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Original Article

Value of Q-switched 755-nm alexandrite laser combined with topical tranexamic acid in the treatment of melasma

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Abstract: Objective: To explore the clinical value of Q-switched 755-nm alexandrite laser combined with topical tranexamic acid in treating melasma. Methods: A total of 121 melasma patients treated at AIST Medical Cosmetology Hospital from July 2022 to January 2024 were retrospectively included. They were divided into two groups: the Laser Treatment Group (LTG, n=61), receiving Q-switched 755-nm alexandrite laser combined with topical tranexamic acid, and the Control Treatment Group (CTG, n=60), receiving only topical tranexamic acid. Clinical efficacy, skin scores before and after treatment, laboratory indicators, melanin index, dermoscopic scores for pigmentation and vascular components, dermoscopic typing improvement, adverse reactions, and recurrence rates were compared. Results: The treatment efficacy rate was 93.44% in the LTG, significantly higher than 81.67% in the CTG ($P<0.05$). After treatment, the LTG showed significantly lower Melasma Area and Severity Index (MASI) scores, skin lesion color, and area scores compared to the CTG (all $P<0.05$). No significant differences were found in malondialdehyde (MDA) and superoxide dismutase (SOD) levels (both $P>0.05$). The LTG had a lower melanin index and dermoscopic scores for telangiectasia and perifollicular pigmentation than the CTG (all $P<0.05$). The incidence of adverse reactions in the LTG was 11.48%, significantly lower than 40.00% in the CTG ($P<0.05$). The LTG also had a lower recurrence rate of 1.64% at 6-month follow-up, compared to 10.00% in the CTG ($P<0.05$). Conclusion: Q-switched 755-nm alexandrite laser combined with topical tranexamic acid is highly effective in treating melasma, improving clinical symptoms, reducing oxidative stress and inflammation, and yielding better results in vascular proliferation and pigmentation. The treatment also demonstrated a low recurrence rate, suggesting its potential for broader use.

Keywords: Melasma, Q-switched 755-nm alexandrite laser, tranexamic acid, combined treatment, clinical efficacy, oxidative stress

Introduction

Melasma is a chronic, acquired pigmentation disorder characterized by excessive melanin deposition in the epidermis and dermis, presenting as irregular light or dark brown patches on the cheeks, forehead, and jaw [1, 2]. The global prevalence of melasma is approximately 1%, with higher rates in high-risk populations, ranging from 9% to 35%. Among Asian women of childbearing age, the prevalence is around 30%, and in areas with intense sunlight, it may exceed 50% [3, 4].

The exact etiology and pathogenesis of melasma remain unclear, though it is believed to be influenced by genetic factors, ultraviolet radiation, and sex hormones. As such, treatment should be tailored to the patient's specific stage and classification. Current treatment principles focus on reducing melanin production, repairing the skin barrier, preventing photoaging, enhancing vascularization, and addressing inflammation [5, 6]. Tranexamic acid, a synthetic lysine derivative, competes with tyrosine to inhibit its catalytic activity, thereby reducing melanin production and helping to alleviate melasma [7, 8]. Recent studies have shown that tranexamic acid can inhibit dermal angiogenesis, reduce mast cell numbers, protect the basement membrane, and repair the compromised stratum corneum barrier [7, 9]. However, melasma is challenging to treat with monotherapy. While early treatment often leads to rapid lesion reduction, long-term use can result in resistance and relapse [10].

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This study found that the Q-switched 755-nm alexandrite laser, which works through subcellular selective photothermolysis, can disrupt melanin particles with low-fluence light, facilitating their phagocytosis and expulsion, thereby effectively treating melasma [5]. Few studies have investigated the combined use of tranexamic acid and the Q-switched 755-nm alexandrite laser for melasma treatment. This study uses skin scores and laboratory indicators to confirm the clinical value of the combined intervention, offering theoretical insights into melasma treatment.

Materials and methods

Study design and patient inclusion and exclusion

This retrospective study was approved by the Ethics Committee of AIST Medical Cosmetology Hospital. The study period spanned from July 2022 to January 2024, with a 6-month follow-up for the included patients, concluding in July 2024. Clinical data were collected using the electronic medical record system of AIST Medical Cosmetology Hospital, focusing on patients diagnosed with melasma according to the diagnostic criteria in the "Consensus on Diagnosis and Treatment of Melasma in China (2021 version)" [11]. A total of 184 patients were initially selected and screened based on the following inclusion and exclusion criteria:

Inclusion criteria: (1) Patients who had not undergone other treatments within three months prior to enrollment; (2) Patients who adhered to a single treatment regimen throughout the study (either tranexamic acid alone or tranexamic acid combined with laser therapy); (3) Patients who completed a six-month follow-up; (4) Patients with complete baseline data, including disease duration, age, Fitzpatrick skin type, type of melasma, clinical efficacy, skin-related scores before and after treatment (Melasma Area and Severity Index (MASI), skin lesion color, and area scores), laboratory indicators before and after treatment (malondialdehyde (MDA) and superoxide dismutase (SOD)), skin melanin index before and after treatment, dermoscopic scores for pigmentation and vascular components, incidence of adverse reactions, and recurrence at six-month follow-up.

