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Successful Treatment of Melasma Using a Combination of Microdermabrasion and Q-Switched Nd:YAG Lasers

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Background and Objective: A common, disfiguring problem in women, melasma is often refractory to treatment, and long-term remissions are difficult to achieve. This study assessed the safety and effectiveness of a procedure combining microdermabrasion, a topical regimen, and low fluence Q-switched Nd:YAG laser treatment.

Materials and Methods: In this observational study of 27 female subjects, phototypes II–V, referred for treatment of mixed-type melasma refractory to previous therapies, low-fluence QS Nd:YAG laser treatment of 1.6–2 J/cm^2 with 5 or 6 mm spot was administered immediately following microdermabrasion. Daily application of a broad-spectrum sunscreen began immediately; subjects used a topical skin care regimen of hydroquinone with tretinoin or vitamin C. Treatments were repeated at 4-week intervals. Follow-up assessment was done 3–12 months after the last treatment. Adverse effects were recorded at each visit. Standardized digital photographs obtained before each treatment session and at follow-up visits were objectively assessed by blinded comparison using a quartile grading system.

Results: Treatment was successful in all skin types, deemed painless by all subjects, and required no anesthesia. Average number of treatments was 2.6. Twenty-two subjects (81%) had >75% clearance of melasma; 11 subjects (40%) achieved >95% clearance. Most subjects showed >50% clearance of their melasma 1 month after the first treatment. Side effects were limited to mild post-treatment erythema, which developed after the microdermabrasion and lasted approximately 30–60 minutes. Four subjects noted temporary exacerbation of melasma after inadvertent sun exposure, but this resolved within several weeks of resuming the topical skin care regime. Remission lasted at least 6 months.

Conclusion: Microdermabrasion plus low-fluence QS Nd:YAG laser treatment is a simple, non-invasive procedure with minimal risk, no recovery time, and long-lasting remission. Treatment works on all skin phototypes in just two to three treatment sessions. Subject compliance with skin care was excellent, probably due to the dramatic improvement observed within 4 weeks. Lasers Surg. Med. 44:117–124, 2012. © 2011 Wiley Periodicals, Inc.

Key words: chloasma; pigment; melanosome; Nd:YAG laser; hyperpigmentation; phototypes; mixed-type melasma; low-fluence laser; microdermabrasion; melanin; melanocytes

INTRODUCTION

Characterized by hyperpigmentation of sun-exposed skin, melasma is a common condition that presents as symmetric, hyperpigmented macules and patches on the face, usually on the cheeks, bridge of nose, forehead, chin, and upper lip [1,2]. More common among individuals with a family history [3,4] and among people with darker skin tones, melasma affects Latinos, Blacks, and Asians more often than whites. Melasma affects an estimated 50–80% of Latinas [5], and in Asian countries, melasma accounts for more than 50% of the aesthetic consultations [6]. Ninety percent of those affected are women [1,3,4,7–9] usually during their reproductive years [2,8]. It is known as chloasma or the "mask of pregnancy" when it occurs during pregnancy [2], and affects an estimated 50–70% of pregnant women in the United States [10]. Patients report that the condition interferes with their leisure activities and their emotional and social well-being [11–14].

While the cause of melasma is unknown, pregnancy, birth control pills, hormone therapy, genetics, photosensitizing medications, cosmetics, and mild ovarian or thyroid dysfunction are the strongest predictors. Sun exposure can trigger melasma because it stimulates melanocytes to produce increased melanin, and even a small amount of sun exposure can worsen the condition [4,10]. Irritation or inflammation of the skin can also stimulate melanin production and worsen melasma [1,4,11,15,16].

