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MELASMA MANAGEMENT: HOW I DO IT

Melasma is a common acquired disorder of hyperpigmentation which has a strong predilection for females and is more common in individuals with Fitzpatrick skin phototypes III-VI.[1] It is most common on the face but can occur on the neck, upper chest, extensor forearms and upper back.[2]

The pathogenesis of melasma is both multifactorial and incompletely understood.[2] There is an increase in epidermal and dermal melanin without a similar increase in the number of melanocytes. Melanocytes are enlarged with elongated dendrites and increased numbers of melanosomes. An increase in mast cells, dermal blood vessels, abnormalities of the basement membrane and solar elastosis can also be seen.[2] The number of blood vessels, vessel size and density are all increased in lesional melasma skin.[2,3] Increasing evidence is emerging that points to melasma as a disorder of photoaging in genetically predisposed individuals.[3,4]

Melasma can cause significant psychological distress and negatively affect quality of life.[1,2] Medical management of melasma has been shown to produce feelings of confidence and influence self-esteem in a positive way making this a very important condition to treat.[2]

Management of melasma is challenging. It is often recalcitrant to treatment and frequently recurs following successful treatment. It can be frustrating to patients and physicians alike when expectations are not met or if/when the condition recurs. Additionally, there is a paucity of strong evidence surrounding treatment as many products are best described as cosmeceuticals or are compounded.

My practice contains a large population of melasma patients, and their treatment is both challenging and rewarding. Several key aspects of management are crucial for a successful therapeutic relationship and the focus of this article will be on topical and oral agents which are the mainstay of my practice.

The most important aspect of management is setting realistic patient expectations. I spend considerable time reviewing the overall natural history of this condition with patients in order to align our goals. I emphasize the fact that there is no cure to this condition. I review the two phases of treatment that they will undergo; an active treatment phase which most often includes topical hydroquinone. During this stage patients will see dramatic improvement in their melasma and overall skin tone and health. Once we are both pleased

with the results, we enter into a maintenance treatment phase which includes a skin care regimen that is entirely safe to continue over the long term and takes advantage of botanical brightening agents without the use of hydroquinone. Often, after the summer season or a significant amount of time in the sun, the hyperpigmentation will return, and the patient returns to the active treatment phase again. Once patients understand the overall treatment approach, they are less surprised if the pigment returns and are able to understand that they are still on track for the successful management of their disease and cope with the fact that their treatment wasn't a failure.

A thorough patient history is key especially with regard to exogeneous hormone use. The use of oral contraceptive pills or hormone replacement therapy can induce or worsen melasma and make it more difficult to treat. A 63-year-old female patient I recently saw with severe melasma had been prescribed an oral contraceptive pill for no clear indication. The discontinuation of the offending medication in this circumstance was enormously helpful.

Photography is another key component to successful treatment. Standardized photographs in the same room, with the same lighting, comparing 'before' and 'after' photographs is essential. Patients are often thrilled to see their progress, and this will help clinicians make objective management decisions.

When treating a patient, I take a full-face approach for almost all patients (except those with only a small patch of melasma limited to the upper lip). When speaking to patients about their treatment goals, it is common to hear the wish for the whole skin to be improved, not just the brown patches. Therefore, all steps in my regimen are applied to the entire face with few exceptions.

In my experience, the results of melasma treatment are much improved with the use of as many brightening and photodamage-repairing ingredients as possible. Of course, hydroquinone plays an essential role in this regard as the gold standard for skin brightening. However, in my clinical experience, the use of glycolic acid, salicylic acid, niacinamide, retinoids, antioxidants and botanical brighteners may help to create even better results. This is certainly supported in the peer-reviewed literature on melasma management by numerous studies demonstrating improved results with hydroquinone if other ingredients are added (such as a retinoid and corticosteroid).[5,6]

Botanical brighteners refer to non-hydroquinone brightening agents including: ascorbic acid, arbutin, green tea, emblica, licorice, mulberry, niacinamide, silymarin and others.[2,5,6,8]

My treatment regimens include a multi-step, multi-layered approach of products applied to the entire face. The overall regimen remains the same throughout the entire treatment period and only the true brightening products are changed over time between hydroquinone and botanical brighteners. I have consistently been impressed with the results my patients achieve with a complete, thorough, multi-step approach to the treatment of their melasma **(Figure 1)**. I have not seen equivalent results with the use of a traditional Kligman's formula to individual melasma patches. It is important to harness the power of each of the individual ingredients and use them all synergistically to help treat this difficult-to-manage skin condition.

Figure 1. Patient results from 'before' and 'after' multi-step treatment approach; photo courtesy of Allison Sutton, MD

There is a paucity of evidence to support the use of most of these agents. For a comprehensive review of the data for each non-hydroquinone brightening ingredient, please review Dr. Miller-Monthrope's excellent summary in Volume 1, Issue 4 of this publication from 2020.[5]

The key ingredients and the steps taken to incorporate these ingredients into the patient's treatment will now be described. Thorough washing and exfoliating will help to shed stratum corneum and prepare the skin for enhanced penetration of leave-on products. In my experience, choosing products with salicylic acid and glycolic acid may help with gentle epidermolysis.

The application of hydroquinone is next, and it is recommended to be used twice daily. I usually begin hydroquinone at 4% but have titrated to a concentration of 10% when needed and have achieved excellent results with the above combinations, without the need to go above a 10% concentration.