Exclusion criteria: (1) Patients with concurrent pigmentary skin conditions (e.g., vitiligo, brown or green spots); (2) Patients who had taken photosensitive medications or experienced photosensitive disorders within the past three months; (3) Pregnant or lactating women; (4) Patients with infectious diseases or scar constitutions; (5) Patients with incomplete information.

Based on these inclusion and exclusion criteria, 121 patients were selected from the original 184 and were divided into two groups based on their treatment regimen: the Control Treatment Group (CTG, n=60), receiving topical tranexamic acid twice daily for eight consecutive weeks, and the Laser Treatment Group (LTG, n=61), receiving Q-switched 755-nm alexandrite laser combined with topical tranexamic acid. The laser therapy was administered once every four weeks for a total of six sessions, in accordance with the safety guidelines outlined in the "Laser Treatment Equipment-Pulsed CO2 Laser Therapy Machines" specifications of the pharmaceutical industry standards of the People's Republic of China.

For patients undergoing tranexamic acid treatment, precautions included avoiding prolonged sun exposure, refraining from driving or engaging in high-altitude tasks after administration, regularly monitoring blood parameters to reduce the risk of thromboembolic events, and avoiding concurrent use of glucocorticoids or nonsteroidal anti-inflammatory drugs. For those receiving combined therapies, additional measures included maintaining proper skin hygiene, hydration, and sun protection following laser treatment to prevent pigmentation. Mild pain post-treatment is expected; however, if severe pain, redness, or swelling occurs, patients should promptly seek follow-up care.

Data collection

This study is a retrospective analysis. Prior to its initiation, the sample size was estimated using the formula for comparing the means of two populations in medical statistics:

$$N = \frac{2\delta^2 (t_a + t_\beta)^2}{(\mu_1 - \mu_2)^2}.$$

Here, δ represents the standard deviation of the two populations, typically chosen as the larger of the two sample deviations. The means

of the populations, μ1 and μ2, are estimated using sample means. With a test power of 0.8 and a significance level of α=0.05, the minimum required sample size per group was estimated to be 50 subjects.

Data were collected from 121 patients, including baseline clinical data (age, disease duration, Fitzpatrick classification, type of melasma, treatment history, dermoscopic classification, family history), clinical efficacy (defined as significant improvement with a post-treatment MASI score reduction of ≥50%, effective with a reduction of 10%-49%, and ineffective with a reduction of <10%) [12], skin-related scores (including MASI score, skin lesion color score, and lesion area score, with the MASI assessing both the area of involvement and pigmentation darkness, the lesion area score subdivided into four regions such as forehead and chin, and scores ranging from 0-6 for area and 0-4 for pigmentation darkness), laboratory indicators (blood samples were collected for SOD and MDA levels before treatment and at the end of treatment), melanin index (measured using a Mexameter MX 18 to determine pre- and post-treatment melanin levels), and dermoscopic scores for pigmentation and vascular components [13] (pre- and post-treatment dermoscopic scores were collected, including pseudoreticular network, globular pattern, dot pattern, arcuate pattern, telangiectasia, and perifollicular pigmentation, with each dimension scored from 0-3, where higher scores indicate more severe symptoms). Additionally, the incidence of adverse reactions (including pigmentation, blisters, erythema, and desquamation) was recorded, as well as recurrence during follow-up (the recurrence of melasma was documented during a 6-month follow-up period).

Outcome measures and statistical methods

A total of 121 patients were included in this study. The primary hypothesis was that patients in the LTG, receiving Q-switched 755-nm alexandrite laser therapy combined with topical tranexamic acid, would demonstrate superior treatment efficacy compared to those in the CTG, who received topical tranexamic acid alone. After treatment, the LTG was expected to show lower skin-related scores and melanin index compared to the CTG, along with reduced levels of SOD and MDA. Additionally, dermoscopic features in the LTG were anticipated to improve, with the combined treatment proving to be safe and resulting in a lower recurrence rate during follow-up.

Data collection was performed using EXCEL 2022, and data analysis was conducted with Statistical Package for the Social Sciences (SPSS) 26.0. Measurement data were normally distributed and expressed as mean ± standard deviation (mean ± SD). Inter-group differences at the same time points were compared using the independent samples t-test, while intra-group comparisons were made using the paired samples t-test. Count data were presented as rates, and inter-group differences were analyzed using the chi-square test. A *P*-value of less than 0.05 was considered statistically significant.

Results

Comparison of general clinical data between the two groups

There were no statistically significant differences in general clinical data between the two groups, including age, disease duration, Fitzpatrick classification, type of melasma, treatment history, dermoscopic classification, and family history (all P>0.05) (**Table 1**).

Comparison of clinical efficacy between the two groups

In the LTG, there were 22 cases with significant improvement, 35 effective cases, and 4 ineffective cases, resulting in an overall efficacy rate of 93.44% (57/61), significantly higher than 81.67% (49/60) in the CTG (P<0.05) (**Figure 1**).

Comparison of skin-related scores between the two groups before and after treatment

There was no statistically significant difference in MASI scores between the two groups before treatment (P>0.05). However, after treatment, the MASI scores in the LTG were significantly lower than those in the CTG (P<0.05) (**Figure 2**). Similarly, there were no significant differences in skin lesion color and area scores between the two groups before treatment (P>0.05). However, after treatment, the LTG showed significantly lower skin lesion color and area scores compared to the CTG (P<0.05) (**Figures 3** and **4**).

