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Combined Efficacy of Q-Switched 785 nm Laser and Tranexamic Acid Cream in the Treatment of Melasma: A Prospective Clinical Study

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Abstract: *Background and Objectives*: Melasma, a hypermelanotic dermatologic condition that mainly affects women, poses challenges due to its complex etiology involving environmental and genetic factors. Its pathophysiology, marked by intricate histological changes, is not fully understood. This study explored the efficacy and safety of a new 785 nm picosecond laser in treating facial melasma. *Materials and Methods*: An 11-participant cohort, comprising women with Fitzpatrick phototypes II-III, underwent a treatment protocol with a new 785 nm picosecond laser. The clinical evaluation used the Global Aesthetic International Score (GAIS) and the Five-Point Likert Scale Questionnaire. The aim of the study was to understand the capacity of the 785 nm wavelength laser to interact with both the pigmentary and vascular components of melasma. *Results*: The GAIS outcomes revealed excellent (18.2%), good (54.5%), poor (18.2%), and no results (9.1%). The Likert Scale responses varied from very satisfied (18.2%) to slightly satisfied (9.1%). Clinical images at three months demonstrated resolution of melasma with no adverse events. *Conclusions*: This non-invasive procedure showed positive outcomes and high patient tolerance, emphasizing its potential in melasma management. However, in order to fully understand the interactions of pigmentary and vascular components with the 785 nm wavelength laser, further research is required. The small cohort represents a limitation for this study, therefore studies that include a larger number of patients are needed to assess the effectiveness of this laser treatment for facial melasma.

Keywords: melasma; laser; skin pigmentation; facial melasma resolution

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1. Introduction

Melasma is an acquired hypermelanotic condition that appears as irregular brown macules on sun-exposed areas such as the face, and results from a combination of environmental and genetic factors. [1,2]. This dermatological condition is more prevalent in Asian women and darker skin types in their thirties and forties [3].

Cellular interactions, gene abnormalities, and neovascularization complicate melasma's treatment, contributing to recurrence and requiring targeted interventions [4]. Histological analysis shows increased VEGF synthesis, inflammatory mediators, and melanin phagocytosis in melasma lesions, contributing to persistent pigmentation [5]. Patients often experience negative psychological effects, impacting their quality of life. Common treatments include topical therapies, chemical peels, and laser technologies. Currently, no

therapy completely alleviates melasma, but laser treatments are effective for refractory cases [6]. The five main laser therapies are QS lasers, IPL, non-ablative and ablative lasers, and picosecond lasers [7]. Picosecond lasers, operating with ultrashort pulses, effectively target pigmentary alterations [8–10]. Laser therapy targets chromophores, minimizing tissue damage and enhancing efficacy and safety. A 785 nm picosecond laser offers heightened peak temperatures with reduced risk of thermal injury [11]. IPL, for instance, targets pigmentation and vascular irregularities, while non-ablative lasers stimulate collagen and disperse pigment. A novel 675 nm non-ablative laser showed promise in treating melanin-based conditions [12]. Fractional ablative lasers create microthermal zones, stimulating a repair response that is effective for scars and melasma [13]. Through this investigative study, our intention was to introduce a novel indication for a laser device emitting light at a wavelength of 785 nm, emitted in a Q-switched picosecond modality. This specific wavelength is highly absorbed by dermal and epidermal melanin and blood vessels, which are all involved in the formation of melasma. The study aimed to assess the 785 nm laser's effectiveness in treating both pigmentary and vascular components of melasma. Furthermore, the ultrashort pulse duration helps to protect the surrounding non-lesional skin from damage. These factors support the efficacy and safety of the 785 nm laser in melasma management.

2. Materials and Methods

2.1. Study Population

For this investigation, a cohort comprising 11 participants was selected. The chosen individuals exhibited Fitzpatrick phototypes spanning from II to III, representing a spectrum of skin pigmentation characteristics. The study cohort exclusively comprised female participants, ranging in age from 34 to 47 years. This gender and age homogeneity was intentional to ensure a more focused exploration of the effects and outcomes within a specific demographic subset, specifically women in their mid-thirties to late forties.

