

The Overall Landscape for the Treatment of Melasma

Dermatology Times: *What makes melasma so difficult to treat?*

Dr. Desai: While for many years, we have talked about melasma, primarily from the aesthetic standpoint—what makes the condition so challenging to treat is that it is also a chronic skin disease. From that perspective, we have to approach melasma in the same manner as psoriasis or atopic dermatitis. It is important to emphasize the chronic nature of melasma in that first patient consult and to set appropriate patient expectations. While our community of board-certified dermatologists are there to help patients manage their condition and improve their symptoms both medically and cosmetically, patients need to understand that this is not a curable disease.

Melasma has a high relapse and recurrence rate because the pigmentation triggered by increased melanin production is always lurking in the background.

Dermatology Times: *Do you have a lot of melasma patients coming in to see you with the expectation that this is a permanently curable condition?*

Dr. Desai: Absolutely. In fact, I would say that the majority of patients I see think that I am going to be able to give them a quick fix to resolve their issues. While there are things we can do rather quickly in some cases to improve patients' melasma-related symptoms, we can't make the disease go away overnight. It takes time.

Dermatology Times: *What are the most common approaches to the treatment of melasma?*

Dr. Desai: In my practice, we take a multidisciplinary approach. Successful treatment often requires combination therapy, and while it's important to recognize that topical therapy remains the gold standard as first-line treatment of melasma, one prescription alone is often not enough for these patients.

I like to start with topical therapy, which usually includes a triple combination that includes hydroquinone, a retinoid and a steroid. In addition to topical therapy, it's important to reinforce the importance of proper sunscreen application and photoprotection. Even though sunscreen is not prescription therapy, it's important that patients understand that it is something they need to apply multiple times each day, especially during prolonged sun exposure.

I also talk to my new melasma patients about topical antioxidants. Specifically, I like to suggest vitamin C, often combined with vitamin E. Topical antioxidants are great to let patients know that they have options besides prescription therapy.

I will typically have melasma patients initiate that therapeutic combination for anywhere from six to 12 weeks before seeing them for an initial follow-up visit. I do tell them before they leave the initial consultation that we may discontinue the hydroquinone at the initial follow-up visit to give their skin a break. Depending upon the level of improvement at this visit, we may move on to second-line topical agents or introduce physical modalities such as chemical peels.

Dermatology Times: *Why is hydroquinone typically considered the anchor drug for the treatment of melasma? Why is it thought to work in these patients?*

Dr. Desai: Hydroquinone is still the gold standard in topical skin lightening. The reason is because it remains the most potent tyrosinase inhibitor available. There are other agents that can target tyrosinase enzyme activity, but we haven't found anything better than hydroquinone in terms of the topical lightening.¹

The problem with hydroquinone is that it is not meant for long-term use, which can be challenging for melasma patients to understand. There are potential side effects when hydroquinone is used for extended periods of time such as irritation, possible risk of ochronosis, initial worsening of pigmentation, peeling, and dryness.² Those things are all important to discuss with patients, and we need to make sure that they understand hydroquinone is given during, what I like to call, the "induction phase" of skin lightening.

I equate our use of hydroquinone in patients with melasma to an overactive car engine that's going too fast. You're trying to slow that engine down and get it back into a normal speed with aggressive measures — that's what we use the hydroquinone for — but then you need to maintain that normal, steady speed with other, longer-term approaches so that there aren't major safety issues.

Dermatology Times: *What is your preferred second-line topical agent for the treatment of melasma?*

Dr. Desai: I use oral tranexamic acid for many of my patients with recalcitrant melasma who don't respond to initial treatment and chemical peels. While it's an off-label use, oral tranexamic acid therapy has been studied in melasma quite extensively in recent years, particularly in Asia.³

While it's been typically dosed in clinical studies between 250–500 mg twice daily, only a 650 mg dose of tranexamic acid is available in the United States. Consequently, I'll have my patients split the medication in half, taking 325 mg in the morning and 325 mg at night.

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There are side effects associated with tranexamic acid, so it's vital to take a detailed medical history of any patient in whom you are considering its use to ensure that they don't have any history of deep vein thrombosis, pulmonary emboli, or hypercoagulability, that they aren't planning on getting pregnant or nursing, that they aren't taking oral contraceptives, and that they're not a smoker.^{3,4} You want to make sure you document the medical record very thoroughly and review all of the potential side effects of tranexamic acid thoroughly.

