

REVIEW

Dermatology: how to manage facial hyperpigmentation in skin of colour

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Abstract

Hyperpigmentation disorders, such as post-inflammatory hyperpigmentation and melasma, are common conditions affecting all skin types. These conditions are largely benign and are influenced by numerous endogenous and exogenous factors impacting melanocyte activity and melanin production. Current treatment modalities for these conditions fall into broad categories, including photoprotection, topical and systemic therapies, chemical peels, and laser or light-based therapies. Biological differences in skin of colour require additional consideration when deciding on treatment and management. This narrative review provides an inclusive summary of these conditions and compares the current treatment options with a specific focus on skin of colour. Photoprotection and sunscreens protective against both UV and visible light are recommended

for all individuals. Topical therapy is the recommended first-line treatment, with the gold standard being hydroquinone, which can be used alone or in combination with other agents. Chemical peels and laser or light-based therapies are also effective adjunctive methods of treatment; however, caution should be taken when used in patients with richly pigmented skin due to the increased risk of post-inflammatory hyperpigmentation.

Keywords: facial hyperpigmentation, melasma, post-inflammatory hyperpigmentation, skin of colour.

Citation

Moolla S, Miller-Monthrope Y. Dermatology: how to manage facial hyperpigmentation in skin of colour. *Drugs Context*. 2022;11:2021-11-2. <https://doi.org/10.7573/dic.2021-11-2>

Introduction

Facial hyperpigmentation is a distressing condition that is more common in people with skin of colour.¹ One form of hyperpigmentation is melasma, also known as chloasma. This is a refractory disorder characterized by brown or grey pigmentation generally involving the face.² Whilst melasma can occur in both sexes it is more common in women, especially during pregnancy.³ Post-inflammatory hyperpigmentation (PIH) is another common hyperpigmentation disorder that occurs due to hypermelanosis after trauma or inflammation of the skin. Unlike melasma, this condition does not have a sex or age bias.⁴

There are multiple approaches for the treatment of hyperpigmentation, including photoprotection, topical treatment, systemic medications and procedural interventions. Common topical treatments include skin lightening agents such as hydroquinone (HQ) and retinoids. More recently, agents such as topical tranexamic acid and 5% cysteamine cream have proven to be effective alternatives to conventional topical agents.⁵ Finally, procedural interventions such as chemical peels and light-based therapies have shown efficacy in treating

hyperpigmentation, but depending on the clinical context, may be associated with adverse effects.^{6,7}

Due to the resistant and relapsing nature of hyperpigmentation, it can be challenging to select an appropriate treatment option to match the patient's unique needs. This narrative review aims to provide an informative up-to-date overview of these disorders as well as a review of common treatment options with a specific focus on skin of colour.

Methods

This is a review article focusing on the management of hyperpigmentation disorders, including melasma and PIH, specifically in skin of colour. Articles were identified from PubMed, MEDLINE and EMBASE, using the various combinations of the keywords "post inflammatory hyperpigmentation", "melasma", "treatment", "richly pigmented", "skin of color", "skin type", "dark skin", "Fitzpatrick scale". Articles were further selected based on their inclusion of patient characteristics, location of the lesions, skin of colour population and primary language.

Review

Epidemiology

Pigmentary disorders are exceedingly common in patients with skin of colour. A survey completed in the United States with more than 1400 patients identified dyschromia as the second most common dermatologic diagnosis in Black and Hispanic populations.¹ This contrasts with white patients, where dyschromia did not even place in the top ten most common diagnoses.

