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Assessing the efficacy of oral tranexamic acid as an adjuvant to triple combination topical treatment in melasma: a meta-analysis of randomized controlled trials

Ocílio Ribeiro Gonçalves,[1] Maria Clara Fogaça de Souza,[2] Alice Volpato Rocha,[3] Gabriel Silva Alves,[2] João Luís Reis Freitas,[4] Benjamim Barbosa de Azevedo,[1] Milene Vitória Sampaio Sobral,[2] Amanda Scrobot Handocha[5] and Caroline Baima de Melo[1]

[1]Federal University of Piauí (UFPI), Teresina, Brazil
[2]University of Western São Paulo (Unoeste), Presidente Prudente, Brazil
[3]Federal University of Paraná (UFPR), Curitiba, Brazil
[4]University of São Paulo (USP), São Paulo, Brazil
[5]University Positivo, Curitiba, Brazil

Correspondence: Ocílio Ribeiro Gonçalves. Email: ocilio41@gmail.com

Abstract

Melasma is a skin pigmentation disorder that lacks consistent treatment success, despite various methods used. Tranexamic acid (TXA) has shown hypopigmentation properties, but whether its administration should be combined with standard treatment has yet to be clarified. We aimed to perform an investigation of the effectiveness and safety of oral TXA as an adjuvant to triple combination cream (TCC) treatment in melasma. We searched PubMed, Embase and Cochrane (CENTRAL) for studies that compared TCC + adjuvant TXA to TCC treatment alone in patients with melasma. Outcomes of interest included change from the baseline Melasma Area and Severity Index (MASI) score, recurrence of melasma and adverse events. Statistical analysis was performed using R Studio 4.3.2. Four trials involving 490 patients were included. In the pooled analysis, the decrease from baseline in MASI score [mean difference –3.10, 95% confidence interval (CI) –5.85 to –0.35] was significantly higher in patients treated with oral TXA as an adjuvant to TCC compared with TCC alone. Melasma recurrence [risk ratio (RR) 0.28; 95% CI 0.16–0.49] was significantly lower in the group treated with TCC and TXA. Regarding erythema (RR 0.63, 95% CI 0.34–1.17) and burning (RR 0.59, 95% CI 0.30–1.17), no statistically significant difference was found. This meta-analysis demonstrated statistically significant benefits of TCC + TXA combination treatment compared with TCC alone. Furthermore, the results suggest that the addition of TXA to TCC treatment may reduce melasma recurrence.

Introduction

Melasma is a chronic common hyperpigmentary disorder characterized by brown or greyish-brown patches on sun-exposed facial skin. Owing to this facial involvement, the disease has a negative impact on the quality of life of affected individuals.[1] The clinical manifestations can vary from asymptomatic light-to-dark-brown hyperpigmentation to a symmetrical disposition with irregular borders; it is usually worse in the summer. Risk factors included ultraviolet (UV) exposure, hormonal changes and a genetic predisposition.[2–4] While the precise cause of melasma remains unclear, researchers speculate that this condition stems from active melanocytes. Studies have identified augmented vascularity in the affected skin and heightened levels of angiogenic factors within the epidermis.[3,5,6] These factors are thought to influence the onset of melasma.

Sun exposure is the most relevant trigger for the onset of melasma.[7] The brown patches with geographical borders found in patients with melasma are observed in three distinct patterns: centrofacial (where lesions extend across the forehead and descend along the midline of the face, including the cheeks); malar (the lesions extend across the cheeks and dorsum of the nose); and mandibular (where lesions follow the jawline). The most common distribution is centrofacial, although mixed patterns are often encountered. Melasma can also be classified by dermoscopy according to the depth of melanin pigment: epidermal, dermal, mixed and the nonapparent Wood lamp type seen in people with Fitzpatrick skin types V and VI. Each histological lesion is characterized by their different responses to treatment, so it is important to know the correct classification before choosing the best treatment.