Melasma may involve the epidermis, the dermis, or, in the case of mixed-type melasma, both. The excess melanin can be visually localized to the epidermis or dermis with the use of a Wood's lamp (340–400 nm). Epidermal melanin is enhanced with Wood's light (340–400 nm) examination; dermal melanin is not [2,17]. Clinically, melasma usually appears as tan to brown patches, but dermal melasma may have a blue or black coloration [2,17]. In dark brown or black skin, Wood's light illumination does not localize the pigment, and these patients are classified as

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"indeterminate" [18]. On histological examination, increased melanin is found in the epidermis, the dermis or, most commonly, both locations. The number of melanocytes is usually not increased, but the melanocytes are usually larger, more dendritic, and more metabolically active [9]. Dermal melanin is found in the superficial and mid-dermis within macrophages, termed melanophages. The melanophages are usually present around small, dilated blood vessels, and there is scant or no inflammation [9].

Melasma may fade on its own [18], but it is usually a lifelong condition, and controlling it requires constant attention.

Treating melasma with topical treatments such as hydroquinone, kojic acid, azelaic acid, ascorbic acid, or alpha arbutin lightens the skin by reducing pigment production in the melanocytes. A common topical treatment regimen combing hydroquinone, tretinoin, and a topical corticosteroid produces temporary lightening or clearing of melasma but can also produce long-term complications [2,9,11,19]. Additionally, topical agents or chemical peeling usually provides only temporary results [2,9,11].

Early studies involving laser treatment often used pigment-specific lasers and light sources at standard parameters used for treating other pigmented skin lesions and tattoos. These high-fluence, single-pass laser treatments often exacerbate the melasma and cause temporary or permanent hypopigmentation [2,10,20–24]. Treatment with ablative carbon dioxide (CO_2) and erbium:YAG (Er:YAG) lasers is painful and involves significant morbidity, requiring sedation or general anesthesia. The healing period is a 1 or 2 weeks of intensive, at-home wound care, and the possible side effects include infection, scarring, and permanent hypopigmentation [25–27]. Ablative laser resurfacing procedures often result in worsening of melasma.

Treatment with non-ablative fractionated lasers is painful and requires a 30- to 60-minute application of a topical anesthetic cream as well as other methods of analgesia such as cold air cooling. Side effects include swelling, redness, and crusting for 3–5 days, and treatments must be performed monthly for 5–6 months [28–30]. While early results with the non-ablative fractionated lasers seemed promising [31], long-term follow-up demonstrated a high frequency of relapse [28,32,33].

Recently, there have been several reports of treating melasma with the Q-Switched neodymium-doped yttrium aluminum garnet (QS Nd:YAG) laser [34]. With a clinical endpoint of erythema plus lesional and hair whitening, the QS Nd:YAG treatments involve 10, 20, or more weekly treatments with as many as 10–20 laser passes per treatment. Complications from these high cumulative fluence procedures include pain, urtication, hyperpigmentation, long-term hypopigmentation (guttate leucoderma), and rebound of melasma [35–39].

Previous studies have shown limited success with the above treatments. Using these results as historical controls, this study reports on the efficacy and safety of a combination procedure to treat melasma. The treatment reported here combines microdermabration and topical treatment with low-fluence, Q-switched Nd:YAG laser rather than high-fluence pigment-specific, ablative, or fractionated lasers.

MATERIALS AND METHODS

Subjects

This was an observational study of 27 female subjects with dermal or mixed-type melasma present for more than 1 year that was refractory to other treatments including topical medications, chemical peeling, and other laser therapies. Subjects presented themselves to the clinical practice and paid for all procedures. Subject informed consent was obtained for publication of their medical results and photographs. Exclusion criteria included subjects who had a known photosensitivity disorder and subjects who were sensitive to hydroquinones. Each subject had a washout period and received no treatment for melasma for at least 2 months prior to receiving the treatment described here.

Laser Treatment

After cleansing the skin, a series of five photographs were taken using a Canfield Omnia System (Fairfield, NJ). Microdermabrasion was performed with a system that combines vacuum suction through a diamond chip wand (DiamondTome, Altair Instruments, Ventura, CA). Two passes were performed over the entire facial skin. Laser treatment was performed immediately after the microdermabrasion. Ten subjects were treated with a 1,064-nm QS Nd:YAG laser with a 5- to 7-ns pulse duration, 6-mm spot size, and fluence of 1.8–2.0 J/cm^2 (Q-YAG 5, Palomar, Burlington, MA). Seventeen subjects were treated with a 1,064-nm QS Nd:YAG laser with 50-ns pulse duration, a 5-mm spot size, and a fluence of 1.6 J/cm^2 (AlexTriVantage, Candela, Wayland, MA). The choice of laser was determined on availability and was deemed to be equivalent for purposes of this study. Treatment sessions were at monthly intervals, and the number of laser treatments was determined by the subject's desire for continued lesion clearance or satisfaction.

