

Treatment of Hyperpigmentation in Darker Skins

Savas Yayli*

Department of Dermatology, Faculty of Medicine, Karadeniz Technical University, Trabzon, Turkey

*Corresponding author: Savas Yayli, Department of Dermatology, Faculty of Medicine, Karadeniz Technical University, Trabzon, Turkey, Tel: 90 462 377 53 88; E-mail: savasyayli@gmail.com

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Introduction

Darker skin or skin of colour means higher Fitzpatrick skin types in a wide range of racial and ethnic groups referring to persons from African, Asian, Native American, Middle Eastern and Hispanic backgrounds. Darker skin types are characterized by higher content of melanin, higher eumelanin to pheomelanin ratio. This is an advantage for protection against ultraviolet (UV) radiation, however it also makes darker skin more vulnerable to postinflammatory dyspigmentation [1,2].

Pigmentary disorders, especially hyperpigmentation is one of the most common complaints in darker skin, and the management is often challenging. A recent review by Cestari et. al listed most common acquired hyperpigmentations in darker skin including melasma, Post Inflammatory Hyperpigmentation (PIH), acanthosis nigricans, phytophotodermatitis, dermatosis papulosa nigra, erythema dyschromicum perstans, periorbital hyperpigmentation, flagellate dermatosis, confluent and reticulated papillomatosis of Gougerot and Carteaud, cervical poikiloderma and primary cutaneous amyloidosis [3]. This presentation will particularly focus on the treatment options of melasma and PIH in darker skin.

Treatment options in Melasma and PIH in Darker Skin

Before the treatment, one should identify and treat any underlying dermatosis or contributing factors. Moreover, the treatment should have rational goals. One should also keep in mind the options with multi-therapy approach. Sun protection should be central with sunscreens and physical barriers, such as hats and clothing which will reduce sun exposure [4].

For melasma, current treatments available remain unsatisfactory. Topical combination therapies are more effective. Triple Combination (TC) including hydroquinone, retinoids and steroids is most effective with clear adverse effects such as erythema and peeling. Chemical peels, especially superficial ones, are generally effective. Laser and light therapies have mixed with an increased risk of irritation and PIH [5].

For PIH, firstly one should aim to treat underlying disorders. It often takes many months. Topical therapy is typically effective for epidermal PIH. Chemical peels and lasers may help in recalcitrant hyperpigmentation. All treatments should be used with great caution to prevent irritation and worsening of PIH [4].

Topical treatments

A list of skin lightening agents are listed in Table 1 [2]. The largest group in those agents is tyrosinase inhibitors, and the most well-known agent is hydroquinone which is often considered as "topical gold standart" in the melasma and hyperpigmentation treatments [4]. However, in last decade concerning the safety reasons about hydroquinone such as ochronosis or theoretical risk of malignancy,

many newer agents are in the market [6]. Beside those newers, fixed TC including hydroquinone 4%, tretinoine 0.05%, flucinolon acetoneide 0.01% is shown as the therapy with highest evidence – still little controlled studies - in Latin guide of melasma or recent reviews. If there is an irritation or allergy to one of compounds of this TC, one may use it as dual combinations. In Latin guide for treatment of melasma, second line therapies are TC plus peels or microdermabrasion, and lastly lasers and light sources [4,7].

Mechanism of action	Compound
Tyrosinase inhibition	Arbutin
	Azelaic acid
	DeoxyArbutin
	Hydroquinone
	Liquorice extract
	Mequinol
	N-Acetylglucosamine
	N-Acetyl-4-S-cysteaminylphenol
Reduction in melanosome transfer	Niacinamide
	Retinoids
	Soybean trypsin inhibitor
Interaction with copper	Ascorbic acid
	Kojic acid
Stimulation of keratinocyte turn over	Glycolic acid
	Retinoids
Inhibition of melanosome maturation	Arbutin
	DeoxyArbutin
Inhibition of protease-activated receptor-2	Soybean trypsin inhibitor
Oxidation and break down of melanin	Lignin peroxidase

Table 1: Skin lightening agents [2].

Hydroquinone is an older depigmenting cream which is effective in 2%-5% formulations. The most well-known adverse effects are irritation, contact allergy, exogenous ochronosis. It is sold with prescription in many countries. It is also a component of famous Kligman's Formula: Hydroquinone 5%, tretinoine 0.1%, dexamethasone 0.1% [8].

One of the few randomized controlled studies comparing fixed TC and hydroquinone 4% in Asian melasma patients showed that TC had superior efficacy (64.2% and 39.4%) in 8-weeks, in all assessed parameters including Melasma Area and Severity Index score and Global Severity Score (GSS). TC was associated with more but mostly mild adverse effects [9].

A recent letter by Kandhari et al. pointed out that topical treatment for melasma might cause many side effects in skin of colour. In their study, 69 melasma patients with darker skin treated topically with or without TC showed frequent side effects including erythema, acneiform eruptions, telangiectasias, hypertrichosis and rosacea like eruption. Of those side effects, erythema and hypertrichosis are significantly higher in TC group [10]. Patient education is crucial on that topical therapy including hydroquinone and TC to prevent mentioned side effects.