Four percent kojic acid is a helpful addition to the compounded hydroquinone formula. Kojic acid has poor efficacy when used as monotherapy, however, can be very effective in combination with hydroquinone.[1] Kojic acid can lead to a significant irritant contact dermatitis. Therefore, if a patient presents with dermatitis, I suggest first removing kojic acid from the modified Kligman's formula to see whether the patient responds. I exclude topical corticosteroids in my modified Kligman's formulas. In my experience, they do not provide significant benefit and may cause corticosteroid-induced acne, telangiectasias and even hypopigmentation as a side effect. I work with a local pharmacist to create a compound that is cosmetically elegant, moisturizing, and as stable as possible.

The next element of my treatment approach involves a layer of 10% glycolic acid lotion, which is used for the above-mentioned reasons.

An antioxidant, particularly one with ascorbic acid, and a sunscreen are the last two layers in the morning routine. Consistent, rigorous, daily photoprotection is a critical aspect of long-term management of this condition. At every appointment it is important to remind the patient of its importance. The goal is to prevent UV light exposure. There is new evidence that visible light can also aggravate melasma, especially short wavelength visible light (415nm).[2] Short wavelength visible light has been shown to induce prolonged hyperpigmentation in healthy volunteers compared to longer wavelength (630 nm) visible light exposure.[7]

A sunscreen must be used every single morning and re-applied at least once a day if not more frequently, depending on exposure. A minimum SPF of 30 is suggested. Physical blockers such as titanium dioxide and zinc oxide protect against UVB, UVA and modestly against visible light.[8] I routinely recommend these; however, they can be difficult to use in skin of color patients due to a white-to-gray sheen they may produce.[2] Iron oxides are also able to block both UV and short wavelength visible light and may be more cosmetically acceptable to skin of color patients as they provide a better color match. In addition to UV and visible light, heat is also thought to be a trigger for melasma, and avoidance should be attempted.[1]

In the evening after washing and exfoliating, hydroquinone is applied a second time followed by a topical retinoid. The choice of topical vitamin A is based on several factors including skin sensitivity, comorbidities, as well as cost.

Given that most of the active ingredients in this approach can be irritating to the skin, it is critical to include some products meant to hydrate and soothe the skin. Implementing this without the use of topical corticosteroids is preferable, and clinicians may consider including a bland emollient in the patient's regimen that contains ingredients such as aloe which can calm the skin.

The newest and most exciting addition to our therapeutic armamentarium has been oral tranexamic acid (TA). Its use in melasma is off-label but there are several studies consistently showing significant improvement in melasma scores with its use. TA's mechanism of action is uncertain but is thought to be based on 1) competitive inhibition of plasminogen activator – this inhibits conversion of plasminogen to plasmin in keratinocytes which in turn reduces arachidonic acid and prostaglandins leading to a decrease in tyrosinase activity 2) a decrease in angiogenesis and mast cells thereby possibly counteracting the vascular component of melasma and 3) competitively antagonizing tyrosinase which further impairs melanogenesis due to its structural similarities to tyrosinase.[2]

I use TA at a dose of 250 mg p.o. b.i.d. and have found this to be generally well-tolerated and extremely helpful in managing melasma. The main clinical issue is to identify the

appropriate treatment duration. Most studies use oral TA for a 3-6 month duration. In practice, most of my patients do not want to discontinue its use, as it is incredibly helpful in improving melasma. Interestingly, I have not found TA to be efficacious in managing other conditions of hyperpigmentation such as post-inflammatory hyperpigmentation.

Patients are provided with written instructions reviewing the steps in which to apply the products and they are also counselled extensively on the anticipated and normal adverse reactions of erythema, scaling and mild pruritus that often accompany the use of this regimen of products.

Patients are seen in follow up at months two, four and six. I will continue use of hydroquinone for a maximum of 6 months, however most patients require a shorter treatment course. As soon as patients demonstrate excellent improvement, the active treatment phase concludes, and a slow taper of hydroquinone begins until it is no longer required. This hydroquinone taper takes place over a period of one month and the introduction of non-hydroquinone brighteners occurs concurrently, which may result in less rebound hyperpigmentation.

I attempt to maintain the patient's improvement on the full regimen of topical agents with botanical brighteners, retinoids, alpha and beta hydroxy acids, antioxidants and photoprotection for as long as possible.

In terms of choosing non-hydroquinone options for the brightening agent, this depends on the clinician's familiarity with cosmeceutical products in your armamentarium. Additionally, comorbidities such as acne are important to consider. Several of the botanical brighteners, including vitamin C-based products, tend to aggravate acne. Therefore, one option to consider when acne is a comorbidity includes the use of topical azelaic acid 15% gel. The majority of evidence for azelaic acid's efficacy in treating melasma is with the 20% cream formulation which is not available in Canada.[1,6] The remaining brightener options are cosmeceuticals and therefore, gaining familiarity with the individual products is the best method to determine their suitability for use in the clinician's practice. Vitamin C, arbutin, green tea, emblica, licorice, mulberry, niacinamide, silymarin and others[2,5,6] are options that have demonstrated improvement in hyperpigmentation in smaller studies. In my experience, they are not as effective as hydroquinone and I therefore use them predominantly in the maintenance phase of management. In certain situations these agents could be first-line treatment options such as in use with a pregnant or lactating patient, one with exogenous ochronosis or with a patient who wishes to avoid hydroquinone use.

Melasma can certainly be challenging to treat, however it can also be extremely rewarding to improve. Melasma patients are generally motivated patients who are pleased with improvement in their skin. It is important to take the extra time to set realistic expectations and to review normal reactions. Finally, the combination of many brightening and anti-photoaging ingredients can lead to better outcomes.

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