A comparative study of low-fluence 1064-nm Q-switched Nd:YAG laser with or without chemical peeling using Jessner’s solution in melasma patients

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Original Article

Abstract

Background: Although low-fluence 1064-nm Q-switched Nd:YAG laser (QSNYL) is widely used for the treatment of melasma, multiple treatments are necessary for clinical improvement. Superficial chemical peeling using Jessner’s solution has been used for treatment of melasma conventionally.

Objectives: To evaluate the additional therapeutic effect and adverse effects of Jessner’s peel when combined with 1064-nm QSNYL for melasma patients in a double-blind, placebo-controlled design.

Methods: Total of 52 patients were included. Patients who received 10 sessions of 1064-nm QSNYL plus chemical peeling with placebo (group A) in a two-week interval and those who received 10 sessions of 1064-nm QSNYL plus chemical peeling with Jessner’s solution (group B) in a two-week interval were analyzed. Responses were evaluated using the Melasma Area and Severity Index (MASI) score, physician’s global assessment (PGA) and subjective self-assessment.

Results: At 8 weeks, the mean MASI score decreased from 8.68 ± 4.06 to 8.60 ± 3.88 in group A and from 8.98 ± 3.72 to 7.13 ± 2.57 in group B, showing a significant difference (p < 0.001). But at 20 weeks, there was no significant difference on reduction of MASI, self-assessment and PGA between the two groups. No serious adverse effects were reported with the additional Jessner’s peeling.

Conclusion: This study suggests Jessner’s peel is a safe and effective method in the early course of treatment for melasma when combined with low-fluence 1064-nm Q-switched Nd:YAG laser.

Introduction

Pigmentary disorders of facial skin pose severe psychosocial stress and significant negative impact on the affected patients’ quality of life (1). Among these pigmentary disorders, melasma, which presents as localized persistent hyperpigmentation of facial skin, is one of the most common disorder and yet the hardest one to treat.

There are two aspects in categorizing melasma. Clinically, it is divided into centrofacial, malar and mandibular type, and histopathologically, it is divided into epidermal, dermal or mixed type, representing the location of melanin pigmentation in the layers of skin (2–4). Epidermal types respond well to topical treatment, whereas dermal and mixed types, which are more common in Asia, respond poorly, hence, combined methods are recommended.

Treatment of melasma is often quite difficult, despite the availability of a range of treatment modalities. Historically, bleaching creams such as topical hydroquinone or chemical peels using glycolic acid (GA), trichloroacetic acid (TCA) and lactic acid have been popular (5–9). However, in darker skin types, the availability of a range of treatment modalities. Historically, bleaching creams such as topical hydroquinone or chemical peels using glycolic acid (GA), trichloroacetic acid (TCA) and lactic acid have been popular (5–9). However, in darker skin types, the limitation is post-inflammatory hyperpigmentation and relapse. Jessner’s solution is a superficial chemical peeling agent composed of lactic acid, salicylic acid, resorcinol and ethanol. It is easier to use than GA, because it does not require neutralization, and relatively safer than TCA because it has superficial depth (8,9). Although it has been used widely in acne and various types of hyperpigmented lesions, there is little published evidence of efficacy on the treatment of melasma.

On the other hand, treatments such as intense pulsed light (IPL), Q-switched Ruby lasers and fractional photothermolysis have also been used to treat melasma with variable results, but such therapy pose risk of inflammation, post-inflammatory hyperpigmentation and thermal damage (10–12).

Recently, the so-called laser toning treatment was introduced that uses a collimated low-fluence 1064-nm Q-switched neodymium-doped yttrium aluminum garnet (Nd:YAG) laser. This laser treatment minimizes thermal damage by using top-hat beam mode, short pulse width, high peak power and low fluence (13–15). Although considered as a safe method, the limitation is prolonged downtime, requiring at least five sessions of treatment for acceptable results.

In recent studies, combined methods such as GA peels combined with 1064-nm QSNYL treatment, topical 20% azelaic acid combined with 1064-nm QSNYL, and triple combination cream combined with 1064-nm QSNYL have yielded better results compared to monotherapy (16–19).