Melasma occurs in all population groups. However, epidemiological studies have reported a higher prevalence among more pigmented phenotypes, including people of East Asian (Japanese, Korean and Chinese), Indian, Pakistani, Middle Eastern and Mediterranean–African descent.[8] It is also

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common among Hispanic Americans and Brazilians who live in intertropical areas, where there is greater exposure to UV radiation.[1] In a 2011 review, the mean age of patients with melasma was 33.45 years and the female-to-male ratio was 4 : 1.[9]

Despite a high demand for therapeutic solutions, melasma does not yet have an established, consistently satisfactory treatment. As melasma is a chronic condition with no known cure, its treatment is based on inducing remission and preventing relapse. The gold standard protocol is sun protection measures (e.g. application of sunscreen and avoidance of sun exposure) and topical bleaching agents, usually triple combination cream (TCC) composed of hydroquinone 2–4% with retinoic acid 0.01–0.05% and hydrocortisone 1%.[10] According to the literature, the complementary use of chemical peels with glycolic acid and retinoic acid may be added to the regimen, while fractionated laser therapy is still not well established. Among the therapeutic possibilities, tranexamic acid (TXA) has shown satisfying results owing to its ability to inhibit the production of melanin – the pigment responsible for skin colour. However, individual response to treatment can vary and, although TXA can be effective,[11] it is not clear whether it should be used on its own or be added to the standardized TCC regimen.

A prior meta-analysis conducted by Feng *et al.* concluded that oral TXA is an available, effective and safe alternative treatment for melasma.[12] However, recognizing the evolving landscape of melasma management, our study sought to explore the potential synergistic benefits of TXA when used as an adjuvant to the TCC regimen. By investigating the combined effects of these interventions, we aimed to contribute valuable insights into the efficacy and safety of this novel approach, potentially refining and expanding the existing treatment options for individuals with melasma. Different routes of TXA administration (oral, topical and localized microinjections) have shown encouraging results; however, efficacy and safety data in treating melasma with TXA lack substantial backing owing to insufficiently robust randomized controlled trials (RCTs). Our objective was to conduct a systematic literature review and meta-analysis to explore the effectiveness and safety of oral TXA as a supplementary treatment in individuals undergoing the gold-standard treatment for melasma.

Materials and methods

Eligibility criteria

To be included in this meta-analysis, studies had to meet all of the following eligibility criteria: (i) RCT; (ii) comparison of TCC treatment alone vs. TCC treatment + adjuvant TXA; (iii) included participants had melasma. In addition, studies were only included if they reported any of the clinical outcomes of interest. We excluded studies with no control group; those that used different intervention modalities; and those that had no outcomes of interest.

Search strategy and data extraction

We systematically searched PubMed, Embase and Cochrane (CENTRAL) from inception to December 2023 with the following search terms: 'melasma', 'fluocinolone-based triple combination cream', 'modified Kligman's formula', 'routine topical treatment', 'oral tranexamic acid' and 'tranexamic acid'. The reference lists from all included studies, previous systematic reviews and meta-analyses were also searched manually for any additional studies. Two authors (A.V.R. and M.C.F.S.) independently extracted the data following predefined search criteria and quality assessment. The prospective meta-analysis protocol was registered in PROSPERO on 20 December 2023 (ID 495718).

Endpoints and subgroup analyses

The main focus of our analysis was a change in the initial Melasma Area and Severity Index (MASI) score and post-treatment recurrence of melasma. Additional outcomes of interest were adverse events such as erythema and burning.

Quality assessment

We evaluated the risk of bias using the Cochrane Risk of Bias assessment tool (version 2). Two independent authors completed the risk-of-bias assessment (M.V.S.S. and O.R.G.). Disagreements were resolved via consensus after discussion.

