Clinical Review:

Melasma and Hyperpigmentation

Melasma is a skin disorder characterized by irregular brown macules. It is typically symmetrically distributed on areas of the body that endure the most sun exposure, the face in particular is often affected.[1] Melasma is more commonly reported among women and those with darker skin tones. The incidence varies widely, and light exposure, hormonal influences, and genetics have all been implicated as potential factors in the etiology of melasma.[2] One common way that melasma is triggered or exacerbated is via UV light. UV light is thought to induce oxidative stress by creating reactive oxygen species, this combined with general UV induced inflammation has been known to trigger melasma.[3] Another common trigger of melasma is hormonal changes, this can occur during pregnancy or can be associated with hormonal contraceptive or hormone replacement therapy in menopause.[1]

A variety of methods can be employed to help improve melasma including topical medications, oral treatments, procedures, or combinations thereof. The goals of treatment include management of photodamage, decreasing inflammation, improving vascularity, and, of course, reducing pigmentation. Generally, topical management of melasma is considered first line management and UV protection/sunscreen is important during all treatments.[2]

Common topical agents include hydroquinone, corticosteroids, retinoids, tranexamic acid, niacinamide, kojic acid, ascorbic acid, azelaic acid, or chemical peels (glycolic acid, salicylic acid etc).[2] Hydroquinone is commonly used between 2-5%, though concentrations of up to 10% are sometimes used.[4] Hydroquinone lightens skin by decreasing formation of melanosomes and increasing degradation of melanosomes. Hydroquinone has the potential to cause permanent bleaching via necrosis of whole melanocytes. Hydroquinone concentrations ranging from 2 to 5% applied once daily has demonstrated efficacy in many studies, with the effects usually becoming evident by 5 to 7 weeks and sometimes earlier.[5,6]

Tretinoin is another agent used frequently on its own or in combination for the treatment of melasma. Retinoids such as tretinoin suppress UVB induced pigmentation and promote increased epidermal turnover to limit contact time between keratinocytes and melanocytes. Tretinoin is also sometimes used in combination with hydroquinone to enhance penetration. Skin lightening benefits may take longer to become apparent as compared with hydroquinone if used as a single agent.[6] Tretinoin used in combination with other agents, usually between 0.01-0.05%, or used as a single agent, up to 0.1%, has been shown in placebo controlled studies to decrease pigmentation.[6,7]

Corticosteroids, such as fluocinolone, also play a role in skin lightening. They are primarily used in combination with other agents, both for synergistic effect and to decrease irritation sometimes associated with other active ingredients that are also being used to treat hyperpigmentation.[6] The mechanism of skin lightening is not well understood, though it may be related to inhibition of inflammatory markers such as prostaglandins which can play a role in melanogenesis. Studies evaluating hydroquinone 5%, tretinoin 0.05%,fluocinolone acetonide 0.01% combination creams have demonstrated benefit by week 8 with continued benefit at the 6-month follow-up.8 Even after 12 months most patients continued to tolerate the cream without adverse effects.[9]

Tranexamic acid is another option currently gaining popularity. The mechanism of action could very well be multimodal, but one suggested mechanism is inhibition of plasmin which plays a role in the release of a growth factor that can stimulate melanocyte growth. Studies evaluating oral 500mg per day dosing over just 8 to 12 weeks have seen benefit in the management of patients with refractory melasma.[11,12] Topical 5% tranexamic acid alone, favored for a lower likelihood of systemic effects, applied twice daily over a period of 12 weeks faired as well as hydroquinone 2% in a skin lightening study without as many adverse events as the hydroquinone group.[12]

Another option commonly used as a combination agent is niacinamide. Niacinamide is a B-vitamin with anti-inflammatory properties that may work to help decrease incidence of melasma by decreasing transfer of melanosomes.[13] A study comparing niacinamide 4% cream with hydroquinone 4% cream over a period of 8 weeks found that while hydroquinone 4% did get slightly more significant results, 44% of patients in the niacinamide group still reported excellent improvement and the incidence of adverse effects was greatly decreased.[13] Similarly, other studies investigating 2% niacinamide have also observed a reduction in area of hyperpigmentation after as little as 4 weeks of treatment.14 Another study evaluating niacinamide 4% in combination with N-acetyl glucosamine 2% over a period of 8 weeks also found significant benefit with a low incidence of adverse effects.[21]

Niacinamide isn't the only vitamin used as a skin lightening agent. Ascorbic acid has also been investigated for its skin lightening effects. One study comparing ascorbic acid 5% to hydroquinone 4% cream over a period of 16 weeks found a slightly lesser benefit with ascorbic acid than with hydroquinone, though 62.5% of patients using the ascorbic acid still reported excellent results. Additionally, the ascorbic acid has an adverse effect rate in the 6% range as opposed to almost 69% of patients who used the hydroquinone.[15] Ascorbic acid is thought to exert this effect via inhibition of tyrosinase, an enzyme responsible for the conversion of tyrosine into melanin.[16]

Azelaic acid is another popular option in the management of hyperpigmentation. Like ascorbic acid, it's mechanism of action is rooted in its inhibition of tyrosinase thereby preventing melanin formation.6 One double-blind randomized study spanning 24 weeks comparing hydroquinone 4% to azelaic acid 20% found no significant difference in improvement between the two groups, with significantly fewer side effects in the azelaic acid group.[17] A similar study of 20% azelaic acid vs 2% hydroquinone over 24 weeks found significantly more improvement in the azelaic acid group.[18]

Kojic acid is yet another common topical agent that works via inhibition of tyrosinase in addition to its action as an antioxidant. It is commonly used in concentrations of 1 to 4% and one double-blind study spanning 12 weeks evaluating kojic acid 2% combined with hydroquinone 2% have found it to be superior to a similar cream containing glycolic acid as the substitute.[20] Though studies have demonstrated efficacy, kojic acid has a higher incidence of irritation than some other options that also inhibit tyrosinase, such as ascorbic acid.[6]

Lastly, chemical peels are another treatment sometimes used for the management of melasma. A chemical peel causes destruction of part of the epidermis and sometimes the dermis (depending on agent and concentration used) leading to the removal of superficial lesions. Generally, glycolic acid solution 30-70%, salicylic 20-30%, trichloroacetic acid 10-30% are considered to be superficial peels, whereas stronger strengths of trichloroacetic acid or some combination products are considered to be deeper peels reaching into the dermis.[19] Many of these preparations are used at an office and use can depend on which agent is used, for example, glycolic acid peels are generally applied every 2-3 weeks with several sessions scheduled in succession. Trichloroacetic acid peels, while effective, are not used as commonly as glycolic acid peels due to higher risk of adverse effects especially in patients with overall dark skin tone including risk of scarring.[19]

In summary, there is a wide variety of options for the management of hyperpigmentation with many of these options having high quality supporting data in the form of head to head trials or placebo-controlled trials. Combination treatments may be the key to both faster results and fewer side effects. Check out our Fagron Academy website for more formulations.

Sources:

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