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Efficacy and Safety of Combination Therapy of Intense Pulsed Light and Topical Tranexamic Acid in the Treatment of Melasma

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Abstract

Background: Melasma is a chronic hypermelanosis requiring effective therapies. Methods: This prospective, randomized controlled trial evaluated intense pulsed light (IPL) and topical tranexamic acid (TXA) versus IPL with placebo. Thirty-three patients completed the 5-month study (group A: TXA + IPL, $n = 17$; group B: Placebo + IPL, $n = 16$). Outcome included VISIA analysis, modified Melasma Area and Severity Index (mMASI), skin melanin index (MI) and erythema index (EI) measurement. Results: At Month 5, both groups showed improved mMASI scores; however, group A demonstrated a significantly greater reduction than group B (−50.52% vs. −38.49%; mean difference −12.03%, 95% CI −23.74% to −0.32%; $p < 0.05$). Excellent improvement was achieved in 70.59% of Group A versus 25% of Group B. Furthermore, Group A exhibited a significant decrease in MI (−36.31%) compared to a negligible change in Group B (−1.28%), with a significant between-group difference ($p = 0.02$). VISIA analysis confirmed superior improvements in brown spots and texture for Group A ($p < 0.05$). No adverse events occurred. Conclusions: Combining topical TXA with IPL is a safe and significantly more effective treatment for melasma than IPL alone, offering superior pigment reduction without increased risks.

Keywords: melasma; tranexamic acid; intense pulsed light; combination therapy

1. Introduction

Melasma, also called chloasma or butterfly mask, is a form of hypermelanosis that involves symmetrical dark patches on areas of the body that are exposed to sunlight [1]. The majority of cases occur in women between the ages of 20 and 50, particularly those with Fitzpatrick's phototypes III–V [2]. It is mainly characterized by brown or grayish-brown patches on the face, especially on the cheeks, forehead, above the upper lip and chin exposed to sunlight [3]. The precise cause of melasma remains elusive. The development of melasma is believed to involve multiple factors, such as genetic predisposition, exposure to sunlight, hormonal fluctuations, impairment of the skin barrier, mechanical irritation, and oxidative stress [4]. Melasma has been demonstrated to have a detrimental effect on a patient's quality of life [5].

The complex pathogenesis makes effective management challenging. There have been a lot of traditional therapeutic approaches in recent years, from topical agents (depigmenting agents, tranexamic acid [TXA] and vitamin C) and pharmacotherapy to more invasive procedures such as chemical peels and dermabrasion [4]. Hydroquinone, a depigmenting agent that is widely studied and widely used, is recognized as the gold standard to treat melasma [6]. However, topical hydroquinone may carry risks, including allergic or irritant

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contact dermatitis, hypopigmentation, post-inflammatory hyperpigmentation, exogenous ochronosis, nail hyperpigmentation, and trimethylaminuria [7]. Tranexamic acid (TXA) has shown superior outcomes compared to hydroquinone in treating epidermal melasma [7]. Its primary function is to decrease the synthesis and deposition of melanin by blocking tyrosinase, a crucial enzyme in melanin synthesis [8]. Topical TXA also may target melasma by inhibiting Endothelin-1, a well-known melanogenic factor that causes pigmentation and tanning reactions when exposed to ultraviolet irradiation [9]. Combining therapy with liposomes, microneedling or lasers is required to improve skin penetration due to the hydrophilic nature of TXA [10].

Intense pulsed light (IPL), a light source with a continuous spectrum from 515 to 1200 nm with low-end cutoff filters, can be filtered to target melanin and hemoglobin [11]. Its mechanism in melasma is not fully understood, but IPL generates microsecond-domain non-coherent light, causing thermal diffusion from melanosomes and widespread destruction of pigmented cells. IPL has been shown to have contradictory results in treating melasma, with a risk of post-inflammatory hyperpigmentation (PIH)—reported in 13% of subjects in one study—particularly in darker skin types (Fitzpatrick III–V) [12]. To mitigate this risk, recent studies have combined IPL with topical or systemic anti-melanogenic or anti-inflammatory agents. This study evaluated the efficacy and safety of combining topical TXA with IPL for melasma.

2. Materials and Methods

2.1. Study Design and Participants

This was a prospective, single-center, randomized, placebo-controlled trial comparing the efficacy and safety of combination therapy with IPL and topical TXA versus IPL for melasma. The study protocol was approved by the Ethics Committee of The First Hospital of China Medical University (Approval number: 2022412). All participants were given informed consent before the study began. This study was conducted according to the Declaration of Helsinki.

Between January 2023 and January 2024, 36 patients with melasma and Fitzpatrick skin Type III or IV were enrolled in this study. The inclusion criteria included subjects who were above 18 years old and had epidermal and mixed-type melasma that was determined by a wood's lamp examination. Before beginning the study, no relevant pharmacological treatments (including hydroquinone, kojic acid and arbutin) were used, and no other cosmetic treatments (such as IPL, chemical peels and laser treatments) were performed in the previous month. Exclusion criteria included pregnancy, breast-feeding, infection on the face from trauma, a history of adverse reactions to cosmetic products, systemic diseases that may affect facial conditions (systemic lupus erythematosus), and unrealistic expectations. Patients who were incapable of avoiding overexposure to sunlight were also excluded.

2.2. Randomization and Blinding

Eligible patients were randomized in a 1:1 ratio using a computer-generated random number sequence prepared by an investigator not involved in patient treatment or outcome assessment. Allocation was concealed using sequentially numbered, opaque, sealed envelopes. Group A received topical TXA cataplasm (Shanghai Easyface Biotechnology Co., Ltd., Shanghai, China) plus IPL (M22™, Lumenis Co., Santa Clara, CA, USA) in combination; Group B received placebo cataplasm (without TXA; Shanghai Easyface Bio-technology Co., Ltd., Shanghai, China) plus IPL in combination. The treating physician was not blinded to treatment assignment due to the nature of the intervention, but outcome assessors (two independent dermatologists who evaluated mMASI scores and clinical photographs)

and patients (both groups applied identical cataplasms) were blinded. The statistician was also blinded to group allocation until after the primary analysis was completed.

