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

Young Woon Park¹
Un Cheol Yeo²

¹Republic of Korea Army, Korea
²Jongno S&U Dermatologic Clinic, Seoul, Korea

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
**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 pathophysiologic 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, 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 COMPLICATIONS**

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
studies performed laser toning and described its effects as well as the complications including hypopigmentation, whereas Chan et al. reported patients who visited the authors for treatment of complications arising after laser toning procedures received elsewhere. The authors admit that they could not identify the treatment parameters (fluence, treatment endpoint, number of passes, spot size, etc.) used in other clinics. The studies on laser toning that were cited in these studies used high fluence levels around 3.5 J/cm$^2$ for laser toning and defined the end point as petechiae or pinpoint bleeding. Considering this, these treatments were performed during the time when the leading trend was to use a high fluence and high cumulative energy. As for the treatment interval, studies report a wide variety of intervals used and it is difficult to estimate an average interval duration. However, another study published by the same authors described a case of hypopigmentation developing after 4 weeks of daily treatments. Moreover, the daily treatment of 1,064 nm QS Nd:YAG laser was proposed by some clinicians in 2005. Based on these data, one can estimate that about 20-30 treatments could have been given with at most one-week intervals in the early days of laser toning. Although the authors did not provide the information on the treatment techniques as their patients had received the treatment elsewhere, but considering the trends of the time, a high fluence, high cumulative energy, excessive tissue response and frequent treatments might have been used in laser toning therapy.

If so, what would be the risk of hypopigmentation occurring as a complication of such a treatment method? Chan et al. examined patients who were referred due to complications and does not provide the total number of patients receiving laser toning. Therefore, the exact incidence of the hypopigmentation could not be identified. However it mentioned that there was “an approximately 10% risk of hypopigmentation from laser toning in Asian patients,” citing other studies that investigated the rate of hypopigmentation.

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 developed 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/cm$^2$. 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 treatment 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.

Cho et al., in 2009, reported that 2 out of 25 Korean patients developed hypopigmentation. The 1,064 nm QS Nd:YAG laser (MedLite C6) was used with the entire face surface (2 passes at a 6 mm spot size and 2.5 J/cm$^2$) and the parameters were changed for 2 more passes given only on melasma lesions (4 mm spot size, 4-5 J/cm$^2$). The treatment interval was 2-week. Judging from the local anesthesia used prior to treatment, they might use a very high fluence. Another study published in 2011 also reported of similar results. This study examined the patients who received laser toning in 2008 at a quite high fluence of 2-4 J/cm$^2$ over 10 weekly treatments. One out of 23 patients with melasma developed hypopigmentation.

Kim et al. reported some interesting results. This study focused on punctate leukoderma developing after laser toning treatments performed in 259 patients. With this large number of patients it provides sufficient statistical power to the rate of hypopigmentation. Also, it was written by the same authors who published the above-mentioned study, and we were able to compare the findings in two studies. In this study, the 1,064 nm QS Nd:YAG laser (MedLite C6) was used with 2-week intervals. Two passes at a fluence of 1.6 J/cm$^2$ and a 6 mm spot size were given over the entire face and two more passes were given only over melasma lesions at 2.2-2.5 J/cm$^2$, and a 4 mm spot size. Three (1.6%) out of 259 patients developed hypopigmentation. In this study, the parameters were maintained the same as the authors’ previous study, except for the fluence which was lowered to about 50-60% of that used in the previous study. It is interesting to note that the rate of hypopigmentation is much lower in this study. Although the fluence was lower than the previous studies, it was still higher than the levels normally used in today’s clinical practice (2.0 J/cm$^2$ or less).

Polnikorn reported the literature which has been extensively cited since its publication in 2008. The author reported two cases of intractable dermal melasma treat-
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. 11 Although the authors did not reveal the exact rate of hypopigmentation, they cautioned against overtreatment 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. 18 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. 19 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 study 20 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. 21 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.” 21 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)” 21 They added that theoretically, treating melasma with an “extremely low fluence (1 J/cm²)” may still be successful. 21

This opinion was shared by another review 22 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. 22

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. 23-25

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.,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/cm², and was followed by another pass at 6 mm, 3.5 J/cm². Then, several passes at 4 mm, 3.2 J/cm² 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 systemic 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.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/cm² 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.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.7,28 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.7-11 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**


