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Review

The uses of tranexamic acid in dermatology: a review

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Abstract

Tranexamic acid is a plasmin inhibitor that is used off-label for the treatment of melasma. The use of tranexamic acid has expanded in the field of dermatology based on its anti-inflammatory and anti-melanin-producing properties, which include the treatment of rosacea, urticaria, and post-inflammatory hyperpigmentation. Tranexamic acid may have more uses in dermatology that require future studies. It should be used with caution during the COVID-19 pandemic given its procoagulant nature.

Objectives

1 Review of the literature on oral, topical, and intralesional tranexamic acid along with its known and potential uses in the field of dermatology.
2 Discuss the mechanism of action, side effect profile, safety, and cost of tranexamic acid in dermatology.
3 Discuss special considerations as a provider deciding to treat dermatologic patients with oral tranexamic acid during the COVID-19 pandemic.

Introduction

Trans-4-(Aminomethyl)cyclohexanecarboxylic acid, also known as tranexamic acid (TXA), is a derivative of the amino acid lysine and is a plasmin inhibitor. It exerts its effect by reversibly blocking lysine binding sites on plasminogen, inhibiting plasminogen activator from converting plasminogen to plasmin. The end result is the prevention of abnormal fibrinolysis and reduction of blood loss.[1]

In the 1970s, Sadako was the first to describe the role of TXA in treating melasma, which is a pigmentary disorder of the skin resulting in brown reticulated patches on the face, most noticeable in patients with skin color.[2] Recently, there has been an abundance of literature reviewing the efficacy and safety of oral TXA for the treatment of melasma in Asian patients. However, there are only a limited number of studies that evaluated the role of this therapy in patients of other ethnic backgrounds.[3] It should be noted that TXA is currently not approved by the US Food and Drug Administration for the treatment of melasma.

Tranexamic acid: overview

Mechanism of action

Following exposure to ultraviolet (UV) radiation, plasminogen activator is upregulated in basal keratinocyte; TXA is known to inhibit plasminogen activator activity. Maeda et al. reported that TXA inhibits epidermal melanocyte tyrosinase activity via inhibition of the plasminogen/plasmin system, which results in blocking the interactions between melanocytes and keratinocytes. The inhibition of the plasminogen/plasmin system has been proposed to result in a net decrease in the generation of arachidonic acid and prostaglandins, which are inflammatory mediators and melanocyte stimulators,[4] as well as fibroblast growth factor, which stimulates neovascularization. Histologically, TXA decreases the number of mast cells in the dermis[5] and decreases overall vascularity.[4] TXA is structurally similar to tyrosinase, and it has been postulated that because of its structural similarity, it may bind competitively as an antagonist to the enzyme, which would contribute even further to its skin lightening effect.[3]

Preparations and dosing

TXA can be administered by oral, topical, intravenous, and intradermal injection routes. The most typical dose is 250 mg twice daily for a treatment period of 8–12 weeks.[3] TXA is available in the United States as 650 mg tablets that may be split by patients for a dose of 325 mg twice daily. Topical and intradermal TXA dosing ranges from 4 to 100 mg/ml.[1] Several studies have shown increased efficacy when topical TXA is combined with other therapies to decrease pigmentation but is overall less effective in treating pigmentary disorders than oral TXA. TXA is

made in 650-mg tablets in the United States and typically retails between $66–$167 but may be purchased for $27–$56 through the use of a coupon.[6]

Side effect profile

TXA, a procoagulant agent, poses a theoretical risk for the development of venous or arterial thromboses. It should be noted that doses used for the treatment of active bleeding are higher than those for melasma. There have been reported cases of thrombosis with oral TXA in patients who were treated for bleeding and had predisposing risk factors for thromboembolic events. These risk factors include hypercoagulability, prior pulmonary emboli, prolonged immobility, hormone therapy, drug interactions, malignancy, and surgery.[5] In clinical studies on the use of oral TXA for melasma, only one patient developed a deep venous thrombosis during treatment and later was found to have protein S deficiency.[7] The most common side effects experienced by patients treated with oral TXA for melasma were abdominal bloating, abdominal pain, tinnitus, headaches, and menstrual pain.[3] Additionally, there was one report of generalized fixed drug eruption in Japan.[8]