2.2. Study Device

In this study, a specialized picosecond laser handpiece was employed, featuring a wavelength emission of 785 nm and powered by a Q-switched laser (El.En Group, Florence, Italy). This handpiece, designed for addressing superficial facial melasma, exhibits versatility by offering the option of equipping a contact sensor. This sensor served a dual purpose, ensuring not only optimal device performance, but also enhancing safety during the treatment process. The incorporation of such technology aligns with the overarching objective of enhancing precision, efficacy, and safety in the application of laser therapy for the targeted treatment of superficial facial melasma.

2.3. Study Protocol

The treatment protocol adhered to specific parameters, wherein the spot size ranged between 2 and 6 mm, the fluence varied from 0.4 to 3 J/cm^2, and the frequency was set between 1 and 5 Hz. To achieve the desired outcome, multiple passes (ranging from 2 to 3) were executed, continuing until the visual whitening of the treated lesion was achieved. The treatment regimen comprised a total of four laser sessions, each spaced at intervals of 6–8 weeks, allowing for the complete recovery of the skin from the preceding therapeutic intervention. Additionally, complementary home therapy was integrated into the protocol, involving the application of a lightening cream containing tranexamic acid (Kromia liposomal emulsion, FB Dermo, Milan, Italy). Three months after the final laser treatment, a conclusive evaluation was conducted, complemented by follow-up visits to ascertain the sustainability of the outcomes and the long-term impact of the combined therapeutic modalities on the melasma-affected skin. This structured treatment plan uses a multifaceted approach, integrating in-office laser sessions and at-home therapy, reflective of a comprehensive strategy to optimize results and uphold the long-term well-being of the patients undergoing treatment for facial melasma.

2.4. Clinical Evaluation

The assessment of treatment outcomes employed a comprehensive approach, utilizing the Global Aesthetic International Score (GAIS) on a 5-point scale (ranging from 0 to 4). This scale facilitated a nuanced evaluation of the overall improvement in the treated area, delineated as follows: 0—no change/worsening; 1—0–25%, mild improvement; 2—25–50%, moderate improvement; 3—50–75%, good improvement; and 4—75–100%, excellent improvement. The assessment of these improvements was carried out by a team of five physicians who are experts in dermatology and aesthetic medicine, who were blinded to the treatment details to ensure a professional and unbiased evaluation. To assess the patients' comfort and satisfaction levels, a Five-Point Likert Scale Questionnaire was employed at the 3-month follow-up (FU). This instrument quantified the satisfaction levels on a scale from 0 to 4 (0 = worse; 1 = little satisfaction or not satisfied; 2 = fairly satisfied; 3 = satisfied; and 4 = very satisfied). The multifaceted evaluation sought to capture not only the clinical efficacy of the treatment but also the subjective experiences and contentment of the patients. Throughout the follow-up period, the patients were diligently monitored to discern both the enduring benefits and any potential undesired effects arising from the treatment. This vigilant observation was instrumental in understanding the long-term impact and safety profile of the therapeutic interventions. In tandem with the assessments, a visual record of the treatment process and its aftermath was meticulously documented. Clinical photographs, captured under visible light, were taken during the treatments as well as during subsequent follow-up visits. These images served as a valuable tool for objectively evaluating the procedural outcomes and identifying any potential side effects. This comprehensive evaluation framework, blending subjective patient satisfaction metrics with objective clinical assessments, underscores the commitment to a thorough understanding of the treatment's efficacy, safety, and long-term implications.

3. Results

The analysis of the Global Aesthetic International Score (GAIS) outcomes disclosed predominantly positive findings within the study cohort. Specifically, the outcomes were categorized as follows: excellent results were noted for two patients, constituting 18.2% of the study population; good results were observed for six patients, accounting for 54.5%; poor results were reported for two patients, representing 18.2%; and for one patient, there were no discernible results, representing 9.1% of the study group. As per the outcomes derived from the Five-Point Likert Scale Questionnaire, a varied range of patient satisfaction was observed. Specifically, 18.2% of the participants (two patients) were classified as Very Satisfied, reflecting a high level of contentment. A substantial majority, constituting 63.6% (seven patients), fell under the category of satisfied. Additionally, 9.1% (one patient) expressed fairly satisfied sentiments, while an equal proportion, also at 9.1% (one patient), indicated a lower degree of satisfaction, characterized as slightly satisfied. At the three-month follow-up, the clinical images substantiated a near-complete resolution of melasma, estimated to be approximately 75–95%, marked by the absence of any discernible adverse events (see Figure 1). This confirmation not only underscores the efficacy of the applied therapeutic interventions but also bolsters the assurance of a favorable safety profile for the treatment protocol.