2.3. Interventions

The treatment parameters were set as follows: an energy density of 13–17 J/cm^2, and a triple pulse mode (3–4 ms pulse and 25–40 ms delay time), depending on the patient's skin type, severity of melasma, and pain tolerability. The endpoint of the treatment was considered to be slight cutaneous erythema. Each group received IPL treatments every four weeks, resulting in a total of four sessions. Protective eyewear was worn by both the patient and the operator during the procedure.

The TXA cataplasm consisted of a hydrophilic polymer matrix containing 3% tranexamic acid as the active ingredient. The placebo cataplasm was identical in appearance, texture, and packaging but contained no TXA. Patients were instructed to apply one piece of cataplasm (205 mm × 180 mm) to the affected facial areas once daily in the evening after thoroughly cleansing the face. Only the lesional skin was treated. The TXA content was calculated to be 0.24 mg per cm^2 of cataplasm. The cataplasm was removed after 20 min without any rinsing. Compliance was monitored by counting returned used cataplasms at each follow-up visit. Throughout the entire study period, all patients were instructed to apply a broad-spectrum sunscreen (SPF $\geq$ 50, PA++++) twice daily (at 8:00 AM and 12:00 PM) and to avoid excessive sun exposure. At each follow-up visit, the topical regimen and sunscreen usage compliance were assessed through collecting of used packages and reviewing of patient diaries.

2.4. Outcome Assessments

After cleaning their faces, patients rested in a room with a 20 °C temperature and 40% humidity control for 30 min. Standardized photographs were taken with the VISIA Complexion Analysis System (Canfield Imaging Systems, Fairfield, NJ, USA) from the front and side of both cheeks. The following parameters were assessed in bilateral facial areas using the VISIA analysis: skin spots, ultraviolet spots, brown spots, red areas, and texture. The score was ranked by percentile, with a higher score indicating better skin condition [13].

Evaluations were conducted at baseline (M0) and at follow-up visits at month 1 (M1) and month 5 (M5), including a self-examination questionnaire and clinical symptoms assessments. To measure clinical improvement and the modified Melasma Area and Severity Index (mMASI) score, two dermatologists who were blind examined the clinical photographs before and after treatments [14]. The total mMASI score ranges from 0 to 48, with higher scores indicating more severe melasma. The final mMASI score for each patient at each time point was the average of the two independent dermatologists' assessments. A Mexameter (MX18, Courage and Khazaka, Electronic GmbH, Cologne, Germany) was also used to measure skin melanin index (MI) and erythema index (EI) on cheekbone at M0, M1 and M5. The device was calibrated before each measurement session according to the manufacturer's instructions. The mean value was calculated after measuring each site three times. At each follow-up visit, patients completed a standardized self-assessment questionnaire rating the degree of improvement in their melasma on a 4-point scale: mild (<25% improvement), moderate (25–50% improvement), good (51–75% improvement), or excellent (>75% improvement).

2.5. Statistical Analysis

Statistical analysis was performed using GraphPad Prism (version 10.0) (GraphPad, San Diego, CA, USA). Hypotheses were tested using two-sided tests with a significance level of $p = 0.05$. Repeated-measures ANOVA was used to compare changes in outcome measures

(mMASI, MI, EI, and VISIA parameters) across three time points (M0, M1, M5) within each group. The assumptions of normality (tested by Shapiro–Wilk test) and sphericity (tested by Mauchly's test) were verified. When sphericity was violated, Greenhouse–Geisser correction was applied. The *t*-test or Mann–Whitney test was applied to compare efficacy between the two groups. The statistical measures used to express the measurements were the mean (standard deviation; SD). Last Observation Carried Forward (LOCF) was used to substitute missing data for continuous variables. The correlation between the disease severity of melasma and objective measurements was assessed by the Spearman correlation test.

3. Results

3.1. Patients' Characteristics

The study design is shown in Figure 1. Table 1 summarizes the baseline demographic and clinical characteristics of the 33 patients who completed the 5-month follow-up. In group A (topical TXA + IPL, $n = 17$), the mean age was 35.53 ± 6.67 years, and in group B (placebo + IPL, $n = 16$), the mean age was 38.56 ± 8.58 years ($p > 0.99$). The baseline mMASI score, melanin index (MI), erythema index (EI), and all VISIA parameters (skin spots, ultraviolet spots, brown spots, red areas, and texture) were comparable between groups ($p > 0.05$ for all comparisons). The discontinuation of treatment occurred due to relocation (one subject in Group A), personal time constraints (one subject in group B), and treatment dissatisfaction (one subject in group B). No subject has discontinued treatment due to side effects.

Table 1. Baseline demographics and clinical characteristics of study participants.

	Group A ($n = 17$)	Group B ($n = 16$)	Difference (95% CI; Adjust p Value)
Age (years)			
Mean (SD)	35.53 (6.67)	38.56 (8.59)	2.5 (−3.00 to 8.00; 0.37)
Sex			>0.99
Male	1	0	
Female	17	16	
mMASI			
Mean (SD)	11.45 (4.05)	9.14 (4.19)	2.30 (−0.67 to 5.27; 0.18)
Melanin index			
Mean (SD)	117.65 (68.66)	93.91 (53.96)	25.80 (−5.75 to 57.35; 0.14)
Erythema index			
Mean (SD)	296.74 (47.00)	306.97 (84.55)	−10.23 (−63.18 to 42.71; 0.95)
Percentage of skin spots			
Mean (SD)	31.47 (18.71)	34.75 (22.51)	−3.60 (−18.81 to 11.61; 0.92)
Percentage of brown spots			
Mean (SD)	48.65 (20.08)	44.63 (29.01)	3.80 (−14.93 to 22.52; 0.94)
Percentage of ultraviolet spots			
Mean (SD)	32.41 (21.86)	30.19 (24.37)	2.09 (−19.26 to 23.43; 0.99)
Percentage of red areas			
Mean (SD)	50.82 (18.78)	57.50 (24.72)	−6.64 (−21.12 to 7.85; 0.60)
Percentage of texture			
Mean (SD)	56.65 (17.76)	69.75 (17.05)	−13.14 (−27.17 to 0.90; 0.07)

mMASI, modified Melasma Area and Severity Index.