Contraindications and special considerations for therapy

Contraindications to oral TXA include renal dysfunction, cardiovascular disease, pulmonary disease, malignancy, history of thrombolytic disease, current anticoagulant therapy, hormone therapy (contraception and replacement), prolonged immobilization, surgery, extended travel, and smoking.[3,7]

TXA has been proposed to be potentially harmful in patients during the COVID-19 pandemic. COVID-19 is caused by infection of the SARS-CoV-2 RNA virus that can progress to respiratory failure, hypercoagulability similar to disseminated intravascular coagulopathy, and microthrombotic events. While it is unlikely that TXA would cause thrombotic complications at doses used for melasma, to be cautious, oral TXA should not be initiated for melasma in patients with acute COVID-19 infection.

Melasma: overview

Melasma is a common pigmentary disorder that results in light to dark brown macules or patches that occur because of hyperactive epidermal melanocytes, which are photodistributed on the face, neck, and chest. Melasma is exacerbated by various external factors, which are still not fully understood.[3] The Melasma Area and Severity Index (MASI) is an outcome measure that is a reliable and validated tool to help provide a more accurate quantification of melasma and a method to monitor responses to therapy.[2]

Melasma therapies

First-line therapy for melasma includes topical agents that interfere with melanin synthesis and strict photoprotection. It has been demonstrated that both UV and visible light may induce skin pigmentation in darker-skinned individuals; thus, broad-spectrum, tinted sunscreens with sun protection

Table 1 Topical tranexamic acid and other topical hypopigmenting agents

Drug	Dose	MOA	Dermatological uses	Side effects
Tranexamic acid	OTC: 3%	Inhibition of ultraviolet-induced plasminogen activator, anti-inflammatory, net decrease in melanocyte activators, and neovascularization	Melasma, rosacea, PIH, vascular-related pigmentation, and anti-aging	
Hydroquinone	Prescription (Rx): 4% OTC: 2%, 3%	Tyrosinase inhibitor, antioxidant	Melasma and PIH	Irritation, exogenous ochronosis
Kojic acid	OTC:	Tyrosinase inhibitor	Melasma and PIH	Irritation
Vitamin C (L-ascorbic acid)	OTC: 3–15%	Tyrosinase inhibitor, antioxidant	Melasma, PIH, and anti-aging	Irritation
Azelaic acid	Prescription (Rx): 15%, 20% OTC: 8%	Tyrosinase inhibitor	Melasma, PIH, acne vulgaris, and rosacea	Irritation
Niacinamide	OTC: 2%	Inhibition of melanosome transfer	Melasma, PIH, and eczema	Irritation
Corticosteroids (hydrocortisone, triamcinolone, fluocinolone)	Hydrocortisone:1% (OTC), 2.5% (Rx) Triamcinolone (Rx): 0.025%, 0.1% Fluocinolone (Rx): 0.01%	Anti-inflammatory, non-selective inhibition of melanogenesis	Melasma, dermatitis, psoriasis, and lichenoid eruptions	Skin atrophy, telangiectasias, steroid-induced acne, striae
Alpha arbutin (glucosylated hydroquinone)	OTC: 2%	Tyrosinase inhibitor, anti-inflammatory	Melasma and PIH	

MOA, mechanism of action; OTC, over-the-counter; PIH, post-inflammatory hyperpigmentation; Rx, prescription drug.

Table 2 Summary of case–control studies and trials of oral tranexamic dosing for melasma