However, if you do have a young, healthy patient with melasma, tranexamic acid can be a good option. We've seen some really impressive results with its use.

Dermatology Times: *How much of a concern is adherence to topical therapy regimens in melasma, knowing that patients are often having to apply one, two, or potentially three topical therapies at a time?*

Dr. Desai: Adherence certainly can be an issue. What I try to explain to my melasma patients is that the main driver of their condition is the fact that their body is making more melanin because the tyrosinase enzyme activity in their cells is being overactive. However, at other levels in that melanogenesis pathway, there are multiple different areas where melanin is either packaged, transferred, or modified, and it's on those therapeutic targets that we need more data.

For example, we are starting to learn more about the transfer of melanosome from the melanocyte to the keratinocyte, the peroxidase enzymes, and the oxidation of melanin production.⁵ That's where combination therapy comes in handy so we can target multiple levels of the disease.

For example, if a patient comes in with recalcitrant melasma, I will usually start them on triple combination topical treatment, antioxidants, and sunscreen. Follow up is in eight to 12 weeks. If they are not improving, we'll talk about either continuing their current regimen and adding a second-line topical agent, such as azelaic acid, and moving on to tranexamic acid or trying a chemical peel.

Dermatology Times: *How commonly will you try a chemical peel in a patient with melasma? How would you characterize the success you have seen with its use?*

Dr. Desai: I have seen a great deal of success with chemical peels. In my opinion, chemical peels are somewhat of a lost art in dermatology. We are luckily talking about it more now. What I find really helpful about chemical peels is that you can tailor their use to a patient's specific skin type and condition.

For example, there are often melasma patients who have concomitant acne, and salicylic acid peels are great for those patients because they help with oil reduction and unclogging pores, while also being beneficial for their melasma-related symptoms.

We are starting to see more studies using a combination of peeling agents. I will often combine lactic acid with pyruvic and glycolic acid into its own peel suspension. We've seen nice results with that combination.

In the literature, the data supporting glycolic acid is likely better than salicylic acid for patients with melasma,⁶ but I will still use salicylic acid in some cases, especially if I have an overly oily patient with blackheads, pustules, open comedones, and significant acne.

Mandelic acid is another chemical peel that I like to use, although it's use for melasma is off-label. It comes typically in a variety of concentrations. Personally, I prefer 40% mandelic acid in my patients with melasma.

The important thing about the use of chemical peels in patients with melasma is that they need to be done every few weeks for at least four to five sessions before you'll see noticeable improvement. One peel alone is rarely going to lead to a major improvement. The other thing you want to tell patients is that they need to stop using any topical retinoid or retinol-containing product at least one week before each chemical peel.

Dermatology Times: *What about laser surgery? Is that ever indicated for the treatment of melasma?*

Dr. Desai: Laser surgery for the treatment of melasma is somewhat controversial. In my practice, it's the option of last resort. Some of my colleagues may disagree, but I don't even bring up laser as an option until we've exhausted all of the other options we've discussed earlier.

When I opt for laser treatment, I use low fluence settings — typically 1.5–2 joules — and fairly small spot sizes. I'll have patients come in for treatment every three to four weeks. That said, laser is rarely used in my personal

practice for the treatment of melasma and, again, usually as a last option. That certainly may change with newer devices and, of course, more clinical study data.

The problem with laser treatment in melasma is that, in a lot of our patients with darker skin types, you run the risk of post-inflammatory hyperpigmentation as well as relapse. There have been several studies showing that laser does work for the treatment of melasma, and especially now that we're moving more into the use of picosecond lasers, there is increasing interest in their use.⁷ Once more data becomes available, I think we'll have a better idea of the best settings for the use of laser in patients with melasma.

Dermatology Times: *Once the initial treatment of melasma is successful, regardless of the therapeutic approach that was taken, what steps do you recommend to your patients that may help them avoid a recurrence of the condition?*

Dr. Desai: This is something that is really important to discuss with melasma patients because the relapse rate is so high. One of the most important things I tell patients is that they need to do their best to avoid excessive sun exposure. Patients need to apply a broad-spectrum sunscreen with a minimum SPF of 30 or higher and reapply frequently. I also tell patients to wear a hat, seek shaded areas, and avoid very sunny or hot parts of the day.

I also talk to patients about the use of oral contraceptives and hormonal therapies and give them somewhat of a precautionary warning that these can exacerbate their melasma and possibly cause a relapse.

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