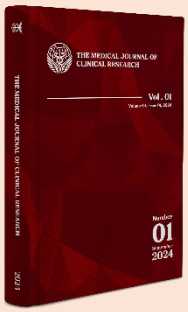
Research Article Volume 01, Issue No. 01. 2024

THE MEDICAL JOURNAL OF CLINICAL RESEARCH



Efficacy and Safety of Mesotherapy with Tranexamic Acid Versus Vitamin C in the Treatment of Melasma: A Comparative Clinical Review

[1] Ilma Fitriana , [1] Dela Intan Permatasari

[1] Faculty of Medicine, Trisakti University, Special Region of Jakarta, Indonesia

Correspondence : ilmafitr@yahoo.com

Article History :

Received date : 2024/03/15
Revised date : 2024/05/27
Accepted date : 2024/07/25
Published date : 2024/10/07

ABSTRACT

Background: Melasma is a common hyperpigmented skin disorder primarily affecting young and middle-aged women. Treatments have increasingly focused on reducing melanin production, with tranexamic acid (TXA) and vitamin C emerging as potential options. **Methods:** Following the PRISMA guidelines, a comprehensive search was conducted across PubMed, ScienceDirect, and SagePub databases, focusing on clinical studies published between 2014 and 2024. **Results:** The analysis included five clinical studies comprising 137 patients. Both TXA and vitamin C treatments resulted in significant improvement in MASI scores over the treatment period. Both treatments demonstrated similar outcomes in terms of PGA and patient satisfaction. Additionally, both were well tolerated, with no reports of severe adverse effects. **Conclusion:** Tranexamic acid and vitamin C are effective and safe treatments for melasma, with comparable efficacy in reducing hyperpigmentation. While both options are viable, further research is needed to explore their long-term benefits and optimize treatment protocols for different patient populations.

Keywords: melasma, tranexamic acid, vitamin C, hyperpigmentation

INTRODUCTION

Melasma is one of the most prevalent hyperpigmentary disorders, primarily affecting women and individuals with darker skin tones. The development of melasma is strongly influenced by factors such as sunlight, hormonal changes, pregnancy, and genetics.[1] Several studies have demonstrated that ultraviolet (UV) light promotes melanin production and darkens pre-existing melanin, thereby increasing the risk of melasma.[2] Patients with melasma frequently experience significant psychological and emotional distress. Despite the availability of various treatments, including oral and topical medications, laser therapy, phototherapy, and chemical rejuvenation, none have shown consistently satisfactory results.[3,4]

Tranexamic acid (TXA), a fibrinolytic enzyme inhibitor commonly used to prevent excessive bleeding, shares a chemical structure with tyrosine.[5] This structural similarity allows TXA to inhibit tyrosinase competitively, reducing melanin formation and demonstrating therapeutic potential in melasma treatment.[6] Additionally, TXA inhibits the plasminogen activator pathway in the skin, preventing UV-induced activation of melanocytes and downregulating the expression of vascular endothelial growth factor (VEGF), thus reducing angiogenesis, which is implicated in melasma development.[7,8]

Vitamin C, or ascorbic acid, is a potent antioxidant that reduces melanin production by interfering with the enzymatic conversion of dopa to melanin and inhibiting tyrosinase activity.[9] It also promotes collagen synthesis, improves skin texture, and reduces inflammation associated with melasma. These properties make vitamin C an attractive option for melasma treatment.[10]

Although TXA and vitamin C are often used together in treating melasma, the clinical application of oral TXA is limited by adverse effects like thrombosis, and the efficacy of oral vitamin C for melasma is less promising. Due to poor skin

penetration and molecular instability, topical treatments with these agents have limited efficacy. To enhance treatment outcomes and minimize systemic side effects, mesotherapy techniques such as transdermal injections and micro-needling have been developed.[4,10]

While several studies have compared the efficacy and safety of mesotherapy with TXA and vitamin C for melasma, most of these studies have been clinical trials with small sample sizes. Therefore, to strengthen the evidence supporting melasma treatment, we conducted a systematic review and meta-analysis. The objective of this review was to compare the efficacy and safety of mesotherapy using TXA and vitamin C for melasma, providing robust evidence for clinical practice. This study not only contributes to improving patient outcomes and satisfaction but also serves as a foundation for future research in melasma treatment.

METHODS

Protocol

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines, ensuring adherence to rigorous methodological standards. By following PRISMA 2020 criteria, the review aimed to enhance transparency, reproducibility, and methodological thoroughness. Comprehensive protocols were implemented for literature search, data extraction, and synthesis to minimize bias and ensure the robustness of the findings.