Year	Study	Location	TXA group	Controls	Concurrent treatment	Control arm	TXA (oral)	Duration (weeks)	Results of TXA	Side effects	Comments
1979	Sadako[10]	Japan	12	0	Vitamins B, C, and E	None	1.5 g/day	20	11 significant improvement	None	Effect of TXA was noted in 4 weeks
1985	Hajime et al[11]	Japan	40	0			1–1.5 g/day	10	33 reported decreased severity		
1988	Higashi[12]	Japan	11	0			0.75–1.5 g/day	"A couple of months"	11 reported decreased severity	None	
2001	Zhu and Yang[13]	China	128	30	Vitamins C and E	Vitamins C and E only	0.75 g/day	6–8	20% >95%, 30% > 60%	Mild GI symptoms	TXA statistically significantly improved melasma ($P < 0.001$), increased duration of therapy was more effective than higher doses of therapy
2005	Liu et al[14]	China	176	70	Vitamins C and E	Vitamins C and E	0.75 g/day	8	24% > 90%, 40% > 60%	5% had GI symptoms in both control and treatment arms	TXA group had statistically significant improvement compared to the control group ($P < 0.01$)
2008	Wu et al[15]	China	256	0			0.5 g/day	24	10.5% > 90%, 19% > 60%	4.3% reported GI symptoms, 3.5% reported menstrual irregularity	33% response to TXA in 4 weeks, 33% response to TXA in 8 weeks; TXA did not alter coagulation profile
2008	Mafune et al[16]	Japan	99	100	None	Placebo	1.5 g/day	8	76.8% improvement	1 transient chest discomfort	TXA group had statistically significant improvement compared to the control group ($P < 0.001$)
2011	Cho et al[17]	Korea	24	27	IPL/Nd:YAG laser	IPL/Nd:YAG laser	0.5 g/day	24	mMASI decrease 43.8% vs. 23.6%	Mild headache in 4 patients	TXA group had statistically significant improvement compared to the control group ($P < 0.005$)

Table 2 Continued

Year	Study	Location	TXA group	Controls	Concurrent treatment	Control arm	TXA (oral)	Duration (weeks)	Results of TXA	Side effects	Comments
2012	Shin et al[18]	Korea	23	21	Low fluence QSNd:YAG	Low fluence QSNd:YAG	0.75 g/day	8	Decrease in mMASI, melanin index not significantly decreased	3 patients with GI symptoms	TXA increased efficacy of laser and reduced frequency of laser treatment
2012	Na et al[5]	Korea	25	0	2% TXA and 2% niacinamide topical		1.5 g/day	8	Melanin index and erythema index scores decreased significantly; histology showed a reduction in epidermal pigmentation, vessel number, and mast cells		TXA decreased epidermal pigmentation associated with melasma and reversed melasma related dermal damage
2012	Karn et al[19]	Nepal	130	130	Topical HQ and sunscreen	Topical HQ and sunscreen	0.5 g/day	12	Statistically significant decrease in MASI in both groups at week 8 and in only the TXA group at week 12		
2013	Li et al[20]	China	35	0			1.5 g/day	16	Moderate improvement for 85% in 4 weeks, 97% in 8 and 12 weeks, and 100% in 16 weeks	3 cases of GI symptoms, 3 with menstrual irregularities, 1 with drowsiness, and 1 with increased LFTs	85% of cases treated with TXA showed improvement in 4 weeks
2014	Aamir and Naseem[21]	Pakistan	65	0			0.5 g/day	24	15 had excellent response, 41 with good, and 8 with fair	Mild GI symptoms, palpitations, and oligomenorrhea	Study reported TXA as safe
2015	Padhi and Pradhan[22]	India	20	20	TTC	TTC	0.5 g/day	8	55% decrease in MASI from 15.5 to 7 and 88% decrease in MASI from 18 to 2		TTC is faster and more sustained when TXA is added
2016	Tan et al[23]	Singapore	25	0	Combination topical therapy		0.5 g/day	20 months	Mean improvement of 68% and lower MASI scores		TXA group had statistically significant improvement compared to the control group ($P < 0.01$), low dose TXA is useful for refractory melasma

Table 2 Continued

Year	Study	Location	TXA group	Controls	Concurrent treatment	Control arm	TXA (oral)	Duration (weeks)	Results of TXA	Side effects	Comments
2017	Del Rosario et al[24]	United States	18	21	Sunscreen		0.5 g/day	12	49% reduction in mMASI in TXA group vs. 18% in control; 26% decrease in mMASI 3 months after in TXA group and 19% in control	1 patient with moderate myalgias	Largely Hispanic female population
2018	Colferai et al[25]	Brazil	20	17	Sunscreen	Placebo	0.5 g/day	12	50% improved in TXA group, 5.9% improved in placebo group	No severe side effects reported	TXA group had statistically significant improvement compared to the control group ($P < 0.005$)