Keywords

1064-nm Q-switched Nd:YAG laser, Jessner’s solution, melasma

History

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We therefore investigated whether Jessner’s solution provides additional effect when combined with 1064-nm QSNYL, and assessed the clinical efficacy and safety of this method. Furthermore, we analyzed which type of melasma responded well to this treatment.

Subjects and methods

This study was performed in accordance with the Declaration of Helsinki (1975) and was approved by the institutional review board of Ulsan University Hospital. Before enrollment, patients were informed of the study procedure, possible risks, benefits and complications. All patients provided written informed consent and fully understood the purpose of this study.

Study design and subjects

This was a single-center, randomized, controlled, double-blinded study comparing a combination of 1064-nm QSNYL plus Jessner’s peel with 1064-nm QSNYL plus placebo in patients with melasma.

Inclusion criteria required a diagnosis of melasma by two dermatologists and confirmed by Wood lamp examination. Exclusion criteria included underlying skin diseases or other skin lesions on the treatment area; pregnancy or breast-feeding; history of poor wound healing; recurrent herpes simplex infection; use of oral medication; hormone replacement therapy; use of topical bleaching agents within 1 month before enrollment; and use of chemical peels, laser therapy or IPL within 6 months before enrollment.

Fifty-two patients participated in this study from September 2011 to August 2012. Patients’ ages ranged from 29 to 53 (mean, 41.7); all were female. Twenty-six patients were each randomly distributed into either group A (1064-nm QSNYL plus placebo) or group B (1064-nm QSNYL followed by Jessner’s peel). All patients were healthy, and none had any dermatologic, endocrinologic, hepatic or any other disorder except for melasma. Patients were instructed not to use any other form of treatment or functional cosmetics during the study period. Wood lamp examination was used to determine which type of melasma is present in each patient.

Treatment methods

Laser treatments were performed for 10 sessions at 2-week intervals, using low-fluence Q-switched Nd:YAG laser (Cosjet TR, Won Technology, Korea) (7-mm spot size, collimated homogenous flat-top beam profile, energy fluence 1.0-1.7J/cm² at 10 Hz). A single physician performed all the treatments using a collimation hand piece and two passes were done per each treatment session.

Chemical peeling using Jessner’s solution (salicylic acid 14 g, resorcinol 14 g and lactic acid 14 g dissolved in 95% ethanol) or placebo (normal saline) was also performed immediately after laser treatment at a 2-week interval for 10 sessions. First, one pass of skin priming was done with alcohol gauze. Then, 1–2 ml of Jessner’s solution or placebo was evenly applied onto melasma lesion using cotton-tipped applicator. The contact time was 2–3 minutes average, until mild frosting developed. Cooling with ice gauze was done after the procedure. A sunscreen with sun protection factor of 50 and moisturizer were provided. Avoidance of direct facial exposure to the sun was recommended.

Efficacy and safety assessments

Responses to treatments and adverse effects were evaluated at a 4-week interval throughout the 20-week treatment period. Standard photographs of both the front and sides of the face were taken using a digital camera (Nikon D7000, Tokyo, Japan), under the same conditions at baseline and at each subsequent follow-up visit. Two blinded independent dermatologists reviewed the photographs to determine the score. The Melasma Area and Severity Index (MASI) scoring system was used to evaluate the severity of melasma, according to the measurements used in previous studies (20).

Physician’s global assessment (PGA) was performed using a five-point scale. In comparing the two photographs taken at baseline and after 10 sessions of treatments, degree of improvements were graded (1: none, 0%, 2: slight, 0–25%, 3: average, 26–50%, 4: good, 51–75%, 5: very good, 76–100%).

In addition, all patients were requested to complete a questionnaire about the perceptions of their overall improvement. Responses were graded in a seven-point scale (−3: greatly worsen, −2: worsen, −1: slightly worsen, 0: no change, 1: slightly improved, 2: improved, 3: much improved).

Adverse events, including any possible complications (erythema, edema, burning sensation, acute urticaria, post-inflammatory hyperpigmentation and hypopigmentation) were recorded at each visit.