Table 1. Comparison of general clinical data between the two groups (mean ± SD)/[n (%)]

General clinical data		LTG (n=61)	CTG (n=60)	t/χ^2	*P*
Average age (years)		36.59±6.59	37.56±8.11	0.723	0.471
Average course of disease (years)		8.69±2.51	8.99±3.65	0.528	0.599
Fitzpatrick classification	Type II	10 (16.39)	6 (10.00)	1.298	0.523
	Type III	26 (42.62)	30 (50.00)		
	Type IV	25 (40.98)	24 (40.00)		
Melasma type	Butterfly-shaped	31 (50.82)	28 (46.67)	0.236	0.816
	Centrofacial	15 (24.59)	13 (21.67)		
	Mandibular	14 (22.95)	15 (25.00)		
	Generalized type	1 (1.64)	4 (6.67)		
Treatment history	Hydroquinone Cream	7 (11.48)	5 (8.33)	0.334	0.563
	Chemical peel	2 (3.28)	1 (1.67)	0.325	0.569
	Tranexamic acid tablets	8 (13.11)	5 (8.33)	0.721	0.396
	Isotretinoin	1 (1.64)	2 (3.33)	0.359	0.549
Dermoscopic classification	Epidemal type	26 (42.62)	25 (41.67)	0.076	0.963
	Dermal type	11 (18.03)	12 (20.00)		
	Mixed type	24 (39.34)	23 (38.33)		
Family history	Yes	23 (37.70)	20 (33.33)	0.252	0.615
	No	38 (62.30)	40 (66.67)		

Note: LTG: Laser Treatment Group; CTG: Laser Treatment Group.

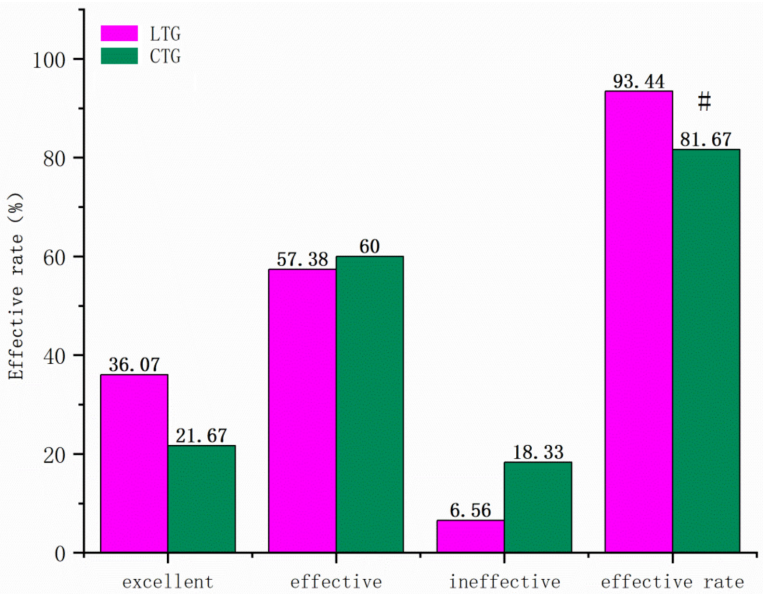

Figure 1. Comparison of clinical efficacy between the two groups. The overall treatment efficacy rate in the LTG was 93.44% (57/61), higher than 81.67% (49/60) in the CTG ($P<0.05$). # represents a statistically significant difference between groups. Note: LTG: Laser Treatment Group ($n=61$); CTG: Control Treatment Group ($n=60$).

Comparison of laboratory indicators between the two groups before and after treatment

There were no statistically significant differences in SOD and MDA levels between the two groups before treatment (both P>0.05). At three months after treatment, no significant differences in MDA and SOD levels were observed between the LTG and CTG (**Figure 5**, both P>0.05).

Comparison of melanin index between the two groups before and after treatment

Before treatment, there was no statistically significant difference in melanin index between the two groups (P>0.05) (**Figure 6A**). After treatment, the melanin index in the LTG was significantly lower than in the CTG (P<0.05) (**Figure 6B**).

Comparison of dermoscopic scores for pigmentation and vascular components between the two groups before and after treatment

Before treatment, there were no significant differences in the pseudoreticular network, globular pattern, dot pattern, arcuate pattern, telangiectasia, and perifollicular pigmentation between the two groups (all P>0.05). After treatment, the LTG showed significantly lower scores

