Overview on Post-Inflammatory Hyperpigmentation

Abstract:

Post inflammatory hyperpigmentation (PIH) can affect people of all skin colours, but it is more common in people of colour, such as African Americans, Hispanics/Latinos, Asians, Native Americans, Pacific Islanders, and those of Middle Eastern descent. There is no distinction between men and women. In darker-skinned acne sufferers, the prevalence of PIH might reach 65 percent. Many studies have demonstrated that topical retinoids, especially in darker skin types, can be beneficial in treating PIH associated with acne. However, Hydroquinone is still a go-to treatment for melasma and hyperpigmentation, and it's commonly referred to as the "gold standard." triple combination fixed treatment has also become a common intervention, with evidence showing that the combination is more successful than hydroquinone monotherapy. In this review article we will be looking at PIH etiology, epidemiology, different treatment options as well as the effectiveness of each medication.

Introduction:

After cutaneous inflammation or injury, postinflammatory hyperpigmentation (PIH) is a kind of acquired hypermelanosis. It can afflict persons of all skin colours, although it is more frequent among people of colour, such as African Americans, Hispanics/Latinos, Asians, Native Americans, Pacific Islanders, and Middle Easterners. Because pigmentary abnormalities occur more frequently and with greater severity in these populations, and are generally more evident in darker skin, PIH can have a significant psychological impact on patients of colour (Fitzpatrick skin types IV through VI). Only a few of the safe and effective treatments for PIH in skin of colour include topical depigmenting agents, chemical peels, and laser and light therapy. [1]

Although the chances of epidermal hyperpigmentation resolving are greater than those of dermal hyperpigmentation, the clinical course of PIH is persistent and unpredictable. PIH can be avoided or reduced. When this happens, the underlying inflammatory problems should be searched out and treated as soon as possible to prevent inflammation and PIH from progressing (which is an inflammatory

consequence). If the inflammatory circumstances improve or if there is no indication of inflammation at the time of diagnosis, PIH therapies should be examined. Understanding the therapy choices available aids the physician in selecting the best treatment for each patient. The development of treatment options for PIH requires the establishment of a repeatable model. [2]

Although epidermal hyperpigmentation has a higher likelihood of healing than dermal hyperpigmentation, the clinical course of PIH is long and unpredictable. It is possible to avoid or lessen PIH. To prevent inflammation and PIH from worsening, the underlying inflammatory disorders should be identified and addressed as soon as feasible (which is an inflammatory consequence). PIH therapy should be considered if the inflammatory conditions ameliorate or if there is no evidence of inflammation at the time of diagnosis. The physician's ability to determine the optimum treatment for each patient is aided by knowledge of the various therapeutic options. The building of a reproducible model is required for the development of therapeutic options for PIH. [3]

Epidemiology:

PIH affects people of all ages, however it is more common in Fitzpatrick skin types III-VI. Hypermelanosis is more severe and persistent in those who have darker skin. No differentiation is made between males and women. The prevalence of PIH might reach 65 percent among acne sufferers with darker skin. [4-6]

According to several epidemiological studies, PIH is more common among skin-of-color patients than among Caucasian patients. Between 1983, Halder et al. released a study comparing the most common dermatoses in African Americans and Caucasians. Pigmentary illnesses, aside from vitiligo, were the third most frequent dermatoses among African-American patients (9 percent), but the seventh most common in Caucasians (1.7 percent). According to a 20073 survey, dyschromias was the second most frequent diagnosis among African-American patients, but it did not make the top ten most common diagnoses among Caucasian patients. The authors of a study conducted in Singapore discovered that PIH was more prevalent among Asians with darker skin, such as Malays and Indians, than among Asians with lighter skin, such as Chinese, hinting that pigmentation, rather than race/ethnicity, may have a larger role in the development of PIH. [1,8-10]

Etiology and Pathophysiology:

Postinflammatory hyperpigmentation, which occurs in epidermal or dermal melanosis, is caused by one of two mechanisms. As a result of the epidermal inflammatory response, arachidonic acid is released and oxidised to prostaglandins, leukotrienes, and other substances (i.e. dermatitis). These inflammatory substances damage both immune cells and melanocytes. When a 35 percent trichloroacetic acid (TCA) solution was applied to skin, TCA-induced postinflammatory hyperpigmentation was found to be a helpful in vivo model for the exploration of acne-induced postinflammatory hyperpigmentation. [2]