Statistical analysis

Statistical Package for Social Sciences (SPSS version 19.0, SPSS Inc, Chicago, IL) was used to all of statistical analysis. Student t-tests were used to evaluate pretreatment homogeneity, mean MASI score, and reduction of MASI score according to melasma types. Significance level was set at 0.05.

Results

Demographics

All 52 patients completed the study. There were no significant difference between the patients of group A and group B. Clinically, malar type was the most common type in both groups, and histologically, mixed type was the most common type in both groups (Table 1).

Melasma Area and Severity Index

The mean MASI score of both groups decreased significantly in a 20-week study period. In group A, the mean MASI score reduced from 8.68 ± 4.06 to 6.22 ± 2.54 (p < 0.001) at completion of treatment, achieving a 28.3% reduction from baseline MASI. In group B, the mean MASI score reduced from 8.98 ± 3.72 to 6.05 ± 2.66 (p < 0.001), achieving 32.6% reduction (Table 2, Figure 1).

Comparison of the MASI score reduction from the baseline of the two groups at 8 weeks and 20 weeks were done. At 8 weeks,
The mean MASI score gradually decreased in a 20-week study period. At 8 weeks, after four sessions of treatment, group B patients showed a significant decrease of mean MASI score than group A patients.

Table 3. Reduction of MASI score in two treatment groups at 8 weeks and 20 weeks are shown. The reduction of MASI score at 8 weeks was significantly bigger in group B than in group A (p<0.001).

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Std.</th>
<th>p</th>
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<tbody>
<tr>
<td>Reduction of MASI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 8 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group A</td>
<td>-0.08</td>
<td>0.88</td>
<td>0.000</td>
</tr>
<tr>
<td>Group B</td>
<td>-1.85</td>
<td>1.96</td>
<td></td>
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<tr>
<td>At 20 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group A</td>
<td>-2.46</td>
<td>2.58</td>
<td>0.477</td>
</tr>
<tr>
<td>Group B</td>
<td>-2.93</td>
<td>2.16</td>
<td></td>
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</tbody>
</table>

Group A = 1064-nm QSNYL alone; Group B = 1064-nm QSNYL plus Jessner’s peel. MASI = Melasma Area and Severity Index.

Discussion

Many therapeutic approaches have been used to treat melasma, including hypopigmenting agents, chemical peels, dermabrasion and laser treatments. Of these, chemical peels are used to create injury at a specific skin depth with the goal of stimulating new epidermal growth and collagen with more evenly distributed melanin (8,9). Chemical peels are classified by the depth of action into superficial, medium and deep peels. Specific peeling agents should be selected based on the disorder to be treated and used with an appropriate peel depth, determined by the histological level or severity of skin pathology to maximize success (9).

The most frequently used peeling agents for melasma are glycolic acid, trichloroacetic acid (TCA) and Jessner’s solution (lactic acid, salicylic acid, resorcinol and ethanol), and the reported efficacy of these agents are variable (21–24). Among these agents, Jessner’s solution, a superficial chemical peeling agent, induces desquamation of epidermis which has melanin and atypical melanophages. It has been used in mild dyschromasias, acne, post-inflammatory hyperpigmentation and actinic keratosis, and is known to cosmetically increase brightness and radiance of skin. Re-epithelization occurs after 3–5 days after desquamation and the scales are minimal. The procedure itself is relatively simple, and it does not require sodium bicarbonate for counter-action, as is the case in glycolic acid peeling. A recent interest in Jessner’s solution is as a combination medium-depth peel along with other agents like GA and TCA (25,26). But the adequate

Figure 1. Effect of low-fluence 1064-nm QSNYL vs. low-fluence 1064-nm QSNYL plus Jessner’s peel on the mean MASI score (the y-axis) in melasma patients. The mean MASI score gradually decreased in a 20-week study period. At 8 weeks, after four sessions of treatment, group B patients showed a significant decrease of mean MASI score than group A patients.

