Efficacy of Combination Treatment with 1064-nm Low-Fluence Q-Switched Nd:YAG Laser (LFQSNY), 595-nm Pulsed Dye Laser (PDL), and Oral Tranexamic Acid for Melasma Complicated by Post-Inflammatory Hyperpigmentation and Hypopigmentation: A Case Report.

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Received: 18 December 2025; Accepted: 14 March 2025; Published: 30 April 2025

Abstract: Treatment for melasma remains challenging due to high recurrence rates and the adverse effects associated with available treatment options. This case report examines the efficacy of a combination therapy involving the 1064-nm Low-Fluence Q-Switched Nd:YAG laser (LFQSNY), 595-nm Pulsed Dye Laser (PDL), and oral tranexamic acid (TA) for managing melasma complicated by post-inflammatory hyperpigmentation (PIH) and hypopigmentation. A 53-year-old Chinese Malaysian woman with Fitzpatrick skin type III presented to the author's clinic with melasma complicated by PIH and hypopigmentation following an ablative laser procedure performed by a non-professional. She underwent 20 sessions of LFQSNY and PDL at 4- to 6-week intervals over a period of 1 year and 6 months. Oral TA was administered at 250 mg once daily for 6 months. Improvement was assessed using a skin analyzer and a modified Melasma Area and Severity Index (mMASI) score. The patient's melasma showed improvement. At the initial consultation, her mMASI score was 4.2, which reduced to 1.20 by the twentieth session. No deterioration in hyperpigmentation or hypopigmentation was observed, and no rebound melasma was reported throughout the treatment course. The combination of 1064-nm LFQSNY, 595-nm PDL, and oral TA appears to be a promising therapeutic option for melasma complicated by PIH and hypopigmentation. Further large-scale studies are essential to validate the efficacy and safety of this combination treatment in the Malaysian population.

Keywords: 1064-nm Low Fluence Q-Switched Nd:YAG laser, 595-nm Pulsed Dye Laser, Hypopigmentation, Melasma, Post-inflammatory hyperpigmentation

Introduction

Melasma, also known as chloasma, is a common pigmentary skin condition characterized by bilateral, irregular brown patches on facial areas frequently exposed to sunlight. [1]. While melasma does not cause physical pain, it often leads to considerable psychological distress due to its cosmetic impact. Sun exposure, genetic factors, and elevated estrogen levels are well-

established contributors to its development and persistence [2].

Melasma significantly impacts quality of life, often lowering self-esteem and causing feelings of frustration and embarrassment [3]. Studies have also found an association between melasma and depressive disorders [4-7]. Because melasma lesions typically appear on the face and are highly visible, they often cause significant stress, negatively affect daily life and emotional well-being, and frequently lead patients to seek dermatological care [8].

Treatment for melasma remains challenging due to its high recurrence rates and the adverse effects associated with available treatment options. Managing the condition can be difficult for both physicians and patients [9]. Melasma management has advanced over time, with available treatments ranging from topical agents to more advanced laser-based therapies. The low-fluence Q-switched Nd:YAG laser (LFQSNY), often referred to as laser toning, has been established as a new benchmark for melasma treatment in Asia. This laser uses low fluence (typically 1–3 J/cm^2), a large spot size, and a frequency of 5–10 Hz. The desired outcome of the procedure is to achieve faint erythema [10]. LFQSNY is recognized for its ability to selectively eliminate melanin in melanophores while sparing melanin-containing cells, resulting in safe depigmentation [11,12].

However, LFQSNY are not without adverse effect. The most frequent complications of LFQSNY include PIH, hypopigmentation, rebound hyperpigmentation, and melasma recurrence. Of these, hypopigmentation is often considered the most concerning [13]. To ensure safer and more effective clinical outcomes, LFQSNY is often combined with other treatment modalities in clinical practice [14,15].