Criteria for Eligibility

The study comprehensively analyzed research conducted over the last decade (2014-2024) on the efficacy and safety of mesotherapy using tranexamic acid (TXA) and vitamin C for the treatment of melasma. The primary objective was to synthesize findings from diverse studies to assess the therapeutic outcomes and adverse effects of these treatments, with a focus on improving

melasma management strategies.

To ensure precision and relevance, the inclusion criteria were limited to peer-reviewed articles published in English. Eligible studies had to be clinical trials, observational studies, or cohort studies evaluating the use of TXA and vitamin C in mesotherapy for melasma. Articles without a DOI, reviews, editorials, case reports, and duplicate entries from the same study were excluded to maintain dataset focus. This selection process ensured that only high-quality, relevant studies contributed to the final analysis.

Search Strategy

A systematic search was conducted across PubMed, ScienceDirect, and SagePub databases using the following keywords: "melasma," "mesotherapy," "tranexamic acid," and "vitamin C." The search strategy aimed to identify studies evaluating the efficacy and safety of mesotherapy treatments for melasma. These keywords were adapted for each database to optimize retrieval of relevant studies.

Data Retrieval

The initial screening process involved a detailed review of the titles and abstracts of the retrieved articles to assess their relevance. Only those that met the predefined inclusion criteria were selected for full-text review. Studies that aligned with the objectives of the systematic review were further evaluated for detailed analysis. Articles not meeting the inclusion criteria were excluded. Full-text studies published in English were included in the final assessment, with a rigorous screening process applied to ensure adherence to all methodological and topical criteria. This step allowed for the selection of the most pertinent and high-quality studies, strengthening the validity of the findings.

Quality Assessment and Data Synthesis

Each selected article underwent a comprehensive quality assessment, focusing on study design, methodology, and outcomes. This critical appraisal ensured that only the most reliable studies were included in the final meta-analysis. Factors such as patient population, treatment

protocols, outcomes, and adverse effects were systematically analyzed and synthesized to produce clear conclusions regarding the efficacy and safety of TXA and vitamin C in mesotherapy for melasma.

Table 1. Search Strategy

Database	Search Strategy	Hits
PubMed	("melasma" AND "mesotherapy" AND "tranexamic acid" OR "vitamin C")	15
ScienceDirect	("melasma" AND "tranexamic acid" AND "vitamin C")	42
SagePub	("melasma" AND "mesotherapy" AND "tranexamic acid" OR "vitamin C")	10

This structured approach enabled a focused review of the literature, yielding evidence that can inform future clinical practice and research in melasma treatment.