Skin Care Regimen

A broad-spectrum sunscreen with a minimum SPF of 40 was applied immediately after laser treatment, and on a daily basis thereafter. Subjects began a skin care regimen 18–24 hours after each laser treatment and continued this regimen until the next treatment session. Skin care for subjects with normal skin consisted of using hydroquinone 4% cream twice daily and 0.05% tretinoin cream at night, and skin care for subjects with sensitive skin consisted of hydroquinone 4% cream twice a day and 15% L-ascorbic acid every morning. The skin care regimen was modified if sensitivity developed to one of the products or after complete clearance was achieved.

Assessment of Response

Clinical and photographic evaluations for improvement (a decrease in the appearance of melasma) and for adverse

effects were conducted at baseline, before each treatment session, and at follow-up visits. Standard digital photographs (Omnia, Canfield Imaging Systems) were taken from the front view and side views under the same lighting conditions at each visit. Any adverse effects were recorded at each treatment session and during follow-up visits. Three blinded investigators performed the grading of the digital images using the following grading system for the percent improvement in the melasma: 0 = <25%, 1 = 25–50%, 2 = 51–75%, 3 = 76–95%, 4 = >95% clearance. Follow-up evaluation was performed 3, 6, and 12 months following the completion of laser treatment, which ranged from one to four treatment sessions.

Statistical Analysis

A Wilcoxon–Mann–Whitney test (Stata 11.2, College Station, TX), a non-parametric analog to the independent samples *t*-test that can be used when it is assumed that the dependent variable is a normally distributed interval variable, was used to compare the subjects who had one or two treatments with subjects who had three or four treatments. Spearman correlation (Stata 11.2) was used to evaluate the interaction between the number of treatments and skin type and the correlation between skin type and percent clearance.

RESULTS

Twenty-seven female subjects, ages 26–61 years old (mean age 42), completed this study. Two subjects chose not to return for photographs at the 6-month follow-up, and 16 subjects chose to not return for photographs at the 12-month follow-up. These paying patients were satisfied with the outcome and saw no reason to return for the photographs. The skin type distribution for phototypes II–V were 4, 11, 7, and 5 subjects, respectively (Fig. 1). The mean number of treatments performed was 2.6 (Fig. 2).

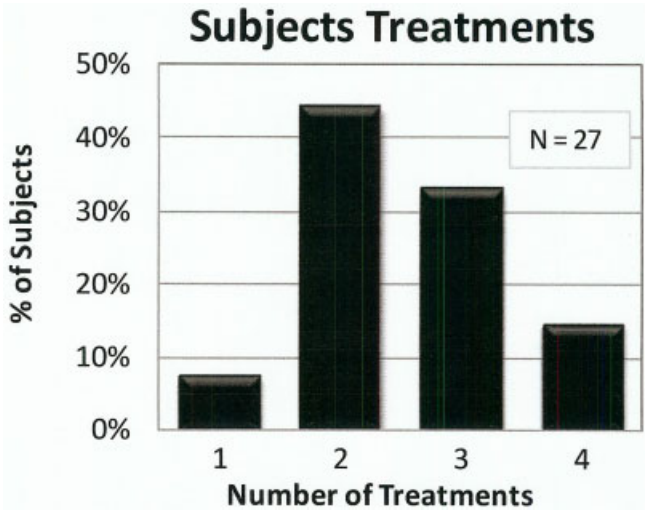

Fig. 2. Percentage of subjects who had 1, 2, 3, or 4 treatments.

