significant decrease of the melanin index was observed in the upper dermis.³⁶ In a review by Agrawal

			Mean ± SD			
Variables		N	Before the Intervention Initiation	3 Months After the Last Intervention Session	Mean Percent Change (%)±SD	P Value
Visioface color	Male	4	-6.71 ± 4.67	-5.01 ± 2.80	-17.19 ± 32.90	0.263
	Female	24	-5.94 ± 2.27	-3.57 ± 1.75	-41.50 ± 21.14	< 0.001
Visioface erythema	Male	4	466.25 ± 63.19	426 ± 62.93	-8.69 ± 4.70	0.031
	Female	24	395.46 ± 73.34	350.80 ± 61.50	-10.23 ± 12.36	< 0.001
Melanin index	Male	4	225 ± 86.90	175.5 ± 61.35	-20.80 ± 5.28	0.032
	Female	24	266.84 ± 75.41	207.04 ± 67.42	-22.37±11.30	< 0.001
Colorimeter (lightness)	Male	4	-9.55 ± 11.15	1.5 ± 13.07	201.03 ± 181.25	0.089
	Female	24	-11.5 ± 11.302	3.34 ± 10.86	153.31 ± 321.31	< 0.001

 Table 2. Efficacy of Fractional QS 1064 nm Nd:YAG Laser Response in the Treatment of Eye Dark Circles in a 6-Month Period of Trial Based on Gender (a 2.5-Month Period of Therapy and a 3-Month Period of Follow-up After the Last Treatment Session)

et al, it was shown that Q-switched Nd:YAG could be a good modality to treat periorbital hyperpigmentation.³⁷ However, in a recent systematic review by Michelle et al, it was concluded that laser treatments are only mildly to moderately efficient in vascular and pigmented types of periorbital hyperpigmentation.²⁵ Also, a recent clinical trial compared this treatment modality with carboxy therapy and showed that less invasive, less expensive and more effective results can be achieved by carboxy therapy in comparison to the Q-switched Nd: YAG laser.³⁸ On the other hand, Mhatre et al claimed that the Q-switched Nd: YAG laser shows variable and inconsistent results in the treatment of facial pigmentary lesions in such a way that some patients may show aggregation of pigmentation, so the patient should be warned about it before starting the treatment and it should be mentioned in informed consent.³⁹ However, in the present study, none of the patients observed significant side effects such as PIH, and only few patients had mild erythema or irritation.

The current pilot study presented promising positive clinical outcomes regarding the effectiveness of Q-switched Nd: YAG by the assessments of biometric parameters. These days one of the most popular lasers for pigmentation is QS 1064 nm Nd:YAG. We used the fractional laser method for patients with EDCSs in 6 months' duration (2.5 months' duration of intervention and around 3 months' duration of follow-up), which resulted in a statistically significant improvement of pigmentary changes with a good safety profile and patients' satisfaction. Although the contribution of the female-male ratio was not proportionate, females, unlike males, exhibited significant changes in all indices. Furthermore, given the fact that nearly 90% of patients exhibited skin types 3 and 4, which are the most prevalent skin type among Iranian people, the outcomes of this study were not analyzed separately for each skin type. The outcome of this clinical trial study showed the beneficial effect of Q-switched Nd:YAG by evaluating its effect by biometric parameters.

In the present study, this treatment approach was utilized

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for only adult patients, so it is recommended to evaluate it in different age groups. Also, it is beneficial to record the duration and etiology of periorbital hyperpigmentation and their relation with treatment success, which should be evaluated in future clinical trials. On the other hand, it is beneficial to assess the effects of the moderation of low-density lipoproteins in serum, which characterize the severity of atherosclerosis and can cause the deposition of bilirubin under the eyes. Furthermore, for more accurate results and recommendations, it is better to conduct studies with larger sample size, equivalent gender and age distribution, and parallel-group designs.

The authors of this study have worked on various aspects of melasma and other pigmentary disorders for better management and therapy,⁴⁰⁻⁴⁵ and now it seems that this hot topic could answer some questions and concerns about one of the most encountered pigmentary disorders in the field of dermatology, namely periorbital hyperpigmentation or dark circles under the eyes.⁴⁴

Conclusion

On the basis of our study, the Fractional QS 1064 nm Nd:YAG laser is an effective and safe therapy in EDCs since objective outcomes like the reduction of the melanin index and improvement in lightness and subjective ones such as the reduction of darkness and erythema were confirmed and observed after the trial. Although there was a significant response regarding the reduction of the melanin index and erythema of DEC in men, the final color and darkness did not show a significant difference after the trial. A safety profile and satisfaction with treatment were appropriate.

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Conflict of Interests

The authors declare that they have no known competing financial

interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethics Considerations

The current study was registered at the IRCT (Iranian Registry of Clinical Trials) and the study protocol was approved by the Ethics Committee of Tehran University of Medical Sciences (IRCT registration number: IRCT20080901001159N31; Ethics committee reference number: IR.TUMS.REC 1394.854).

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Informed consent

Informed consent was obtained from the patients for participating in the study, and the right of the subjects was protected.

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