Table 2. Effect of low-fluence 1064-nm QSNYL vs. low-fluence 1064-nm QSNYL plus Jessner’s peel on the mean MASI score in melasma patients. The mean MASI score gradually decreased in a 20-week study period.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>4 weeks</th>
<th>8 weeks</th>
<th>12 weeks</th>
<th>16 weeks</th>
<th>20 weeks</th>
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<tbody>
<tr>
<td>Mean MASI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group A</td>
<td>8.68 ± 4.06</td>
<td>8.88 ± 4.05</td>
<td>8.60 ± 3.88</td>
<td>7.48 ± 3.69</td>
<td>6.70 ± 3.06</td>
<td>6.22 ± 2.54</td>
</tr>
<tr>
<td>Group B</td>
<td>8.98 ± 3.72</td>
<td>8.89 ± 3.80</td>
<td>7.13 ± 2.57</td>
<td>7.01 ± 2.90</td>
<td>6.53 ± 2.64</td>
<td>6.05 ± 2.66</td>
</tr>
</tbody>
</table>

Group A = 1064-nm QSNYL alone; Group B = 1064-nm QSNYL plus Jessner’s peel; MASI = Melasma Area and Severity Index.

Subjective assessment

After 20 weeks of treatment, the patients were asked to assess the treatment results. There were no patients who reported gravely worsen or worsen in both groups. In group A, 2 patients reported slightly worsen, 3 reported no change, 4 reported slightly improved, 11 reported improved and 6 reported much improved. In group B, none of the patients reported slightly worsen, 2 reported no change, 7 reported slightly improved, 10 reported improved and 7 reported much improved. Overall, patients’ subjective satisfaction was similar in both groups, but the percentage of patients who reported better than slightly improved was insignificantly bigger in group B, the combined therapy group (Figure 4).

Recurrence and adverse effects

In terms of Jessner’s solution application, four patients experienced burning sensation during and after Jessner’s solution application, which subsided within the following week. No other complications occurred. The adverse events that occurred after laser treatments were mild pain and erythema. Punctate leukoedema, post-inflammatory hyperpigmentation or hypopigmentation did not occur in any patient.
Figure 2. Serial photographs of representative melasma patients treated with 1064-nm Q-switched Nd:YAG laser plus and Jessner’s peel (upper) with 1064-nm Q-switched Nd:YAG laser alone (lower). Relatively rapid clearing of melasma was seen in the combined therapy group.

Table 4. Reduction of MASI score at 20 weeks according to each clinical and histologic types of both groups. The differences between the types were not significant ($p > 0.05$).

<table>
<thead>
<tr>
<th>Clinical type</th>
<th>Group A</th>
<th>Group B</th>
<th>Histologic type</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction of MASI</td>
<td>Epidermal</td>
<td>$-1.60 \pm 3.03$</td>
<td>$-2.18 \pm 2.01$</td>
<td>Centrofacial</td>
<td>$-1.50 \pm 1.29$</td>
</tr>
<tr>
<td></td>
<td>Dermal</td>
<td>$-2.89 \pm 2.04$</td>
<td>$-3.77 \pm 2.59$</td>
<td>Malar</td>
<td>$-2.87 \pm 2.95$</td>
</tr>
<tr>
<td></td>
<td>Mixed</td>
<td>$-2.40 \pm 2.86$</td>
<td>$-2.74 \pm 2.02$</td>
<td>Mandibular</td>
<td>$-1.65 \pm 0.21$</td>
</tr>
<tr>
<td>$p$ Value</td>
<td>0.770</td>
<td>0.454</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$p$ Value</td>
<td>0.496</td>
<td>0.187</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Group A = 1064-nm QSNYL alone; Group B = 1064-nm QSNYL plus Jessner’s peel.

Figure 3. Overall evaluation of the efficacy of combined treatment (1064-nm QSNYL plus Jessner’s peel) vs. monotherapy with 1064-nm QSNYL alone by Physician’s global assessment. The $y$-axis represents the percentage of patients, and efficacy of treatment is expressed in a five grade (from none to very good). The numbers of patients within each grade are shown.

