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Advances in the Treatment of Melasma

An Evidence-Based Approach

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KEYWORDS
• Melasma • Laser • Light • Hyperpigmentation • Pigmentary disorders

KEY POINTS

- Melasma is a chronic and dynamic condition involving hyperactivity of melanocytes and deposition of melanin within the epidermis, dermis, or both. Clinically, it presents as focal hyperpigmented patches most commonly on the face. Well-established risk factors include sun exposure, oral contraceptives, pregnancy, family history, and Fitzpatrick skin types (III–V).
- The goal for effective treatment of melasma includes removal of the excess melanin in the epidermis and dermis as well as suppression of further melanogenesis. Without these 2 steps, there is high risk for relapse of melasma after treatment.
- Topical therapy remains the gold standard for first-line therapy for melasma using broad-spectrum sunscreens and either hydroquinone 4% cream, tretinoin, or triple-combination creams.
- In recalcitrant cases and in dermal melasma, the addition of laser treatment using low-fluence QS-Nd:YAG laser or other pigmented specific laser and light devices can be used.
- Melasma is difficult to treat and single-modality treatment approaches usually do not yield favorable long-term results.

INTRODUCTION

Melasma, formerly known as chloasma, is an acquired hyperpigmentation disorder most commonly affecting women. It is characterized by irregular brown to brown-gray macules and patches on the face, in 3 predominant clinical patterns: centrofacial, malar, and mandibular [1]. Of these patterns, the centrofacial is most common and involves the forehead, nose, upper lip excluding the philtrum, cheeks, and chin [2,3]. The malar pattern involves the malar cheeks, and the mandibular pattern involves the jawline and chin. More recently the term "extrafacial melasma" has been used to describe a melasma pattern occurring on nonfacial body parts [4].

Although the exact cause of melasma is unknown, risk factors are well established and include sun exposure, Fitzpatrick skin types III to V, family history of melasma, pregnancy, and exogenous hormones (oral contraceptives and hormone replacement therapy) [1–3,5,6]. Recently, reports of visible light inducing

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increased and sustained pigmentation in the skin highlight another potential risk factor for melasma development and persistence [7,8].

Melasma, has been classified into epidermal, dermal, and mixed-type based on the location of pigment deposition [1]. In the epidermal form characterized by brown color, melanin is found in the basal and suprabasal layer. In dermal melasma, clinically more blue-gray in appearance, melanin is found in the superficial and deep perivascular melanosomes. Mixed-type melasma is characterized by both epidermal and dermal pigment deposition. Woods lamp (340–400 nm) examination was thought to enhance epidermal melasma lesions and aid in distinguishing it from dermal melasma, in which the pigment does not enhance with Woods lamp. However, recent study suggests that Woods lamp examination does not accurately detect dermal melasma as well as previously thought [9]. The location of excess melanin is important clinically, as it can guide treatment choice. The epidermal form is easier to treat and more amenable to topical therapy, whereas the dermal or mixed type of melasma is more resistant to treatment. It is thought that it is the presence of the deeper, dermal melanin that contributes to the difficulty in melasma treatment [1]. This is because destruction of these melanosomes is often accompanied by significant inflammation that in turn stimulates further melanogenesis [10].

Aside from the clear role that melanocytes and melanosomes play in pathogenesis of melasma, there is increasing evidence that melasma also has a significant vascular component. This has been demonstrated by the increased number and size of dermal blood vessels in melasma lesions compared with unaffected perilesional skin, as well as greater expression of vascular endothelial growth factor in keratinocytes of melasma lesions [11]. Furthermore, the study by Kim and colleagues [11] found a significant relationship between the number of blood vessels and pigmentation in melasma. The exact mechanism and relationship between this vascular phenomenon and melasma is not yet fully understood and is the subject of ongoing investigation.

Various treatments, including topical, oral, resurfacing techniques, as well as numerous light and laser treatments have been used for treatment of melasma, both alone and in combination. Unfortunately, treatments have often produced inconsistent and generally unsatisfactory results, and to this day achieving long-term clearance in melasma remains a clinical challenge. Given the clinical and therapeutic challenges of patients with melasma, we present a practical approach to the evaluation and treatment of these patients, focusing on the most effective, safe, evidence-based treatments available currently for melasma.

PRETREATMENT PLANNING

Patient History

Given the complexity of melasma and interplay of both genetic and environmental factors in pathogenesis of the disease, a thorough history and physical examination of the patient is of utmost importance. History should include investigation of onset or worsening of hyperpigmentation and any relationship to pregnancy or the initiation of hormone therapy of any type. It is recommended that patients who develop melasma while taking an oral contraceptive pill stop the medication and avoid future use of similar drugs if possible [6]. Patients also should be asked about presence of previous inflammation at the hyperpigmented sites, as this can point away from diagnosis of melasma. Furthermore, extent of ultraviolet light exposure and patient's compliance with daily sun protection should be assessed. Importance of strict photoprotection before, during, and after the treatment must be reviewed and emphasized to all patients. Patients should understand that failure of appropriate compliance with strict photoprotection can lead to recurrence and at times worsening of hyperpigmentation after treatment. Patients' medications also should be carefully reviewed for presence of any phototoxic medications, as drug-induced pigmentation can be confused for melasma. Given that family history is an important risk factor for development of melasma [12,13], patients should be asked about family members who have had similar symptoms, which can help support the diagnosis of melasma.

Physical Examination

Pretreatment physical examination should include assessment of patient's Fitzpatrick skin type, because patients of darker skin types with melasma (Fitzpatrick type IV–VI) are at a higher risk of adverse events after treatment [14,15], including postinflammatory hyperpigmentation (PIH) and melasma recurrence, and extreme caution should be exercised in selecting the appropriate treatment modality in these patients. Because assessment of melasma involvement can be more challenging in skin of color, Woods lamp examination can be helpful in better visualization of hyperpigmentation (in all Fitzpatrick skin types.)