Percent Clearance

As determined by the blinded investigators, mean clearance scores were: 3.3 at 3-month follow-up ($n = 27$), 3.2 at 6 month follow-up ($n = 25$). The Wilcoxon–Mann–Whitney test showed significant difference at 3-month follow-up (Fig. 3) but not at 6-month follow-up (Fig. 4) between subjects who had 1 or 2 treatments compared with those who had 3 or 4 treatments, with *P* values of 0.02 and 0.09, respectively. At 12-month follow-up, mean clearance score was 3.3 ($n = 9$). Given the low number of subjects, no additional statistics were employed on data collected at 12-month follow-up.

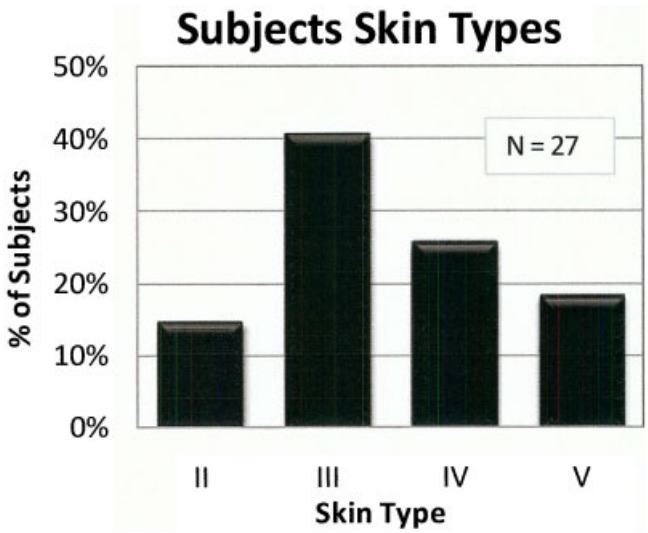

Fig. 1. Percentage of subjects with skin phototype II, III, IV, or V who completed the 3-month follow-up.

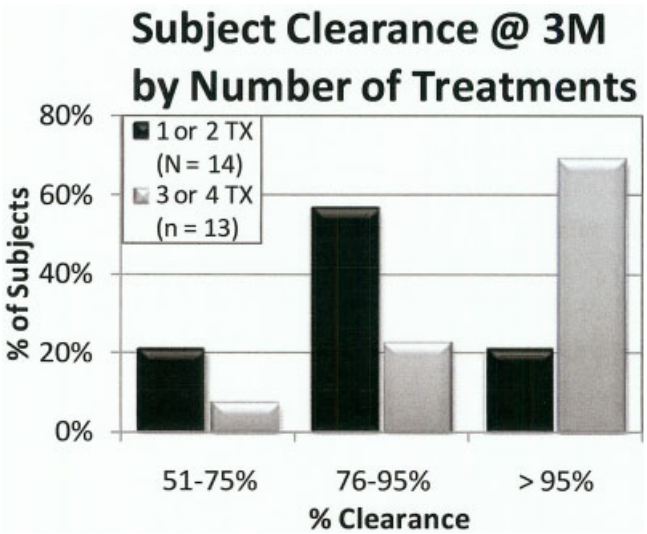

Fig. 3. Clearance rates at 3-month follow-up for those who chose to have 1 or 2 treatments versus those who chose to have 3 or 4 treatments.

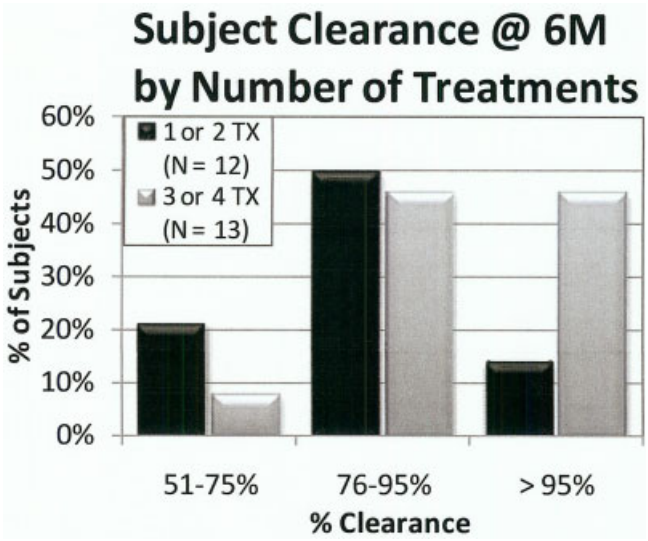

Fig. 4. Clearance rates at 6-month follow-up for those who chose to have 1 or 2 treatments versus those who chose to have 3 or 4 treatments.

