Addressing Disorders of Hyperpigmentation With Combination Therapy: A Marriage of Mother Nature, Medicine, and Modalities

Fran E. Cook-Bolden, MD

Cosmetic procedures have gained popularity as the treatments of choice for many dermatologic concerns, when possible. This trend is certainly true when addressing disorders of hyperpigmentation. Common cosmetic procedures for the treatment of hyperpigmentation include chemical peels, microdermabrasion, light sources, and lasers. These modalities rarely are utilized as monotherapies and frequently are paired with topical prescription medications or cosmeceuticals, or both.

The quest for beauty has been an important goal since the beginning of time. This quest includes skin devoid of irregularities and blemishes. Historically, chemical exfoliation has been used to smooth out the skin, make it soft and supple, and even skin tone. Cleopatra understood the currency of good looks and enhanced her power by using the mystique of beauty. She used lactic acid in the form of milk baths to achieve these results.[1]

As the population ages and becomes more diverse, and as our ozone layer disappears, hyperpigmentation disorders rival acne for the number 1 spot as the most common dermatologic disorder. Patients are inherently embarrassed by hyperpigmentation, sometimes avoiding public exposure and personal relationships. Additionally, patients often are frustrated at the slow response or lack of response from prior treatments. Therefore, the need to gain greater expertise at evaluating and treating hyperpigmentation disorders is crucial. Treatment modalities include the use of medicines, cosmeceuticals, and cosmetic procedures. In addition, physicians must take into account the underlying disorder, etiologic factors, skin type, patient expectations (rate of results), tolerability, safety, and budget.

Hydroquinone (HQ) has been the mainstay of therapy for hyperpigmentation disorders for more than 50 years. It has been reported that more than 60 companies in the United States sell more than 200 different types of skin-lightening products that contain up to 2% HQ,[2] reflecting the magnitude of the problem of dyschromia and the desire to find an acceptable treatment of hyperpigmentation. Although many physicians achieve success with HQ products, at least temporarily, the conditions can be persistent, resistant to treatment, and recurrent in nature, with response being unpredictable and too often met with limited and/or temporary success, further increasing patient frustration and desperation.

Patients often present with a bag full of potions that they have tried, including over-the-counter treatments, prescription treatments, and home remedies. Patients report that the various treatments initially worked and then stopped working, or never worked at all.

Response to treatment is difficult to predict. In addition to a thorough patient history and physical examination, basic techniques such as Wood lamp examination can be used as a guide to assist in predicting the prognosis based on the location of the pigment (dermal or epidermal).

From Skin Specialty Dermatology and the Ethnic Skin Specialty Group, New York, New York.
The author reports no conflicts of interest in relation to this article.

However, Wood lamp examination provides only a cursory or gross predictor of prognosis due to a number of other contributing factors, including success of sun protection and avoidance, tolerability of treatment, and overall compliance.

Prescription-strength HQ (4% concentration) when used as monotherapy can have varied and limited short-term success, even with ideal compliance of treatment including optimal dosing, frequent reapplication of sunscreens, and other forms of sun protection and sun avoidance.

In the early 2000s, there was an explosion of new prescription lightening agents. These products were primarily HQs combined with botanicals; other cosmeceuticals; or other ingredients such as glycolic acid, retinol, sunscreen, hyaluronic acid, corticosteroids, and vitamin C to enhance efficacy. This period was shortly followed by a boom in chemical peel solutions and systems as well as antiaging serums and systems that all promised to be superior in evening skin tone, eliminating unwanted pigment, and maintaining long-lasting clear skin. They also purported to possess other unique antiaging properties that gave the user the best chance at eternal youth.

In 2006, a halt in the development of all HQ treatments occurred when the US Food and Drug Administration proposed a ban on the sale of over-the-counter cosmetic products containing HQ.[2] The reason cited for the proposed ban was that animal studies showed some evidence that HQ may act as a carcinogen, though cancer-causing properties have not been proven in humans. In addition to concerns of carcinogenicity, HQ has been identified as an immunotoxicant as well as a developmental and reproductive toxicant, posing concerns of risk to various organ systems, the endocrine system, and neurotoxicity according to the Environmental Working Group's Skin Deep Cosmetics Database.[3]

Although to date we have been able to stay the fate of HQ and it is not known if and when the proposed ban would take effect in the United States, HQ has already been banned in Australia, the European Union, and Japan. It has now become a virtual "HQ ghost town," with many products (prescription and over-the-counter) disappearing or being difficult to find, along with heightened consumer concern regarding the use of HQs. Where do we go from here?

With the uncertainties of the plight of HQ, there has been a shift in the paradigm for treatment protocols focusing on botanicals and cosmeceuticals, most often combined with physical modalities such as chemical peels, microdermabrasion, light sources, and lasers to address these concerns and fill the possible void. We have again recruited Mother Nature and science to help us address the concerns of hyperpigmentation and to augment and possibly replace, if that is the fate at some point, the use of HQ. Alternative treatments include retinoids, vitamin C, ferulic acid, arbutin, mulberry bark extract, licorice root extract, bearberry leaf extract, soy, azelaic acid, kojic acid, lactic acid, mequinol, aloesin, *N*-acetylglucosamine, and lignin peroxidase (Melanozyme, Syneron Medical Ltd).

Physical modalities also have been successfully utilized to treat postinflammatory hyperpigmentation, melasma, lentigo, and other hyperpigmentation disorders. Challenges still exist in developing protocols suitable for large numbers of patients with various skin types that yield consistent and reproducible results. Intense pulsed light, for example, has been successful for the treatment of sun-damaged skin and other dyschromia in Fitzpatrick skin types I to III (and even IV) but is not recommended in skin types V and VI. The heat associated with some laser therapies, and certainly with use of the wrong laser device, has been implicated as worsening the hyperpigmentation and extending it to previously uninvolved skin. It is important that additional research efforts on physical devices for the treatment of pigmentation disorders continue, but physicians must proceed with caution. Great care should be taken to avoid physical modalities that are too aggressive or generate excessive amounts of heat, which can worsen the pigment or spread the pigment to adjacent areas.

Although combination therapy still remains the key to success, it is important to keep it simple and to use a stepwise approach in which less is more when choosing which therapies to combine. Keep in mind that pigment often can subside spontaneously, particularly with diligent sun protection and avoidance or if the pigmentation is new onset, postinflammatory in nature, and limited in extent. Oftentimes, treating the underlying condition can result in resolution of the pigmentation.

Even with multiple treatments, there is no guarantee that the pigmentation will substantially or permanently improve, especially if it has been present for an extended period of time. Therefore, patient expectations need to be managed through education. All treatments should be tailored to the individual patient based on history of treatment (successes or failures), patient characteristics, and the nature of the dyschromia itself.

The best chance at achieving optimal results lies in attaining a delicate balance between the various options, whether topical prescriptions, gifts from Mother Nature,

or modalities; our knowledge and expertise; and patient education and compliance.

References

1. Cook-Bolden F, Downie J. *Beautiful Skin of Color.* New York, NY: Harper Collins Publishers; 2003.
2. Skin bleaching drug products for over-the-counter human use; Proposed Rule. *Fed Registr.* 2006;71(167):51146-51155. To be codified at 21 CFR §130.
3. Environmental Working Group. Skin Deep Cosmetics Database. http://www.ewg.org/skindeep/ingredient/703041/HYDROQUINONE/#multiple. Accessed October 17, 2011. ■