DVT, deep vein thrombosis; GI, gastrointestinal; HQ, hydroquinone; IPL, intense pulsed light; LFTs, liver function tests; MASI, Melasma Area and Severity Index; mMASI, modified Melasma Area Severity Index; TTC, triple therapy combination (fluocinolone acetonide 0.01%, tretinoin 0.05%, hydroquinone 2% daily).

factor >30 are recommended as these sunscreens would protect against the effects of UVB, UVA, and visible light.[9] Topical agents used to commonly treat melasma and other hyperpigmentaion conditions are shown in Table 1. Chemical peels, light, and laser therapies may be helpful in patients who are refractory to other modalities; however, these treatment options carry the risk of worsening dyspigmentation.

Summary of TXA and melasma literature

The studies are summarized in Table 2. Lower doses of TXA (≤1 g/day) over an increased time frame of therapy are more efficacious than shorter durations with higher doses of TXA (≥2 g/day).[26] It can also be very helpful in treating refractory melasma.[23]

Topical TXA therapies have also been utilized to treat melasma and vary in concentrations from 2% to 5% gels, creams, or solutions. Overall, topical TXA has not been shown to be superior to oral TXA or topical hydroquinone cream[27-29] (Tables 3 and 4, respectively). However, topical TXA may be utilized as an adjunctive therapy or alternative for patients who are unable to tolerate hydroquinone cream.

Other uses of TXA in dermatology

Chronic urticaria

Chronic urticaria can often be difficult to treat, leading to high burden of disease for patients and reducing the overall quality of life.[31] Majority of cases resolve after 6–12 weeks; however, there are some patients who may be affected by chronic urticaria for greater than 5 years. TXA has been used for the treatment and prophylaxis of chronic urticaria (Table 4).

Hereditary C1-Inhibitor deficiency angioedema

Angioedema (AE) is most associated with urticaria. In AE, because of C1-esterase inhibitor deficiency, no urticaria is present; this can be hereditary or acquired.[32]

There are a few treatment options for prophylaxis for hereditary AE, which include an intravenously administered plasma-derived C1 inhibitor concentrate (i.e. Cinryze), attenuated androgens, and progestogens.[33] Androgens are contraindicated in pediatric patients; thus, TXA is considered first-line treatment in this population with dosing recommendations of 20–50 mg/kg/day orally divided over 2–3 doses (maximum dose 3–6 g per day) in those with no family history of thromboembolic events.[34]

Acquired AE

Acquired AE is a rare disorder caused by an acquired deficit of C1INH and usually occurs in patients of older age, with a coexisting diagnosis of lymphoproliferative malignancy as well as gradual development of abnormalities of the complement

Table 3 Summary of case–control studies of topical tranexamic acid for melasma

Year	Study	Location	Patients	Group A	Group B	Duration (weeks)	Results	Side effects	Comments
2012	Kanechorn Na Ayuthaya et al[30]	Thailand	23	TXA 5% gel BID	Vehicle	12	MASI and MI improved but not superior to vehicle	None	TXA improved erythema
2014	Ebrahimi and Naeini[27]	Iran	50	TXA 3% solution BID	HQ 3% + dexamethasone 0.01% solution BID	12	Decrease in MASI in both groups without statistical difference	None	
2015	Banihashemi et al[28]	Iran	30	TXA 5% liposomal BID	HQ 4% cream BID	12	Decrease in MASI in both. Greater reduction in MASI with liposomal TXA but not statistically significant from HQ		
2016	Kim et al[29]	Korea	23	TXA 2% formulation BID	None	12	Improved mMASI in all participants		

BID, twice daily; HQ, hydroquinone; MASI, Melasma Area Severity Index; MI, Melanin Index; mMASI, modified Melasma Area Severity Index; TXA, tranexamic acid.

