Medical Safety and Global Health

Extended Abstract

Cosmetology 2015: Review of topical lightening agents- Shuba Dharmana- Evangelist LeJeune Medspa, India-Shuba Dharmana- Evangelist LeJeune Medspa, India

Abstract

There are many topical skin lightening agents in the dermatologists armamentarium for treating hyperpigmentation. Apart from treating the underlying cause of the pigmentation it causes a lot of distress esp. in dark skinned individuals hence this needs treatment alongside sun avoidance measures. Amongst the varied agents, hydroquinone and triple combination cream are the foremost studied and widely used but retinoid, azelaic acid, mequinol, kojic acid, arbutin, niacin amide, N-acetyl glucosamine, vitamin C , liquorice extract, soy products are just a few of the others which will be considered. Treatments involving chemical peels and laser therapies can also target excess melanin and current research is throwing light on more emerging lightening agents and coverings.

Introduction

Hyperpigmentation occurs when there is an increase in melanin content in the skin. It can be localised i.e. limited to a certain area or it can be diffuse i.e. occurring all over the body. Localised sort of hyperpigmentation can happen as a results of injury or inflammation from conditions like Acne, dermatitis , lupus etc. referred to as post inflammatory hyperpigmentation or Melasma. Diffuse generally results from a systemic disease, drug or neoplasm. Localised hyperpigmentation like PIH and melasma can cause tons of psychological distress with skin type IV and above being particularly susceptible. It is not only important to find the cause of pigmentation in order to arrest further progression but it is also important to treat the pigmented lesions. Further prevention should advocate the utilization of daily sun protection with sunscreen agents and other sun avoidance measures. Topical Agents Number of topical agents is employed to treat PIH. The most commonly used agent is hydroquinone between 2 to 10% though 2 to 4% of hydroquinone alone or with of tretinoin 0.05 to 0.1% is used. Hydroquinone may be a hydroxyphenolic chemical classically utilized in melasma treatment. Hydroquinone Hydroquinone is one among the important agents when treating PIH. It is a phenol compound which inhibits tyrosinase, thereby reducing the conversion of dihydroxyphenylalanine (DOPA) to melanin. In the US, hydroquinone is available over the counter (OTC) at 2% and in prescription strength from 3% to 10%, although hydroquinone is typically used at 2–4% concentrations. Daily concomitant use of a broad-spectrum sunscreen can also be beneficial as sun exposure can hinder the effects of hydroquinone, leading to repigmentation. Antioxidants like 0.5% vitamin C (vitamin C) and retinoid also as a-hydroxyl acids are used as additives to extend penetration and enhance efficacy. Cook- Bolden and Hamilton conducted a 12-week, open-label study of microencapsulated 4% hydroquinone and 0.15% retinol with antioxidants within the treatment of 21 patients (17 PIH, 4 melasma). Significant

decreases in lesion size, pigmentation, and disease severity were noted as early as 4 weeks after initiating treatment and remained significantly decreased throughout the study. The majority of patients (63%) experienced either marked improvement (75% overall improvement) or complete clearing (95% or greater overall improvement), and reflectance spectrophotometer readings showed statistically significant reductions in melanin content as early as week 4. Similar results were obtained in a previous study. The 5% concentration of hydroquinone can also be compounded with 0.5% vitamin C during a low-potency corticosteroid base to extend penetration and reduce irritation, respectively. An improvement within the hyperpigmentation could also be noticeable after 4 weeks of therapy but the optimal effect is usually achieved after 6–10 weeks of therapy. Prolonged daily use of 4–5% hydroquinone can cause a high incidence of irritant reactions particularly when combined with retinoic acid. A triple combination cream during a stabilized formulation, containing 4% hydroquinone, 0.05% tretinoin, and 0.01% fluocinolone acetonide, has been demonstrated to be both safe and effective within the treatment of moderate to severe melasma and has also been successfully used in the treatment of PIH, although formal clinical studies are needed. In 1982, the US FDA originally proposed that OTC hydroquinone at 1.5–2% concentrations was generally safe and effective. However, in 2006, the FDA released a press release proposing a ban on all OTC hydroquinone agents and a requirement for any currently marketed hydroquinone product to submit New Drug Application (NDA) or be withdrawn from the market. This change in position was supported rodent studies, which suggested that oral hydroquinone could also be a carcinogen. The FDA has yet to form a final ruling. In light of the controversy surrounding the utilization of topical hydroquinone, clinicians are looking to other products with depigmenting effects. Mequinol, tretinoin monotherapy, and azelaic acid have also been proven to be effective within the treatment of PIH.

Mequinol

Mequinol (4-hydroxyanisole) may be a derivative of hydroquinone but may cause less skin irritation than its parent compound. Mequinol may involve in competitive inhibition of tyrosinase thereby inhibiting melanin formation. An open-label, split face, non-inferiority, comparison study of twenty-two mequinol/0.01% tretinoin versus 4% hydroquinone cream was conducted in 61 patients with mild to moderate facial PIH. Patients applied 2% mequinol/0.01% tretinoin to at least one side of the face and 4% hydroquinone to the contra lateral side for 12 weeks. The mequinol/tretinoin solution was found to be non-inferior to the hydroquinone cream within the treatment of PIH as 81% of mequinol/tretinoin-treated and 85% of hydroquinone-treated patient's experienced clinical success.

Retinoid

Tretinoin (all-trans retinoic acid), a vitamin A analog, wont to treat hyperpigmentation of photo aged skin, post inflammatory hyperpigmentation, and melasma. Tretinoin 0.1% has been wont to successfully treat melasma in Black patients; improvements of up to 73% were seen after 40 weeks of treatment. Erythema and peeling within the area of application are adverse effects of tretinoin 0.05 to 0.1%; post inflammatory hyperpigmentation also can occur. Concentrations range from 0.01% to 0.1%. However, irritant dermatitis is often a frequent adverse effect, and caution should be used when prescribing higher concentrations of tretinoin in darker skin types, since the irritation can lead to

further PIH. To determine the safety and efficacy of 0.1% tretinoin in the treatment of PIH, a randomized, double-blind, vehicle-controlled clinical trial was conducted in 54 Black patients. Patients applied either tretinoin or vehicle cream to the face, arms, or both areas daily for 40 weeks. At the study endpoint, the PIH lesions of the tretinoin-treated group were significantly lighter than those of the vehicle-treated group as assessed by clinical and colorimetric (p=0.05) examinations. However, it's important to notice that patients treated with tretinoin experienced minimal lightening of normal skin and 50% of those patients also developed retinoid dermatitis. It is possible to reduce this irritation by reducing dose and titrating to higher doses gradually or by using cream based formulations or even diluting it with a moisturizer. Other retinoid compounds are also available including isotretinoin, adapalene, and tazarotene. Isotretinoin is out there in both oral and topical formulations and is widely utilized in the treatment of acne.

Azelaic acid

Topical azelaic acid 15 to twenty are often as efficacious as hydroquinone, but is a smaller amount of an irritant. Azelaic acid may be a dicarboxylic acid isolated from Pityrosporum ovale, the organism liable for pityriasis versia colour. Studies have shown that 20% azelaic acid cream produces significantly greater decreases in pigmentary intensity than the vehicle and, when combined with 15–20% glycolic acid, is as effective as 4% hydroquinone within the treatment of facial hyperpigmentation including melasma and PIH. Azelaic acid is usually well tolerated with only mild adverse effects reported, like pruritus, transient erythema, scaling, and irritation, which disappear during a few weeks.

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