PIH specifically has been shown to occur in patients of all ages and with no predominance in either sex.⁸ This condition does seem to be directly related to an individual's skin tone, with an increased prevalence in skin types III–VI.⁹ Within specific ethnic populations, PIH is more likely to be reported in those with darker complexions, as seen in one study of Arab Americans.¹⁰

As with PIH, melasma is more prevalent in patients with darker skin tones.¹¹ Other predisposing factors include ethnicity, geographical location and pregnancy, with the prevalence of melasma ranging from 9% to 50% in certain populations.^{12–14} Despite these similarities, melasma does have a clear predominance in women, with women-to-men ratio ranging from 4:1 in an Indian study to 39:1 in Brazil.^{15,16}

Pathophysiology

The pathogenesis of melasma is complex and can be triggered and exacerbated by several factors, including UV light, visible light (VL), positive family history and hormonal influences.^{11,17} UV light is thought to impact skin pigmentation by inducing the production of reactive oxygen species, thereby promoting melanogenesis.¹⁶ VL and UV light also induce pigmentation through the secretion of stem cell factor, the ligand of the tyrosine kinase receptor c-kit, which leads to the proliferation of melanocytes. Another possible mechanism is through the stimulation of vascular endothelial growth factor from keratinocytes after UV exposure, which causes increased activity in melanocytes.¹¹ UV light is linked to the downregulation of lipid metabolism-associated genes in melasma skin, which impairs the skin's barrier function and can contribute to the pathogenesis of the condition.¹⁸ Hormones seem to play an important role in the development of hyperpigmentation, with the epithelium of melasma lesions in women demonstrating an increased expression of both oestrogen and progesterone receptors.^{19,20} Finally, there is also a strong familial component in melasma, with some studies reporting a positive family history in as much as 61% of affected patients.²¹

PIH occurs due to cutaneous inflammation leading to the overproduction of melanin or uneven dispersion of pigment in the skin.²² This response can be triggered by both endogenous and exogenous factors such as acne or trauma to the skin.⁴ PIH can occur in the epidermis or the dermis. Whilst the exact mechanism of PIH in the epidermis is unknown, there

is an increase in melanocyte activity that is associated with inflammatory mediators and reactive oxygen species. Studies have shown that prostaglandins E2 and D2, leukotrienes LT-C4 and LT-D4, thromboxane 2, IL-1, IL-6, epidermal growth factor, nitric oxide, TNF and other cytokines may all be associated with increased melanocyte stimulation.²³ In the dermis, basal keratinocytes are damaged by inflammation, which results in a large release of melanin. Macrophages phagocytose the released free pigment to form melanophages. The melanophages then reside in the upper dermis and appear as a blue-grey patch at the site of injury, which can persist for years.²⁴

Treatments

The appearance of hyperpigmentation and melasma can be extremely distressing for patients and an understanding of available treatment modalities is a useful tool for medical professionals. There are various topical, oral and procedural treatments that aim to reduce the appearance of these lesions by targeting different aspects of their pathogenesis (Table 1).

Sunscreen/photoprotection

It is widely understood that sun exposure is a contributing factor in the formation and appearance of hyperpigmentation disorders and that photoprotection should be paramount to the treatment of these conditions. Conventionally, it was believed that UV radiation was central to the development of melanotic dyschromia, which was the basis for the recommendation of sunscreen for these conditions.²⁵ A study including 185 pregnant Moroccan women investigated the effects of a broad-spectrum SPF 50+, UVA protection factor 28 sunscreen for the management of melasma. This study discovered that its use every 2 hours reduced the incidence of melasma from approximately 53% in similar populations to only 2.7%.²⁶ In addition, approximately 67% of patients with pre-existing melasma saw marked improvements in the appearance of their skin. More recent studies have discovered that VL also contributes to pigmentary changes by acting synergistically with UVA1 exposure.^{27,28} A study including 68 Mexican patients assessed the effectiveness of UV-blocking and VL-blocking sunscreen compared to regular UV-blocking sunscreen. Patients were randomized into two groups and treated with either sunscreen alongside HQ. It was discovered that, at 8 weeks, there was a statistically significant reduction in colorimetric values and Melasma Area and Severity Index (MASI) scores of 28% and 15%, respectively in the UV-VL sunscreen group when compared to the UV sunscreen group.²⁹ A study also found that sunscreen with iron oxide improved the appearance of pigmentation compared to mineral SPF 50+ sunscreen and controls in skin phototypes above type II.³⁰ Thus, VL blocking sunscreens, such as iron oxide-containing formulations, should be included in initial recommendations for all patients seeking care for hyperpigmentation disorders.