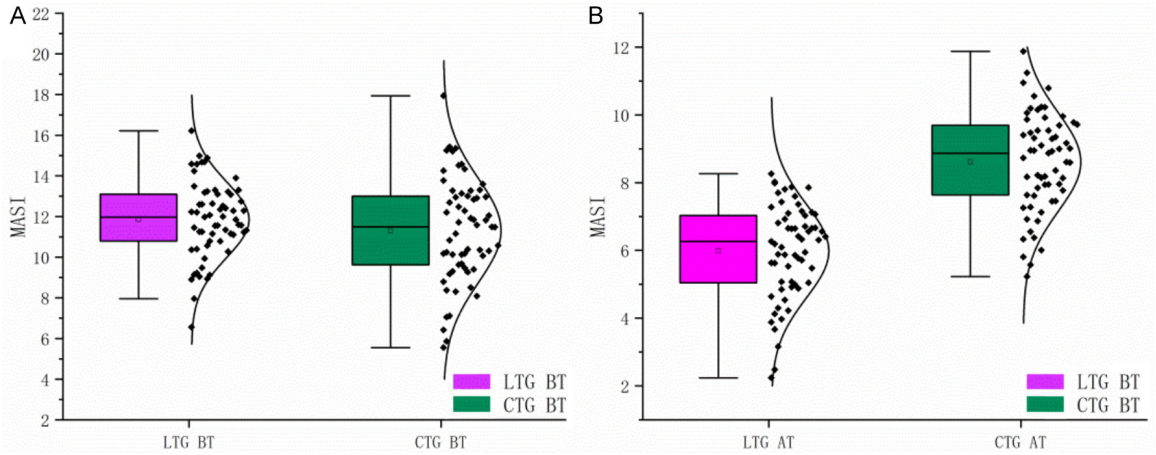

Figure 2. Comparison of MSAI scores between the two groups before and after treatment. Before treatment (A), there was no statistically significant difference in MASI scores between the two groups ($P>0.05$). After treatment (B), the LTG had lower MASI scores than the CTG ($P<0.05$). # indicates a statistically significant difference between groups. Note: MASI: Melasma Area and Severity Index; LTG: Laser Treatment Group ($n=61$); CTG: Control Treatment Group ($n=60$); BT: before treatment; AT: after treatment.

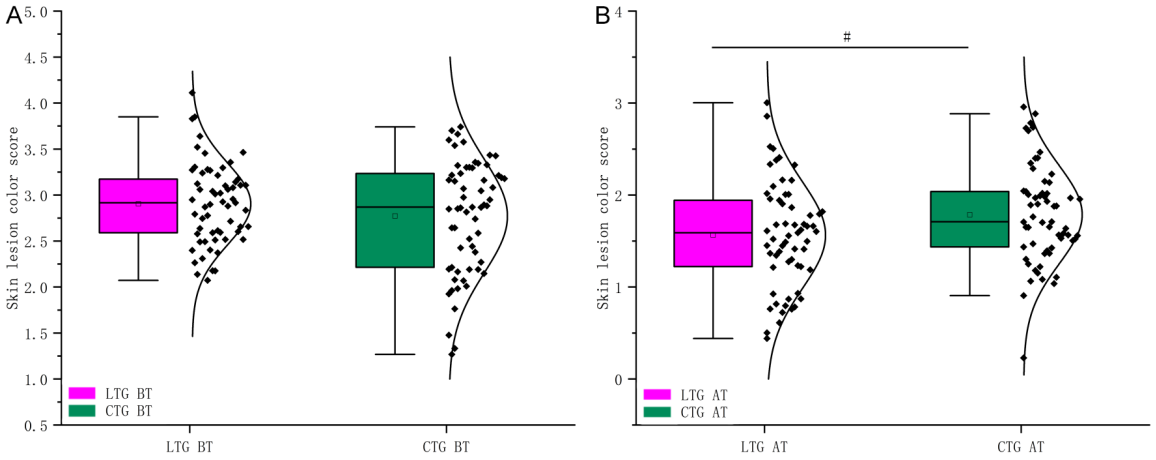

Figure 3. Comparison of skin lesion color scores between the two groups before and after treatment. Before treatment (A), there was no statistically significant difference in skin lesion color scores between the two groups ($P>0.05$). After treatment (B), the LTG had lower lesion color scores than the CTG ($P<0.05$). # indicates a statistically significant difference between groups. Note: LTG: Laser Treatment Group ($n=61$); CTG: Control Treatment Group ($n=60$); BT: before treatment; AT: after treatment.

for telangiectasia and perifollicular pigmentation compared to the CTG (**Figure 7**, all P<0.05).

Comparison of incidence of adverse reactions between the two groups

Follow-up data revealed 3 cases of pigmentation, 1 case of blisters, 2 cases of erythema, and 1 case of desquamation in the LTG, resulting in an overall adverse reaction incidence of 11.48% (7/61), significantly lower than 40.00% (24/60) in the CTG (P<0.05) (**Figure 8**).

Comparison of follow-up recurrence between the two groups

During the six-month follow-up, only one case of recurrence was observed in the LTG, resulting in a recurrence rate of 1.64% (1/61), significantly lower than 10.00% (10/60) in the CTG (P<0.05) (**Figure 9**).