Statistical analysis

This systematic review and meta-analysis were performed and reported according to the Cochrane Collaboration Handbook for Systematic Review of Interventions and the PRISMA statement (https://www.prisma-statement.org).[13] Standardized mean differences with 95% confidence intervals (CIs) were used to compare continuous outcomes. We assessed heterogeneity with I^2 statistics and Cochran's Q test; P-values < 0.10 and $I^2 > 25\%$ were considered to be statistically significant for heterogeneity. Statistical analysis was performed using R Studio 4.3.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Study selection and characteristics

The initial search yielded 79 results (Figure 1). After the removal of duplicate records and ineligible studies, eight remained and were fully reviewed based on the inclusion criteria. Of these, 4 RCTs were included in the systematic review and meta-analysis, comprising 490 patients.[2,14–16] In total, 245 (50.0%) patients received TCC + oral TXA and 245 (50.0%) received TCC. The characteristics of each of the included studies are reported in Table 1. Significant between-study variability existed with regard to the treatment duration of TCC + oral TXA, as well as the duration of follow-up. Risk-of-bias analysis was applied to the four studies.

Pooled analysis of all studies

In participants who received TCC + oral TXA, there was a general trend of decrease from baseline in MASI score

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Table 1 Baseline characteristics of patients in the studies included in the systematic review and meta-analysis

Study (country)	Patients (TCC+TXA/TCC), *n*	Female (TCC+TXA/TCC), %	Age (TCC+TXA/TCC), years*	Duration of follow-up (TCC+TXA/TCC), months	Melasma type			Melasma distribution		
					Epidermal (TCC+TXA/TCC)	Dermal (TCC+TXA/TCC)	Mixed (TCC+TXA/TCC)	Frontal (TCC+TXA/TCC), %	Central facial (TCC+TXA/TCC), %	Chin (TCC+TXA/TCC), %
Basit *et al.* (Pakistan)[2]	30/30	87/77	30/32	6	NA	NA	NA	29/36	36/29	0
Minni and Poojary (India)[14]	65/65	92/92	36/38	9	NA	NA	NA	NA	NA	NA
Padhi and Pradhan (India)[15]	20/20	85/75	36/36	6	NA	NA	NA	NA	NA	NA
Karn *et al.* (Nepal)[16]	130/130	84/83	NA	3	93/80	14/14	23/36	15/14	102/107	13/9

*Mean or median. NA, not available; TCC, triple combination cream; TXA, tranexamic acid.

Figure 1 PRISMA flow diagram of study screening and selection.

[mean difference (MD) −3.10, 95% CI −5.85 to −0.35; $P=0.03$, $I^2=83\%$ (Figure 2a)]. Melasma recurrence [risk ratio (RR) 0.28, 95% CI 0.16–0.49; $P<0.001$ (Figure 2b)] was significantly lower in the group of patients treated with TCC+adjuvant TXA. There was no statistically significant difference between the groups in terms of erythema [RR 0.63, 95% CI 0.34–1.17; $P=0.15$; $I^2=0\%$ (Figure 2c)] and burning [RR 0.59, 95% CI 0.30–1.17; $P=0.13$, $I^2=0\%$ (Figure 2d)]. The sensitivity analysis with adjusted risk estimates could not be performed owing to the low number of observational studies reporting adjusted risk estimates.

Quality assessment

The Cochrane Risk of Bias assessment tool (version 2) was used for quality assessment. Individual risk-of-bias appraisal for each of the RCTs is reported in Table 2. Four studies lost points in domains related to the randomization process. Two lost points for deviations from the intended interventions. One study lost points in the 'measurement of outcomes' domain. The studies were considered to be at low risk of bias for all other domains.

Discussion

In this systematic review and meta-analysis of 4 studies and 490 patients,[2,14–16] we compared TCC alone to TCC treatment with adjuvant oral TXA in people with melasma. The main findings from the pooled analyses included a decrease in MASI score with the use of TCC+adjuvant TXA; melasma recurrence was significantly lower in the group treated with TCC+adjuvant TXA; and there was no statistically