3.2. Clinical Assessment and Safety

All patients with melasma showed improvements in skin lesions at M5. The representative photographs are illustrated in Figure 2.

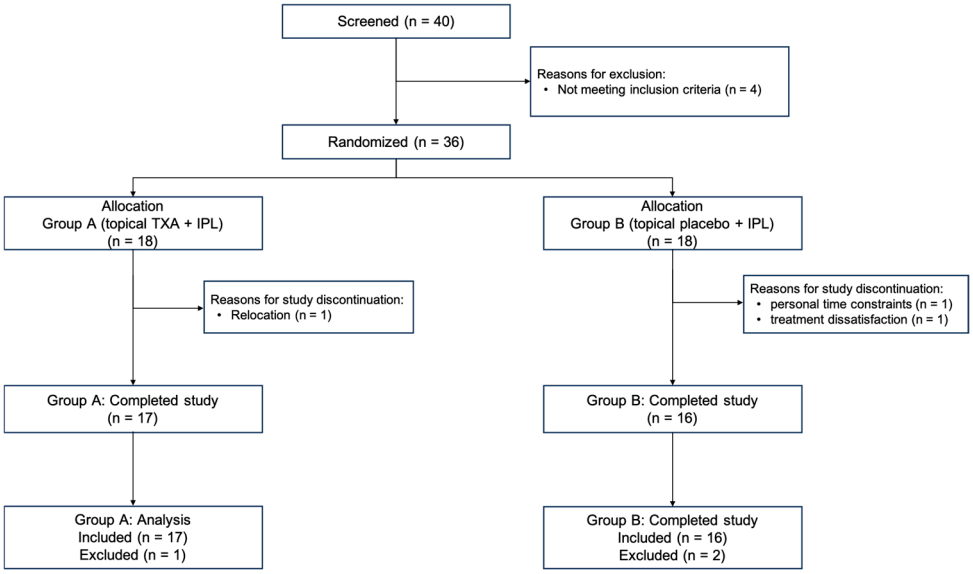


Figure 1. CONSORT diagram.

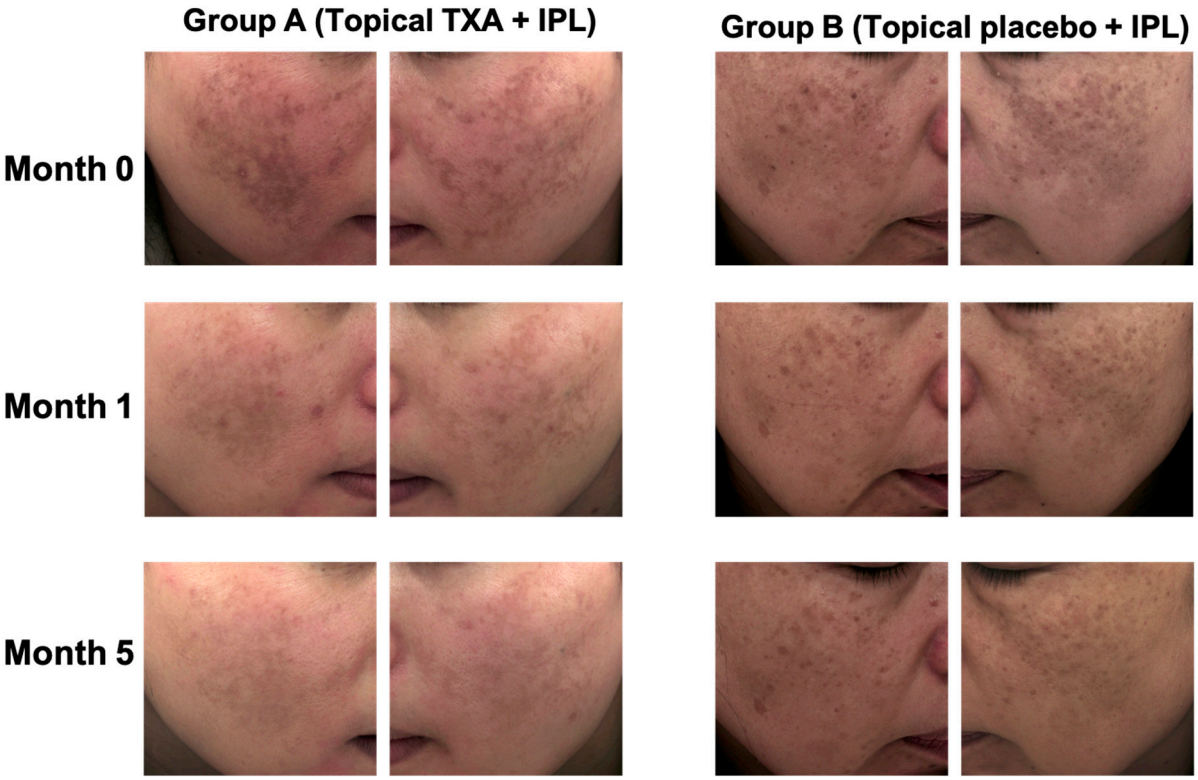


Figure 2. Clinical photographs of a representative patient taken at baseline (M0), after 1 month and 5 months of combination therapy with topical TXA and IPL (group A). Clinical photographs of a representative patient taken at Month 0, Month 1 and Month 5 of combination therapy with topical placebo and IPL (group B). IPL, intense pulsed light; TXA, tranexamic acid.

At M5, the mean (SD) mMASI score was reduced by 5.94 points (change, −50.52%) in group A, and 3.34 points (change, −38.49%) in group B (Figure 3A,B). The difference in percentage change between the two groups was –12.03% (95% CI –23.74% to –0.32%; $p < 0.05$), indicating a statistically significant advantage of the combination therapy with topical TXA over placebo.