Pulsed-dye laser (PDL), regarded as the gold standard for treating cutaneous vascular lesions [16], has also demonstrated effectiveness in managing melasma when combined with pigment-targeted therapies, as reported in several studies [17-20]. PDL operates on the principle of selective thermolysis, utilizing light to heat and destroy specific target structures. It emits pulses of visible light at wavelengths of 585 or 595 nm. PDL plays a crucial role in treating vascular conditions by delivering light energy at a wavelength that selectively targets oxyhemoglobin. Its precision ensures minimal or no damage to surrounding tissues, effectively eliminating only the targeted vessels. Over time, the damaged vessels are absorbed by the body, leading to a reduction in symptoms caused by abnormal vasodilation or the overgrowth of cutaneous vessels [21], both of which play key roles in the development of PIH.

Tranexamic acid (TA) has been used for melasma treatment either as monotherapy or in combination with other therapies. It is a synthetic derivative of the amino acid lysine, binding to lysine sites on plasminogen and blocking its activation to plasmin. This, in turn, inhibits melanogenesis [22]. TA has been reported to improve melasma when used either orally or topically [23,24]. TA suppresses angiogenesis and neovascularization induced by basic fibroblast growth factor, helping to reduce both erythema and pigmentation [25]. Its anti-angiogenic effect is thought to result from lowered expression of vascular endothelial growth factor and endothelin-1, key elements in the vascular theory of melasma pathogenesis [26]. Various routes of TA administration, including oral intake, intradermal injections, microneedling, iontophoresis, and topical application, have been employed in the treatment of melasma [27]. However, studies indicate that oral TA is more effective and preferable for managing melasma compared to other routes [28].

The optimal treatment strategy can be achieved by combining multiple approaches to address several factors, such as using topical agents to inhibit melanin production and transfer to keratinocytes, along with laser or light therapies to enhance melanin clearance [29]. Therefore, this case report will assess the efficacy and safety of treating a Malaysian patient with

melasma complicated by PIH and mottled hypopigmentation using a combination of 1064-nm LFQSNY, 595-nm PDL, and oral TA.

Case Presentation

This case report presents a 53-year-old Chinese woman with melasma complicated by both hyperpigmentation and hypopigmentation following six sessions of monthly ablative laser therapy administered by a beautician for facial melasma treatment. She has no pre-existing medical conditions and no personal or family history of vitiligo, though her mother has melasma. After each treatment session by the beautician, she experienced skin irritation lasting over a week, which worsened with sun exposure. Otherwise, she was in good systemic health.

Her initial consultation took place when she noticed mottled hypopigmentation on her cheek area. Upon examination, bilateral malar melasma was observed, along with PIH and several areas of mottled hypopigmentation. No dyspigmentation was noted on the forehead or chin. Skin analysis using the ISEMECO® S7 device (Guangzhou Newlife New Material Co., Ltd., Guangzhou, China) revealed more distinct areas of hyperpigmentation and hypopigmentation, as well as an inflamed skin base **(Figure 2).**

Management and Outcome

The patient received a combination of LFQSNY and PDL treatments, along with oral tranexamic acid, for her melasma complicated by post-inflammatory hyperpigmentation and hypopigmentation. The LFQSNY (Spectra XT™, Lutronic Corporation, Korea) was set with a fluence of 0.7 J/cm², a frequency of 10 Hz, and a spot size of 8 mm, with 3 passes per session. The 595 nm PDL (Spectra XT™, Lutronic Corporation, Korea) was set with a fluence of 0.24 J/cm², a frequency of 2 Hz, and a spot size of 5 mm, with 1 pass per session. Both lasers were administered for a total of 20 sessions, conducted at 4- to 6-week intervals over a period of 1 year and 6 months. She was also prescribed oral tranexamic acid at a dosage of 250 mg once daily for 6 months, starting from the second session and continuing until the eighth session. Although she was advised to begin oral tranexamic acid at the initial treatment session, the patient gave consent only at the second session.