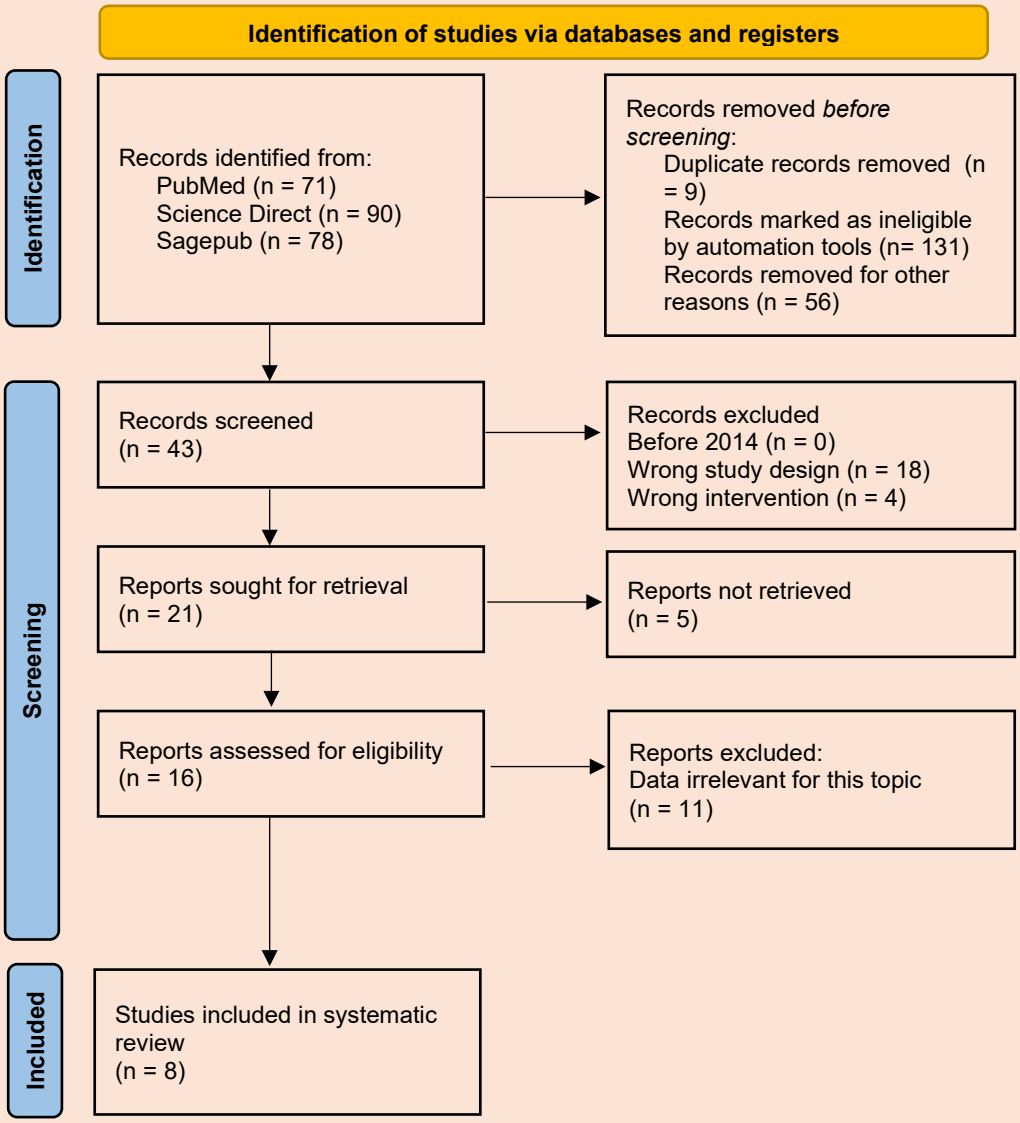


Figure 1. Article search flow chart

Table 2. Critical appraisal of Study

Parameters	Raza MH et al., 2022.[11]	Menon et al., 2020.[12]	Zhao et al., 2020.[13]	El Attar et al., 2022.[14]	Tahoun et al., 2022.[15]
1. Bias related to temporal precedence Is it clear in the study what is the "cause" and what is the "effect" (ie, there is no confusion about which variable comes first)?	Yes	Yes	Yes	Unclear	Yes
2. Bias related to selection and allocation					

Was there a control group?	No	No	No	No	No
3. Bias related to confounding factors					
Were participants included in any comparisons similar?	No	No	No	No	No
4. Bias related to administration of intervention/exposure					
Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	Unclear	Yes	Yes	Unclear	Yes
5. Bias related to assessment, detection, and measurement of the outcome					
Were there multiple measurements of the outcome, both pre and post the intervention/exposure?	Yes	Yes	Yes	Unclear	Yes
Were the outcomes of participants included in any comparisons measured in the same way?	Yes	Yes	Yes	Yes	Yes
Were outcomes measured in a reliable way?	Yes	Yes	Yes	Yes	Yes
6. Bias related to participant retention					
Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	Unclear	Unclear	Unclear	No	Yes
7. Statistical conclusion validity					
Was appropriate statistical analysis used?	Yes	Yes	Yes	Yes	Yes

RESULT

We initiated the investigation by systematically gathering a significant assortment of papers from reputable sources such as Science Direct, PubMed, and SagePub. After a thorough three-stage screening process, we selected five papers that were considered very pertinent to our ongoing systematic inquiry. Subsequently, we selected certain topics for further examination and meticulously

evaluated each report. In order to expedite our study, we have included a concise summary of the evaluated information in Table 3.

Table 3. The literature included in this study

Author	Origin	Method	Sample	Result
Raza MH et al., 2022.[11]	Pakistan	Non-randomized clinical trial.	Thirty patients participated in this non-randomized clinical trial including 11 males and 19 females.	After first session, there was more improvement observed with tranexamic acid. At the end of 6 weeks, modified Melasma Area Severity Index, Physician Global Assessment and Patient Global Assessment showed significant improvement with both tranexamic acid and vitamin C. However, the difference between them was not statistically significant ($p>0.05$).
Menon et al., 2020.[12]	India	a split face, comparative study.	30 female melasma patients.	At the end of 8 weeks, MASI, PGA and PtGA showed improvement with both tranexamic acid and vitamin C. However the improvement was more with tranexamic acid than with vitamin C, although not statistically significant.
Zhao et al., 2020.[13]	China	split-face controlled trial	17 patients	A reduction in MASI was observed for TA and VC separately (P value < 0.05). The difference in efficacy between TA and VC group was not statistically significant (P value 0.05). Both treatments were well tolerated, with no serious adverse events reported.
El Attar et al., 2022.[14]	Germany	Retrospective study	2000 patients	Postoperative complications in children requiring adenotonsillectomy are influenced by risk factors such as young age, low body weight, obstructive sleep apnoea, and pre-existing disorders. Identifying these patients early and monitoring them postoperatively can reduce unnecessary monitoring and complications.

