Clinical effectiveness of low-fluence 585 nm Q-switched Nd:YAG laser treatment on persistent facial erythema after adult type acne treatment: A Preliminary Study

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ABSTRACT

Acne remains a problem for dermatologists worldwide, but persistent erythema after successful acne treatment can present an even greater problem. The aim of the present study was to clarify the efficacy of low-fluence 585 nm Q-switched Nd:YAG laser treatment (Gold Toning™) for persistent facial erythema after acne treatment. Twenty female patients participated in the study (ages from 21 to 31 yr) randomly divided into 2 groups of 10, the Control and Treatment groups. Both groups first underwent superficial chemical peeling and physical comedone extraction, then the Treatment group received a number of low-fluence Gold Toning sessions (Q-switched 585 nm, 5-10 ns, 5 mm spot, 0.25-0.40 J/cm^2). Objective assessment from the clinical photography and subjective patient assessment were performed at the 8-week follow-up. Both the subjective and objective assessments showed significant improvement for the Gold Toning-treated group. This minimally-invasive approach therefore offers good results for persistent erythema post-acne treatment, and a potential range of other conditions.

INTRODUCTION

Acne is a common, chronic and relapsing inflammatory disease of the pilosebaceous units. It is very commonly seen in adolescence, and currently specific presentation is notable also in adults.

Conventional treatment has been dependent on drug therapy such as topical or systemic agents including antibiotics, keratolytics and retinoids[1]. The efficacy of these drugs varies, and they are associated with a variety of side effects, which limits their usage in the patient population at large[2].

For persistent erythema during or after any treatment, conventional treatments showed unmatched responses with other features of acne, including papules, pustules and the paradoxical reappearance of comedones. This interferes with the compliance of the patients, and prolongs the period for the patients to return to their normal lives. This problem is notably important for those patients with active working ages, and often results in a limitation of the overall treatment satisfaction even after successful treatments of papules and pustules. No drug has shown any efficacy for persistent erythema, and some of the acne drugs are known to even exacerbate this problem[3].

Erythema surrounding follicular openings often remains for a relatively longer time. This is postulated as being due to a change in the microvascular structure or caused by exogenous stimuli, nevertheless the mechanism for this long-lasting phenomenon after treatment for acne has not been elucidated. If persistent erythema is considered as being due to dilated microvascular structures in the superficial dermis, which is not detectable to the naked eye as visible telangiectasia, it can be regarded as a change in smaller vascular structures like microcapillaries.

The 585 nm wavelength is commonly used in vascular treatment with long pulse durations measured in milliseconds, and targets the endothelium and wall structure of various vessels under the extended theory of selective photothermolysis. At this wavelength, the absorption by melanin and oxyhemoglobin is very high, and almost the same. This is coupled with an acceptable penetration depth into tissue that can reach the superficial dermis. The 585 nm was considered one of 'gold-standard' wavelengths for the treatment of blood vessels. The pulsed dye laser (PDL) currently delivers wavelengths from 585 to 595 nm, which was an improvement on the 577 nm delivered by earlier versions[4].

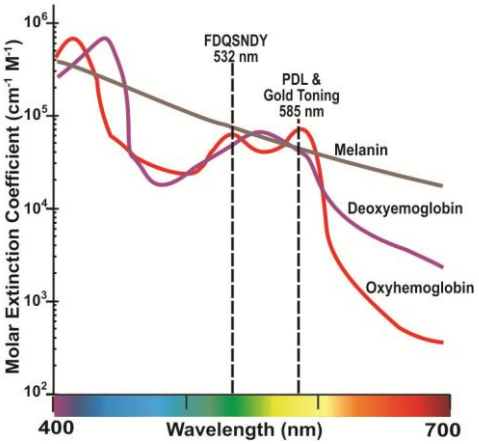

Fig 1: Absorption spectra of melanin, oxy- and deoxyhemoglobin. (PDL: Pulsed dye laser; FDQSNDY: Frequency-doubled, Q-switched, neodymium-doped yttrium-aluminum-garnet laser)

Considering the postulated size of the microvascular structures in acne-induced erythema, shorter pulse widths in the microsecond domain could be applied to vascular treatment[5]. Previously, the Q-switched Nd:YAG laser wavelength of 1064 nm, or frequency-doubled at 532 nm, has been reportedly used for vascular treatment associated with melasma and rosacea[5,6,7].

