Mottled Hypopigmentation from Laser Toning in the Treatment of Melasma: A Catastrophic or Manageable Complication?

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Melasma is a common acquired pigmentary disorder and difficult to treat with a high rate of recurrence. Conventional methods in the treatment of melasma have drawbacks and limitations. The so-called "laser toning" treatment, which uses a collimated low-fluence 1,064 nm Q-switched neodymium-doped yttrium aluminum garnet laser, was introduced a few years ago for the treatment of melasma. Laser toning has attracted much popularity and attention, and has become a crucial method for treatment of melasma. Laser toning is now a mainstay for treatment and management of melasma, however some dermatologists have excessive concerns about the risk of hypopigmentation. This inordinate fear may have originated from a few studies which insisted that laser toning therapy has a high risk of hypopigmentation and should be considered as a second-line treatment, not a first-line treatment for melasma. In the current study, we suggest that hypopigmentation after laser toning is a preventable and controllable complication based on our clinical experiences and reviews of various literatures.

Key words
Complication; Hypopigmentation; Laser toning; Low fluence; Melasma

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INTRODUCTION

Melasma is a type of acquired hyperpigmentation that generally manifests in symmetrical brown patches over the face. The patches are light brown to dark brown in color and irregular in shape. Its etiology is yet to be fully understood and various causal factors and pathophysiological processes are thought to be involved. Melasma tends to be more common in women of darker skin tones. In particular, East Asians including Koreans are prone to developing melasma and most eagerly seek treatment.

Most cases of melasma are intractable and traditional treatment options are topical UV blocking agent, topical whitening agent, and peeling, etc. For quite some time now, lasers and intense pulsed light (IPL) have been used for the treatment of melasma. For removal of pigment, the Q-switched laser (alexandrite laser (755 nm), ruby laser (694 nm), or neodymium-doped yttrium aluminum garnet laser (532 nm)) and IPL were often used. However, these treatment modalities had a high risk of complications including hyperpigmentation or exacerbation of melasma. Such complications were thought to be associated with skin inflammation caused by excessive thermal damage with a high fluence. In more recent years, a collimated low-fluence, 1,064 nm Q-switched neodymium-doped yttrium aluminum garnet (QS Nd:YAG) laser with the top-hat beam mode, short pulse width, high peak power, and low fluence was used in the so-called “laser toning” treatment that minimizes thermal damage while clarifying the skin of melasma. Laser toning became a hot trend in East Asia and subsequently throughout the world. As many aesthetic clinicians have experienced and proven its effects and safety, laser toning has become an important treatment method of melasma.

Despite its popularity, laser toning is not without complications which have proven to be a source of a headache for many dermatologists. The most common complications are postinflammatory hyperpigmentation (PIH), hypopigmentation, rebound hyperpigmentation, and recurrence of melasma. Among these, hypopigmentation may be the most dreaded complication of melasma treatment. Hypopigmentation is also referred to as depigmentation, guttate hypopigmentation, mottled hypopigmentation, facial depigmentation, and punctate leukoderma, depending on the scholar. In this article, the word “hypopigmentation” will refer to all of the above conditions. This makes the outcome of laser toning disappointing and lower the patient satisfaction as well as cause permanent damage in some cases. Unlike other complications, some of the hypopigmented lesions are irreversible in spite of active treatment for repigmentation over a long time span. Precautions about the risk of hypopigmentation with laser toning is somewhat justified in that it can lead to better treatment outcome, however, excessive fear may not be helpful. Such an overblown fear may have stemmed from several reports such as case series of facial depigmentation associated with low fluence Q-switched 1,064 nm Nd:YAG laser for skin rejuvenation and melasma which emphasized the risk of hypopigmentation with laser toning, questioning the appropriateness of using laser toning in the treatment of melasma. Various studies have pointed out that laser toning is associated with a high incidence of hypopigmentation. We would like to share our clinical experiences and include a literature review regarding whether hypopigmentation is truly a catastrophic and unavoidable complication of laser toning.

To start the discussion on this topic, we first need to answer the question, “why does hypopigmentation occur during laser toning therapy?” Many dermatologists suspect that a high fluence and cumulative energy coupled with short treatment intervals and a large number of treatments, etc. to be the causes of this unwanted complication. However, there are very few studies in the literature that systematically examined the therapeutic outcome and incidence of complications associated with laser parameters. One can speculate about which causative factors of hypopigmentation associated with laser toning from literature review and examination of changes in treatment methods throughout time.