Improvement of melasma was assessed using the modified Melasma Area and Severity Index (mMASI). At the initial consultation, the mMASI score was 4.2. By the tenth session, notable improvement was observed, with the score reduced to 2.40. Further progress was seen at the twentieth session, culminating in a final mMASI score of 1.20 **(Table 1).** Hyperpigmentation of the bilateral malar region improved after five sessions of combined treatment with PDL, LFQSNY, and oral tranexamic acid, with no new cases of PIH, hypopigmentation, or rebound melasma.

Along with the improvements in melasma, both PIH and hypopigmentation showed enhancement. However, it is important to note that complete resolution of all hypopigmentation was not achieved, although considerable progress was observed throughout the treatment regimen **(Figure 1).**

Figure 1. Clinical photographs of the patient at the 1st (A), 5th (B), and 8th (C) treatment sessions, showing front, left, and right views. Improvement in hyperpigmentation was observed by the 8th session.

Table 1. mMASI score of the patient.

Session	mMasi score
1	4.2
5	3.6
8	2.4
10	2.4
15	2.4
18	2.4
20	1.2

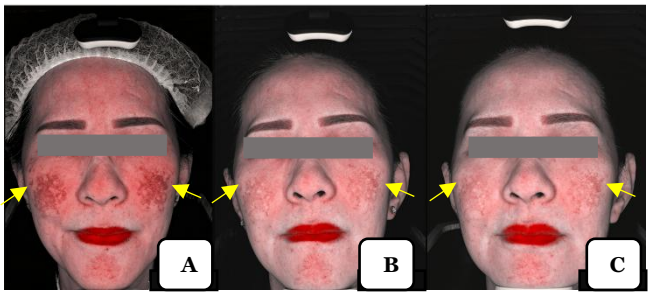

Figure 3. ISEMECO® AI skin analysis images at the 1st (a), 5th (b), and 8th (c) treatment sessions. Yellow arrows indicate areas of inflammation. Progressive improvement in inflamed areas was observed over the course of the 8 sessions.

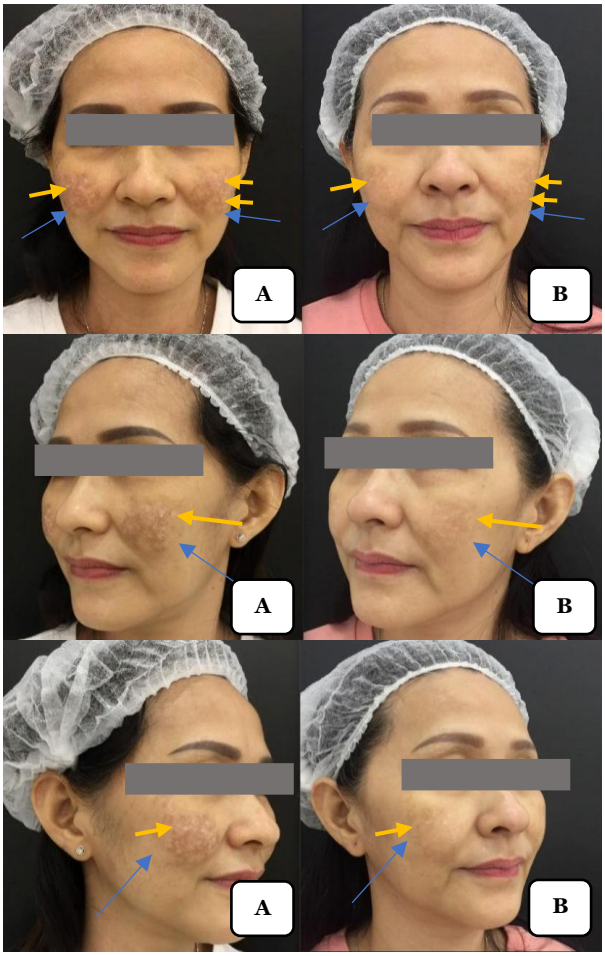

Figure 2. Clinical photographs of the patient at the 1st session (A) and 20th session (B), showing front, left, and right views. Blue arrows indicate areas of hyperpigmentation; yellow arrows indicate areas of hypopigmentation. Improvement in both hyperpigmentation and hypopigmentation was observed after the 20th session.