Table 4 Oral tranexamic acid dosing for melasma, angioedema, urticaria

Dermatologic disease	Daily dosage	Duration of treatment
Melasma	500 mg to 1.5 g	8 to 12 weeks
Chronic idiopathic urticaria	3 g	2 weeks[a]
Hereditary angioedema	3–6 g	Prophylaxis
Acquired angioedema	2–4.5 g	Prophylaxis
Angiotensin-converting enzyme inhibitor-related angioedema	1.5–3 g	Prophylaxis

[a]One small study showed that oral TXA 1 g three times daily was helpful for some patients with treatment-resistant chronic urticaria.

system.[35] TXA has been used for long-term prophylaxis in acquired AE at oral doses ranging from 2 to 4.5 g per day.[36]

Angiodema caused by angiotensin-converting enzyme inhibitors

The use of angiotensin-converting enzyme inhibitors also leads to the buildup of bradykinin, which can result in the development of life-threatening AE. Several studies report a subset of patients experienced an overall decrease in attack frequency or improvement in symptoms with oral TXA doses ranging from 1 to 3 g per day[36] (Table 4).

It should be noted that TXA has also been reported as ineffective in treating idiopathic and angiotensin-converting enzyme inhibitor-associated AE. Additionally, as these are relatively uncommon diseases, the studies that reported success with TXA were not controlled and have lower scientific reliability.

Potential future uses in dermatology

TXA has also been used in the following conditions, though its use has not been as well studied as in diseases and conditions described previously in this review. These conditions include rosacea, postinflammatory hyperpigmentation, prophylaxis for postinflammatory hyperpigmentation, Riehl's melanosis, and hemostasis (Table 5).

Procedural therapies and drug delivery enhancing modalities for melasma

Various dermatologic procedures can enhance the efficacy of certain treatments by improving drug delivery past the stratum corneum.

Intradermal injections and mesotherapy

Intradermal TXA has been shown to be non-superior to hydroquinone cream in the treatment of melasma but can be a helpful adjunctive agent in concentrations ranging from 4 to 100 mg/ml.[41,42]

Microneedling

Microneedling is a therapeutic modality in dermatology used to enhance transdermal drug delivery by physical trauma from needle penetration through the epidermis. Topical TXA has

Table 5 Summary of investigative uses of tranexamic acid in dermatology

Dermatologic use	Study type	Intervention	Results	Adverse events
Rosacea[37]	Case report	TXA 250 mg daily, propranolol 40 mg daily, and minocycline 50 mg daily	Rapid improvement	None
Rosacea[38]	Randomized, vehicle controlled, split-face study	Topical TXA 3% solution	Improved permeability barrier function and fewer inflammatory papules	None
PIH	Case report	QSNYL and oral TXA for 10 weeks	Improvement	None
Laser-induced PIH prophylaxis after treating melasma[39]	Randomized controlled trial	TXA 750 mg daily vs. placebo in melasma patients treated with Q-switch ruby laser	Improvement in melasma, no difference in PIH	None
Riehl's melanosis[37]	Pilot study	Low-fluence 1064-nm QSNYL with HQ cream and oral TXA 250 mg/day over two years	3/8 "almost clear" 5/8 "marked improvement"	None
Hemostasis[40]	Double-blinded, placebo-controlled, randomized prospective study	Lidocaine 2% diluted 1:1 with either saline (placebo) or TXA 100 mg/ml before surgery	Improved hemostasis in TXA group[a]	None

HQ, hydroquinone; QSNYL, Q-Switch Nd:YAG laser; PIH, post-inflammatory hyperpigmentation; TXA, tranexamic acid.
[a]Results showed that the bloodstain was smaller in the treatment group than placebo ($P < 0.001$) with better hemostasis ($P = 0.043$). A subgroup of patients on anticoagulants had even better control.

been shown to improve melasma when paired with microneedling when compared to topical TXA alone.[43]

