Summary

Background: Increased pigmentation is a common response to induced inflammation. In order to rejuvenate the skin we utilize modalities like Superficial Chemical Peel, Percutaneous Collagen Induction, Intense Pulse Light between the less minimal invasive intervention and Full and Fractional Ablatives Lasers at the most invasive end of modalities. They all can lead to post inflammatory hyperpigmentation. Imperative for any Aesthetic Medicine Practitioner to properly handle this condition on all skin colors.

Aim: This review examined the use of depigmenting molecules, their safety and efficacy.

Methods: Data Collection Methods are based on the collection of Continuing Medical Education Need and Assessment from 2003 to the present. Surveys of documenting perceptions, attitudes and beliefs of faculty and board certify physicians in Aesthetic Medicine. Open-end questions that yield qualitative data analyzed by interviews, focus groups in order to capture similarities and differences in viewpoints. Context analysis of research article from 1980 to 2019 was also revised.

Results: Significant efficacy, safety and tolerability are achieved if the patient particular characteristics are matched with the specific combinations for the particular skin type: oily vs dry; sensitive vs resistant; pigmented vs non pigmented; elastotic vs tight.

Conclusion: This review exposes the value of specific protocols, modalities and ingredients in formulations to treat post inflammatory hyperpigmentation.

Key words

Post Inflammatory Hyperpigmentation (PIH), Depigmentation, Skin Lightening.

Introduction

Post Inflammatory Hyperpigmentation (PIH) is more likely to happen among skin of color. Probably the leading causes can be acne, insect bites and aesthetic and cosmetic surgical medical procedures.

In any case, when addressing PIH, any depigmenting component will work the best if the skin is properly conditioned.

In the author experience, exfoliative ingredients like glycolic acid, lactic acid, salicylic acid, mandelic acid and others over the counter formulation ranging from 2 to 5 percent, apply daily will increase exfoliation, decreasing thickness of the stratum corneum and allowing better penetration of the following steps of the skin conditioning program indicated for properly depigmenting the skin .

Review of Post-Inflammatory Hyperpigmentation Management:

Safety and Efficacy of Skin Lightening Ingredients

by Dr. Marcelo A. Suarez-Bigetti

Moisturization as the second pillar of skin conditioning will warrant patient compliance by reducing dryness and consequent irritation.

Sun Protection base on Zinc Oxide and Titanium Dioxide, are the most effective in protecting any wavelength of UVA or UVB as they act as a mirror, reflective all 200 to 400 nm of the spectrum.

From the early 90s, replenish vitamin C topical 20% serum when tolerated or a lower dose if skin sensitivity. More importantly, when the patient is on the middle 30s, time that the physiological concentration on the granular layer start to naturally decrease making the maximum oral daily dose insufficient.

Finally, vitamin A 0.025, 0.05 and 0.1 depending on patient tolerance, will promote essential physiological functions like cell growth and differentiation, synergistically working with the exfoliants to increase cell removal and turnover, inducing some clearance of the hyperpigmented skin.[1]

With a colorful history of plants leaves and roots teas and powders, we found back to the 16th century documentation addressing the use of whitening agents.[2]

Anatomy and physiology of the coloration of all skin types have in common same functions: number, size and distribution of the melanosomes. Although, genetics of pigmentation indicate differences for sun response where studies are showing a variation of more than 100 fold in sensitivity to ultraviolet radiation and also the risk of melanoma and non-melanoma skin cancer.[3,4,5,6]

Making the selection of the best formulation shows an amply spectrum of variations between researchers and practitioners. Current research is developing a progression from the fairly effective most interesting ingredients to more effective but less irritating ingredients.
The study ingredients include:

- Hydroquinone/Derivatives
- Tyrosinase Inhibitors
- Retinoids: Retinol-Retinic Acids
- Ascorbic Acid/Derivatives like Magnesium ascorbyl phosphate (more stable)
- Ion Chelators

Hydroquinone and Derivatives

Introduced as a skin-lightening agent in 1961, widely used for melisma, PIH, and other hyperpigmentations. Causing a reversible inhibition of cellular metabolism affecting synthesis of DNA and RNA, reduced by 90% tyrosinase activity.[7]

Naturally occurs in plants, beer, wine and coffee, needing a higher dose to inhibit metabolism in nonmelanotic cell. Concentrations range is from 2% to 5%. Can cause contact dermatitis and PIH. Serious but rare side effect, macular hyperchromia known as ochronosis, (histological degeneration of collagen and elastic fibers) can occur if high concentrations are used for prolonged periods of time. Preventable if used for 8 to 12 weeks at 4% and been substitute by an alternative depigmented agent like kojic acid 4%, for example. Been possible to repeat a course after 3 months.[8]