In addition to successfully lightening tattoos, epidermal and dermal pigmented lesions, these wavelengths have been demonstrated to induce injury to human vascular structures[8,9]. Only a few reports have appeared on their clinical application.

The 585 nm wavelength can be generated in Q-switched nanosecond domain pulse durations by wavelength conversion. Solid dye in a handpiece is used for this, to convert the 532 nm from a frequency-doubled KTP/Nd:YAG into 585 nm. (Figure 2)

This aim of this study was to clarify the efficacy of low-fluence 585 nm Q-switched Nd:YAG laser treatment of persistent facial erythema after acne treatment.

Fig 2: Solid dye block inserted in the handpiece to generate the 585 nm wavelength

MATERIALS & METHODS

1. Subjects

Twenty adult acne patients were voluntarily enrolled from October of 2012 to January of 2013, in Kim's Dermatology Clinic in Suwon, Korea. All the patients were female. The ages varied from 21 to 31 yr, with a median age of 25.4 yr.

Inclusion criteria were the presence of acne vulgaris with persistent erythema after pustules or papules had been improved within one year from the diagnosis, regardless of the previous treatments. All subjects were screened by the severity grading under the Korean acne grading system (KAGS)[10] ranged from 'severe' or higher and scored as the 2nd to 4th grade.

Table 1: Total patient population broken down by study center.

Score	Definition
Grade 1	Papule ≤10
Grade 2	Papules 11~30
Grade 3	Papules ≥31, nodules ≤10
Grade 4	Nodule 11~20, ±mild ongoing scars
Grade 5	Nodule 21~30, ±moderate ongoing scars
Grade 6	Nodule ≥31, ±severe ongoing scars, ±sinus tracts

Screening was performed based on the following exclusion criteria: uncontrolled severe acne conglobata or acne cystica; noticeable change in severity related to the menstrual cycle; any concomitant skin diseases or conditions; any history of photosensitivity disorders; any history of systemic drugs taken within four weeks before the enrollment, including systemic corticosteroids, antibiotics, isotretinoins, or hormonal treatment; any histories of topical steroid or antibiotic treatment within two weeks before enrollment; pregnancy; or lactation.

2. Methods

A Q-switched Nd:YAG laser (SPECTRA™, Lutronic corporation, Goyang, Korea) with the 585 nm Gold Toning™ handpiece was used for this study. Fixed parameters were used with a spot size 5 mm in diameter, pulse duration of 5 ~ 10 nanoseconds and fluences from 0.25 to 0.40 J/cm^2. Different fluences were applied based on the degree of disease severity, with changes proportional to the amount of erythema.

A split-group study was designed with control and treatment groups. Each group contained ten patients with randomization on enrollment. The control group underwent superficial chemical peeling and physical comedone extraction. The treatment group received Gold Toning treatment after the same baseline treatment as the control group. The treatment interval was two weeks. The number of treatment sessions was determined as follows based on the disease severity and KAGS scale: 2 sessions for patients with KAGS grade 3 and under, and 3 sessions for those with a KAGS grade over 3.

Each patient was followed up per one or two weeks. On each visit, light photography using a Nikon D80 camera and AF Micro 60 mm 2.8 lens under standard lighting conditions was performed for the objective rating. The final assessment was carried out at eight weeks after the initial treatment.

3. Assessment

1) Objective assessment

Digital photographic documentation under the same conditions (light source, room, and camera settings) was obtained before treatment and during each session. Improvement was assessed from the clinical photography after the final session and at 8 weeks thereafter on a five-point scale as follows:

1. Excellent improvement (>75%).
2. Good improvement (50-75%),
3. Fair improvement (25-50%);
4. Some improvement (10-25%);
5. Little or no improvement (0-10%);

Assessment was performed by two independent certified dermatologists. The raters were blinded to the descriptive information of the patients and their treatment.