Table 1. Review of treatments for melasma and post-inflammatory hyperpigmentation.

Treatment	Mechanism of action	Disadvantages	Strength of Recommendation Taxonomy (SORT)
Photoprotection	- Reduces UV and visible light exposure, which is known to induce inflammatory responses stimulating and exacerbating pre-existing hyperpigmentation	- Needs to be reapplied regularly - Is not an active treatment for depigmentation	B
Topical/systemic			
Hydroquinone and combinations	- Inhibit tyrosinase activity - Promote melanocyte destruction - Promote degradation of melanosomes	- Erythema, burning, pruritis, desquamation - Hydroquinone halo - Ochronosis	A
Retinoid	- Vitamin A derivative - Increase epidermal cell turnover - Express anti-inflammatory properties	- Burning, dryness - Retinoid dermatitis - Risk of post-inflammatory hyperpigmentation	B
Azelaic acid	- Inhibit tyrosinase activity - Selective antiproliferative and cytotoxic effects on melanocytes	- Transient erythema, irritation, pruritis, dryness, burning	B
Kojic acid	- Inhibit catecholase activity of tyrosinase	- Transient erythema - Risk of contact dermatitis	B
Tranexamic acid	- Inhibits UV-induced plasmin activity and impairs melanogenesis	- Erythema, scaling, dryness - Oral side effects include abdominal discomfort, bloating, headache, hypomenorrhea - Risk of thrombotic events in specific populations	B
Cysteamine	- Inhibit tyrosinase and peroxidase - Chelate metal ions required for melanin synthesis - Scavenging dopaquinone	- Transient dryness, burning - Malodorous	B
Chemical peels: <i>glycolic acid, salicylic acid, Jessner solution, trichloroacetic acid</i>	- Controlled destruction of skin layers depending on peel depth - Increase keratinocyte turnover	- Post-inflammatory pigmentary changes - Burns, erythema, irritation, desquamation - Scarring	B
Laser			
Ablative laser	- Causes controlled damage to and removes layers of skin	- High risk of post-inflammatory pigmentary changes - Burns, erythema, pain - Scarring	Not recommended
Non-ablative fractioning laser	- Produce coagulative damage within the dermis below the wounding threshold causing melanin extrusion	- Risk of post-inflammatory pigmentary changes in darker skin tones - Burns, erythema, pain - Requires optimization based on patient's skin type	B

(Continued)

Table 1. (Continued)

Low-fluence Q-switched laser	- Selectively destroys melanin pigments	- Risk of post-inflammatory pigmentary changes in darker skin tones - Burns, erythema, pain - Requires optimization based on patient's skin type	B
Picosecond laser	- Produce short pulse durations with higher pulse energies leading to lower thermal effect and greater fragmentation of melanin	- Erythema, pain, blister formation - Still has risk of post-inflammatory pigmentary changes - Limited studies in skin of colour	B

Whilst the evidence is clear that photoprotection is important, healthcare workers recommend photoprotection for their white patients at significantly higher rates than for their patients with richly pigmented skin. In a survey completed in the United States, photoprotection was only the sixth most recommended treatment option for dyschromia in African Americans compared to the third most recommended treatment for white populations.³¹ Even more troublesome is the fact that African Americans are less likely to use sunscreen compared to other races.³² This further enforces the idea that adequate education and counselling are required when dealing with these at-risk populations.

Topical therapies

Hydroquinone

Topical HQ is regarded as the gold standard for the treatment of facial hyperpigmentation. HQ is a bleaching agent that acts by inhibiting tyrosinase to limit melanin production in the skin.³³ Additional studies have hypothesized that at certain concentrations, HQ can promote melanocyte destruction and the degradation of melanosomes.³⁴ The most common concentrations for HQ monotherapy are 2–4% with 4% having the strongest evidence for use in melasma. HQ has been well studied and used as a baseline comparator for numerous alternative treatments in skin of colour, including ascorbic acid, liquiritin, niacinamide, *Rumex occidentalis* and thiamidol.^{35–39} These therapies may be used as an adjunct to traditional treatments or as monotherapy for patients seeking 'natural' remedies.