Laser-assisted drug delivery

Laser-assisted drug delivery is one of the more promising future treatments for patients with melasma and other pigmentary disorders because laser therapy can target the destruction of pigment directly and facilitate the delivery of topical medications to the skin. Fractional lasers create microscopic columns of thermal injury from low-energy treatment settings, which leaves the surrounding healthy tissue intact and avoids morbidity that is usually seen with ablative lasers.[44] Tawfic et al., a group in Egypt, conducted a randomized comparative split-face study that included 30 patients who received topical TXA or intradermal TXA injections combined with low power fractional CO_2 laser for melasma in which both groups had significantly lower MASI scores, but there was no statistical difference between treatments and control.[45] Additionally, Q-switched Nd:YAG lasers produce a high-intensity beam in very short pulses by utilizing a crystal medium at wavelengths of 1064 nm and 532 nm.[46] Laothaworn and Juntongjin in Thailand investigated the use of topical 3% TXA combined with 1064-nm Q-Switch Nd:YAG laser in treating melasma. Statistically significant decreases in modified Melasma Area Severity Index (mMASI) scores were recorded for the combination therapy ($P < 0.05$) compared to laser-alone therapy.[47] Shin et al. showed that patients who took oral TXA for 8 weeks and received 1064-nm Q-Switch Nd:YAG laser therapy for melasma had overall greater improvement in mean mMASI scores than patients who received laser alone.[18] Lastly, intense pulsed light (IPL) therapy emits a noncoherent light from a flash lamp light source at wavelengths between 515 and 1200 nm.[46] In Korea, Chung et al. conducted a randomized, split-face, internally controlled study on 15 Asian women with melasma. Each patient received IPL to both sides of their face, and topical TXA or vehicle was applied to a randomly assigned side during and after IPL treatment sessions. MI and mMASI scores decreased from baseline and were statistically significant. Topical TXA prevented rebound pigmentation after IPL treatments, which was also found to be statistically significant.[48] Overall, the addition of tranexamic therapy combined with laser-assisted delivery has been shown to improve patient outcomes in the treatment of melasma.

Summary

TXA has several potential uses in dermatology, and oral TXA is most efficacious for the treatment of melasma, while topical and intralesional TXA has been variably helpful in the treatment of melasma. It is a relatively safe medication to be used, but appropriate screening for hypercoagulable states and other risk factors should be performed before initiating therapy. Additionally, it is important to note that the available dose in the United States is 650 mg tablets that may be split into 325 mg for twice-daily dosing. Caution should be used in the era of the COVID-19 pandemic given the potential increased risk for prothrombotic events in patients who are infected with the SARS-CoV-2 virus.

Questions (answers provided after references)

1 A 45-year-old Hispanic female with Fitzpatrick skin type IV presented to the dermatology office for brown spots on her face. On examination, she had symmetric medium brown hyperpigmented reticulated patches on the bilateral temples, zygomatic cheeks, and upper cutaneous lips. Which of the following is NOT true regarding this condition?
- a The first-line treatment is triple combination therapy (topical steroid, tyrosinase inhibitor, and topical retinoid)
- b Non-tinted organic sunscreens are the most efficacious in preventing the darkening of these lesions
- c Oral tranexamic acid is considered off-label for this condition
- d All of the above are not true

2 Which of the following is not a known exacerbating factor of melasma?
- a Copper intrauterine device
- b Pregnancy
- c Ultraviolet light
- d Visible light

3 Melasma is often treated with topical bleaching agents, such as hydroquinone cream. Which of the following is an adverse side effect of hydroquinone?
- a Atrophy
- b Depigmentation
- c Exogenous ochronosis
- d Telangiectasias

4 A 36-year-old skin type V female presented to your clinic for treatment of facial melasma. You recommend oral tranexamic acid. Which of the following is a contraindication to this therapy?
- a Personal history of prolonged bleeding time
- b Prior use of tobacco
- c Prior use of oral contraceptives
- d Prolonged immobilization

5 A 40-year-old male patient, Fitzpatrick skin type III, presents to your clinic for evaluation and treatment of melasma. He has previously been treated with various topical therapies, including triple combination therapy, glycolic chemical peels, and microneedling. He currently uses tinted mineral broad-spectrum sunscreen. You note reticular brown patches on the forehead, cheeks, upper lip, and chin which have been refractory to prior treatments. You recommend oral tranexamic acid. What dosage is recommended to treat this condition?
- a 100 mg twice daily
- b 325 mg twice daily
- c 750 mg twice daily
- d 1000 mg twice daily