2) Subjective assessment

Patient subjective assessment was performed and collected by a blinded investigator after eight weeks using the following five-point scale:

1. Excellent
2. Satisfied
3. Fair
4. Unsatisfied
5. Very unsatisfied

3) Safety assessment

On every follow-up visit, any abnormal signs and symptoms were collected by history taking. Well-known side effects and complications like pruritus, irritation, dryness, tingling sensation, burning sensation, scaling, burns, pain and pigmentary changes were separately checked.

4. Statistical analysis

The paired Student's *t*-test and the Wilcoxon rank test were used for the comparison before and after the treatment, as an inter-group assessment. The Wilcoxon rank test was used for the comparison between the groups. Statistical analyses were carried out using SPSS version 19.0 for Windows (IBM SPSS statistics, IBM corporation, Armonk, NY, USA) Statistical significance was defined and agreed when the p value was under 0.05.

RESULTS

A total of twenty patients were enrolled in the study and randomly grouped. A total of three patients dropped out and their data were not included in the analysis of the results due to missing the final follow-up (2 from the control group and 1 from the treatment group).

The results of the objective and subjective assessments are shown in Table 2.

Both the objective and subjective assessments showed statistically significant improvements in the treatment group compared to the control group. (objective assessment, $p = 0.026$; subjective assessment, $p = 0.017$)

Table 2: Objective and subjective assessment

Control group				
No.	**Sex/age**	**KAGS**	**objective**	**subjective**
case 1	F/27	Grade 3	4	3
case 2	F/22	Grade 4	3	3
case 3	F/21	Grade 2	2	2
case 4	F/23	Grade 3	3	2
case 5	F/25	Grade 4	5	5
case 6	F/31	Grade 3	3	3
case 7	F/28	Grade 3	3	3
case 8	F/22	Grade 2	3	3
Test group				
No.	**Sex/age**	**KAGS**	**objective**	**subjective**
case 1	F/25	Grade 2	2	2
case 2	F/25	Grade 4	3	1
case 3	F/31	Grade 2	3	2
case 4	F/21	Grade 3	1	1
case 5	F/28	Grade 4	2	2
case 6	F/25	Grade 3	2	3
case 7	F/28	Grade 4	3	2
case 8	F/29	Grade 3	1	1
case 9	F/21	Grade 2	3	3

No complications were reported during the study, such as seen in other studies using different lasers (e.g., pruritus, irritation, dryness, tingling sensation, burning sensation, scaling, burns, pain, pigmentary changes) in 3 to 6 months of follow-up. The side effects were minimal and transient, mostly presenting as slight edema.

Fig 3: Clinical findings of the treatment result (experimental group, case 4) / A, Baseline; B, 2 weeks after 2 sessions

DISCUSSION

The Q-switched Nd:YAG laser is a well-known treatment of choice for pigmentary lesions of skin or tattoo removal. Recently various applications have been additionally reported. For example, low-fluence, multi-pass Q-switched 1064 nm treatment is a well known treatment for melasma, which was explained based on a unique type of highly specific photothermal effect, termed subcellular selective photothermolysis[11]. A combination treatment involving the application of carbon suspension application and quasi-long pulse delivery followed by the Q-switched mode showed an effect on the reduction of the size of enlarged facial pores[12].

The combination of 1064 nm Q-switched and quasi-long pulsed low fluence treatments showed an effect on rejuvenation and melasma treatment, especially in the case of increased and overlapping vascular prominence in the lesion[6,11].

In the present study, laser energy was delivered in ultrashort Q-switched pulses (in the nanosecond domain) using the 585 nm wavelength. This wavelength is generated with a handpiece containing a solid dye cylinder, pumped by the 532 nm frequency-doubled Q-switched beam of the 1064 nm Nd:YAG laser.

Many studies have demonstrated the significance of wavelength and pulse duration in treating vascular and pigmented lesions. The FLPDL, with a 585 nm wavelength and 450-microsecond pulse duration, has been reported as safe and efficacious when used for the treatment of vascular lesions.