Discussion

Melasma is an acquired skin condition characterized by excessive melanin deposition in the

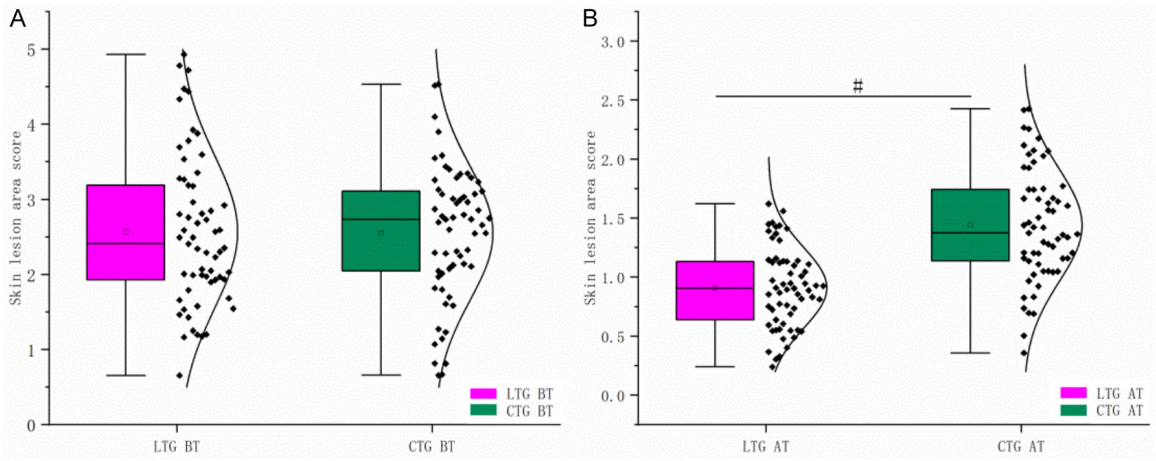

Figure 4. Comparison of skin lesion area scores between the two groups before and after treatment. Before treatment (A), there was no statistically significant difference in skin lesion area scores between the two groups ($P>0.05$). After treatment (B), the LTG had lower lesion area scores than the CTG ($P<0.05$). # indicates a statistically significant difference between groups. Note: LTG: Laser Treatment Group ($n=61$); CTG: Control Treatment Group ($n=60$); BT: before treatment; AT: after treatment.

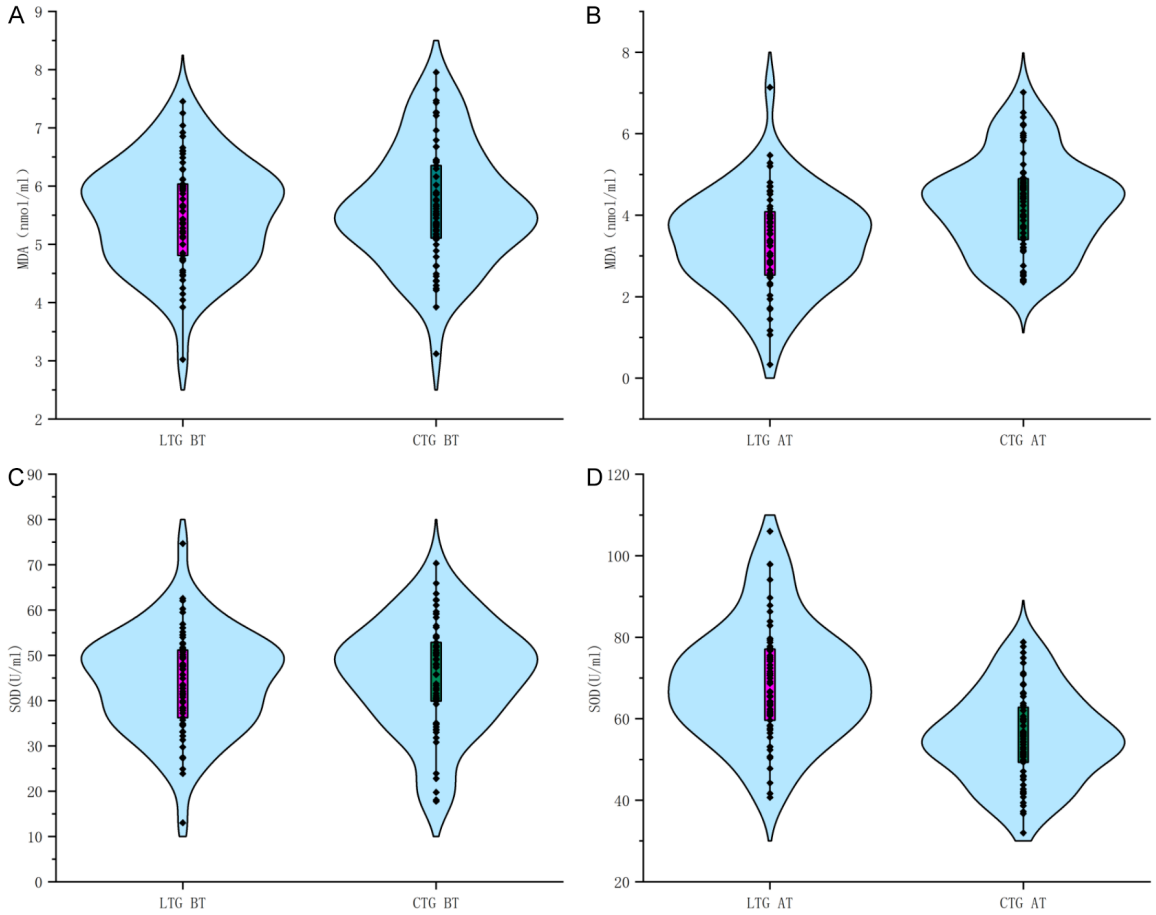

Figure 5. Comparison of laboratory indicators between the two groups before and after treatment. No significant differences were observed in MDA and SOD levels between the two groups before and after treatment ($P>0.05$). Note: LTG: Laser Treatment Group ($n=61$); CTG: Control Treatment Group ($n=60$); BT: before treatment; AT: after treatment.

