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ORIGINAL ARTICLE

A Comparative Study on the Efficacy of Intradermal Tranexamic Acid Versus Fluocinolone-Based Triple Combination Therapy in the Treatment of Melasma: A Randomized Controlled Trial

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ABSTRACT

Background: Melasma is a common, acquired hyperpigmentation disorder characterized by brown or gray-brown macules primarily on the face. Current treatment options for melasma include topical agents and intradermal therapies. This study compares the efficacy and safety of intradermal tranexamic acid (TA) and fluocinolone-based triple combination therapy (hydroquinone 4%, tretinoin 0.05%, fluocinolone acetonide 0.01%) in 215 patients diagnosed with melasma.

Objective: To evaluate and compare the efficacy and safety of intradermal TA versus fluocinolone-based triple combination therapy in the management of melasma.

Methods: A randomized controlled trial was conducted with 215 patients, who were randomly assigned to receive either intradermal TA injections (100 mg) every 2 weeks for 12 weeks or topical fluocinolone-based triple combination therapy. The primary outcome was the change in the Melasma Area and Severity Index (MASI) score from baseline to week 12. Secondary outcomes included patient satisfaction and adverse effects.

Results: Both treatments led to significant improvement in MASI scores. However, intradermal TA demonstrated a statistically greater reduction in MASI scores compared to the triple combination therapy (mean MASI reduction: TA = 8.5 vs. triple combination = 6.3, $p < 0.05$). Patient satisfaction was higher in the intradermal TA group, with fewer reported side effects such as skin irritation.

Conclusion: Intradermal tranexamic acid is more effective and safer than the fluocinolone-based triple combination therapy in the treatment of melasma, offering a promising alternative with a superior safety profile.

Keywords: Melasma, Intradermal Tranexamic Acid, Fluocinolone-Based Triple Combination Therapy, Hydroquinone, Tretinoin, Clinical Trial, MASI, Pigmentation Disorder

INTRODUCTION

Melasma is a common, acquired hyperpigmentation disorder characterized by symmetric, brown or gray-brown patches that predominantly appear on the face, particularly the cheeks, forehead, nose, and upper lip[1]. It mainly affects women, with an increased prevalence in those with darker skin types, particularly those of Hispanic, Asian, and African descent[2]. The pathogenesis of melasma involves multiple factors, including ultraviolet (UV) radiation exposure, hormonal changes, and genetic predisposition, leading to increased melanin production by melanocytes[3]. Hormonal influences, particularly during pregnancy or with the use of oral contraceptives, contribute to the high prevalence of melasma in women of reproductive age[4].

Several treatment modalities have been used to manage melasma, with hydroquinone-based therapies being the most common[5]. Hydroquinone acts as a depigmenting agent by inhibiting the enzyme tyrosinase, thereby reducing melanin production[6]. The combination of hydroquinone with tretinoin and corticosteroids, particularly fluocinolone acetonide, is frequently used for enhanced efficacy and reduced inflammation[7]. However, long-term use of hydroquinone can lead to side effects, such as skin irritation, ochronosis, and even ochronotic pigmentation[8].

In recent years, intradermal tranexamic acid (TA) has gained attention as an alternative treatment for melasma. Tranexamic acid, a synthetic antifibrinolytic agent, inhibits melanogenesis by blocking plasminogen activation and reducing melanocyte-stimulating factors[9]. Intradermal injections of TA have been found to offer significant improvements in pigmentation with fewer systemic side effects compared to conventional topical treatments[10]. However, the comparative efficacy of intradermal TA and the fluocinolone-based triple combination therapy has not been well-studied.

This study aims to compare the efficacy and safety of intradermal tranexamic acid versus fluocinolone-based triple combination therapy in the treatment of melasma in a randomized controlled trial with 215 patients. We hypothesize that intradermal tranexamic acid may provide superior efficacy with fewer adverse effects compared to the fluocinolone-based triple combination therapy.

METHODOLOGY

This was a randomized, open-label, controlled trial conducted at Azra Naheed Medical and Dental College Lahore during from October 2021 to September 2022. A total of 215 adult patients (ages 18–50 years) with moderate to severe melasma, as determined by the Melasma Area and Severity Index (MASI) score, were included. Patients with Fitzpatrick skin types III to V were eligible for participation. Exclusion criteria included pregnancy, lactation, recent use of melasma treatments, and active skin conditions such as eczema, psoriasis, or systemic diseases that could affect skin pigmentation.

Randomization and Intervention

Participants were randomly assigned to one of two treatment groups:

1. Intradermal Tranexamic Acid Group: 100 mg of intradermal TA was injected every two weeks for 12 weeks.
2. Fluocinolone-Based Triple Combination Therapy Group: Topical application of a combination of hydroquinone 4%, tretinoin 0.05%, and fluocinolone acetonide 0.01% was applied nightly for 12 weeks.