All phototypes treated in this study improved with treatment. Figure 5 shows a 33-year-old female with phototype IV skin who had >95% clearance 6 months after one treatment. Over 95% clearance was achieved and maintained at 6-month follow-up after two treatments for a 61-year-old female with phototype V skin (Fig. 6). Figure 7 shows a 38-year-old woman with phototype II skin who underwent three treatments and had >95% clearance at 6-month follow-up.

Table 1 shows melasma clearance by phototype at 3 and 6 months follow-up. After 3 months, 23 of 27 subjects (85%) scored a 3 (76–95% reduction) or higher, and 12 subjects (44%) scored a 4 (>95% reduction). Twenty-one of 25 subjects (84%) evaluated at 6-months follow-up maintained their clearance. Four subjects (16%) had a 1-point decrease in their clearance. Of the nine subjects evaluated at 12-months follow-up, eight subjects (89%) maintained their clearance, and only one subject (11%) had a 1-point decrease in the clearance score from the 6-month follow-up.

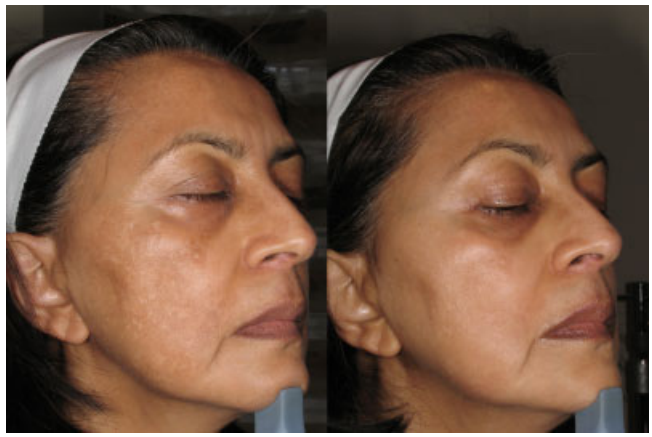

Fig. 6. Sixty-one-year-old female with phototype V skin. **A**: Before treatment with QS Nd:Yag laser and daily skin care regimen. **B**: Six months after treatment showing greater than 95% clearance of melasma.

Correlation of Skin Type With Number of Treatments and Percent Clearance

A Spearman correlation of 23% was calculated for the interaction between the number of treatments and skin type and was not significant ($P = 0.24$). The correlation between skin type and the percent clearance was 26%, and therefore not significant ($P = 0.19$).

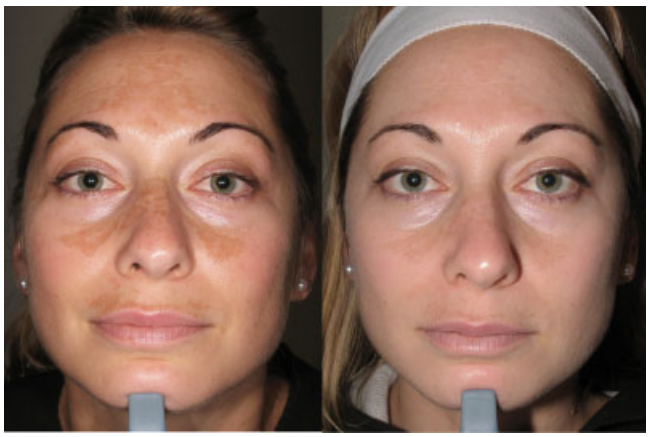

Fig. 5. Thirty-three-year-old female with phototype IV skin. **A**: Before treatment with QS Nd:Yag laser and daily skin care regimen. **B**: Six months after treatment showing greater than 95% clearance of melasma.