STUDIES THAT WARN AGAINST LASER TONING EMPHASIZE THE RISK OF HYPOPIGMENTATION AS ONE OF ITS COMPICATIONS

There are studies that are frequently cited in the discussions on post-laser toning hypopigmentation. These studies that focus on the risk of hypopigmentation related with laser toning therapy were published in the years of 2008-2010. Laser toning started being widely used slightly before this period which means that the studies were conducted while the treatment method was still in its early stage. In other words, the treatment techniques were not yet matured and may have been more prone to complications compared to the techniques that were improved later.

At a closer look, Chan et al. looked at the use of laser toning for the purpose of skin rejuvenation or treatment of melasma, and the other four reports performed laser toning for treatment of melasma alone. These four
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Let us take a look at the parameters and techniques used in other studies on laser toning-related hypopigmentation. In 2010, Wattanakrai et al. reported that 3 (13.6%) out of 22 patients with melasma received laser toning and showed a case of hypopigmentation. Laser toning was performed using a 1,064 nm QS Nd:YAG laser (MedLite C6; Hoya ConBio, Fremont, CA, USA), with a 6 mm spot size and a fluence of 3.0-3.8 J/cm². The patients received five weekly treatments. When 5-10 treatments were given in addition to the first five treatments, 8 out of 22 patients developed confetti-like hypopigmentation. The authors concluded that laser toning is risky and advised to limit the number of treatments to 5 or less with sufficient intervals in between to prevent hypopigmentation. They also emphasized the importance of closely monitoring the signs of hypopigmentation and if they are found, discontinue treatment immediately. They did not directly attribute hypopigmentation to a high fluence, however, they report having used high fluence levels in their laser toning treatments.
ed with a 1,064 nm QS Nd:YAG laser. It was mentioned that they treated dermal melasma with “repeated sub-threshold photothermolysis using a 1,064 nm QS Nd:YAG laser” in over 500 cases in the past two years. Although the authors did not reveal the exact rate of hypopigmentation, they cautioned against overtreating with MedLite C6 due to the risk of mottling hypopigmentation. However, the two melasma patients were given 10 weekly treatments using 20 passes at a 6 mm spot size and a fluence of 3.4 J/cm², which can be considered an “overtreatment”, compared to the milder parameters used today. Another study, which were published in 2011 by the same authors, combined topical arbutin therapy with laser toning using a 1,064 nm QS Nd:YAG laser in 35 patients. They used 20 passes at a fluence of 3.0-3.4 J/cm² in 10 weekly treatments and found that 8.6% of patients developed guttate hypopigmentation. Again, these parameters are much more aggressive than those used in today’s clinical practice.

The above studies that we have reviewed reported of the risk of hypopigmentation inherent in laser toning therapy. They were all published from 2008 to 2010 when laser toning treatment was still in its early phase. All these studies used much more aggressive laser parameters [high fluence, high cumulative energy, short treatment interval and a high number of treatments, etc] compared to those generally used today.

EFFORTS FOR REDUCING THE RISK OF HYPOPIGMENTATION

Jeong et al. presented their study “New treatment for melasma with the collimated low fluence Q-switched Nd:YAG laser” at the 2009 Annual Conference of American Society for Laser Medicine and Surgery. This study compared treatment outcomes and the risk of complications between laser parameters. The first group was given 3-10 passes at 2.0-2.5 J/cm², and the second group was given 2 passes at 1.6-2.0 J/cm². Both groups received 8 weekly treatments. In the first group, hypopigmentation occurred in 3 (17.6%) out of 17 patients, whereas it did not occur in the second group. Although statistical data was not given, their results indicated that laser toning-induced hypopigmentation occurred due to aggressive treatment. However, as no other studies have directly assessed the risk of hypopigmentation associated with laser parameters, it would be helpful to review expert opinions as well as other literature reviews on this topic.

First, let us take a look at the study20 and review,21 which were published following a slate of reports published in 2008-2010 regarding the risk of hypopigmentation with laser toning. Jeong et al.20 aimed to compare the treatment outcomes between different orders of treatment where a combination of laser toning and triple combination cream (4% hydroquinone, 0.05% tretinoin, 0.01% fluocinolone acetonide) was used. The authors performed 8 weekly laser toning treatments using 2 passes at a spot size 7 mm, low (1.6-2.0 J/cm²) fluences and achieved treatment success without any complication over a long-term follow-up. This supports our notion that hypopigmentation can be mostly prevented by using a low fluence. In 2011, Bevec published the review citing this study. The review emphasized the superior efficacy and safety of low-fluence laser toning. The authors concluded, “The result of various studies indicate that even very low fluences [1.6 J/cm²] can be effective.” They also suggested that fluences around 3.0 J/cm² can often cause hypopigmentation and a better alternative would be using a ‘very low fluence (around 1.6 J/cm²)’. They added that theoretically, treating melasma with an “extremely low fluence [1 J/cm²]” may still be successful.