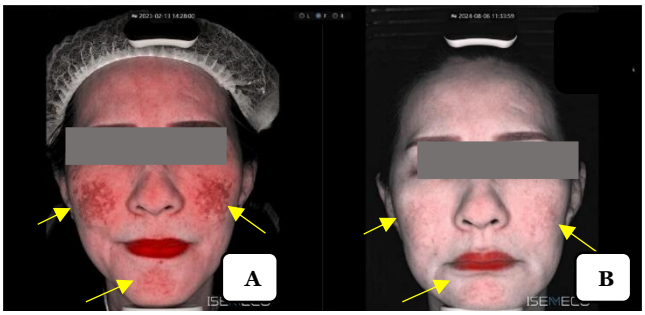

Figure 4. ISEMECO® skin analysis infrared images at the 1st session (A) and 20th session (B). Yellow arrows indicate areas of inflammation. Notable improvement in skin inflammation was observed after the 20th session.

Discussion

LFQSNY as treatment of melasma has shown promising results [30-32]. However, the risk of developing hypopigmentation remains a significant concern with this treatment, as spontaneous recovery is rare [33]. Furthermore, in contrast to other complications, certain hypopigmented lesions may persist permanently despite prolonged and active repigmentation treatments [31-36].

Combination therapy may enhance clinical efficacy and reduce the adverse effects associated with LFQSNY treatment. Therefore, in this case report, the author aims to evaluate the safety and efficacy of combination therapy involving LFQSNY, PDL, and oral TA. The patient in this case report presented with melasma, along with PIH and hypopigmentation resulting from ablative laser treatment performed by a non-professional. Furthermore, skin analysis revealed significant inflammation. Therefore, in addition to targeting melasma, incorporating therapy that addresses the vascular component would be particularly beneficial for this patient.

Patient have shown improvement combined treatment with PDL, LFQSNY, and oral TA, with no new cases of PIH, hypopigmentation, or rebound melasma. Combining therapy with different targeted approach might be the possible reason for patient improvement in this case report.

Increased vascularity may significantly contribute to the pathogenesis of melasma and the development of PIH following laser therapy, through the elevated release of cytokines and soluble factors from proliferating vessels [37]. According to Kong et al., using lasers such as PDL to target blood vessels could reduce melanocyte stimulation and help prevent relapse. Therefore, by addressing both melanin and vascular components, the combination of PDL with LFQSNY may offer an effective and promising treatment strategy for melasma [16].

Additionally, the inclusion of oral tranexamic acid (TA) could further enhance treatment efficacy in this patient, as a study found that oral TA improves the effectiveness and reduces the side effects of LFQSNY therapy [38]. Besides melasma, TA has also shown effectiveness in treating other hyperpigmentation disorders, including PIH [39].

Therefore, by addressing melanin production, vascularization, and PIH in the patient, the combination of LFQSNY with PDL and oral TA could provide an effective treatment strategy for melasma complicated by PIH and hypopigmentation. However, despite improvements in the pigmented lesions, the hypopigmentation was not fully resolved, although some progress was observed throughout the treatment course.

Conclusion

In conclusion, the combination of 1064-nm LFQSNY, 595-nm PDL, and oral TA demonstrated promising results in treating melasma complicated by PIH and hypopigmentation, with no observed worsening of PIH, hypopigmentation, or rebound melasma. Nevertheless, further large-scale studies are warranted to confirm the efficacy and safety of this combination approach in the Malaysian population.

Acknowledgement

I would like to acknowledge with thanks to Prof Adibah Hanim binti Ismail@Daud, Dr Nicole Ng I, and everyone who have directly and indirectly guided me in medical aesthetic training. I would also like to express my gratitude to UR Klinik for giving me this opportunity in conducting and writing this report.

Potential Conflict of Interest

The author declares no potential conflict of interest.

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