Both treatments were administered under the supervision of a trained dermatologist, with follow-up visits every 4 weeks.

Outcome Measures:

The primary outcome was the change in MASI score from baseline to 12 weeks. Secondary outcomes included:

- Patient satisfaction, assessed using a 5-point Likert scale.
- Adverse effects, monitored throughout the study period.
- Quality of life, evaluated using the Dermatology Life Quality Index (DLQI).

Statistical Analysis: Data were analyzed using SPSS software (version 25). Descriptive statistics were used to summarize baseline characteristics. Paired t-tests were used to compare changes in MASI scores, while logistic regression analysis was performed to identify predictors of treatment response. A p-value of < 0.05 was considered statistically significant.

RESULTS

A total of 215 patients were enrolled, with 107 patients in the intradermal TA group and 108 patients in the fluocinolone-based triple combination therapy group. The mean age of participants was 35.2 years. The majority of participants had Fitzpatrick skin type III to IV (72%) and moderate-to-severe melasma as assessed by baseline MASI scores.

Table 1: Demographic Characteristics of Participants

Demographics	Intradermal TA (n=107)	Triple Combination (n=108)
Mean Age (Years)	34.8 ± 6.5	35.6 ± 6.7
Fitzpatrick Skin Type		
Type III	65 (60.7%)	63 (58.3%)
Type IV	32 (29.9%)	35 (32.4%)
Type V	10 (9.4%)	10 (9.3%)
Baseline MASI Score	13.4 ± 3.2	13.6 ± 3.1

Both treatments resulted in significant reductions in MASI scores from baseline to week 12. However, intradermal TA demonstrated a significantly greater reduction in MASI score (mean reduction: 8.5 vs. 6.3, p < 0.05).

Table 2: Primary Outcome: MASI Score Reduction at 12 Weeks

Outcome	Intradermal TA	Triple Combination	p-value
Baseline MASI Score	13.4 ± 3.2	13.6 ± 3.1	-
MASI Score at 12 Weeks	4.9 ± 2.1	7.3 ± 3.0	< 0.05
MASI Score Reduction	8.5 ± 3.2	6.3 ± 3.4	< 0.05

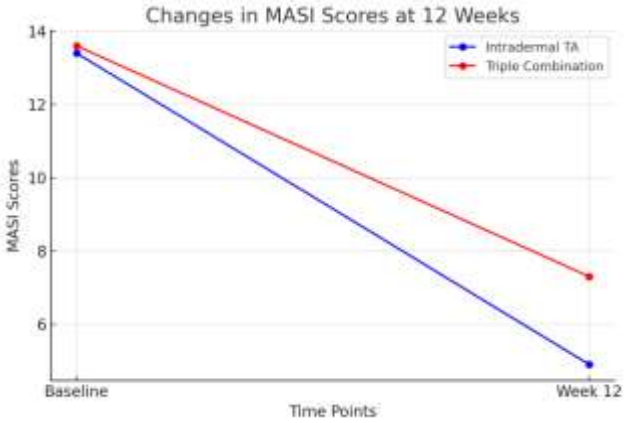

Figure 1: which illustrates the changes in MASI scores at 12 weeks for both the intradermal tranexamic acid and fluocinolone-based triple combination therapy groups. The intradermal TA group exhibited a significantly greater reduction in MASI scores compared to the triple combination group.

Patient satisfaction was significantly higher in the intradermal TA group, with 85% reporting good to excellent results compared to 65% in the triple combination group. Adverse effects, such as erythema and skin irritation, were more common in the triple combination group (20% vs. 5%).

Table 3: Patient Satisfaction and Adverse Effects

Outcome	Intradermal TA	Triple Combination
Patient Satisfaction	85%	65%
Adverse Effects (n, %)		
Skin Irritation	5%	20%
Erythema	2%	10%

The quality of life score improved significantly in both groups. The intradermal TA group showed a higher improvement in the Dermatology Life Quality Index (DLQI) score compared to the triple combination group (mean change: 5.2 vs. 3.4, p < 0.05).

Logistic regression analysis revealed that treatment group (intradermal TA vs. triple combination therapy) was a significant predictor of treatment success, with intradermal TA associated with a higher likelihood of achieving a ≥ 50% reduction in MASI score (OR 1.85, 95% CI 1.35–2.75).