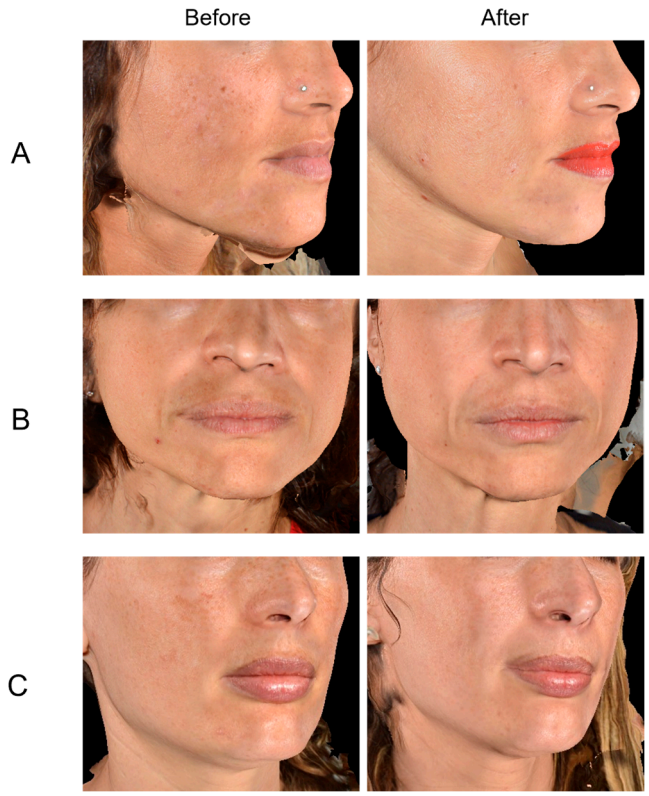

Figure 1. Clinical pictures were acquired with the QuantifiCare system (Biot, France). They show the pre-and post-treatment images of three patients included in the study. They were treated for superficial facial melasma with the 785 nm wavelength laser. (**A**) Melasma on the cheek. (**B**) Melasma on the upper lip area. (**C**) Melasma on the cheeks and nose. After the treatment, there was a near-complete (75–95%) resolution of melasma symptoms.

4. Discussion

Melasma stands out among hyperpigmentary disorders due to its dual presentation involving both pigmentary and vascular components, rendering it arguably the most complex condition within this category. The etiology of melasma remains incompletely understood, adding to its complexity. The microvascular network involved in melasma exhibits a unique and relatively straightforward anatomical structure. Capillaries, which solely comprising an outer basal membrane (BM or basal lamina) and an inner monolayer of endothelial cells, are seemingly uncomplicated but contribute significantly to the overall complexity of melasma's pathophysiology. The basal membrane (BM), a critical component in the microvascular architecture, constitutes a specialized layer of the extracellular matrix (ECM), with a thickness ranging between 50 and 100 nanometers. This ECM is predominantly composed of laminin and type IV collagen. Acquired hyperpigmentations and congenital ones are usually treated with Q-switched lasers that use different wavelengths and target specifically epidermal and dermal pigmentations; in general, acquired pigmentations tend to have better results than the congenital ones. Q-switched laser treatment is typically well tolerated. The side effects may include pain, erythema, edema, pinpoint bleeding, crusting, blistering, scarring, and post-inflammatory hyperpigmentation. Recent studies showed the effectiveness of lasers in brown epidermal lesions, with better results when treating the extremities or the trunk and lighter phototypes [14]. In our study, the rationale behind employing 785 nm wavelength light was grounded in the strategic objective of optimizing melanin absorption while minimizing interference from blood absorption. This wavelength selection aimed to enhance the specificity of the therapeutic intervention by prioritizing melanin as the primary target for effective treatment. Several approaches have demonstrated notable success in the treatment of melasma, albeit often accompanied by