HQ has also been used in combination with other treatments to improve its efficacy and reduce the occurrence of its side effects. The most common combination is known as the Kligman formula, or triple combination therapy (TCT), where HQ is combined with a topical retinoid and a corticosteroid.⁴⁰ Numerous randomized control studies (RCTs) in skin of colour as well as a Cochrane review have assessed the efficacy of TCT and found it to be more effective than HC monotherapy.^{41–44} The side effects most frequently reported are transient erythema, burning, pruritus and

desquamation. In some cases, HQ can cause a phenomenon known as the 'hydroquinone halo', where hypopigmentation occurs surrounding treated areas.⁴⁵ Ironically, the most concerning side effects caused by HQ are hyperpigmentation and even exogenous ochronosis or paradoxical increased permanent pigmentation of the skin. It should be noted that the association of these effects is extremely rare and typically seen with extended use of the therapy.² The safety of TCT has also been demonstrated in a year-long study where patients used TCT daily until lesion clearance and then restarted for an 8-week course if the lesions recurred. Approximately 57% of patients experienced at least one side effect, including burning, desquamation, erythema or dryness, with most effects being mild. There were no reports of ochronosis or skin atrophy; however, 2% of the patients did develop telangiectasias with most of them resolving during the study.⁴⁶

Retinoids

Retinoids are another topical treatment for pigmentary disorders efficacious both in combination with other agents such as in TCT and as monotherapy. These compounds are structurally and functionally similar to vitamin A. They are effective in lightening skin by modulating cell proliferation and through anti-inflammatory properties.^{47,48} The most commonly prescribed retinoids are tretinoin, tazarotene and adapalene.⁴⁹ There have been numerous studies in patients with skin of colour demonstrating the effectiveness of retinoids. In a double-blinded RCT of 54 Black women, 0.1% tretinoin was found to be superior in lightening the skin of patients with PIH when compared to the vehicle. There was an approximate 40% lightening effect noticed in hyperpigmented lesions in those treated with the 0.1% tretinoin cream compared to only 18% in the vehicle control group. Despite these promising results, patients in the tretinoin group did notice that there was lightening of non-hyperpigmented skin, and 50% of treated patients developed retinoid dermatitis.⁵⁰ In another RCT of 28 Black women with melasma, 0.1% topical tretinoin was noted to cause a 32% improvement in the MASI score of compared

to only a 10% improvement in the vehicle control group. In this study, however, 67% of patients in the treatment group developed retinoid dermatitis.⁵¹ This side effect of retinoid dermatitis is concerning because this condition might cause or exacerbate PIH in patients with darker skin.⁵² It has been suggested that starting at lower dosages and slowly increasing the concentration of the retinoid might help mitigate these side effects.⁵²

Studies have also found that synthetic retinoids, such as adapalene 0.1% gel and tazarotene 0.1% cream, are just as effective in managing acne associated with PIH in patients with skin of colour with minimal side effects.^{53,54} When compared against each other in a multiracial RCT, tazarotene 0.1% cream was discovered to induce a statistically greater ($p < 0.018$) reduction in the appearance of PIH lesions.⁵⁵ In addition, these agents also seemed to be more tolerated than topical tretinoin with only approximately 10% of patients in each group presenting with mild adverse effects such as burning and dryness.⁵⁵ There was no mention of any patients in this study developing retinoid dermatitis. Recently, a formulation of tazarotene 0.045% lotion with promising effectiveness and seemingly better tolerability was approved for clinical use in the United States.⁵⁶ These newer options should be considered for patients seeking treatment for both acne and hyperpigmentation.