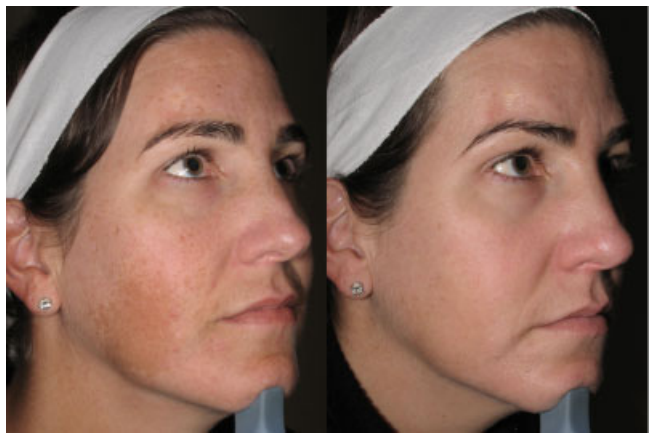

Fig. 7. Thirty-eight-year-old female with phototype II skin. **A**: Before treatment with QS Nd:Yag laser and daily skin care regimen. **B**: Six months after treatment showing greater than 95% clearance of melasma.

TABLE 1. Skin Type and Percent Clearance at 3- and 6-Month (Bold) Follow-Up

	Number of subjects with a % clearance at 3M | 6M		
Skin type	51–75%	76–95%	> 95%
II	2 | **2**	2 | **1**	0 | **0**
III	1 | **1**	4 | **6**	6 | **4**
IV	1 | **0**	2 | **3**	4 | **3**
V	0 | **1**	3 | **3**	2 | **1**
Total	4 | **4**	11 | **13**	12 | **8**
% of total	15% | **16%**	41% | **52%**	44% | **32%**

Side Effects

Side effects were limited, but some subjects required modification of skin care regimen. There was no pain reported during microdermabrasion or laser treatment. Immediately after microdermabrasion, faint erythema developed that lasted approximately 30–60 minutes. There appeared to be no increased erythema or edema after treatment with the QS Nd:YAG laser. During laser treatment, there was no apparent immediate skin or hair whitening. There was no swelling, crusting, blistering, post-inflammatory hyperpigmention, or scarring. No long-term hypopigmentation or guttate leukoderma was observed. Seven out of 27 subjects (17%) developed significant irritation from their skin care regimen requiring the discontinuation of tretinoin. Four out of 27 subjects (15%) had mild irritation from their skin care regimen, and the frequency of hydroquinone and retinoid application was modified.

DISCUSSION

Nanosecond domain QS lasers have been widely used to treat a variety of pigmented lesions because of their low potential for scarring [40–42]. The QS lasers selectively target melanosomes present in melanocytes, keratinocytes, and phagocytes. The effectiveness of these QS lasers is based on the theory of selective photothermolysis, which requires that a specific wavelength of energy be delivered in a period of time shorter than the thermal relaxation time of the target chromophore (melanosome) in order to restrict injury to the target while minimizing collateral damage. QS lasers induce selective photothermolysis of melanosomes by producing high local temperature gradients between the melanosome and its surrounding structures, resulting in subsequent melanosome fracture. High-pressure acoustic waves are produced and often result in melanocyte death. Laser treatment of pigmented lesions therefore relies on a combination of confined thermal damage and thermally initiated mechanical injury. The destruction of melanosomes is pulse-width dependent. A typical 1.0 μm melanosome has a thermal relaxation time in the range of 0.5–1.0 μs. Studies demonstrate that pulse durations of 40 and 750 ns selectively disrupt melanosomes; however, longer pulse durations, such as 400 μs, do not cause specific melanosomal damage [43]. Nevertheless, when QS lasers are used for the treatment of melasma at standard fluences for pigmented lesions, they produce poor melasma clearance and a high incidence of complications including hypopigmentation, hyperpigmentation, and melasma recurrence [20–23].