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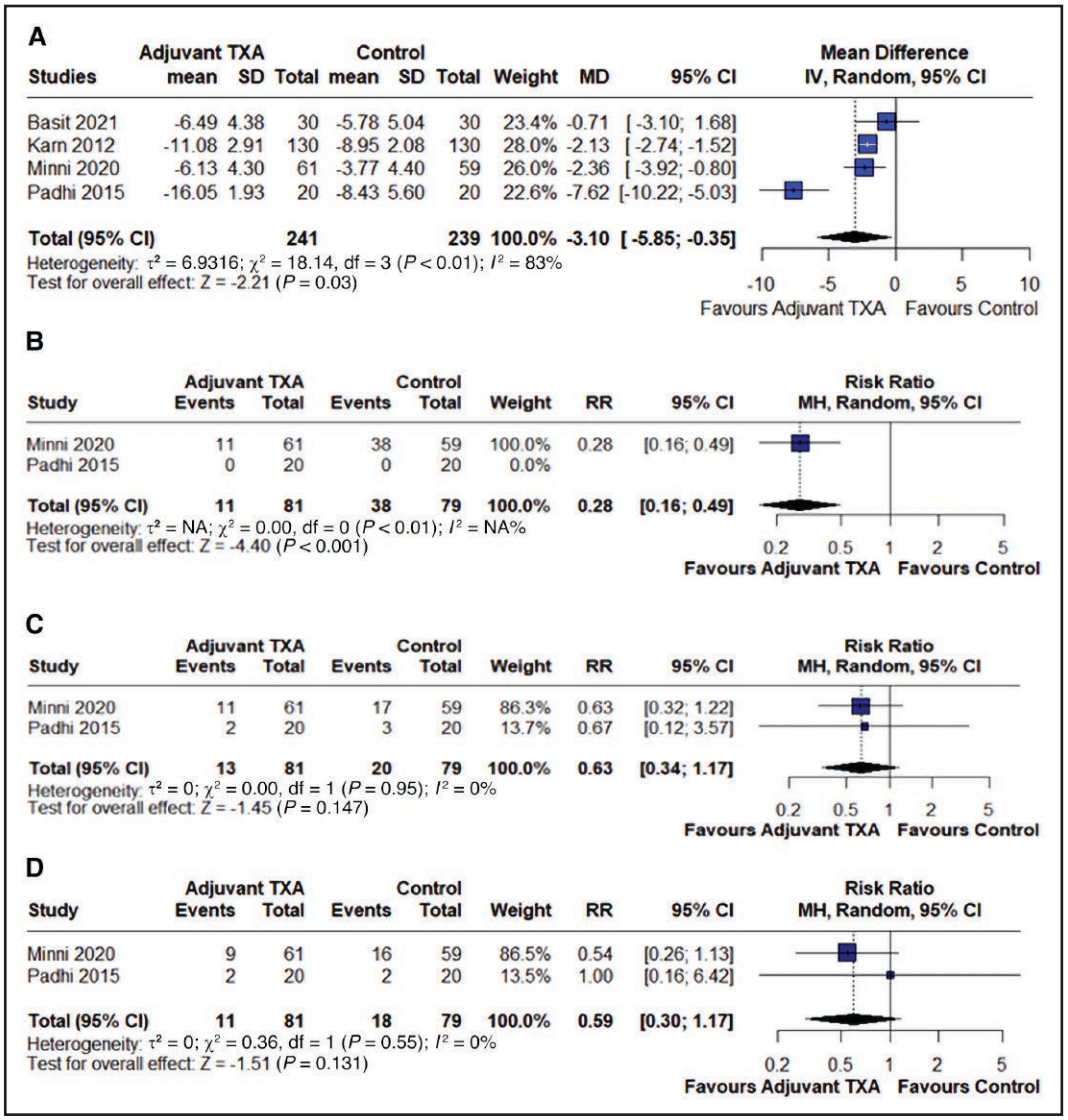


Figure 2 (a) There was a significantly higher decrease in the Melasma Area and Severity Index (MASI) score in patients in the triple combination cream (TCC) + adjuvant tranexamic acid (TXA) group compared with patients in the TCC monotherapy group (control). (b) Melasma recurrence rates were significantly lower in patients in the TCC + adjuvant TXA group compared with patients in the TCC group. (c) There was no statistically significant difference in the risk of erythema in patients in the TCC + adjuvant TXA group vs. the TCC (control) group. (d) There was no statistically significant difference in the risk of burning in patients in the TCC + adjuvant TXA group vs. the TCC (control) group. CI, confidence interval; MD, mean difference; MH, Mantel–Haenszel; NA, not available; RR, risk ratio; SD, standard deviation.

significant difference between the groups with regard to the adverse events of erythema and burning.