One example for newer therapies in melasma that has been recently reported in the literature is the effects of methimazole. It is a potent peroxidase inhibitor, and peroxidase is known as important in final steps of melanogenesis. Methimazole is not melanocytotoxic, even at high concentrations. A recent report by Malek et al showed impressive results with methimazole in a patient with hydroquinone resistant melasma after 2-month therapy [11].

Another example of newers is 4-n-butylresorcinol, which has been shown a higher inhibitory capacity on human tyrosinase activity than hydroquinone, arbutin and kojic acid [12]. Another potent tyrosinase inhibitor, decapeptide-12 has been recently shown very effective with a marked improvement of PIH after 8-week therapy. It is not also melanocytotoxic [13].

Chemical peels

Chemical peels are generally effective in darker skin, especially superficial ones. Because of increased risk of PIH, deep peelings should be avoided. Pretreatment with a course of hydroquinone may improve the results. Topical retinoids should be stopped before seven days. Standard options are glycolic acid 10-70%, salicylic acid 20-30%, trichloroacetic acid (TCA) 10-25% and Jessner's solution. In a recent review, the newers are listed as tretinoin, pyruvic acid, β -lipohydroxy acid, mandelic acid and amino fruit acids [14].

In terms of glycolic acid and salicylic acid, both peels have been shown beneficial for melasma and PIH. A study by Grimes et al. showed that five salicylic acid peels 20-30% with 2-week interval for PIH had more than 75% improvement in 80% of patients with skin of colour [15]. In another study by Grover et al, eight glycolic acid peels 10-30% with 2-week interval was found useful for superficial scarring and melasma [16].

For the newer peels, Ilknur et al who compared the efficacy of amino fruit acid (AFA) and glycolic acid, showed that both of them were effective, however AFA peel was better tolerated [17].

A recent study from Egypt, comparing the efficacy of different formulations of TCA (20%, 25%, 30%) and different wavelength of q-switched Nd:YAG laser (532 nm and 1064 nm) found that TCA 25% is the most effective, according to the mean improvement percentage of MASI scores. Q-switched Nd:YAG laser with 532 nm had the highest complications [18].

Lasers and light sources

Lasers are the last options for the recalcitrant cases of melasma and PIH with great caution. Many reports have pointed out that the safest and efficient laser for melasma and PIH in darker skin was q-switched Nd:YAG laser with its longer wavelength (1064 nm). Q-switched Ruby laser with 694 nm is not recommended in darker skin. Intense pulse light (IPL) has mixed results [19].

Some reports have shown that low fluence q-switched Nd:YAG laser with 1064 nm was beneficial for melasma and PIH in darker skin. A study by Cho et al. [20] from Korea has reported high patient satisfaction (50-100% improvement) in 18 of 25 patient with five sessions q-switched Nd:YAG laser with 2 week interval. The fluence was between 2.0-3.5 J/cm². Another study with the same laser by Choi [21] et al. has showed that the mean MASI scores were significantly decreased after five sessions with 1-week interval. The fluence was also 2.0-3.5 J/cm². However, a study by Wattanakrai has reported only temporary improvement with 5 sessions q-switched Nd:YAG laser with 1-week interval. The fluence was between 3.0-3.8 J/cm². Four of 22 patients had rebound hyperpigmentation, and all patients had recurrence of melasma [22].

In a recent study by Chung et al., they compared the efficacy of pulse-in-pulse IPL (PIP-IPL) and the combination of IPL and q-switched Nd:YAG laser. After 6 months, they found same efficacy on melanin index for both therapy, and concluded that PIP-IPL might be a safe and promising treatment for melasma in darker skin [23].

In terms of fractional lasers, in a study by Wanitphakdeedecha et al., they concluded that fractional photothermolysis laser 1410 nm was safe and temporary effective, but long term follow up was still needed. They suggested that only 5% coverage should be used to minimize risks [24]. In a case report by Katz et al., fractional photothermolysis laser 1550 nm had been shown to be effective in a recalcitrant PIH with 3 sessions with 4-8 week interval [25]. Another case report from Turkey by Oram et al. showed that fractional CO₂ laser was beneficial for a recalcitrant PIH with two sessions [26].

Conclusion

The management of pigmentary disorders in darker skin is often challenging. Melasma and PIH are the most common problems in skin of colour. Firstly, one should identify and treat any underlying and/or contributing factors and have rational treatment goals. Sun protection is essential, and multi-therapy approach is needed in most cases. In most cases, especially superficial ones, first-line therapy is topicals with TC or newers. Second-line therapy is chemical peels with topicals. Lasers and light therapies should be used with special attention for the type of it, skin type and fluence. Low fluence q-switched Nd:YAG laser with 1064 nm has been reported with more benefits.

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