QS lasers in combination with ablative CO_2 and erbium:YAG lasers have produced similarly disappointing results [25–27]. Non-ablative fractional lasers deliver a pattern of very small laser beams, on the order of 50–200 μm that produce microthermal zones of coagulated tissue or wounds that are a stimulus for skin rejuvenation [44]. Fractional lasers were developed for the purpose of skin rejuvenation, and when used to treat photodamage, pigment lightening occurs over a series of successive treatments by means of pixilated destruction of columns of epidermal and dermal tissue, which are subsequently eliminated from the skin surface [44,45]. Due to the pixilated delivery of laser light and the tissue destruction, fractional laser treatment of melasma requires an average of five to six treatment sessions in order to produce uniform lightening of pigmented skin lesions. Furthermore, each treatment is associated with several days of erythema, edema, and crusting, and although fractional lasers have produced excellent lightening of melasma, long-term follow-up studies demonstrated a high incidence of recurrence [28,32,33]. A recent study using the 1,927-nm thulium laser in Chinese patients showed a high incidence of post-inflammatory hyperpigmentation and rebound melasma [46]. When used to treat melasma, high-fluence lasers cause excessive thermal damage and inflammation plus subsequent increased pigmentation leading to rebound hyperpigmentation and melasma recurrence. In an effort to avoid these adverse effects, several investigators have examined lower fluence QS YAG treatments. Polnikorn et al. treated 35 patients with refractory melasma with a 5- to 7-ns 1,064-nm QS Nd:YAG laser in conjunction with the daily application of 7% alpha arbutin. Each subject underwent 10 weekly plus 2 monthly laser treatments. A 6 mm spot size was used with fluences of 3.0–3.4 J/cm^2 in conjunction with cold air cooling. Twenty laser passes were used to treat each 3 cm × 3 cm area of skin with 10% overlap of each pulse to achieve an endpoint of erythema. Six months after treatment, 30% of subjects had greater than 80% reduction in melasma, 37% of subjects had 51–80% reduction in melasma, 8.6% of subjects experienced hypopigmentation, and 5.7% of subjects experienced melasma recurrence. Adverse effects included pain during treatment, hair and pigment whitening, and urticaria that developed immediately after treatment [35]. Suh et al. treated 23 Korean patients with 10 weekly treatments of a 5- to 7-ns QS YAG laser with fluences of 2.0–4.0 J/cm^2. After three months, there was significant clearance of melasma, however, treatment produced immediate erythema and edema, and both hyper- and hypopigmentation were observed at 3 months follow-up [36]. Wattanakrai et al. conducted a split face study of 22 subjects with dermal or mixed-type melasma using a QS YAG laser in conjunction with 2% hydroquinone

versus 2% hydroquinone alone. Subjects received 5 weekly laser treatments with a 1,064-nm laser, using a 6 mm spot size and fluences of 3.0–3.8 J/cm^2 in conjunction with cold-air cooling. Twelve-week follow-up showed 92% improvement in the relative lightness index versus 19.7% on the control side, but melasma had recurred in all 22 subjects, 3 subjects developed punctuate leukoderma, and 4 subjects developed hyperpigmentation [37].

Chan et al. [38] and Kim et al. [39,47] have recently reported on the development of permanent depigmentation following multiple, repetitive QS YAG laser treatments. These depigmented macules are thought to be the same entity as leukoderma punctata, which has been observed after long-term psoralen and UVA (PUVA) therapy. Melasma recurrence, post-inflammatory hyperpigmentation, and punctate leukoderma noted in the prior studies using QS Nd:YAG laser to treatment is likely a consequence of the delivery of a high cumulative fluence of QS YAG irradiation. In all of these studies, multiple laser passes (10–20) were used at higher fluences than the present study to produce an endpoint of erythema plus skin and hair whitening, and multiple weekly laser treatments were employed.