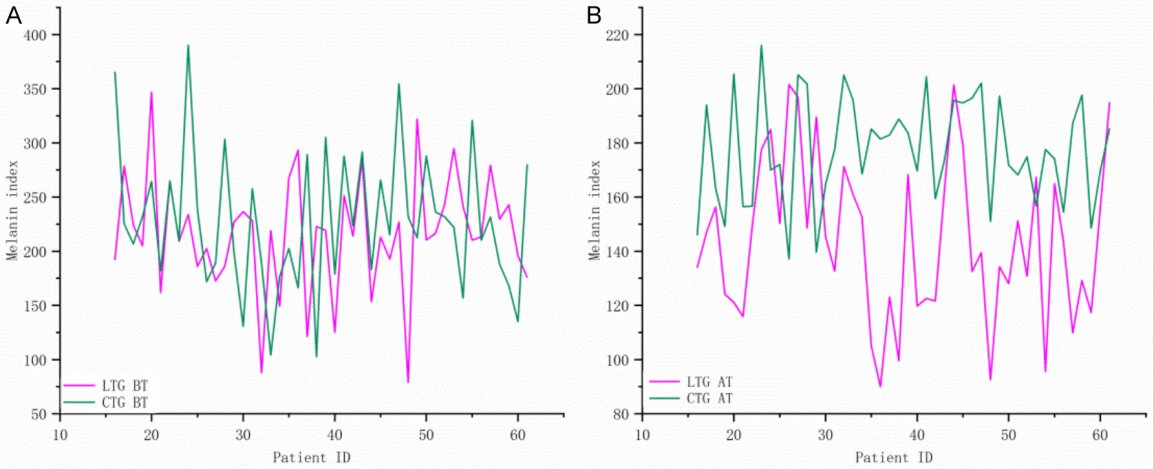

Figure 6. Comparison of melanin index between the two groups before and after treatment. Before treatment, there was no statistically significant difference in melanin index between the two groups (P>0.05) (A). After treatment, the melanin index of the LTG was lower than that of the CTG (P<0.05) (B). Note: LTG: Laser Treatment Group (n=61); CTG: Control Treatment Group (n=60); BT: before treatment; AT: after treatment.

epidermis and dermis. It is known for its high recurrence rate and difficulty in achieving complete cure [14]. While melasma does not significantly affect overall health, it can impact appearance, leading to negative emotions and adversely affecting social interactions [15]. Although topical treatments can alleviate clinical symptoms to some extent, they are often hindered by high recurrence rates and low cure rates. As such, the search for combined interventions remains a key focus in melasma research.

This retrospective analysis found that combining traditional topical tranexamic acid with Q-switched 755-nm alexandrite laser therapy significantly improved the treatment efficacy of melasma. These results align with a meta-analysis by Khan et al. [16], which concluded that all nine included studies demonstrated that laser therapy combined with topical tranexamic acid effectively reduced MASI scores, with the optimal results achieved through monthly laser treatments paired with bi-monthly topical tranexamic acid applications. Elkamshoushi et al. [17] also reported that oral administration of 4% tranexamic acid combined with low-fluence laser therapy twice every four weeks significantly improved treatment efficacy, particularly in alleviating telangiectasia.

The occurrence of melasma is primarily associated with pigmentation at the lesion site and local changes in skin structure and function. Sun exposure contributes to dermal elastic fiber degeneration and promotes dysregulation of various cytokine expressions, which collectively lead to melasma development [18, 19]. Tranexamic acid exerts its pharmacological effects by interfering with melanin biosynthesis. Once administered orally or topically, it reaches the deeper layers of the skin via blood circulation, targeting melanocytes to reduce melanin production and secretion [20]. However, relying solely on pharmacological intervention is limited by significant adverse reactions and a slow onset of efficacy. In contrast, Q-switched 755-nm alexandrite laser therapy employs pulsed laser-induced thermal effects to target localized skin, fragmenting and absorbing melanin, thereby achieving therapeutic benefits for melasma. This is supported by the comparative results of treatment outcomes and melanin index in the patient groups discussed in this study.

Previous studies [21] have advised against the use of lasers in treating melasma, as laser therapy may trigger photodamage and inflammatory reactions. This is particularly relevant for patients with melasma in the active phase, as laser therapy can irritate the skin, leading to new pigmentation and worsening clinical symptoms. To validate this, we compared the differences in cytokine levels between the two patient groups after treatment. The results indicated that the combination of Q-switched 755-nm alexandrite laser and tranexamic acid did