The pulse duration used in this study was much shorter than the thermal relaxation time of the microvasculature (arterioles and venules). Nevertheless, The Q-switched Nd:YAG laser can produce a combination of high peak power and ultrashort pulse duration which induces a combination of a photoacoustic and photothermal effect, quite distinct from the selective photothermal effect associated with the quasi-long pulsed laser (Figure 4).

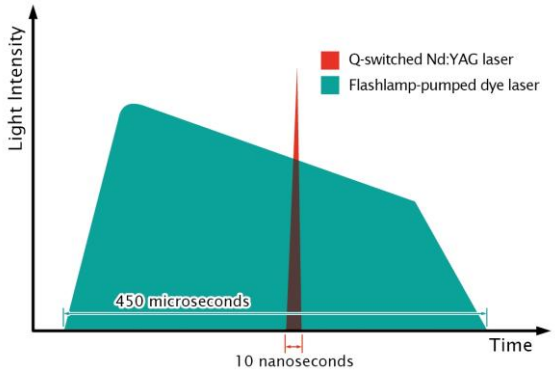

Fig 4: Difference in energy intensity of flashlamp-pumped pulsed dye laser and Q-switched Nd:YAG laser

The physiology of facial flushing, or constantly maintained erythema, is not yet well understood. Usually the most distal vessels of the peripheral circulation consist of a certain thin arrangement of endothelial cells, which have a very short thermal relaxation time compared with that of the multi-layered structure of larger vessels. Purpura as a result of vascular wall rupture is very common in laser treatment with longer pulse duration: the treatment with Gold Toning in the current study was, in contrast, subpurpuric. The correlation between the destruction and revascularization of vascular structures is not completely elucidated. We were unable to observe any clinical signs of direct vascular destruction in any of the Gold Toning-treated patients, such as purpura, since the erythema appearing after acne treatments usually does not appear as vascular structures visible to the naked eye.

Clinically this approach can be used in expanded indications from this postulation. Suggested applications are summarized in Table 3.

Table 3: Possible clinical indications targeting the underlying microvascular structure, invisible to the naked eye

• Cosmetically problematic erythema related with inflammatory diseases
• Telangiectatic type of rosacea (combination with other vascular lasers)
• Persistent erythematous papules and macules after various energy-delivery system
• Melasma with overlapped vascular prominence

Subsequent studies study will target the above indications. For example, persistent erythema as a side effect of fractional laser treatment is hard to treat. It is also hard to screen for or anticipate before treatment. Kang *et al.* suggested the role of increased vasculature in melasma[11].

Vasculature and melanocytes may have an influence on the development of hyperpigmentation in the overlying epidermis. In some types of melasma, pronounced telangiectatic erythema confined to the melasma lesion is frequently observed. Histologically increased vascularity is one of the major findings in this type of melasma. VEGF may be a major angiogenic factor for altered vessels in melasma. The potential application of an anti-angiogenic laser for the treatment of melasma especially when accompanied by pronounced telangiectasia in Asian skin is a possible treatment option. By targeting the vascular component in melasma lesions, a high-fluence PDL (585 nm) may decrease the melanocyte stimulation and subsequently the relapses. These results emphasize the necessity for a broader approach to melasma treatment targeting all components of this complex disorder[14].

Laser treatment using wavelengths in the visible yellow spectrum has also shown an effect on melasma and vascular lesions. The yellow beam (578 nm) of the copper bromide laser affects the altered dermal vasculature in melasma lesions[15].

The precise mechanism of the laser-tissue interaction behind these findings is not clarified yet. Just as seen in low-fluence, multi-passed 1064 nm Q-switched selective laser treatment of the melanocytic melanosomes in melasma patients, low-fluence yellow light could possibly have some kind of photoinhibitory effect on the endothelial physiology, or simple photodestruction as in the extended theory of selective photothermolysis, targeting the sub-visible microvasculature. Further studies on the microvasculature associated with pathologic conditions will enable more targeted and customized treatments for patients.

The limitation of this study is a relatively short follow-up period. Moreover, more objective measurement of erythema should be considered in subsequent studies.

CONCLUSIONS

In this study, Q-switched Nd:YAG laser treatment at 585 nm showed good efficacy in treating persistent erythema after acne treatment. The user satisfaction rate was significantly high.

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