In this study, melasma clearance was excellent using a combination treatment consisting of microbermabrasion, QS Nd:YAG laser at fluences of 1.6–2.0 J/cm^2, and a hydroquinone-based skin care regimen. Patients were satisfied with their melasma improvement after a maximum of 4 monthly laser treatments and a mean of 2.6 treatment sessions. All subjects achieved at least a 50% improvement in the appearance of their melasma. More than 80% of the subjects experienced greater than 76% improvement in melasma at 3-, 6-, and 12-month follow-up. In the 25 subjects observed at 6-month follow-up, there was only a 1-point, or 25% decrease, in pigment clearance in 16% of subjects, and in the 9 subjects who had 1-year follow-up, there was a 1-point decrease in clearance score in 11% of subjects from the 6-month follow-up. Approximately 80% of subjects maintained their melasma clearance for up to 12 months.

The procedure in this study was effective in all skin types, and no correlation was found between skin type and number of treatment sessions or the laser used. Furthermore, data suggest that the paying patients saw an improvement with each treatment and elected to continue with treatments as desired. At the 6-month follow-up there was a statistically significant relationship between the number of treatments and the percent clearance, but this relationship did not hold up at the 9-month follow-up (since some subjects saw a decrease in their clearance).

The design of this observational study does not allow for a detailed statistical comparison between the two skin care regimens, the two lasers used, skin types, ethnicity, and prior melasma treatments the subjects underwent. Larger randomized controltrials would be required to answer these questions.

The low incidence of adverse effects in this study is likely a result of the low total fluences used and limited number of treatment sessions. In this study, total cumulative fluence delivered 10–20 times less than in other "low fluence" studies. With the low fluences employed, there was no pain during treatment and no immediate side effects such as urtication and skin or hair whitening. Additionally, there were no long-term side effects such as leukoderma punctata or rebound hyperpigmentation. The success of this treatment is likely due to the synergistic effect of the microdermabrasion, the low-fluence QS Nd:YAG treatment, and the maintenance skin care regimen. The microdermabrasion decreases scattering of laser light, improving the depth of penetration of the QS Nd:YAG laser and also increases epidermal skin turnover, which speeds the elimination of epidermal melanin. The skin care regimen suppresses melanin production and protects from ultraviolet exposure that can exacerbate melasma. The QS Nd:YAG laser, even at the very low fluences employed, appears to selectively damage melanocytes and dermal melanosomes. Mun et al. [48] recently reported on the effect of low-fluence QS Nd:YAG laser treatment on the structure of melanocytes and melanosomes in patients with melasma. Biopsies were obtained for ultrastructural analysis immediately after treatment with a 5–7-ns QS Nd:YAG laser, using a 7-mm spot size and fluence 1.6–2.0 J/cm^2 with a total of two laser passes. Scanning electron microscopy demonstrated fewer dendrites in epidermal melanocytes as well as a decrease in melanocyte volume after laser treatment. Transmission electron microscopy showed a decrease in stage IV melanosomes, demonstrating the ability to produce selective photothermolysis of melanosomes with such low fluence [48].

In the vast majority of individuals, melasma is a chronic condition, easily exacerbated by inadvertent ultraviolet light exposure or inflammation of the affected areas. Consequently, the most practical treatment approach would be a non-invasive, minimal risk procedure with no recovery time that would efficiently induce remission. The combination of microdermabrasion, low-fluence Nd:YAG laser treatment, and a skin care regimen aimed at suppressing melanin production produced excellent results in this study. While controlled trials are lacking, it is important to note that all of the subjects treated in this study had previously failed other interventions including laser treatments and aggressive topical therapy.

CONCLUSION

This study demonstrates that this unique combination of microdermabrasion and low-fluence QS Nd:YAG laser treatment in conjunction with a pigment-reducing skin care regimen is a safe and effective treatment for melasma for patients of all skin types. Compared to results in published reports of the modalities when used alone, this new combination treatment provides improved results. Furthermore, this low-fluence laser treatment offers substantial benefits over more invasive, high risk, costly procedures such as non-ablative or ablative fractional laser treatment. More than 80% of subjects achieved at least a 75% improvement in their melasma in 1–4 treatments. The treatments are fast and painless, and treatments can

be repeated if melasma rebounds. Randomized, control trials of this procedure are currently underway by the author in order to more definitively examine the benefits of this combination procedure.

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