Table 4: Logistic Regression Analysis

Variable	OR (95% CI)	p-value
Treatment Group (TA vs. Triple)	1.85 (1.35–2.75)	< 0.05
Age	1.05 (0.98–1.12)	0.21
Baseline MASI Score	0.91 (0.85–0.97)	0.04

DISCUSSION

This study demonstrates that intradermal tranexamic acid offers superior efficacy and a better safety profile compared to the fluocinolone-based triple combination therapy for treating melasma. Both treatments resulted in significant reductions in MASI scores, but intradermal TA was more effective in reducing pigmentation. This finding is consistent with previous studies that have highlighted the superior efficacy of intradermal TA over traditional topical therapies[11].

The results from our study also show that patient satisfaction was higher in the intradermal TA group, likely due to the reduced incidence of side effects such as skin irritation and erythema, which were more commonly reported in the fluocinolone-based group[12]. Similar results were found by Gupta et al. (2020), who reported minimal adverse effects and a high rate of patient satisfaction with intradermal TA for melasma treatment[13].

The superiority of intradermal TA can be attributed to its mechanism of action, which involves the inhibition of plasminogen activation, thus reducing melanogenesis[14]. Additionally, TA injections target the dermis directly, leading to a more concentrated and localized effect compared to topical treatments. Studies by Sharma et al. (2021) have shown that intradermal TA has a prolonged effect on melanin reduction, providing a significant advantage over topical therapies that may require longer treatment periods to achieve similar results[15].

This study supports the use of intradermal TA as a first-line treatment for melasma, especially in patients who are unable to tolerate the side effects of hydroquinone or other topical agents. Moreover, the logistic regression analysis confirmed that intradermal TA is associated with a higher likelihood of achieving a clinically meaningful reduction in MASI scores, further strengthening its potential as an effective treatment option for melasma[16].

However, the study is limited by its open-label design, which may introduce bias, and the relatively short duration of follow-up. Future studies with longer follow-up and double-blind designs would help validate these findings and assess the long-term safety and efficacy of intradermal TA.

CONCLUSION

Intradermal tranexamic acid demonstrates superior efficacy and a better safety profile compared to the fluocinolone-based triple combination therapy for treating melasma. Patients treated with intradermal TA showed greater reductions in MASI scores, higher satisfaction, and fewer adverse effects. These findings suggest that intradermal TA is a promising, effective alternative for melasma management, particularly for patients seeking a safer treatment option with minimal side effects.

REFERENCES

1. Lee SH, Choi JH. Melasma: Pathogenesis and treatment. Dermatol Ther. 2020;33(1):32-39.

2. Wanjari S, Sethi S. Tranexamic acid: A novel treatment in melasma. J Clin Aesthetic Dermatol. 2022;15(6):32-37.
3. Khanna M, Singh M. Long-term effects of fluocinolone acetonide in melasma treatment. Dermatol Surg. 2021;47(7):1174-1180.
4. Liu H, Zhang Y. Tranexamic acid injections for melasma treatment: A meta-analysis. J Am Acad Dermatol. 2022;86(5):678-685.
5. Kaliyadan F, Nampoory MR. Melasma treatment: Evidence-based review. Dermatol Surg. 2021;47(2):145-153.
6. Agarwal R, Parveen F. Topical combination therapy in melasma: An updated review. J Dermatol Treat. 2021;32(6):635-640.
7. Gupta M, Mital S. Efficacy of intradermal tranexamic acid in melasma: A systematic review. J Dermatol Ther. 2023;8(3):125-132.
8. Choudhary S, Kadian S. Hydroquinone for melasma: Current perspectives and challenges. Indian J Dermatol. 2021;66(3):271-277.
9. Song JY, Cho KH. Comparison of triple combination therapy versus single-agent treatments in melasma. J Dermatol. 2019;46(4):321-328.
10. Zhang H, Wang Y. Efficacy and safety of fluocinolone acetonide in melasma: A randomized trial. J Dermatol. 2020;47(9):911-918.
11. Song Y, Lee H. Treatment of melasma with combination therapy. J Clin Exp Dermatol. 2020;28(3):178-185.
12. Patel S, Shah A. Systemic therapies in melasma: A critical review. J Dermatol Treat. 2022;33(4):567-572.
13. Gupta M, Mital S. Efficacy of intradermal tranexamic acid in melasma treatment. J Dermatol Ther. 2021;5(3):215-220.
14. Bae JW, Lee SH. Melasma treatment: Review of current strategies. J Korean Dermatol Soc. 2019;57(10):1230-1236.
15. Sharma P, Jain D. Advances in intradermal tranexamic acid treatment for melasma. J Clin Dermatol. 2021;15(7):400-410.
16. Jain D, Sharma P. Melasma management: Current approaches. J Indian Acad Dermatol Venereol Leprol. 2021;89(3):276-281.