Compared to the baseline, group A (2.45; 95% CI 1.33 to 3.56; $p < 0.01$) and group B (1.36; 95% CI 0.22 to 2.51; $p = 0.02$) both experienced significant improvements in their

mMASI scores at M1. However, the between-group difference at M1 was not statistically significant ($p = 0.19$). At M5, the absolute mMASI scores were similar between groups ($p = 0.99$), but the percentage improvement from baseline remained superior in group A ($p < 0.05$).

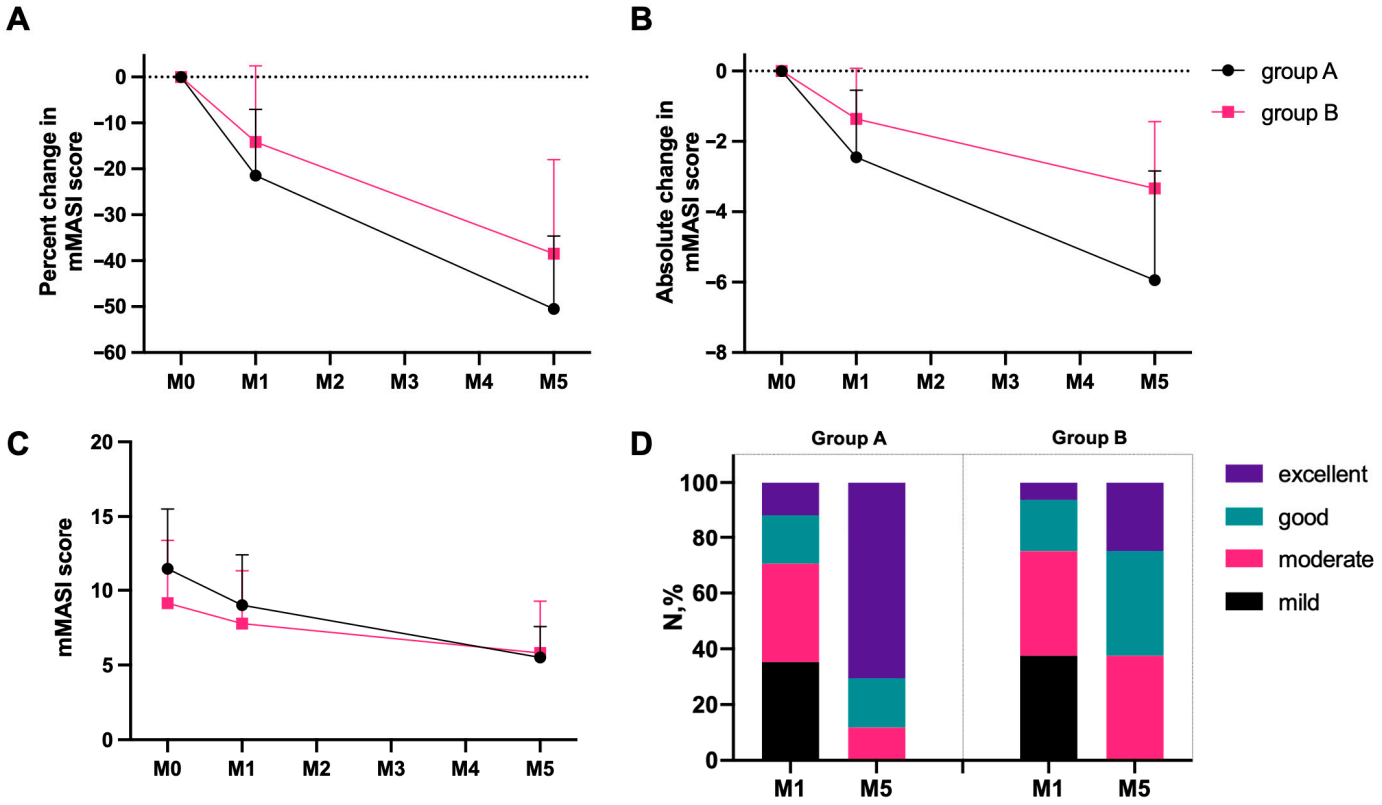


Figure 3. (**A**) Percent change in modified Melasma Area and Severity Index (mMASI) score of patients with melasma at baseline (M0), and after 1 month (M1) and 5 months (M5) of treatment. (**B**) Absolute change in mMASI score of patients with melasma at M0, M1 and M5. (**C**) Change in mMASI score of patients with melasma at M0, M1 and M5. (**D**) Percent of improvement after treatment.

Regarding patient self-assessment, 12 out of 17 patients (70.59%) in group A rated their condition as "excellent" at M5, whereas only 4 out of 16 patients (25%) in group B reported an excellent outcome. No adverse events, including erythema, blistering, post-inflammatory hyperpigmentation, or hypopigmentation, were observed in either group during the entire study period.

3.3. MI/EI Assessment

At baseline, there were no differences in MI and EI between the 2 groups: 117.647 (68.66) and 296.74 (47.00) in group A versus 93.91 (53.96) and 306.97 (84.55) in group B ($p > 0.05$, respectively). During the treatment period, the mean EI values progressively decreased in both groups, but the between-group difference at M5 was not statistically significant ($p = 0.32$; Figure 4A). This suggests that the effect on erythema was largely driven by IPL rather than by topical TXA. In contrast, the MI values showed a striking difference between groups. The MI of group A decreased by 7.81% from the baseline at M1, and continued to decline, resulting in a 36.31% decrease at M5 (Figure 4B). In contrast, the MI scores of group B increased by 1.62% at M1, then decreased and reached just −1.28% at M5. This indicated that there could be a possibility of early post-inflammatory hyperpigmentation after IPL alone. At M5, the mean percent change in MI scores showed a significant difference between the two groups (−35.03%; 95% CI −64.67% to −5.39%;

p = 0.02; Table 2). These findings indicate that adding topical TXA effectively prevents the post-inflammatory hyperpigmentation that can occur after IPL monotherapy.