Azelaic acid

Whilst azelaic acid (AA) is an accepted treatment for rosacea, numerous studies have investigated its effectiveness in treating pigmentary disorders in skin of colour.^{57,58} AA works to depigment lesions by acting as a tyrosinase inhibitor as well as producing selective cytotoxic and antiproliferative effects on melanocytes, ultimately decreasing melanogenesis.⁵⁹ In a mixed racial comparative study, patients with melasma were randomly assigned to either a 4% HQ or 20% AA treatment group. Over the treatment period of 24 weeks, 20% AA was discovered to be as effective as 4% HQ in reducing the appearance of melasma lesions.⁶⁰ Additional comparative studies between HQ and AA have also yielded similar results with some studies finding AA monotherapy to be even more effective than 2% HQ for treating melasma.^{61,62} Side effects associated with AA are generally transient, most commonly presenting as erythema, irritation, dryness, burning and pruritus.⁵⁸

Kojic acid

Kojic acid (KJA) is a naturally occurring metabolite produced by various fungal species. It is an effective depigmenting agent that works by inhibiting the catecholase activity of tyrosinase.⁶³ KJA has mainly been studied in patients with melasma and not PIH. In a study comparing the efficacy of 0.75% KJA to 4% HQ in an Indian population with melasma, KJA was found to be less effective than HQ. The side effects discovered in this study were transient with only 3.3% of patients in the KJA group reporting erythema.⁶⁴ However, KJA use has commonly been associated

with the development of allergic contact dermatitis in the literature as KJA is a potential sensitizing agent.^{65,66} Whilst KJA monotherapy might not be as effective as HQ, various combination trials in skin of colour have demonstrated its effectiveness in combination with other agents.^{67–69}

Tranexamic acid

Tranexamic acid (TXA) is a plasmin inhibitor mainly used to achieve haemostasis in the context of active blood loss. More recently, both oral and topical formulations of TXA have been gaining popularity for the management of pigmentation disorders due to their favourable safety profile. Additional studies have also validated its use in melasma as an adjunct to microneedling and as an intradermal treatment.^{70,71} The mechanism behind how TXA acts in these pigmentary conditions is not fully understood but it is postulated that TXA inhibits UV-induced plasmin activity, causing a reduction in prostaglandins and arachidonic acid. This ultimately leads to decreased tyrosinase activity and subsequent impaired melanogenesis.^{70,72}

Numerous studies have investigated the use of topical TXA 2–5% for the treatment of melasma in richly pigmented skin. In a split-face comparative trial of patients with skin type III–V, 5% liposomal TXA was found to be as effective as 4% HQ in improving the appearance of melasma lesions. In addition, the TXA-treated arm had no adverse reactions when compared to the HQ-treated arm, which had three events of mild skin irritation.⁷³ Similarly, promising results were noted in another split-face study comparing 3% TXA to dual therapy of 3% HQ and 0.01% dexamethasone. Over the 12-week study period, both sides showed significant improvements in the MASI score of the lesions with no statistically significant difference between them. Once again, the TXA-treated side was better tolerated with significantly fewer adverse events ($p < 0.01$) than the HQ dual therapy side.⁷⁴ When used topically, the most common side effects are transient erythema, scaling and dryness, but it still possesses a theoretical risk of precipitating a thrombotic event.⁷⁵

Oral TXA has been shown to be a promising systemic treatment for melasma. When used in this context, the dosage is generally 250 mg twice daily, which is far less than when compared to a dosage of 3900 mg for haemostasis.⁵ Numerous studies have demonstrated the effectiveness of oral TXA as monotherapy for melasma.^{76–78} In addition, studies have also discovered that oral TXA can be used as an effective adjunct with other therapies, such as TCT and HQ, and with laser therapy.^{79–81} When used orally, common side effects include abdominal pain, bloating, headache and hypomenorrhoea.⁸² Even though studies have shown the safety profile for oral TXA to be favourable at this reduced dosage, there was one reported case of a thrombotic event in a patient with a familial protein-S deficiency.⁸³ Due to this, caution should be taken when considering oral or topical TXA in patients with histories of thrombotic events or malignancies or in pregnancy, which can increase a patient's

risk for developing deep vein thromboses. Patients usually require a careful medical history prior to the initiation of oral TXA to minimize risks.