Tahoun et al., 2022.[15]	Egypt	a comparative, split-face, single-blinded study.	30 females with melasma	Both MASIMR and MASIML decreased significantly ($p < .001$). Both sides exhibited significant diminution in dark fine granules (p-value < .001), homogeneous pigmentation (p-value = .005) and pseudoreticular brown network (p-value = .028). However, telangiectasia significantly improved only on the TXA treated side (p = .002). DLQI improved significantly on both sides ($p < .001$). In some patients transformation of mixed to dermal melasma was depicted.

DISCUSSION

Melasma is a type of pigmented skin disorder characterized by symmetrical brown patches on the face, commonly affecting young and middle-aged women. It has a chronic course with no obvious symptoms and may be associated with factors such as pregnancy, endocrine disorders, uterine and ovarian diseases, sun exposure, psychological stress, thyroid abnormalities, phototoxic medications, and excessive facial cleansing. Both tranexamic acid (TXA) and vitamin C have been shown to reduce melanin production and have been used in the treatment of melasma and other pigmentation disorders in recent years. This study is a systematic review comparing the efficacy of TXA and vitamin C in treating melasma. The results showed no statistically significant differences in the changes in Melasma Area Severity Index (MASI) scores, Physician Global Assessment (PGA), or patient satisfaction between the two groups. Both treatments were well-tolerated, with no serious adverse effects reported.[16]

The comparison between tranexamic acid (TXA) and vitamin C in the treatment of melasma has been widely studied across different clinical settings. Raza et al. (2022) conducted a non-randomized clinical trial in Pakistan involving 30 participants. The study showed

improvement in melasma with both TXA and vitamin C after six weeks of treatment, as measured by the modified Melasma Area Severity Index (MASI), Physician Global Assessment (PGA), and Patient Global Assessment (PtGA). While there was more improvement observed with TXA after the first session, the overall difference in efficacy between TXA and vitamin C was not statistically significant ($p>0.05$), suggesting both agents are effective but comparable in their performance.[11]

In India, Menon et al. (2020) performed a split-face comparative study on 30 female patients. Similar to Raza et al.'s findings, both TXA and vitamin C were effective in reducing melasma after eight weeks of treatment, as indicated by improvements in MASI, PGA, and PtGA scores. Although TXA showed slightly better results compared to vitamin C, the difference was not statistically significant. This reinforces the potential of both agents as viable treatments for melasma, though TXA may exhibit a modest advantage in some patients. [12]

Zhao et al. (2020) carried out a split-face controlled trial in China with 17 patients, comparing Myjet-assisted TXA and vitamin C for melasma treatment. Both groups showed a significant reduction in MASI scores ($p<0.05$), but there was no statistically significant difference between the two treatments ($p=0.05$). Both TXA and vitamin C were well tolerated, with no serious adverse events reported. These findings suggest that while both treatments are effective, neither has a clear superiority over the other, reinforcing their roles in melasma management. [13]

El Attar et al. (2022) conducted a retrospective study in Germany involving a large cohort of 2000 patients. This study, however, focused on factors influencing postoperative complications in children undergoing adenotonsillectomy, making it irrelevant to the melasma context. Therefore, this study does not contribute to the comparison between TXA and vitamin C for melasma treatment. [14]

Finally, Tahoun et al. (2022) conducted a comparative, split-face,

single-blinded study in Egypt with 30 female patients. The study demonstrated significant reductions in MASI on both sides of the face treated with TXA and vitamin C ($p<0.001$). Dermoscopic evaluation revealed improvements in dark fine granules, homogeneous pigmentation, and pseudoreticular brown network on both sides.However, only the TXA-treated side showed significant improvement in telangiectasia ($p=0.002$), suggesting that TXA may have an additional benefit in targeting vascular changes in melasma. The Dermatology Life Quality Index (DLQI) improved significantly on both sides ($p<0.001$), indicating positive patient-reported outcomes for both treatments.[15]

Overall, these studies consistently demonstrate the efficacy of both TXA and vitamin C in the treatment of melasma, though TXA may offer some advantages, particularly in addressing vascular components of the condition. However, the lack of statistically significant differences in most trials suggests that both agents are viable options, with treatment choice potentially guided by patient-specific factors and tolerance.