This opinion was shared by another review published in 2012. The author demonstrated that depigmentation occurred after the treatment with a “repetitive high-fluence QS Nd:YAG laser”. They assumed that “high cumulative laser fluences in these studies” [studies that reported of hypopigmentation developing after laser toning] caused skin inflammation and epidermal disruption leading to hypopigmentation. They also recommended using the “very low fluences”, where selective damage of melanosomes is still possible, for better effects and safety.

Before studies emphasizing the need for lowering the fluence in laser toning were released, clinicians had already switched to gentler parameters based on their first-hand experience of complications. Therefore, using a lower fluence were quickly established as a standard in laser toning. Most subsequent studies used fluences below 2.0 J/cm² with 1-2 weeks of interval, and 2-3 passes (the treatment was discontinued not after clear signs of petechiae or erythema but even a milder tissue response) and showed that such safe parameters were able to bring sufficient results at minimal risk of complications.

IMPACT OF EACH PARAMETER ON THE RISK OF HYPOPIGMENTATION

At this point, one may ask, “which laser toning parameters and techniques have the biggest impact on the development of hypopigmentation?” No study has so far
compared the relationship between individual parameters and the risk of complications. Most of the published studies have examined the harmful effects of a high fluence. However, some are also wary of high cumulative energy. Between the traditional methods with a higher risk of hypopigmentation and the later methods that have proven to be safer, the most striking difference is the fluence level. This may lead one to focus on the fluence, however, high cumulative energy, short intervals, number of passes, the degree of tissue response observed, or the total number of treatments may also affect the risk of complications.

A few studies have emphasized the importance of the treatment interval. Lee et al.,\textsuperscript{26} in 2015, performed laser toning at a high fluence with 1,064 nm QS Nd:YAG in patients with melasma. The first pass used a spot size 8 mm, a fluence of 2.0 J/cm\textsuperscript{2}, and was followed by another pass at 6 mm, 3.5 J/cm\textsuperscript{2}. Then, several passes at 4 mm, 3.2 J/cm\textsuperscript{2} were given over large lesions. In total, four monthly treatments were given with the endpoint defined as mild erythema and swelling. In discussion, the authors argued that the longer treatment interval of a month allowed sufficient time for recovery between laser treatments and prevented complications such as hypopigmentation. It is difficult to accept their claims as the number of treatments was very low and they only examined 8 patients. However, the authors have raised an important point and turned our attention from the fluence to other important factors that may impact the safety and efficacy of laser toning. This study emphasized the need for more systematic analysis of all the factors involved, which were studied in some of the more recent studies.

A similar study that drew our attention performed laser toning in 147 patients and analyzed hypopigmentation.\textsuperscript{27} They used 2,000 to 3,000 shots of the 1,064 nm QS Nd:YAG, (spot size 5 mm, 1.6-2.0 J/cm\textsuperscript{2} fluences) until erythema developed. In Group A, who received treatments with 1-2 weeks of interval, 3 out of 75 patients developed hypopigmentation. In Group B, where the interval was increased to 1 month, 0 out of 75 developed hypopigmentation. However, there was no statistical difference between groups. This study also categorized hypopigmentation into type 1 and 2 leukoderma, based on manifestations. They described the cause of type 1 leukoderma to be the “total cumulative dose” delivered through multiple treatments. As the complication developed gradually, the authors found UV imaging useful in early detection. They reported that type 2 leukoderma was caused by direct phototoxicity of laser regardless of the number of treatment and could not be identified early with UV imaging due to its quick and distinct clinical manifestations. The categorization and etiology the authors provided are based on their assumption rather than scientific evidence, however, their claims sound plausible to clinical dermatologists. Further research is needed in this regard in the future.

Few studies have examined the difference in the risk of complications and efficacy of laser toning associated with the spot size, however, Kim et al.\textsuperscript{23} suggested that the fluence should be lowered when using a QS Nd:YAG laser (MedLite C3 and others) that do not emit a flat-top collimated beam, as the Gaussian mode at the same fluence level may be more likely to cause hypopigmentation. Other studies have also mentioned that the nonuniform output can contribute to the development of hypopigmentation.\textsuperscript{28} In my personal experience, some QS Nd:YAG devices occasionally emit a much higher fluence than the set level and one cannot rule out the possibility of such inconsistency causing hypopigmentation.