Cysteamine

Cysteamine is another promising topical agent that has recently been gaining popularity due to its favourable safety profile.⁷⁵ It is a naturally produced aminothiols in mammalian cells and is thought to produce its skin lightening effects through various mechanisms, including the inhibition of tyrosinase and peroxidase, scavenging dopaquinone, and chelating metal ions required for melanin synthesis.⁸⁴ The safety of cysteamine has been extensively studied and is also thought to demonstrate anticarcinogenic effects.⁸⁵ Its depigmentation effects have been known for decades; however, it was only until recently that technological advancement allowed the creation of reduced malodorous topical formulations.⁸⁴ Recent studies have compared the efficacy of 5% cysteamine to HQ and TCT in skin of colour, finding it to be as effective or better at clearing melasma lesions whilst being considerably better tolerated.^{84,86} A case report also suggested that it might also be useful in the treatment of TCT-resistant PIH in skin of colour.⁸⁷ The most common adverse effects associated with its use are mild and transient dryness, burning, and a prominent odor.^{82,88} The favourable safety profile and promising results of cysteamine make it a compelling alternative to HQ or TCT in patients with melasma.

Cosmeceuticals

Agents such as arbutin, ascorbic acid, liquiritin and niacinamide have all shown therapeutic benefits in treating pigmentary disorders in richly pigmented skin.^{34–36,89} These agents are generally well tolerated; however, more robust long-term studies are lacking. These compounds should be considered for patients preferring a natural treatment option for their PIH or melasma in addition to photoprotection and behavioural modifications.

Chemical peels

Chemical peels act by causing controlled damage to various layers of the skin depending on the agent and methodology used.⁹⁰ Caution must be taken when administering these agents, and a thorough history should be obtained before starting treatment.⁹¹ Side effects of chemical peels are variable, from mild transient effects, such as burning and skin irritation, to more serious adverse effects such as scarring, infections and unwanted pigmentary shifts. When using chemical peels, studies have found that photoprotection and the use of HQ prior to administering the chemical peel can reduce the incidence of PIH.⁶

Glycolic acid

Glycolic acid is a naturally occurring α -hydroxyamide from sugarcane. Treatment concentrations range from 20% to 70% depending on the depths of peeling required, and

neutralization can be achieved with water. This is generally considered the gold standard chemical peel for the treatment of melasma and can also improve fine wrinkles and sun-damaged skin.⁹¹ Numerous studies have examined the additive effects of glycolic acid in treating pigmentary disorders in skin of colour with therapies such as laser or TCT. Reported adverse events include transient irritation, burning and desquamation, with no reports of PIH.^{92,93}

Salicylic acid

Salicylic acid (SA) is a naturally occurring β -hydroxy acid from willow tree bark. Treatment concentrations range from 20% to 30%, depending on the study, and SA does not require neutralization.⁹⁴ At these concentrations, numerous studies have shown SA to be well tolerated and effective in treating melasma in skin of colour. Only one study has reported its use in PIH. These studies have demonstrated that SA generally only causes mild side effects, such as dryness, itchiness and erythema.^{95–97} Additional comparison studies in skin of colour have also suggested that SA is as effective in treating melasma as 4% HQ, Jessner solution (JS) and topical tretinoin.^{98–101}

Jessner solution

JS is a common combination peel consisting of resorcinol, SA, lactic acid and ethanol. This combination of different substances seems to work synergistically, ultimately allowing for reduced strengths of each individual component. Newer modified combinations of JS have also been popularized due to the possibility of potential allergic reactions to resorcinol.¹⁰² In a comparative study to 20% trichloroacetic acid, JS had similar efficacy post treatment with fewer reports of PIH in richly pigmented skin.¹⁰³ In addition, when used in combination with a lower strength of 15% trichloroacetic acid, JS was also shown to be even more effective than monotherapy with fewer reports of PIH post treatment.¹⁰⁴

Trichloroacetic acid

Trichloroacetic acid (TCA) is an inorganic peel that can be used at varying concentrations as both a superficial and medium depth peel. Due to the risk of scarring or PIH with TCA, a 10–25% concentration is used in skin of colour to achieve a superficial peel.⁹¹ A meta-analysis assessing various chemical peels found that, whilst TCA monotherapy might be similarly as effective as GA, its higher risk of adverse events makes it less preferable in skin of colour.¹⁰⁵ However, TCA has still shown promising results when used at lower concentrations in combination with JS and GA.^{92,106}

Laser/light therapy

Laser therapy is an extensively studied treatment modality for pigmentary lesions. The major drawback with these treatment options for melasma, especially in skin of colour, is the high risk of PIH post treatment and recurrence.⁷ It is due to this risk that caution must be taken when selecting these treatment options specifically in darker skin phototypes.