Melasma presents a challenge in its treatment, often leading to recurrence.[17] Treatment strategies focus on reducing melanin biosynthesis, transport and transfer, as well as decreasing epidermal melanin content.[17,18] TXA exhibits multifaceted action in the pathophysiology of melasma, acting via various mechanisms. It inhibits the binding of plasminogen to lysine-binding sites on keratinocytes, resulting in decreased levels of free arachidonic acid and, consequently, reduced prostaglandin production.[11,17–21] Moreover, it contributes to decreasing endothelin-1 levels in keratinocytes, thus mitigating keratinocyte-induced angiogenesis.[11,17–22]

The 2012 study of Wu *et al.* demonstrated that TXA was a safe and effective treatment.[23] In their study, only 4% of 74 patients who received oral TXA at a dose of 250 mg twice daily for 6 months experienced poor results, without any worsening. However, 96% of those undergoing treatment with TXA showed improvement. Despite hydroquinone cream being the most common treatment for melasma, with substantial positive outcomes, it is linked to a higher number of side-effects such as burning, itching, dryness, erythema and contact dermatitis.[24,25] In contrast, individuals treated with TXA in the study by Wu *et al.* did not experience significant complications.[23]

Although it is a safe treatment, TXA has contraindications such as allergy, intracranial bleeding, defective colour vision, history or active venous or arterial thromboembolism.[26]

We aimed to demonstrate the adjuvant effect of TXA; indeed, it appeared to be superior when compared with TCC treatment alone. Our meta-analysis of RCTs revealed consistent findings regarding the addition of TXA to the

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Table 2 Risk of bias assessment of the included studies performed with the Cochrane Risk of Bias assessment tool (version 2)

Study	Bias from randomization process	Bias due to deviations from intended interventions	Bias due to missing outcome data	Bias in selection of reported results	Overall risk of bias
Basit *et al*. (Pakistan)[2]	Some concerns	Low	Low	Low	Some concerns
Karn *et al*. (Nepal)[16]	Some concerns	Low	Low	Low	Some concerns
Minni and Poojary (India)[14]	Low	Low	Low	Low	Low
Padhi and Pradhan (India)[15]	Some concerns	Some concerns	Low	Low	Some concerns

melasma treatment regimen, and there was a general trend of decrease from baseline in MASI score.

A study by Minni and Poojary concluded that patients undergoing adjuvant therapy with TXA experience a reduced recurrence of melasma.[14] In their study, the TXA adjuvant treatment group showed a recurrence rate of 18.0% vs. 64.4% in the TCC monotherapy group. Additionally, in the study by Wu *et al*.,[23] it was found that of the seven patients who experienced melasma recurrence (9.5%), all were satisfactorily retreated with TXA. The results of our study corroborate the findings of these other studies, with less recurrence being found in the TXA adjuvant group.

Kim *et al*. published a systematic review and meta-analysis comparing the reduction in MASI score among groups using diverse forms of routine treatment alone vs. routine treatment with TXA as an adjuvant or on TXA alone.[27] In this study, TXA was administered in various ways, including as microinjections, orally, topically and via microneedling. The quality of included studies that evaluated TXA treatment was, for the most part, low. The study found a reduction in MASI score of 2.46 (95% CI 1.13–3.80; $P<0.001$) with oral TXA, 1.42 (95% CI 0.98–1.87; $P<0.001$) with TXA injection and 1.36 (95% CI −0.17 to 2.90; $P=0.08$) with topical TXA treatment.

Feng *et al*. also conducted a systematic review and meta-analysis of RCTs that compared TXA alone, TXA as an adjuvant to routine treatment, and placebo.[12] Various pharmaceutical forms and routes of administration were utilized, with the outcome being a reduction in MASI score. Overall, the reduction in MASI score was significant, with an MD of 6.55 (95% CI 2.62–10.48) after 16 weeks when comparing diverse routine treatment with routine treatment + TXA. Superiority was not observed when topical or intradermal treatment was adopted.