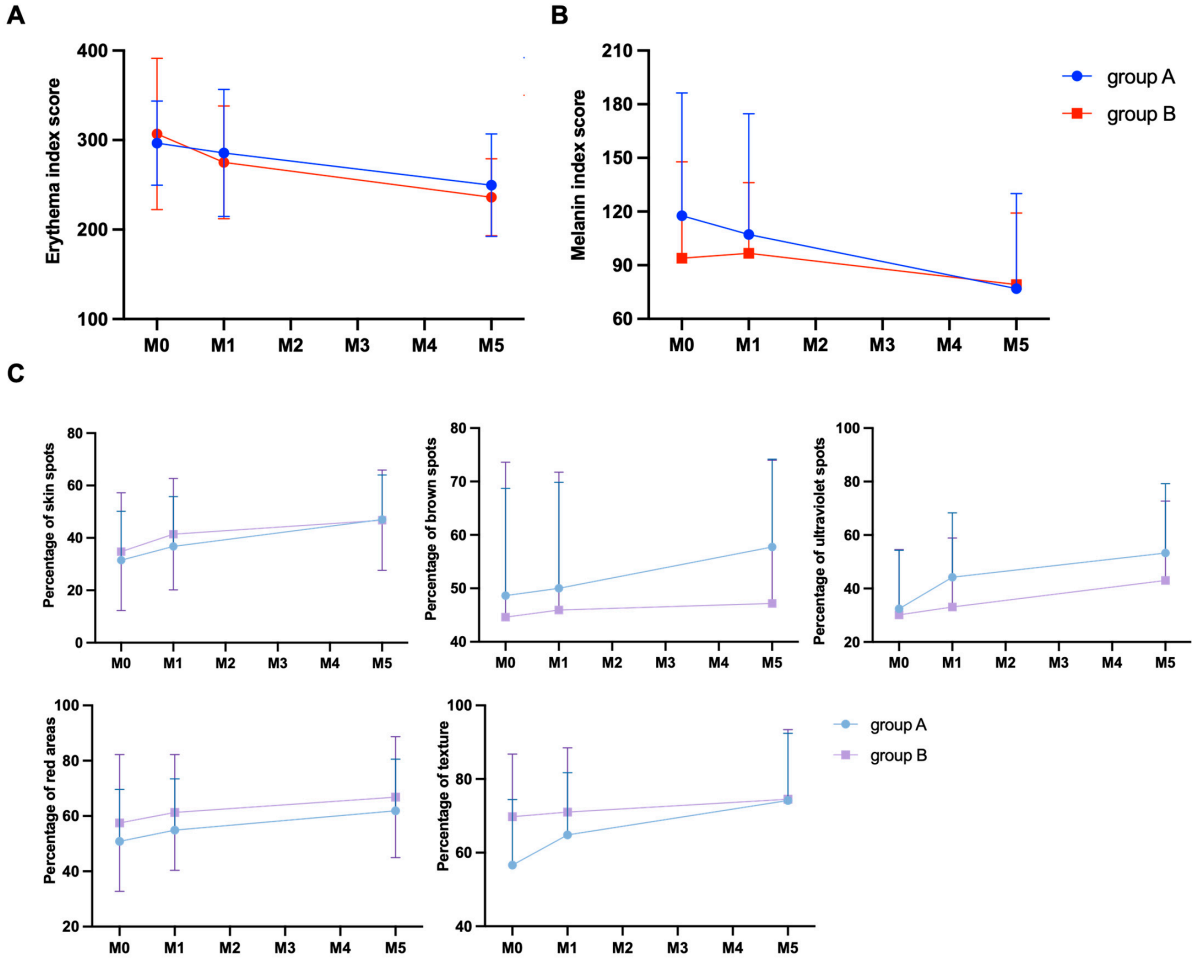


Figure 4. (**A**) Change in erythema index score of patients with melasma at baseline (M0), and after 1 month (M1) and 5 months (M5) of treatment. (**B**) Change in melanin index score of patients with melasma at M0, M1 and M5. (**C**) Change in percentage of skin spots, brown spots, ultraviolet spots, red areas, and texture score of patients with melasma at M0, M1 and M5.

Table 2. Efficacy Assessments.

	Group A (n = 17)	Group B (n = 16)	Difference (95% CI; Adjust p Value)
mMASI			
Mean absolute score change at M1	−2.45	−1.36	−1.09 (−2.60 to 0.43; 0.23)
Mean percent score change at M1 (%)	−21.47	−14.16	−7.31 (−19.01 to 4.40; 0.35)
Mean absolute score change at M5	−5.94	−3.34	−2.60 (−4.12 to −1.09; <0.01)
Mean percent score change at M5 (%)	−50.52	−38.49	−12.03 (−23.7 to −0.32; 0.04)
Melanin index			
Mean absolute score change at M1	−10.41	2.81	−13.13 (−32.84 to 6.59; 0.29)
Mean percent score change at M1 (%)	−7.81	21.60	−29.41 (−59.05 to 0.23; 0.05)
Mean absolute score change at M5	−40.74	−14.69	−26.26 (−45.98 to −6.55; <0.01)
Mean percent score change at M5 (%)	−36.31	−1.28	−35.03 (−64.67 to −5.39; 0.02)
Erythema index			
Mean absolute score change at M1	−11.00	−31.97	20.97 (−19.99 to 61.93; 0.52)
Mean percent score change at M1 (%)	−3.67	−7.95	4.45 (−6.72 to 15.61; 0.70)
Mean absolute score change at M5	−47.15	−70.88	23.73 (−17.23 to 64.69; 0.41)
Mean percent score change at M5 (%)	−15.59	−20.00	4.42 (−6.74 to 15.58; 0.70)

mMASI, modified Melasma Area and Severity Index; M, month.