Ablative lasers

Ablative lasers include CO₂ lasers and erbium:YAG lasers that ultimately function by causing damage and removing layers of the skin.¹⁰⁷ Whilst studies have shown this modality to be useful in the treatment of melasma, it is not preferred in skin of colour due to the high incidence of PIH. In a chart review of patients treated with CO₂ lasers, it was found that there was a 37% risk of PIH in all patients with an increasing risk in darker complexions.¹⁰⁸

Non-ablative fractioning lasers

Non-ablative lasers function by causing controlled coagulative damage within the dermis that is below the wounding threshold of the skin. In doing so, these therapies are thought to be better tolerated with fewer side effects when compared to ablative techniques. Varying wavelengths have been studied, with 1550 nm being the wavelength preferred for the treatment of melasma.¹⁰⁹ An RCT comparison in patients of skin type II–IV found non-ablative fraction lasers to be equally as effective in treating melasma, with similar rates of recurrence and side effects when compared to TCT.¹¹⁰ Despite this, there is still a risk of PIH in darker skin tones.¹¹¹ Some preventative PIH methods include optimizing the settings as well as therapy to suit the patient's skin type. By altering the treatment density, reducing the number of passes and extending the time between treatment, the risk of PIH is significantly reduced.¹¹²

Low-fluence Q-switched lasers

Low-fluence Q-switched lasers (LFQSL) are a newer variant of the older Q-switched lasers, which have been shown to be effective in treating melasma in skin of colour. This newer version utilizes a lower fluence that is sub-photothermolytic and is thought to selectively destroy melanin pigment whilst leaving cells intact.¹¹³ This allows for less skin damage and fewer adverse effects; however, PIH is still a complication that is associated with its use in darker skin.¹¹⁴ A randomized split-face comparison trial between LFQSL and 2% HQ found LFQSL to be more effective than the topical treatment as a monotherapy, and additional synergetic effects were observed when used in combination for the treatment of melasma. Despite these promising results, patients who were treated with these lasers did develop post-treatment hypopigmentation and had a high rate of recurrence.¹¹⁵

Picosecond laser

This is a newer class of laser that was designed to produce shorter laser pulse durations and ultimately lead to less photothermal damage to the skin.⁷ Recent studies have been very promising in the treatment of hyperpigmentation and melasma in Asian skin but there has been limited research on darker skin types.^{116,117} Further information is required in skin of colour before recommendations can be made.

Emerging treatments

Research understanding the mechanisms surrounding PIH and melasma is still ongoing and, as such, novel therapeutic options are continuing to be developed. One area which has shown promising results is the use of alternative vehicles for drug administration. For example, the use of solid lipid nanoparticles can increase topical drug bioavailability and drug stability. Solid lipid nanoparticle-prepared HQ has shown improved efficacy when compared to standard topical HQ.¹¹⁸ In addition, other drug vehicles, such as liposomes and microemulsions, have also shown encouraging results.^{119,120}

Emerging pharmacological therapeutics include topical metformin, flutamide, isobutylamido thiazoyl resorcinol and platelet-rich plasma for the treatment of melasma and PIH.^{121–124} Newer non-pharmacological options include the use of microneedling and picosecond lasers.¹²⁵ All these treatments have shown positive results in their respective studies; however, stronger more robust studies and their efficacy and safety profile in skin of colour are still lacking. As such, additional research is required before possible recommendations can be made regarding their use.