Our systematic review and meta-analysis, distinct from any other as it included only RCTs, compared and restricted the statistical analysis to the oral use of TXA as an adjuvant to TCC treatment vs. TCC alone. The studies included in this review had not been previously compared in any meta-analysis, enabling a highly reliable and specific comparison between the proposed treatments, with the aim of optimizing efficacy and reducing adverse effects experience by patients.

This study had limitations. Our choice to combine data from studies that employed various methods of TXA administration and diverse treatment protocols (including differences in dosage, frequency of procedures, timing of treatments, concurrent therapies, etc.) introduced some heterogeneity. Notwithstanding these challenges, this systematic review and meta-analysis offers a comprehensive overview of the most robust evidence presently available regarding the use of TXA in melasma treatment.

Conclusions

Our comprehensive analysis highlights the clinical significance of incorporating oral TXA as a complementary element to standard melasma treatment. The synthesis of available evidence indicates that oral TXA confers clinical benefits, contributing to the enhancement of treatment outcomes in melasma when used in conjunction with TCC treatment. Moreover, our findings suggest a promising avenue for minimizing melasma recurrence associated with the standard treatment regimen.

Learning points

- The study demonstrates the adjuvant effect of tranexamic acid (TXA) in treating melasma.
- Using TXA in combination with triple combination cream (TCC) is superior to TCC alone.
- There was a significant decrease in the Melasma Severity Area Index score when adjuvant TXA was used in combination with TCC to treat melasma.

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Conflicts of interest

The authors declare no conflicts of interest.

Data availability

The data underlying this article are available in the article.

Ethics statement

Not applicable.

References

1 Handel AC, Miot LD, Miot HA. Melasma: a clinical and epidemiological review. *An Bras Dermatol* 2014; **89**:771–82.
2 Basit H, Godse KV, Al Aboud AM. Melasma [updated 8 August 2023]. Available at: https://pubmed.ncbi.nlm.nih.gov/29083744/(last accessed 15 July 2024).
3 Sarkar R, Arora P, Garg VK *et al*. Melasma update. *Indian Dermatol Online J* 2014; **5**:426–35.
4 Handel AC, Lima PB, Tonolli VM *et al*. Risk factors for facial melasma in women: a case–control study. *Br J Dermatol* 2014; **171**:588–94.