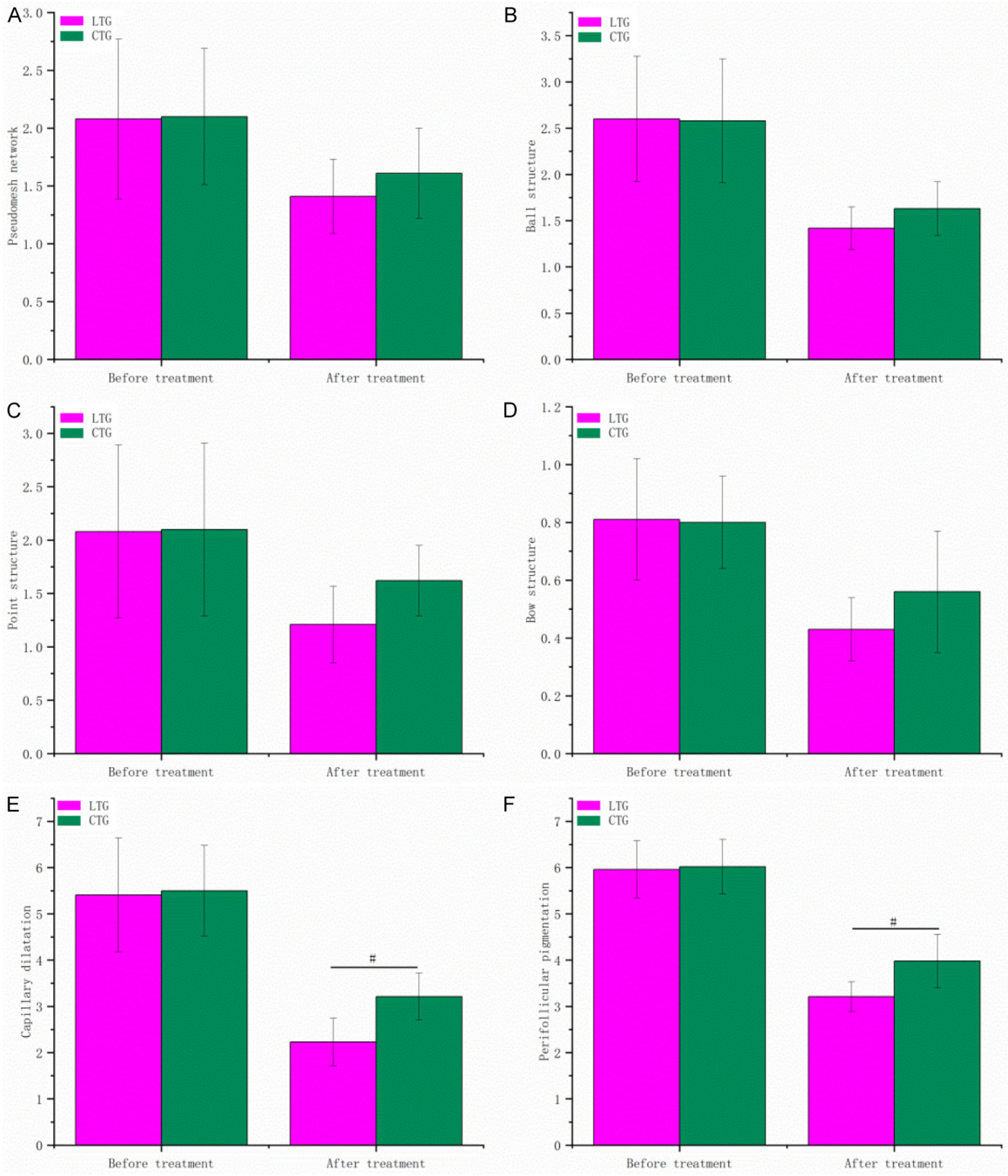

Figure 7. Comparison of dermoscopic scores for pigmentation and vascular components between the two groups before and after treatment. Before treatment, there were no statistically significant differences in pseudoreticular network (A), globular pattern (B), dot pattern (C), arcuate pattern (D), telangiectasia (E), and perifollicular pigmentation (F) between the two groups ($P>0.05$). After treatment, the scores for telangiectasia and perifollicular pigmentation in the LTG were lower than those in the CTG ($P<0.05$). # indicates a statistically significant difference between groups. Note: LTG: Laser Treatment Group ($n=61$); CTG: Control Treatment Group ($n=60$).

not increase MDA levels nor significantly reduce SOD levels. SOD is a key antioxidant enzyme that eliminates superoxide radicals and mitigates oxidative damage, while MDA, the end product of lipid peroxidation, serves as a marker of oxidative stress. In melasma patients, MDA and SOD levels often differ from those in healthy individuals, suggesting that oxidative stress plays a critical role in the pathogenesis of melasma. The reduced antioxidant defense