3.4. VISIA Imaging Analysis

The VISIA imaging system analysis showed that pigmentation-, vascular- and texture-related parameters, including skin spots, ultraviolet spots, brown spots, red areas, and texture, were improved in both groups. Both groups showed significant improvements in skin spots at M1 and M5 versus baseline, with no between-group differences ($p = 0.34$ at M5). However, ultraviolet spots and brown spots improved significantly only in group A (ultraviolet spots: $p < 0.01$ at both M1 and M5; brown spots: $p = 0.01$ at M5), and the between-group differences at M5 favored group A ($p = 0.03$ and $p = 0.04$, respectively), suggesting that topical TXA offers superior protection against cumulative sun damage and deeper pigmentation. Red area scores increased progressively in both groups (indicating reduced erythema), with similar changes between groups ($p = 0.48$ at M5), consistent with the EI measurements and confirming that IPL primarily targets the vascular component of melasma without added benefit from TXA. Texture scores improved significantly only in group A at M5 (mean increase 11.3 points; 95% CI 4.8–17.8; $p = 0.01$), while group B showed a non-significant trend ($p = 0.09$); the between-group difference was significant ($p = 0.04$), indicating that combination therapy may also improve skin surface roughness and photoaging.

Spearman correlation analysis was performed to explore the relationship between melasma severity (mMASI score) and objective measurements across all time points (Figure 5). mMASI score showed a positive correlation with EI scores (r = 0.50; $p < 0.01$) and MI (r = 0.34; $p < 0.01$), but negative correlations with skin spots (r = −0.42, $p < 0.01$), red areas (r = −0.54, $p < 0.01$) and texture (r = −0.41, $p < 0.01$).