PIH can be caused by infections such as dermatophytoses or viral exanthems, allergic reactions such as insect bites or contact dermatitis, papulosquamous diseases such as psoriasis or lichen planus, medication-induced PIH from hypersensitivity reactions, or cutaneous injury from irritants, burns, or cosmetic procedures. In individuals of colour, acne vulgaris, atopic dermatitis, and impetigo are all common causes of PIH. Among reality, PIH is a fairly common acne sequela in dark-skinned persons. Acne-induced PIH was found in 65.3 percent of African-Americans, 52.7 percent of Hispanics, and 47.4 percent of Asians in a 2002 study of acne in persons of colour. Another common inflammatory dermatosis that causes PIH is pseudofolliculitis barbae (PFB), which is thought to affect 45 to 83 percent of African Americans. In a study by Perry et al, 90.1 percent of 71 African American and Hispanic patients with PFB had hyperpigmentation; as a result, the authors believe that PIH may be a common clinical finding in PFB. [1,11-14]

According to Callender, transient PIH is common in those with darker complexions who are getting acne treatment with chemical peels. YAG laser resurfacing has been associated to a 68 percent risk of PIH in Fitzpatrick skin type IV. After laser resurfacing, PIH appears 32 days later and lasts an average of 112 days. Laser hair eradication has also been associated to PIH. Weisberg and Greenbaum identified a group of people with a hyperpigmented ring arrangement that transformed into a thin, wafer-like crust. The consequence was hypopigmentation, which was followed by a gradual return to normal skin tone. [5]

UV light, as well as various chemicals and therapies such as tetracycline, bleomycin, doxorubicin, 5-fluorouracil, busulfan, arsenicals, silver, gold, antimalarial medicines, hormones, and clofazimine, can darken postinflammatory

hyperpigmentation spots. Following foamed bleomycin sclerotherapy for vascular anomalies, hyperpigmentation was seen. [2]

Effectiveness of different medication:

Topical Retinoids: Many studies have shown that topical retinoids, particularly in darker skin types, can help to alleviate PIH associated with acne. Patients who received tretinoin 0.1 percent for 50 weeks and tazarotene 0.1 percent for up to 18 weeks had a significantly higher reduction in clinical assessment of PIH than those who received placebo. In a study of 65 acne patients, therapy with adapalene 0.1 percent gel for 12 weeks decreased hyperpigmented macules and density of hyperpigmentation in 2/3 of the "highly pigmented" cases. Furthermore, two studies investigate the use of topical retinoids in combination with other topical therapies. A topical clindamycin 1.2 percent plus tretinoin 0.025 percent gel for people with facial acne and PIH had no effect on melanin chromameter measurement or clinical evaluation of PIH when compared to placebo. 5 75 percent of 50 acne patients (60 percent of whom had PIH) who took a 0.3 percent adapalene gel/benzoyl peroxide 2.5 percent gel daily for 16 weeks had no PIH or very mild PIH, with a 27 percent reduction in PIH severity score. While topical retinoids alone may be effective in the treatment of acne-related PIH, the ideal combination therapy has yet to be discovered. [15]

Hydroquinone (HQ): HQ is still the cornerstone of PIH treatment. It's a phenolic compound that suppresses the conversion of dihydroxyphenylalanine (DOPA) to melanin by inhibiting tyrosinase. Its method of action might include inhibition of deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) generation, selective cytotoxicity targeting melanocytes, and melanosome destruction. HQ is often recommended in doses of 2 to 4%, although it can be prescribed up to 10%, and it is available over the counter (OTC) in the United States at a concentration of 2%. [1,16-18]

Hydroquinone is beneficial for PIH when administered in combination with a retinoid, according to studies. A combination of 5% hydroquinone, 7% lactic acid ointment, and either 0.1 percent all trans retinoic acid ointment or gel used twice day helped four individuals with PIH. Two studies combined microencapsulated hydroquinone 4 percent with retinol 0.15 percent twice daily for 12 weeks; one study found that melanin content was significantly diminished by week 4 as

evaluated by spectrophotometer; and both studies found that clinically analysed disease severity was dramatically improved by week 4 compared to baseline. [15]

Long-term daily use of HQ at 4% or above may trigger inflammatory reactions, especially when used with other irritants such retinoids. Concurrent use of a topical corticosteroid, on the other hand, might reduce irritation and hence the risk of further hyperpigmentation. Because of the high levels of tretinoin and the presence of a potent fluorinated steroid, Kligman's formula, which comprised 5% HQ, 0.1 percent tretinoin, and 0.1 percent dexamethasone, is an example of an early formulation that was effective yet difficult. TriLuma® (Galderma, Fort Worth, Texas) was recently developed as a less irritative combination medication, including 4% HQ, 0.05% tretinoin, and 0.01 percent fluocinolone acetonide. [1,19-22]