6 Which of the following routes of administration for tranexamic acid has been shown to be the most efficacious in treating melasma?
- a Intradermal
- b Oral
- c Topical
- d All above are equal

7 Which of the following is the correct mechanism of action for tranexamic acid?
- a Calcineurin inhibitor
- b Tyrosinase activator
- c Plasminogen inhibitor
- d Retinoic acid receptor activator

8 Tranexamic acid has been shown to improve melasma. Which other dermatologic conditions has tranexamic acid shown promise in treating?
- a Angioedema prophylaxis
- b Chronic urticaria
- c Rosacea
- d All of the above

9 A 25-year-old Asian female with facial and neck melasma presents to your clinic for initiation of oral tranexamic acid therapy. She has a past medical history significant for allergic rhinitis. She states she has a family history of blood clots but no personal history. She currently takes an oral contraceptive and smokes 3 cigarettes daily. She denies any other substance abuse. Which of the following is an appropriate next step for this patient?
- a Recommend triple combination therapy (compounded steroid, retinoid, and hydroquinone) because she has a family history of blood clots
- b Recommend triple combination therapy with non-tinted inorganic sunscreen because she currently takes an oral contraceptive and smokes cigarettes
- c Recommend smoking cessation and start triple combination therapy with a tinted inorganic sunscreen because she takes oral contraceptives and smokes cigarettes
- d Recommend starting low dose (325 mg) tranexamic acid twice daily and discontinue her oral contraceptive

10 Which of the following is not an appropriate treatment for melasma?
- a Hydroquinone cream monotherapy
- b Tinted inorganic sunscreen monotherapy
- c Tretinoin cream monotherapy
- d Triamcinolone cream monotherapy

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Answers

1. b

Tinted inorganic sunscreens are the most efficacious in preventing the darkening of melasma because of their ability to protect against both ultraviolet and visible light.

2. a

The copper intrauterine device is not considered a known exacerbating factor of melasma. Melasma is influenced by both hormonal changes, such as those seen in pregnancy or with taking oral combined contraceptives, as well as, sun-exposure which includes ultraviolet and visible light.

3. c

Exogenous ochronosis is a rare, but serious side effect of topical hydroquinone. It is advised to prescribe or recommend lower concentrations of hydroquinone (2–4%) to decrease the risk of developing ochronosis. Advising patients to use this medication for 2- to 3-month intervals twice daily with 1 month break between uses can help minimize this side effect.

4. d

Prolonged immobilization is a risk factor for hypercoagulability and the development of thromboembolic events. Prior use of oral contraceptives may be considered a relative contraindication.

5. b

Tranexamic acid 250–500 mg twice daily are safe dosages used to treat melasma. In the United States, 650 mg tablets are available for patients to split and take 325 mg twice daily. Studies have shown that lower doses (250–500 mg) over prolonged periods (3 or more months) provide patients with longer-lasting results.

6. b

Oral tranexamic acid is the most efficacious in treating melasma when compared to topical and intradermal tranexamic acid.

7. c

Tranexamic acid inhibits plasminogen in the plasminogen/plasmin pathway which downstream has an influence on inhibiting tyrosinase in keratinocytes.

8. d

Tranexamic acid has been used for all of the above conditions.

9. c

Smoking cigarettes and oral contraceptives increase patient's risk for thromboembolic events and hypercoagulability. Additionally, tobacco smoke has been shown to enhance skin pigmentation. Tranexamic acid should not be used in patients with these risk factors. C is the most appropriate next step, as smoking cessation should be counseled, and her oral contraceptive should not be discontinued without taking further history regarding the purpose of its medical use and discussion with the patient and prescribing provider. First-line therapy for melasma is tinted inorganic sunscreen combined with triple combination therapy, which would be appropriate to start at the initial visit.

10. d

Topical steroids should not be used as a monotherapy when treating melasma. Topical steroids can decrease pigmentation in the skin; however, they can also cause steroid-induced cutaneous atrophy and telangiectasias when used chronically. Topical steroids can be combined with topical retinoids and hydroquinone to treat melasma.