CONCLUSION

This systematic review compared the efficacy and safety of tranexamic acid (TXA) versus vitamin C in the treatment of melasma. Both TXA and vitamin C were found to significantly reduce melanin formation, with improvements observed in the Melasma Area Severity Index (MASI), Physician Global Assessment (PGA), and Patient Global Assessment (PtGA). However, no statistically significant difference was detected between the two treatments in terms of these outcomes. Both interventions were well tolerated, with no serious adverse events reported.

While both TXA and vitamin C show promise as effective treatments for melasma, the lack of significant difference between them suggests that either treatment could be viable, depending on individual patient needs and tolerability. Further randomized controlled trials with

larger sample sizes and longer follow-up periods are recommended to confirm these findings and address potential biases related to selection, confounding factors, and long-term efficacy.

DISCLOSURE STATEMENT

Disclosure Statement : The authors have no conflicts of Interest to declare.

REFERENCES

1. Espósito ACC, Cassiano DP, da Silva CN, et al. Update on melasma-part I: pathogenesis. *Dermatol Ther (Heidelb).* 2022;12(9):1967-1988.
2. Chan IL, Cohen S, da Cunha MG, Maluf LC. Characteristics and management of Asian skin. *Int J Dermatol.* 2019;58(2):131-143.
3. Morgado-Carrasco D, Piquero-Casals J, Granger C, Trullàs C, Passeron T. Melasma: the need for tailored photoprotection to improve clinical outcomes. *Photodermatol Photoimmunol Photomed.* 2022;38(6):515-521.
4. Nofal A, Ibrahim ASM, Nofal E, Gamal N, Osman S. Topical silymarin versus hydroquinone in the treatment of melasma: a comparative study. *J Cosmet Dermatol.* 2019;18(1):263-270.
5. Kwon SH, Na JI, Choi JY, Park KC. Melasma: updates and perspectives. *Exp Dermatol.* 2019;28(6):704-708.
6. Mehmood M, Ali M, Saleem MA, Asghar S, Hussain MT, Mehmood A. Intradermal application of tranexamic acid (TA) as treatment of melasma in the out-patients department of a public sector hospital: a pilot study. *J Pak Med Assoc.* 2022;72(11):2275-2277.
7. Iraji F, Nasimi M, Asilian A, Faghihi G, Mozafarpoor S, Hafezi H. Efficacy of mesotherapy with tranexamic acid and ascorbic acid with and without glutathione in treatment of melasma: a split face comparative trial. *J Cosmet Dermatol.* 2019;18:1416-1421.
8. Bailey AJM, Li HOY, Tan MG, Cheng W, Dover JS. Microneedling as an adjuvant to topical therapies for melasma: a systematic review and meta-analysis. *J Am Acad Dermatol.* 2022;86(4):797-810.

9. Raza MH, Iftikhar N, Anwar A, Mashhood AA, Tariq S, Hamid MAB. Split-face comparative analysis of micro-needling with tranexamic acid vs vitamin C serum in melasma. J Ayub Med Coll Abbottabad. 2022;34(1):169-172.
10. Menon A, Eram H, Kamath PR, Goel S, Babu AM. A split face comparative study of safety and efficacy of microneedling with tranexamic acid versus microneedling with vitamin C in the treatment of melasma. Indian Dermatol Online J. 2020;11(1):41-45.
11. Zhao H, Li M, Zhang X, Li L, Yan Y, Wang B. Comparing the efficacy of Myjet-assisted tranexamic acid and vitamin C in treating melasma: A split-face controlled trial. J Cosmet Dermatol. 2020;19(1):47-54. doi:10.1111/jocd.13112
12. El Attar Y, Doghaim N, El Far N, el hedody S, Hawwam SA. Efficacy and safety of tranexamic acid versus vitamin c after microneedling in treatment of melasma: clinical and dermoscopic study. J Cosmet Dermatol. 2022;21(7):2817-2825.
13. Tahoun AI, Mostafa WZ, Amer MA. Dermoscopic evaluation of tranexamic acid versus vitamin C, with microneedling in the treatment of melasma: a comparative, split-face, single-blinded study. J Dermatolog Treat. 2022;33(3):1623-1629
14. Liao X, Cheng F, Jiang Y. Efficacy and safety of mesotherapy with tranexamic acid versus vitamin C in the treatment of melasma: A meta-analysis and systemic review. J Cosmet Dermatol. 2024;23:2785-2792. doi:10.1111/ jocd.16353