Postinflammatory Hyperpigmentation in Patients With Skin of Color

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Postinflammatory hyperpigmentation (PIH) has posed a substantial challenge for patients with higher Fitzpatrick skin types, specifically types III to VI. Treatment modalities pose a number of limitations due to the number of treatments required, potential side effects, and overall efficacy. Fortunately, multiple therapies have been delineated that can be moderately to highly efficacious in treating PIH in patients with skin of color. This article will review some of these modalities and procedures for this common patient concern.

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Postinflammatory hyperpigmentation (PIH) develops as darkly pigmented macules that occur after an inflammatory process of the skin such as acne, folliculitis, eczema, or shaving irritation. Patients with Fitzpatrick skin types III to VI usually are most commonly affected, and for many, the remnant pigmentation can be an even greater concern than the original inflammatory process.[1,2] Reported treatments of PIH include tretinoin, hydroquinone, azelaic acid, and chemical peels. The ideal combination of therapy has yet to be delineated.

Tretinoin (Vitamin A Derivative)

Bulengo-Ransby et al[3] performed one of the first clinical trials testing tretinoin cream 0.1% for PIH in patients with Fitzpatrick skin types IV to VI . The study included 54 patients (24 applied tretinoin and 30 applied a vehicle) with moderate to severe PIH on the face and arms. The patients were divided into therapy and placebo groups and were evaluated for 40 weeks. Changes were evaluated through colorimetry, light microscopy, histology, and photography, with significant clinical improvement in the tretinoin-treated group ($P<.001$).[3] A double-blind, randomized study of 45 photoaged Chinese and Japanese patients using tretinoin cream 0.1% also was conducted for treatment of photoaging-associated hyperpigmented lesions of the face and hands. Assessment was done with clinical, colorimetric, and histological evaluation, with an overall statistical improvement noted in hyperpigmentation.[4] Both of the above studies showed mild irritation (ie, retinoid dermatitis) with application of tretinoin, which creates a compliance issue in patients who are recommended to continue therapy with higher-strength tretinoin. This side-effect profile can be circumvented through gradual elevation in the strength of tretinoin.[5]

Combination Therapies

Combination therapies with tretinoin also have been used to improve PIH. Callender et al[6] conducted a study evaluating the efficacy of clindamycin phosphate 1.2%–tretinoin 0.025% gel for the treatment of PIH secondary to mild to moderate acne in patients with Fitzpatrick skin types IV to VI. Thirty patients participated in the randomized, double-blinded, placebo-controlled study, with 15 patients in the clindamycin-tretinoin gel group and 15 in the placebo control group. Based on objective assessment using a chromameter and evaluator global acne severity scale score, clinical efficacy was demonstrated for treating acne and PIH as well as preventing further PIH.[6]

Hydroquinone Formulation (Tyrosine Inhibitor)

Hydroquinone bleaching cream has been the standard therapy for hyperpigmentation. It works by blocking

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the conversion of dihydroxyphenylalanine to melanin by inhibiting tyrosinase.[7] Topical steroids directly inhibit the synthesis of melanin, and when combined with hydroquinone and tretinoin, they can be effective for short periods of time and may decrease the irritation of application.[7,8] The most widely accepted formula consists of a topical steroid (triamcinolone cream 0.1%) in combination with hydroquinone 4% and tretinoin cream 0.05%.[8] In a similar 12-week open-label study of 25 patients with darker skin types, Grimes[9] used an alternative combination formula of hydroquinone 4% and retinol 0.15%. Overall improvement and tolerance was demonstrated through the use of colorimetry measurement. A combination of hydroquinone 4%, tretinoin 0.05%, and fluocinolone acetonide 0.01% also has been used effectively for the treatment of melasma.[10] This formulation has been used more anecdotally for the treatment of PIH and has yet to have a randomized-controlled trial. The concern with repeated long-term use of hydroquinone remains. Permanent leukoderma, exogenous ochronosis, and hyperpigmentation of the surrounding normal skin (halo effect) can occur.