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5 Handel AC, Bartoli Miot LD, Miot HA. Melasma: a clinical and epidemiological review. *An Bras Dermatol* 2014; **89**:771–82.
6 Kim EH, Kim YC, Lee ES, Kang HY. The vascular characteristics of melasma. *J Dermatol Sci* 2007; **46**:111–16.
7 Conahan LJ, Robertson S. Sun-protective behaviors in patients with melasma. *J Nurse Pract* 2023; **19**:104452.
8 Ho SG, Chan HH. The Asian dermatologic patient: review of common pigmentary disorders and cutaneous diseases. *Am J Clin Dermatol* 2009; **10**:153–68.
9 Sheth VM, Pandya AG. Melasma: a comprehensive update: part I. *J Am Acad Dermatol* 2011; **65**:689–97.
10 Rubem DA, Azulay-Abulafia L. *Dermatologia*, 8th edn. Rio de Janeiro: Guanabara Koogan, 2022.
11 Rendon M, Berneburg M, Arellano I, Picardo M. Treatment of melasma. *J Am Acad Dermatol* 2006; **54**(5 Suppl. 2):S272–81.
12 Feng X, Su H, Xie J. Efficacy and safety of tranexamic acid in the treatment of adult melasma: an updated meta-analysis of randomized controlled trials. *J Clin Pharm Ther* 2021; **46**:1263–73.
13 Higgins JPT, Thomas J, Chandler J *et al. Cochrane Handbook for Systematic Reviews of Interventions*, version 6.4 (updated August 2023). Cochrane, 2023.
14 Minni K, Poojary S. Efficacy and safety of oral tranexamic acid as an adjuvant in Indian patients with melasma: a prospective, interventional, single-centre, triple-blind, randomized, placebo-control, parallel group study. *J Eur Acad Dermatol Venereol* 2020; **34**:2636–44.
15 Padhi T, Pradhan S. Oral tranexamic acid with fluocinolone-based triple combination cream versus fluocinolone-based triple combination cream alone in melasma: an open labeled randomized comparative trial. *Indian J Dermatol* 2015; **60**:520.
16 Karn D, Kc S, Amatya A *et al.* Oral tranexamic acid for the treatment of melasma. *Kathmandu Univ Med J* 2012; **10**:40–3.
17 Bagherani N, Gianfaldoni S, Smoller B. An overview on melasma. *Pigment Disord* 2015; **2**:21.
18 Gupta AK, Gover MD, Nouri K, Taylor S. The treatment of melasma: a review of clinical trials. *J Am Acad Dermatol* 2006; **55**:1048–65.
19 Lee JH, Park JG, Lim SH *et al.* Localized intradermal microinjection of tranexamic acid for treatment of melasma in Asian patients: a preliminary clinical trial. *Dermatol Surg* 2006; **32**:626–31.
20 Na JI, Choi SY, Yang SH *et al.* Effect of tranexamic acid on melasma: a clinical trial with histological evaluation. *J Eur Acad Dermatol Venereol* 2013; **27**:1035–9.
21 Poojary S, Minni K. Tranexamic acid in melasma: a review. *J Pigment Disord* 2015; **2**:228.
22 Dunn CJ, Goa KL. Tranexamic acid: a review of its use in surgery and other indications. *Drugs* 1999; **57**:1005–32.
23 Wu S, Shi H, Wu H *et al.* Treatment of melasma with oral administration of tranexamic acid. *Aesthetic Plast Surg* 2012; **36**:964–70.
24 Prignano F, Ortonne JP, Buggiani G, Lotti T. Therapeutical approaches in melasma. *Dermatol Clin* 2007; **25**:337–42.
25 Rodrigues M, Pandya AG. Melasma: clinical diagnosis and management options. *Australas J Dermatol* 2015; **56**:111–16.
26 Chauncey JM, Wieters JS. Tranexamic acid. Available at: https://pubmed.ncbi.nlm.nih.gov/30422504/(last accessed 15 July 2024).
27 Kim HJ, Moon SH, Cho SH *et al.* Efficacy and safety of tranexamic acid in melasma: a meta-analysis and systematic review. *Acta Derm Venereol* 2017; **97**:776–81.

CPD questions

Learning objective

To become more familiar with the treatment of melasma.

Question 1

Which demographic is most commonly affected by melasma?

(a) Children.
(b) Elderly men.
(c) Postmenopausal women.
(d) Young males.
(e) Young to middle-aged women.

Question 2

Which factor is considered to be a significant risk for the development of melasma?

(a) Chronic physical exertion.
(b) Consumption of dairy products.
(c) Diet high in carbohydrates.
(d) High protein intake.
(e) Hormonal changes, such as pregnancy or oral contraceptive use.

Question 3

What is the first-line treatment option for melasma?

(a) Laser therapy.
(b) Oral corticosteroids.
(c) Salicylic acid peels.
(d) Triple combination cream (hydroquinone, corticosteroids and retinoids).
(e) Vitamin C serum.

Question 4

Which external factor can exacerbate melasma?

(a) Cold weather.
(b) High altitudes.
(c) High humidity.
(d) Indoor lighting.
(e) Sun exposure.

Question 5

According to the article, what is the primary benefit of adding oral tranexamic acid to topical triple combination cream treatment in patients with melasma?

(a) Decreased need for sun protection measures.
(b) Faster achievement of initial pigmentation reduction.
(c) Improvement in the Melasma Area and Severity Index (MASI) score.
(d) Improved tolerance of topical treatments.
(e) Reduced risk of systemic side-effects.

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