Combination of different ingredients start in 1975 by Albert Kingman: retinoic acid 0.1 + hydroquinone 5% + dexamethasone 0.1%. Following by other alternatives: hydroquinone ester + retinoic acid; plain hydroquinone + phenol + vitamin C and hydroquinone 4% + retinoic acid 0.05% + fluocinolone acetonide 0.01 %.[9-14] A less irritating form, hydroquinone mono methyl ether is less toxic, combined with retinoic acid 0.01% showing that potentiate each other in a large number of subjects with dyschromias.[15]

Tyrosinase Inhibitors

Flavonoids from the roots of licorice: glabrene, isoliquiritigenin, licochalcone, licuraside and glabridin. This last one with light estrogenic effects[16-17]. Beta Arbutin from strawberry tree and bearberry is a hydroquinone derivative, a popular ingredient for treating PIH at 6%. Alpha Arbutin is a twenty time stronger than the beta version used at 2%. Several studies demonstrated similar efficacy as hydroquinone with less toxicity.[18-19] A synthetic version of arbutin is not safe at greater than 3% accordingly to the Scientific Committee on Consumer Safety. Kojic Acid produced by fermentation of fungus (Aspergillus orizae) also is a copper chelator and free radical neutralizer. Available from 1 to 4%. A popular combination of 2% with hydroquinone shows to improve melasma lesions. None clear efficacy has been demonstrated for it uses on patients with PIH. Contact dermatitis and increased sensitizations has been also frequently reported.[20-21] In terms of efficacy, kojic acid combinations with vitamin C shows to be several times weaker than 4% hydroquinone.

Retinoids: Retinol-Retinoic Acids

Retinol concentrations ranges from 0.04% to 0.07%, intracellularly is oxidized o retinaldehyde and then to retinoic acid requiring certain degree of cell vitality in order to make possible the conversions, decreasing its efficacy in patient with severe environmental damage. Contraindicated on pregnancy base on clear evidence that radio-labeling studies shows 7% of the skin dose is systemically detected. Retinoic acid classic concentrations range from 0.025% to 0.1%. Its biological effects are modulation of cell proliferation, differentiation, induction of apoptosis, and decreased cell cohesiveness. Significantly great efficacy lightning PIH. Because of the high

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incidence of dermatitis, titration is key. Third generation retinoids like adapalene 0.1 to 0.3% and tazarotene gel 0.05 to 0.1% are effective to certain degree but much better tolerated. Several studies report safety and efficacy particularly in dark skin for acne induced PIH.[22-25]

L-Ascorbic Acid and Derivatives

L-ascorbic acid is the predominant antioxidant in skin, many times more than Vitamin E, glutathione and ubiquinone. A six-time fold greater in epidermis than in the dermis, acting as a first line antioxidant just below the corneocytes. A natural decline occurs after the middle thirties preventing the adequate concentration of the vitamin on this antioxidant mantle. Lipid peroxidation that cause apoptosis, cell death and lead to carcinogenesis is inhibited facilitating the reduction of oxidized precursors to alpha tocopherol.[26-30] The most stable derivatives: ascorbyl palmitate and magnesium-L-ascorbyl-2-phosphate (MAP). Blocking oxidation on the steps that transform tyrosine into melanin. The interaction with copper (essential cofactor of tyrosinase activity) explains the inhibitory tyrosinase effect. Usual effective concentrations range from 5% to 20%.[31-32]

Future Research: Miscellaneous Skin Lightening

Germano and Cacciola investigated the Ethanol extract from Betula pendula leaves and its Cupper ions chelators' effects polyphenolic characterization and potential uses as skin depigmenting ingredient.[33]

Himani and Madhuri work is related to several edible fruits from northwestern Himalayans with antityrosinase activities.[34]

A Chinese herbal tea containing the active ingredient aupafolin, a flavonoid with skin lightening properties by inhibiting tyrosinase.[35]

Conclusions

Effective and well tolerated ingredients in the group of depigmenting agents from natural and synthetic sources have the potential of integration into the cosmetic industry. More studies with human clinical trial are required. Early treatment initiation and testing for the best possible titration are critical when implementing any particular protocol. Synergism is of paramount importance. Great percentage of patients do not understand and do not comply with sun protection protocols, time is needed to teach them the importance of it.

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