Figure 4. Subjective self-assessments of combined treatment (1064-nm QSNYL plus Jessner’s peel) vs. monotherapy with 1064-nm QSNYL alone by melasma patients. The $y$-axis represents the percentage of patients, and efficacy of treatment is expressed in a five grade (from slightly worsen to much improved). The numbers of patients within each grade are shown.
number of sessions and intervals of chemical peeling procedures are not determined.

On the other hand, “laser toning”, which uses a collimated low-fluence, 1064-nm Q-switched Nd:YAG laser has recently been used for melasma in Asian practice (13–15). Although it is frequently used in the cosmetic market, the reported efficacy is variable, and it requires prolonged downtime in everyday practice. This laser is known to minimize thermal damage by selectively destroying abundant melanin pigments. These pigments are removed by epidermal desquamation, hence superficial chemical peeling after laser treatment may accelerate desquamation of melanin, enhancing the efficacy of laser treatment alone. Prior study which compared glycolic acid peeling before 1064-nm QSNYL and laser alone suggested that the combination therapy was more effective due to deeper penetration depth (18).

In this study, we compared the efficacy of 1064-nm QSNYL followed by Jessner’s peel versus laser treatment followed by placebo application (normal saline). Both treatments were effective after 10 sessions of treatment but the final difference between the two groups were not significant.

The most notable finding of this study was that the mean MASI score was significantly reduced from 8.98 ± 3.72 to 7.13 ± 2.57, showing 23% improvement after four sessions of treatment in the combined therapy group, whereas in monotherapy group, the score reduced from 8.68 ± 4.06 to 8.60 ± 3.88. From this data, we can postulate that Jessner’s solution had an early additive effect to laser treatment, but this effect was not consistent after four sessions of treatment (Table 2, Figure 1).

The epidermal turnover time, which is the sum of the turnover time of proliferative compartment, differentiated compartment and stratum corneum is reported to be 47–48 days (27). The marked improvement after four sessions of Jessner’s peel might be explained in the context that epidermis containing melanin pigment was replaced in an 8-week period. Afterwards, additional Jessner’s peel could not yield clinical effect due to newly replaced epithelium.

Although chemical peels including Jessner’s solution has extensively been used in melasma, the reasonable number of treatment sessions and intervals are not precisely determined. From this data, we may suggest that four to six sessions of Jessner’s peel is adequate and further treatment might be of no benefit in melasma patients.

In the treatment of melasma, the type and extent of the pigment deposits determine the type and invasiveness of the necessary treatment. The main factor to consider in determining the prognosis and therapeutic approach is the location and extent of the abnormal pigment deposits (2–4). Epidermal types usually respond well to topical treatment, whereas dermal and mixed types respond poorly and have high recurrence rates, and thus, treatment methods should be tailored to the melasma type (4). However, the majority of patients with melasma are of the mixed type, as in this study group, therefore, combined modalities are recommended.

With a relatively large group of melasma patients, we investigated which type of melanin responded better and faster to either combination therapy or monotherapy. Although the reduction of mean MASI score was the biggest in malar and dermal types, the degree of improvements between the clinical and histological types was not statistically significant (Table 4).

It has been reported that repetitive chemical peeling cause adverse effects, such as irritation and post-inflammatory hyperpigmentation, a serious cosmetic problem, but we found no significant adverse effects. Variable reported clinical response and recurrence are probably due to factors such as skin sensitivity, telangiectasia, inflammation and erythema after chemical peel. Especially in dark-skinned patients (Fitzpatrick skin type IV–V), medium-to-deep chemical peel is used with caution due to the risk of prolonged hyperpigmentation. In this study, Jessner’s solution proved to be safe, simple and effective method in combination with 1064-nm Nd:YAG laser.

In conclusion, our results indicate that laser treatment using a collimated low-fluence 1064-nm Q-switched Nd:YAG laser with or without Jessner’s peeling is a safe and effective method for melasma treatment. The combination treatment for four sessions at a 2-week interval promises to be most effective and further sessions of chemical peeling may not be necessary. Furthermore, our findings showed that repetitive Jessner’s peeling can be considered as safe, simple and effective method in melasma cases that are resistant to laser treatment alone, or in patients who expect to see earlier outcome.

Declaration of interest
The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

References