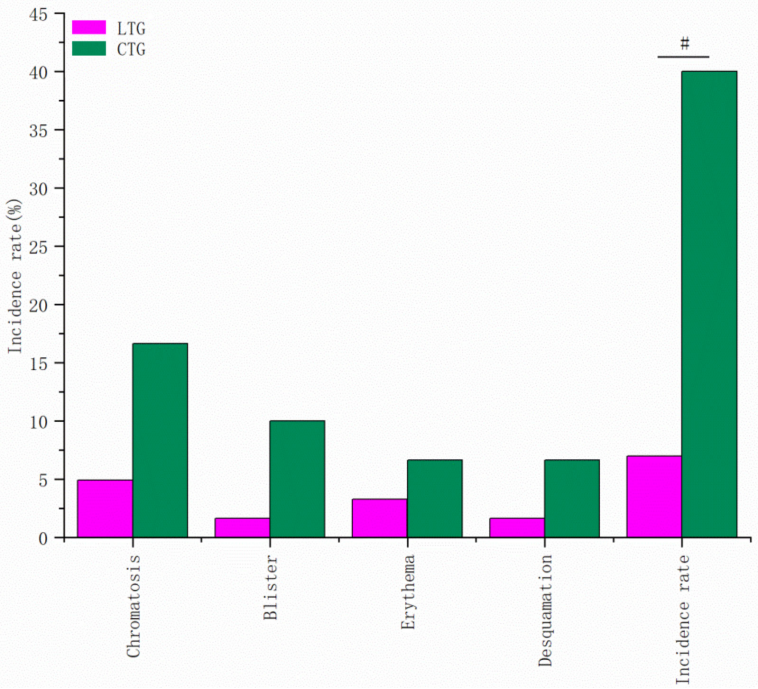

Figure 8. Comparison of incidence of adverse reactions between the two groups. The incidence of adverse reactions in the LTG was 11.48% (7/61), significantly lower than 40.00% (24/60) observed in the CTG (P<0.05). # represents a statistically significant difference between groups. Note: LTG: Laser Treatment Group (n=61); CTG: Control Treatment Group (n=60).

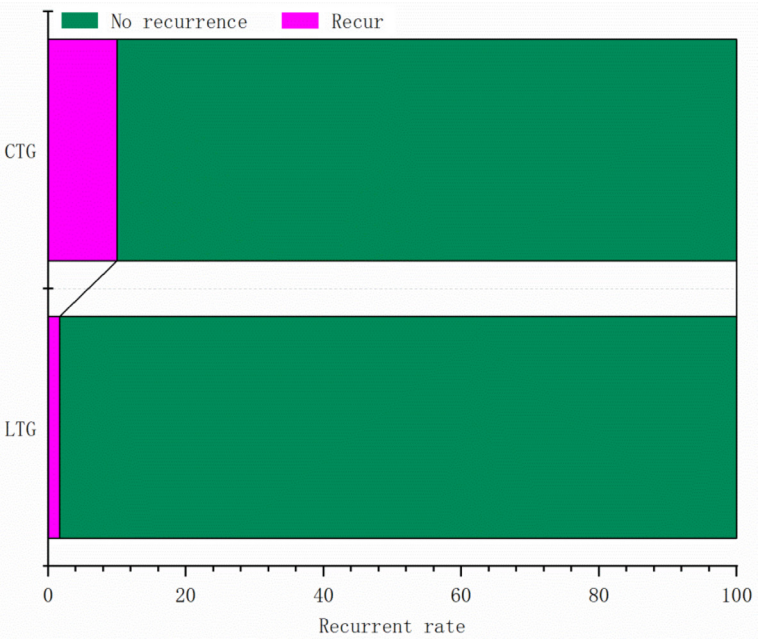

Figure 9. Comparison of follow-up recurrence between the two groups. During the 6-month follow-up, the recurrence rate in the LTG was 1.64% (1/61), notably lower than 10.00% (10/60) in the CTG (P<0.05). Note: LTG: Laser Treatment Group (n=61); CTG: Control Treatment Group (n=60).

in these patients hinders the effective clearance of excessive free radicals, contributing to melasma progression [22]. The activation of melanocytes releases free radicals, such as MDA, which exacerbates both inflammation and oxidative stress responses in melanocytes [23]. The lack of a significant increase in MDA levels after combined laser treatment in this study may be due to the relatively low laser fluence and the antioxidative, anti-inflammatory, and anti-irritant properties of tranexamic acid. Thus, the combined treatment does not trigger new symptoms of melasma.

Additionally, dermoscopic comparisons in this study showed that the combined treatment was more effective in improving telangiectasia and perifollicular pigmentation. This outcome is consistent with the mechanisms of tranexamic acid and laser therapy. Tranexamic acid reduces melanogenic factors and inhibits angiogenesis, while laser therapy targets melanin fragmentation, reducing pigmentation [24, 25]. As a result, the combined treatment is more effective in improving localized telangiectasia and perifollicular pigmentation in melasma patients, making it a promising option for clinical application. Finally, comparisons of adverse reaction and recurrence rates between the two groups indicated that the combined treatment was not only safer but also resulted in a higher cure rate, providing valuable data to support its clinical use.

The study's limitations include a small sample size and its

single-center design. Future multi-center, prospective studies will be valuable in further validating the efficacy and safety of this combined treatment.

In conclusion, Q-switched 755-nm alexandrite laser therapy combined with topical tranexamic acid demonstrates significant efficacy in treating melasma. This combination effectively alleviates clinical symptoms, reduces oxidative stress and inflammatory responses, and shows superior results in vascular proliferation and epidermal pigmentation. Additionally, the recurrence rate was relatively low following the combined treatment, suggesting considerable potential for broader clinical application. The innovation of this study lies in utilizing oxidative stress indicators to demonstrate the efficacy and safety of the combined treatment, as well as quantifying improvements in clinical manifestations of melasma through dermoscopic scores.

Disclosure of conflict of interest

None.

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