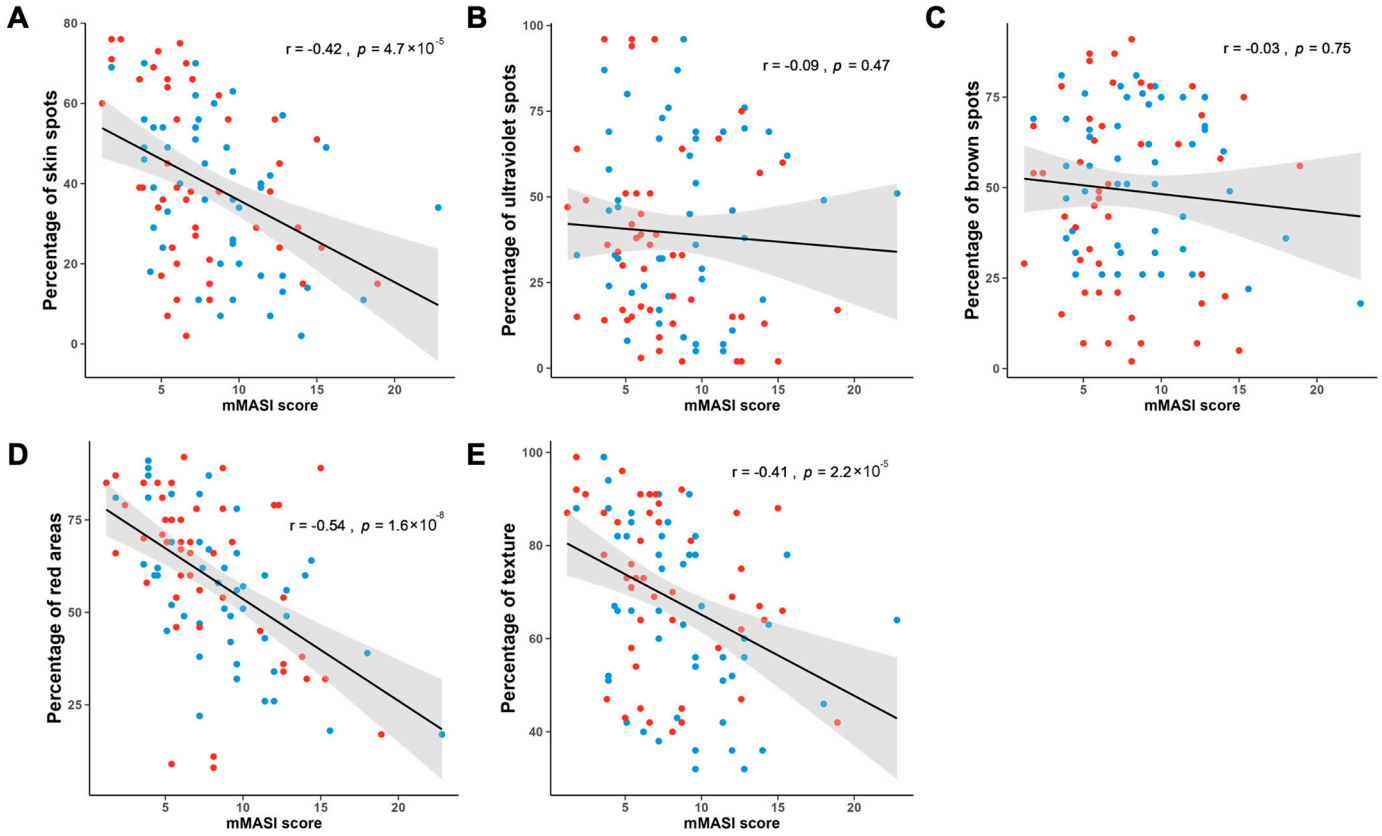


Figure 5. *Cont.*

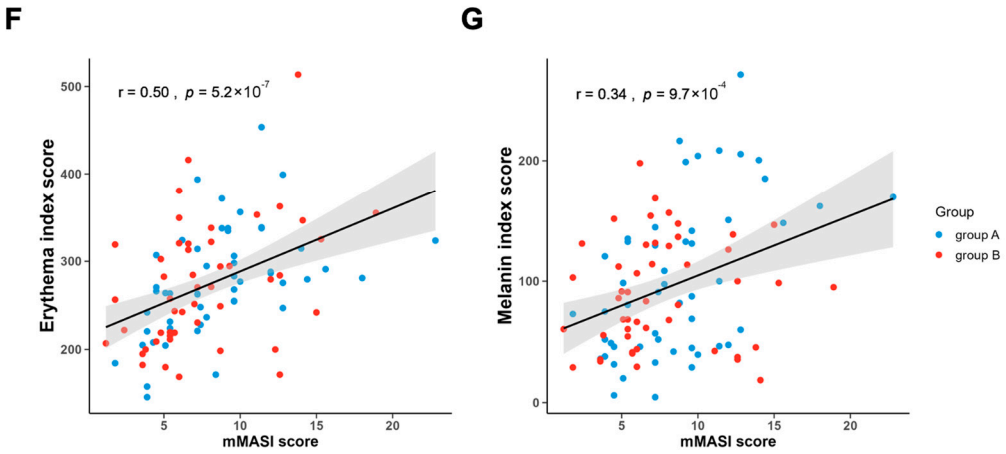


Figure 5. The Spearman correlations between modified Melasma Area and Severity Index (mMASI) score and various skin parameters in patients with melasma. (**A**) percentage of skin spots, (**B**) percentage of ultraviolet spots, (**C**) percentage of brown spots, (**D**) percentage of red areas, (**E**) percentage of texture scores, (**F**) erythema index score, and (**G**) melanin index score. The solid lines are a fitting line for linear regression. A 95% confidence interval (CI) is indicated by the gray shading surrounding each line.

4. Discussion

In this prospective, randomized, placebo-controlled trial, we evaluated the efficacy and safety of using topical TXA daily in combination with IPL over a 4-month treatment period in Chinese patients with melasma. The key findings are: (1) the combination therapy produced a significantly greater percentage reduction in mMASI score at month 5 compared with IPL plus placebo (–50.5% vs. –38.5%; $p < 0.05$); (2) the combination therapy prevented the early rebound increase in melanin index observed with IPL alone and achieved a 36.3% reduction in MI at month 5; (3) only the combination group showed significant improvements in ultraviolet spots, brown spots, and skin texture on VISIA analysis; and (4) no adverse events were recorded in either group. The combination therapy with IPL and topical TXA seems to be a good choice, which undoubtedly resolves some of the risk of systemic side effects and post-inflammatory hyperpigmentation.

Our findings are consistent with and extend previous research on TXA in melasma. A recent study by Xu et al. reported that intradermal injection of TXA combined with broadband light achieved a 58.6% ± 9.7% reduction in mMASI after 12 weeks [15], which is similar to the 50.5% reduction observed in our study. However, intradermal injections are associated with injection-related pain, bruising, and the need for trained medical personnel. Our topical cataplasm approach is non-invasive, can be self-administered by patients at home, and carries no risk of needle-related adverse events. In contrast to oral TXA, which has a slight but not significant risk of thrombo-embolic events, topical TXA prevents systemic absorption and is safer for long-term use, especially in patients with risk factors for thrombosis. Our combination approach has the potential to provide an adaptable approach to treating melasma in clinical practice.

The superior outcomes of the combination therapy can be explained by the complementary mechanisms of IPL and TXA. IPL targets melanin and hemoglobin as chromophores, leading to photothermolysis of pigmented lesions and reduction of telangiectasias. However, IPL also induces a controlled inflammatory response that can paradoxically stimulate melanogenesis and lead to PIH [12], as reflected by the transient increase in MI at M1 in group B. TXA has anti-inflammatory effects that can reduce the inflammatory response induced by pigmentation and enhance the condition of pigmented skin by blocking the citric acid pathway [16]. This can explain why MI scores in combination therapy decreased sig-

nificantly. Previous reports suggested that topical TXA can prevent rebound pigmentation after IPL sessions, and this finding is consistent with that [17].

Using VISIA imaging system, we noticed marked improvements in skin aging in group A, specifically in brown spots, ultraviolet spots and texture. Skin spots being reduced indicates a decrease in hyperpigmentation and discoloration, and ultraviolet spots being lightened suggests less melanin deposit due to sun damage [18]. Moreover, TXA has been shown to reduce mast cell infiltration and vascular endothelial growth factor (VEGF) expression in melasma lesions, which may contribute to the improvement in ultraviolet spots and texture observed only in group A. Interestingly, compared with baseline, the scores of red areas increased in both groups. However, the difference between two groups was not significant at both M1 and M5. Broad-spectrum IPL is capable of targeting hemoglobin and melanin as primary chromophores in a selective way. Our findings support that topical TXA has a limited ability to alter dermal structures due to its limited penetration into the dermis.

Several limitations of this study should be noted. First, the study population was limited to Chinese patients with Fitzpatrick skin types III–IV, which restricts generalizability to other ethnicities or darker skin types. Second, the sample size was small, limiting statistical power for subgroup analyses. Third, the follow-up period ended at 5 months, and no longer-term assessment was performed; therefore, the durability of treatment effects beyond completion remains unknown. Future studies with larger, more diverse cohorts and extended post-treatment follow-up are needed to confirm long-term efficacy.

5. Conclusions

In conclusion, this randomized controlled trial demonstrates that the combination of topical 3% TXA cataplasm applied daily for 20 min and monthly IPL sessions for 4 months is significantly more effective than IPL alone in reducing melasma severity, preventing post-inflammatory hyperpigmentation, and improving signs of photoaging. The combination therapy represents a well-tolerated, promising, non-invasive, and patient-friendly option for the treatment of melasma, particularly in individuals with Fitzpatrick skin types III–IV. Future large-scale, long-term studies are warranted to confirm these findings and to optimize the treatment regimen.

Author Contributions: Conceptualization, L.G. and Y.W.; methodology, Y.X. and Y.W.; validation, S.Q.; formal analysis, S.Q.; investigation, Y.L. and X.X.; resources, L.G.; data curation, Y.L.; writing—original draft preparation, Y.X.; writing—review and editing, Y.L., X.X., S.Q., L.G. and Y.W.; visualization, Y.X.; project administration, Y.W.; funding acquisition, Y.X. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: This study was reviewed and approved by the Ethics Committee of The First Hospital of China Medical University (Approval number: 2022412, Approval date: 10 October 2022). This study was conducted according to the Declaration of Helsinki.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patient(s) to publish this paper.