Azelaic Acid (Tyrosinase Inhibitor)

Azelaic acid is a dicarboxylic acid isolated from pityriasis versicolor that acts similar to a tyrosine inhibitor and has an antiproliferative effect toward abnormal melanocytes. Lowe et al[11] conducted a randomized, double-blind, vehicle-controlled trial in patients with Fitzpatrick skin types IV through VI with facial hyperpigmentation using azelaic acid cream 20%. Over the course of 24 weeks, patients noted a decrease in overall pigment using both an investigator subjective scale and chromometer analysis.[11]

Kojic Acid (Tyrosinase Inhibitor)

Kojic acid is a tyrosinase inhibitor found in fungal metabolite species such as *Acetobacter, Aspergillus,* and *Penicillium*. It is commonly combined with other skin lightening agents such as hydroquinone or vitamin C to further enhance its efficacy. A randomized, 12-week, split-face study of Chinese women with melasma compared treatment with a glycolic acid 10%–hydroquinone 2% gel versus the combination plus kojic acid 2%. The results showed that 60% (24/40) of patients improved with the use of kojic acid as compared to those using the medication without kojic acid.[12] Anecdotal data suggest kojic acid may be effective for PIH[13]; however, no studies specifically for PIH have been conducted.

Chemical Peels

Chemical peels have been used for a number of years, though their benefits in patients with skin of color is still being elucidated. The ideal chemical peels for Fitzpatrick skin types IV through VI are superficial to medium-depth peeling agents and techniques.[14] Glycolic acid is a naturally occurring α-hydroxy acid that causes an increase in collagen synthesis, stimulates epidermolysis, and disperses basal layer melanin. Neutralization of glycolic acid peels can be done with the use of water, sodium bicarbonate, or sodium hydroxide to avoid unnecessary epidermal damage. Multiple clinical trials have been conducted to determine the response of glycolic acid peels in clearing PIH in patients with skin of color. Kessler et al[15] compared glycolic acid 30% to salicylic acid 30% in 20 patients with mild to moderate acne and associated PIH. Chemical peels were performed every 2 weeks for 12 weeks. The study showed that salicylic acid was better tolerated than glycolic acid and both were equally effective after the second application ($P<.05$) for PIH.[15] Finally, another study conducted for PIH in patients with Fitzpatrick skin types III and IV utilized glycolic acid peels with 20%, 35%, and 70% concentrations. The results showed overall improvement of PIH and acne from the use of all concentrations of glycolic peels, though faster efficacy was noted at higher concentrations.[16]

Other self-neutralizing peeling agents include salicylic acid and Jessner solution. Salicylic acid is a β-hydroxy acid that works through keratolysis and disrupting intercellular linkages. Jessner solution is a combination of resorcinol 14%, lactic acid 14%, and salicylic acid 14% in an alcohol base. Salicylic acid is well-tolerated in patients with Fitzpatrick skin types I through VI and has been helpful in treating acne, rosacea, melasma, hyperpigmentation, texturally rough skin, and mild photoaging. Jessner peeling solution has been used for a number of years and works as a keratolytic agent causing intercellular and intracellular edema, and due to its self-neutralizing agent, it is fairly superficial.[17] Overall, superficial peeling agents should be used on patients with darker skin types to avoid the risk for worsening dyspigmentation, keloid formation, or deep scarring.[18]

Conclusion

These treatments are only some of the topical and chemical modalities for PIH in patients with skin of color. The patient history, evaluation, skin type, and underlying medical problems should be considered prior to using any topical or peeling agent. Lastly, photoprotection should be heavily emphasized with both sun protective gear and use of broad-spectrum sunscreens with a high sun protection factor, as UV radiation can cause darkening of PIH areas regardless of skin type and can reverse the progress made by a given therapy.[18]

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