Skin bleaching and glutathione

Skin bleaching refers to the act of purposefully lightening skin tone. This global phenomenon is rooted in the ideals of colourism which promotes the concept that beauty is associated with lighter skin tones.¹²⁶ A commonly used skin bleaching agent is glutathione, used for its antimelanogenic effects.¹²⁷ It is hypothesized that glutathione promotes skin lightening through numerous mechanisms, including its antioxidant properties, the production of pheomelanin, the inhibition of tyrosinase activity and the transfer of tyrosinase.¹²⁶ Whilst glutathione is often marketed as a safe treatment, studies regarding its use for skin lightening are lacking, with the majority of studies having limitations including small sample sizes, short study durations, short follow-up periods and the lack of glutathione bioavailability.^{127,128} In addition, the use of IV glutathione has been associated with several complications, including Stevens–Johnson syndrome, abdominal pain, kidney dysfunction, brain toxicity and liver dysfunction.¹²⁷ Given the lack of research regarding its use, glutathione is not currently recommended for the treatment of melasma or PIH.

Conclusion

PIH and melasma are common relapsing disorders that are notoriously difficult to manage. Over the past decade, the management of these conditions has been altered due to newer agents gaining popularity as well as technological advancements. Currently, the single most important treatment option that should be included in the management of these disorders is robust photoprotection, which is both UV and VL blocking. HQ and HQ-containing combinations,

such as TCT, remain the most well-studied options for topical management; however, cysteamine and topical TXA are reasonable alternatives. Oral TXA is a potential systemic treatment for patients' refractory to topical therapies. Chemical peels, such as GA and JS, could be useful for certain patients as an adjunctive therapy. Finally, LFOQL could be useful for patients with treatment-resistant

lesions; however, extreme caution should be taken when considering procedural options in darker skin tones due to a high rate of recurrence and risk of post-treatment pigmentary anomalies. Treatment of melasma and post-inflammatory hyperpigmentation is an evolving area of research and therapies are expected to continue to develop.

Key practice points

- Photoprotection and sunscreen use are the cornerstones of therapy (strength of recommendation: B)
 - >30 SPF iron oxide-containing sunscreen is preferred
- First-line therapies include hydroquinone 4% or combinations containing hydroquinone, including triple combination therapy (strength of recommendation: A)
 - The maximum recommended duration of treatment is 6 months
 - Common adverse effects include erythema, burning, pruritus and desquamation
 - Ochronosis is a rare but possible side effect
- Retinoids including tretinoin 0.1%, adapalene 0.1% or tazarotene 0.1% can also be used as first-line therapy (strength of recommendation: B)
 - Can be helpful in patients with comorbid acne
 - Adverse effects include burning, skin dryness, retinoid dermatitis and post-inflammatory hyperpigmentation
- Second-line topical treatments include azelaic acid, cosmeceuticals, topical tranexamic acid, kojic acid and cysteamine (strength of recommendation: B)
 - Kojic acid has an increased risk of contact dermatitis
 - These treatment options have less evidence when compared to hydroquinone therapies
- For patients preferring an oral medication, oral tranexamic acid can be used (strength of recommendation: B)
 - Careful history for possible clotting disorders and risks is required
 - Adverse effects include abdominal bloating, headache and hypomenorrhea in women
- Chemical peels and laser-based therapies are only recommended for refractory or persistent lesions (strength of recommendation: B)
 - Low-fluence Q-switched lasers or picosecond lasers are preferred due to more favourable side effect profiles
 - Both chemical peels and lasers have an increased risk of post-inflammatory pigmentary changes in patients with skin of colour

Contributions: All authors contributed equally to the preparation of this manuscript. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Disclosure and potential conflicts of interest: The authors declare that they have no conflicts of interest relevant to this manuscript. The International Committee of Medical Journal Editors (ICMJE) Potential Conflicts of Interests form for the authors is available for download at: <https://www.drugsincontext.com/wp-content/uploads/2022/05/dic.2021-11-2-COI.pdf>

Acknowledgements: None.

Funding declaration: There was no funding associated with the preparation of this article.

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Provenance: Invited; externally peer reviewed.

Submitted: 4 November 2021; **Accepted:** 11 February 2022; **Publication date:** 31 May 2022.

Drugs in Context is published by BioExcel Publishing Ltd. Registered office: Plaza Building, Lee High Road, London, England, SE13 5PT.

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