Data Availability Statement: The data presented in this study are available on request from the corresponding author due to privacy and ethical restrictions.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Passeron, T.; Picardo, M. Melasma, a photoaging disorder. *Pigment Cell Melanoma Res.* **2018**, *31*, 461–465. [CrossRef] [PubMed]
2. Rocio, J.; Pittet, J.C.; Sachdev, M.; Kovylkina, N.; Deloche Bensmaine, C.; Passeron, T. Evaluation of the Efficacy of a Serum Containing Niacinamide, Tranexamic Acid, Vitamin C, and Hydroxy Acid Compared to 4% Hydroquinone in the Management of Melasma. *J. Cosmet. Dermatol.* **2025**, *24*, e70097. [CrossRef] [PubMed]
3. Neagu, N.; Conforti, C.; Agozzino, M.; Marangi, G.F.; Morariu, S.H.; Pellacani, G.; Persichetti, P.; Piccolo, D.; Segreto, F.; Zalaudek, I.; et al. Melasma treatment: A systematic review. *J. Dermatol. Treat.* **2022**, *33*, 1816–1837. [CrossRef] [PubMed]
4. Ke, C.; Huang, Y.; Chen, C.; Chen, X.; Ke, Y. Comparative observation of the efficacy of Q-switched Nd:YAG laser with PhotoAcoustic Technology Pulse vs. traditional mode in treating melasma. *J. Dermatol. Treat.* **2025**, *36*, 2477257. [CrossRef] [PubMed]
5. Kagha, K.; Fabi, S.; Goldman, M.P. Melasma's Impact on Quality of Life. *J. Drugs Dermatol.* **2020**, *19*, 184–187. [CrossRef] [PubMed]
6. Kusumawardani, A.; Murasmita, A.; Rosmarwati, E.; Norawati Ashadi, L.; Setiawan, S.V.; Murlistyarini, S.; Wahyu Fitriyani, N. Efficacy of overnight leave-on sandwich therapy with 5% cysteamine and ectoine cream compared to hydroquinone 4% cream for treatment of melasma: A double-blind randomized controlled trial. *Acta Dermatovenerol. Alp. Pannonica Adriat.* **2025**, *34*, 1–4. [CrossRef] [PubMed]
7. Fabian, I.M.; Sinnathamby, E.S.; Flanagan, C.J.; Lindberg, A.; Tynes, B.; Kelkar, R.A.; Varrassi, G.; Ahmadzadeh, S.; Shekoohi, S.; Kaye, A.D. Topical Hydroquinone for Hyperpigmentation: A Narrative Review. *Cureus* **2023**, *15*, e48840. [CrossRef] [PubMed]
8. Sarkar, R.; Bansal, A.; Ailawadi, P. Future therapies in melasma: What lies ahead? *Indian J. Dermatol. Venereol. Leprol.* **2020**, *86*, 8–17. [CrossRef] [PubMed]
9. Kim, S.J.; Park, J.Y.; Shibata, T.; Fujiwara, R.; Kang, H.Y. Efficacy and possible mechanisms of topical tranexamic acid in melasma. *Clin. Exp. Dermatol.* **2016**, *41*, 480–485. [CrossRef] [PubMed]
10. Cheng, L.; Pettersen, D.; Ohlsson, B.; Schell, P.; Karle, M.; Evertsson, E.; Pahlén, S.; Jonforsen, M.; Plowright, A.T.; Boström, J.; et al. Discovery of the Fibrinolysis Inhibitor AZD6564, Acting via Interference of a Protein-Protein Interaction. *ACS Med. Chem. Lett.* **2014**, *5*, 538–543. [CrossRef] [PubMed]
11. Li, Y.H.; Chen, J.Z.; Wei, H.C.; Wu, Y.; Liu, M.; Xu, Y.Y.; Dong, G.H.; Chen, H.D. Efficacy and safety of intense pulsed light in treatment of melasma in Chinese patients. *Dermatol. Surg.* **2008**, *34*, 693–700. [CrossRef]
12. Wang, C.C.; Hui, C.Y.; Sue, Y.M.; Wong, W.R.; Hong, H.S. Intense pulsed light for the treatment of refractory melasma in Asian persons. *Dermatol. Surg.* **2004**, *30*, 1196–1200. [CrossRef] [PubMed]
13. Goldsberry, A.; Hanke, C.W.; Hanke, K.E. VISIA system: A possible tool in the cosmetic practice. *J. Drugs Dermatol.* **2014**, *13*, 1312–1314. [PubMed]
14. Pandya, A.G.; Hynan, L.S.; Bhore, R.; Riley, F.C.; Guevara, I.L.; Grimes, P.; Nordlund, J.J.; Rendon, M.; Taylor, S.; Gottschalk, R.W.; et al. Reliability assessment and validation of the Melasma Area and Severity Index (MASI) and a new modified MASI scoring method. *J. Am. Acad. Dermatol.* **2011**, *64*, 78–83.e2. [CrossRef] [PubMed]
15. Jia, Z.; Tian, K.; Zhong, Y.; Wang, X.; Gao, S.; Xu, W.; Li, K.; Wu, L. Effectiveness of combination therapy of broadband light and intradermal injection of tranexamic acid in the treatment of chloasma. *J. Cosmet. Dermatol.* **2023**, *22*, 1536–1544. [CrossRef] [PubMed]
16. Wang, J.V.; Jhawar, N.; Saedi, N. Tranexamic Acid for Melasma: Evaluating the Various Formulations. *J. Clin. Aesthet. Dermatol.* **2019**, *12*, E73–E74. [PubMed]
17. Chung, J.Y.; Lee, J.H.; Lee, J.H. Topical tranexamic acid as an adjuvant treatment in melasma: Side-by-side comparison clinical study. *J. Dermatol. Treat.* **2016**, *27*, 373–377. [CrossRef] [PubMed]
18. Chen, Y.T.; Lin, E.T.; Chang, C.C.; Lin, B.S.; Chiang, H.M.; Huang, Y.H.; Lin, H.Y.; Wang, K.Y.; Chang, T.M. Efficacy and Safety Evaluation of Picosecond Alexandrite Laser with a Diffractive Lens Array for Treatment of Melasma in Asian Patients by VISIA Imaging System. *Photobiomodul. Photomed. Laser Surg.* **2019**, *37*, 559–566. [CrossRef] [PubMed]

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