protracted recovery periods, impeding the immediate resumption of normal activities. Devices emitting light at 730 nm present potential advantages for treating lightly pigmented lesions, while those emitting at 785 nm may be preferred for darker lesions and skin types. This preference stems from the anticipation of a 30% greater melanin absorption coefficient at 730 nm compared to 785 nm, underscoring the importance of wavelength selection in optimizing treatment specificity. Furthermore, the utilization of wavelengths such as 730 nm and 785 nm may be deemed more advantageous in comparison to 1064 nm and 532 nm when specifically targeting skin pigment. This preference is rooted in melanin's inherent proclivity for absorption over hemoglobin, as elucidated by previous research [15]. On the other hand, the investigations of Nisticò et al. (2021) [14] and Silvestri et al. (2021) [16] have underscored the efficacy of Q-switched 1064/532 nm laser systems in the treatment of hyperpigmentation. Interestingly, the research conducted by Cannarozzo et al. [17] shed light on the notable improvement in melasma when utilizing a picosecond laser with a 1064 nm wavelength, particularly in darker phototypes such as Asians. This specific modality not only proved to be safe and well-tolerated by patients, but also exhibited a diminished risk of post-inflammatory hyperpigmentation, while acknowledging the inherent challenge of achieving complete resolution. The consideration of wavelengths, as highlighted in the studies, showcases a meticulous approach to treatment, aiming for enhanced specificity in targeting melanin absorption while mitigating potential risks associated with different skin types. Indeed, despite the apparent superiority of this particular laser in comparison to other laser modalities, further studies are needed as the physical treatment of melasma continues to be a subject of contention and debate within the scientific literature [18–20]. For this reason, and given the complicated nature of melasma, achieving an optimal therapeutic outcome may necessitate the integration of diverse treatment modalities. Behavioral methods such as sun avoidance and the use of appropriate sunscreens are mandatory.

General medical advice should include rigorous daily sun protection and the incorporation of a tinted sunscreen with topical bleaching agents, which may have a different action on melanogenesis. Physical treatments and procedures are also useful in the management of melasma. Microneedling is a low-cost technique with few adverse effects that complements topical treatments. Chemical peels act mainly via epidermal renewal. Cosmetic interventions may include depigmenting products, stringent photoprotection measures, and chemical interventions like topical tranexamic acid and various chemical peeling treatments [21,22]. In severe and/or resistant cases, oral drugs should be prescribed. Tranexamic acid has the best evidence for treating melasma; however, it is a thrombophilic drug and thus should be prescribed to select patients. There is also accumulating evidence for the use of pycnogenol as a systemic adjuvant in the treatment of melasma [23,24].

Employing a comprehensive strategy that combines various therapeutic elements should be used to address the diverse aspects of melasma, potentially enhancing treatment efficacy and promoting a more holistic resolution of the condition.

5. Conclusions

There is ongoing research exploring new treatments targeting oxidative stress, melanogenesis, and autophagy induction. Sun protection and treatments targeting melanogenesis and dermal repair are central to the current strategies. Lasers may be used to target different chromophores at various levels of depth. Long-pulsed lasers may cause burns or scarring through prolonged heating. Q-switched lasers use ultrashort pulses in terms of nanoseconds or picoseconds. The release of the energy is limited to the target, and side effects are minimal. Lasers that target water, such as Erbium and CO_2 lasers, have an ablative effect and are widely used in dermatological surgery procedures. In fractional mode, these devices have been used to treat various conditions, including signs of photoaging. The safety and efficacy of intense pulsed light, Q-switched lasers, and non-ablative fractional lasers for melasma have been well described in many studies and systematic reviews [25]. In this study, our intention was to introduce a novel indication for a laser device emitting light at a wavelength of 785 nm in a Q-switched modality. This specific wavelength is

highly absorbed by dermal and epidermal melanin and blood vessels, which are all involved in the formation of melasma. The ultrashort pulse duration ensures selective action with minimal side effects, effectively targeting both pigmentary and vascular components. With minimal side effects, this treatment could be combined with other therapies, though further studies are needed. The patients showed a high tolerance to and satisfaction with the treatment. This noteworthy outcome was consistent across patients, independent of their skin phototype. Further research is needed to understand the interaction between pigmentary and vascular components and the 785 nm wavelength laser. Increasing the number of participants is necessary to strengthen the results. Enlarging the patient cohort will contribute to a more comprehensive evaluation, allowing for a better understanding of the laser's effectiveness in the treatment of facial melasma. Future research should include larger, more diverse populations for more generalizable results.

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