**CONCLUSION**

In summary, several studies have reported of hypopigmentation and depigmentation occurring after laser toning treatments.\textsuperscript{2-11} Because they claimed that the incidence of hypopigmentation caused by laser toning was found to be about 10% in Asians, there was a growing concern regarding laser toning-related complications. However, as we have mentioned above, this may be due to the more aggressive parameters used in the early days of laser toning. Recent laser toning techniques are much more evolved and use lower fluences, less number of passes, sufficient treatment intervals and less tissue responses. Therefore, one can conclude that excessive worry and fear about laser toning-induced hypopigmentation are not necessary. Although a low risk of complications still remains, using gentler treatment approaches (lower the fluence and total cumulative energy and adjust the treatment interval according to treatment response, etc.), close monitoring of signs of complications and immediate discontinuation once hypopigmentation is suspected can help optimize the therapeutic outcome and avoid irreversible hypopigmentation in laser toning treatment.

**REFERENCES**

1. Pandya AG, Guevara IL. Disorders of hyperpigmentation. Dermatol Clin 2000;18:91-8.
2. Naito SK. Fractional photothermolysis treatment for resistant melasma in Chinese females. J Cosmet Laser Ther 2007;9:161-3.
3. Gupta AK, Gover MD, Nouri K, Taylor S. The treatment of melasma: a review of clinical trials. J Am Acad Dermatol 2006;
4. Halachmi S, Haedersdal M, Lapidoth M. Melasma and laser treatment: an evidenced-based analysis. Lasers Med Sci 2014; 29:589-98.
5. Taylor CR, Anderson RR. Ineffective treatment of refractory melasma and postinflammatory hyperpigmentation by Q-switched ruby laser. J Dermatol Surg Oncol 1994;20:592-7.
6. Jeong SY, Chang SE, Bak H, Choi JH, Kim IH. New melasma treatment by collimated low fluence Q-switched Nd : YAG Laser. Korean J Dermatol 2008;46:1163-70.
7. Chan NP, Ho SG, Shek SY, Yeung CK, Chan HH. A case series of facial depigmentation associated with low fluence Q-switched 1,064 nm Nd:YAG laser for skin rejuvenation and melasma. Lasers Surg Med 2010;42:712-9.
8. Wattanakrai P, Mornchan R, Eimpunth S. Low-fluence Q-switched neodymium-doped yttrium aluminium garnet (1,064 nm) laser for the treatment of facial melasma in Asians. Dermatol Surg 2010;36:76-87.
9. Cho SB, Kim JS, Kim MJ. Melasma treatment in Korean women using a 1064-nm Q-switched Nd:YAG laser with low pulse energy. Clin Exp Dermatol 2009;34:e847-50.
10. Kim MJ, Kim JS, Cho SB. Punctate leucoderma after melasma treatment using 1064-nm Q-switched Nd:YAG laser. Dermatol Surg 2009;35:929-32.
11. Polnikorn N. Treatment of refractory dermal melasma with the MedLite C6 Q-switched Nd:YAG laser: two case reports. J Cosmet Laser Ther 2010;12:126-31.
12. Kauvar AN. The evolution of melasma therapy: targeting melanosomes using low-fluence Q-switched neodymium-doped yttrium aluminium garnet lasers. Semin Cutan Med Surg 2012;31:126-32.
13. Goldberg DJ, Silapunt S. Histologic evaluation of a Q-switched Nd:YAG laser in the nonablative treatment of wrinkles. Dermatol Surg 2001;27:444-6.
14. Chan HH, Yang CH, Leung JC, Wei WI, Lai KN. An animal study of the effects on p16 and PCNA expression of repeated treatment with high energy and intense pulsed light exposure. Lasers Surg Med 2007;39:8-13.
15. Lee MC, Hu S, Chen MC, Shih YC, Huang YL, Lee SH. Skin rejuvenation with 1,064-nm Q-switched Nd:YAG laser in Asian patients. Dermatol Surg 2009;35:929-32.
16. Karabudak O, Dogan B, Baloglu H. Histologic evidence of new collagen formation using a Q-switched Nd:YAG laser in periorbital rhytids. J Dermatol Treat 2008;19:300-4.
17. Goh SH. A systematic protocol of the Q Switched Nd:YAG laser [Medlite 4 and C6] in aesthetic medicine. Proceedings of the anti-aging symposium; 2005 Sep 11; Taipei: Laser and Photonics Medicine Society of the R.O.C.; 2005. p.23.