Azelaic acid: Azelaic acid, a topical treatment for acne vulgaris, is also beneficial for postinflammatory hyperpigmentation. For acne patients who are prone to postinflammatory hyperpigmentation, azelaic acid may be an effective treatment option. Tazarotene 0.1 percent cream's effectiveness in the treatment of dyschromia linked with photoaging and acne vulgaris, particularly in people with dark skin tones, may also be beneficial. [2] Azelaic acid has antibacterial effects in addition to blocking tyrosinase. It comes in the form of a cream and has to be used over a period of time. This product should be used alongside sunscreen. In a 24-week, multicenter, double-blind study, 52 subjects with skin types IV to VI were administered azelaic acid or a placebo. According to the investigator's subjective scale and chromometer studies, azelaic acid induced much larger decreases in pigmentary intensity in the subset of patients with PIH, as well as significantly superior overall recovery at week 24. None of the patients tested positive for PIH. Patients who administered azelaic acid had significantly more burning and stinging at weeks 4 and 12. [5]

Combination Therapy: The efficacy and safety of a combination therapy regimen involving sequential GA peels, topical azelaic acid cream, and adapalene gel in the management of refractory melasma were investigated in 28 patients in a prospective, randomised, controlled research that lasted 20 weeks. For those receiving chemical peels, serial GA peels were combined with topical azelaic acid 20% cream (used twice daily) and adapalene 0.1 percent gel (4 times daily,

applied at night). Serial GA peels in conjunction with azelaic acid cream and adapalene gel might be an effective and reliable therapy for resistant melasma. Lepidium apetalum, according to Choi et al, might be a UV-induced hyperpigmentation inhibitor. [2]

The triple combination fixed treatment of fluocinolone acetonide 0.01 percent, hydroquinone 4 percent, and tretinoin 0.05 percent has also become popular, with research indicating that the mixture is more effective than hydroquinone monotherapy. 129 patients were randomly assigned to the triple combination group and 131 to hydroquinone-only treatment in a multicenter, randomised, controlled investigation of Southeast and East Asian patients. During the eight-week study, patient satisfaction and melasma severity (Global Severity Score [GSS], Melasma Area and Severity Index score [MASI]) were examined. Even though it came with more adverse effects, triple combination treatment surpassed monotherapy in terms of GSS and other aspects.

In a trial of predominantly women with PIH associated to acne, Mexameter readings revealed a decrease in pigmentation as soon as four weeks after starting medication. All of the patients' pigmentation had faded at the 12-week period. In a subset of patients with moderate to severe dyschromia and actinic photodamage, treatment with hydroquinone + glycolic acid, tretinoin, or hydroquinone + glycolic acid + tretinoin for 16 weeks showed continued improvement from weeks 12 to 16, whereas improvement slowed in subjects using tretinoin alone. According to investigator assessment at week 16, improvements in PIH were 35.4 percent, 16.9 percent, and 30.6 percent, respectively. [5]

Discussion:

Epidermal postinflammatory hyperpigmentation has been treated with a number of topical therapies, with varied degrees of efficacy. Hydroquinone, tretinoin cream, corticosteroids, glycolic acid (GA), and azelaic acid are examples of these agents. One of the previously mentioned topical medicines may be used to lighten hyperpigmented regions; however, for considerable improvement, a combination of topical creams and gels, chemical peels, and sunscreens may be required. They're solely good for hyperpigmentation on the epidermis. The combination of a salicylic acid peel and topical tretinoin therapy was shown to be more effective

than either treatment alone in one research. Another study found that combining glycolic acid peels with a modified Kligman formula of 2 percent hydroquinone, 0.05 percent tretinoin, and 1 percent hydrocortisone helped dark-skinned Indians with face postinflammatory hyperpigmentation. [7,23-26]

Long-term daily usage of 4 percent or greater HQ might cause irritant responses, especially when combined with other irritants such retinoids. Concomitant usage of a topical corticosteroid, on the other hand, can minimise discomfort and hence the likelihood of additional hyperpigmentation. Kligman's formula, which contained 5% HQ, 0.1 percent tretinoin, and 0.1 percent dexamethasone, is an example of an early formulation that was beneficial yet troublesome because to the high amounts of tretinoin and the inclusion of a powerful fluorinated steroid. TriLuma, which comprises 4% HQ, 0.05% tretinoin, and 0.01 percent fluocinolone acetonide, has recently been created as a less irritative combination medication. This triple combination drug has been found to be safe and effective in the treatment of melasma and photoaging in skin of colour, and it is now being utilised to treat PIH in clinical practise. To further investigate its usage in PIH, proper clinical investigations are still needed. [1,27-32]

Conclusion:

Hydroquinone is still the golden standard for treating post-inflammatory hyperpigmentation, although there’s strong evidence suggesting that multiple combination therapy such as the one that uses (Fluocinolone acetonide 0.01 percent, hydroquinone 4 percent, and tretinoin) which seems to be more effective than monotherapy, yet monotherapy is still recommended due to less side effects. However, such combination can be used if the patient can tolerate the side effects and want better results from the treatment.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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