

The Application of Skin Care Product in Melasma Treatment

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Abstract: Melasma is an acquired and chronic hyperpigmentation disorder which is recognized as one of the most psychologically distressing and difficult to cure forms of skin hyperpigmentation. It is associated with substantial quality of life impairments. Treatments of melasma include local application, oral medication, physical laser therapy and program combination therapy. However, routine treatment usually leads to the damage of skin barrier function, resulting in adverse reactions such as erythema, pruritus, post-inflammatory pigmentation and even scar. Skin care products contain a variety of active ingredients, which are widely concerned by cosmetic dermatologists because of high safety, good tolerance and the effect of improving the damaged skin barrier. Using skin care products alone or in combination with routine treatment not only can improve the curative effect for melasma, reduce side effects and recurrence rate, but also improve patient satisfaction. This article mainly describes the application of skin care products in the treatment of melasma.

Keywords: skin care product, melasma, treatment

Introduction

Melasma is an acquired disorder of hyperpigmentation that typically presents as irregular pigmented spot on the sun-exposed areas of skin, especially on the face and neck.¹ Its pathogenesis has not been fully elucidated. The triggers for melasma are diverse, including inheritance, ultraviolet light, inflammation, oxidative stress, disruption of the skin barrier, angiogenesis and estrogen.¹ The prevention of sun-light and hyperpigmentation is the therapeutic goal of melasma, but melasma is intractable and readily recurrent currently.^{1,2} Despite available multimodal treatments, which include various topical agents, systemic agents, and laser therapy, treatment outcomes have been disappointing. To this date, no single therapeutic approach has been proved entirely effective. Skin care products are daily chemical industrial products that are spread over human skin and its appendages by smearing, spraying or other similar methods to clean, skin care, beauty, sunscreen, and modify.³ Impairment of the skin barrier function is a significant cause of melasma.⁴ At the same time, routine treatments could lead to various adverse effects, such as impairment of the skin barrier function, inflammation, post-inflammatory pigmentation, scar and depigmentation.⁵ Skin care products contain many active ingredients, for example, aloe, oleracea, nicotinamide, titania, hyaluronic acid that possess a variety of beneficial effects in whitening, moisturizing, anti-inflammatory and sun protecting.⁶ Consequently, using skin care products not only can improve melasma lesions and reduce the incidence of adverse reactions but also

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can prevent recurrence as maintenance treatment.⁵ Now, more and more studies indicate that skin care products combined with routine treatment can improve the efficacy, tolerability and compliance in patients with high safety.

Sunscreen Products

UV light is a well-known extrinsic factor in the occurrence and development of melasma. Histopathology of melasma showed increased melanin content in all layers of the epidermis.⁷ Melanin is synthesized by hydroxylation of L-phenylalanine to L-tyrosine or directly from L-tyrosine.⁸ Any factor involved in the pathway for melanin synthesis will affect the synthesis of melanin. First of all, ultraviolet radiation up-regulate the expression of microphthalmia-associated transcription factor (MITF), tyrosinase (TYR), tyrosinase-related protein 1 (TRP-1) and dopachrome tautomerase (DCT) in skin.⁹ Among these, MITF serves a crucial function in the synthesis of melanin.⁸ Secondly, UV light stimulates melanogenesis by activating tyrosinase expression through various signaling pathways, such as MSH/cAMP signaling pathways, SCF/KIT signaling pathways and so on.^{10,11} UV radiation can also trigger keratinocytes produces and releases histamine, when histamine binds to H2-receptors, tyrosinase is activated to induce melanin production.^{12,13} UV light causes basement membrane damage by activating MMP2 and MMP9 to degrade type IV collagen and type VI collagen, the major component of the basement membrane.¹⁴ Basement membrane damage enables melanocytes and melanolipofuscin granules to move down into the dermis, making melasma persistent and recurrent.¹⁵ Finally, UV light can influence skin fatty acid metabolism that could bring about skin-barrier disruption.¹⁶ Therefore, rational and effective use of sunscreens can reduce the production of melanin, avoid the occurrence of skin inflammation, protect the skin barrier, and prevent the recurrence of melasma, which is an important adjuvant therapy and the basis for the treatment of melasma. At the same time, some moisturizing ingredients added to sunscreens can also help repair skin barrier function.¹⁷

A recent study showed that 100 participants were required to apply sunscreen (Garnier White Complete®SPF19 PA+++) during the daytime every 3 hours (approximate 3 mL each time) and found that modified Melasma Area Severity Index (mMASI) score, Hi-MELASQOL score decline, and mMASI score was marginally associated with Hi-MELASQOL score after 12 consecutive weeks of treatment.¹⁸ This study confirmed that use of sunscreen alone can improve the skin lesions and the quality of life of patients with melasma. In one study by Lakhdar et al,¹⁹ the researchers have found that the clinical

improvement was observed in 8 out of 12 volunteers who were affected by a pre-existing melasma and regular application of sunscreen in 185 pregnant women could prevent melasma and only five new cases of melasma occurred. The Indian expert panel recommended that patients with melasma use broad-spectrum anti-UV A and B sunscreens with physical blocking agents like ZnO and TiO₂ (SPF >30) regularly.² Especially for pregnant patients, sunscreen may be the only therapeutic option available.²⁰ At present, visible light (VL) is also thought to be involved in the pathogenesis of melasma, so anti-VL agents should be added to sunscreen.²¹

Whitening Products

As mentioned previously, melasma is characterized by excessive accumulation of melanin in the epidermis and dermis. Melanin is synthesized and stored in melanocytes through a series of oxidative reactions, and through dendritic processes of melanocytes transfer to the neighboring keratinocytes, then some brown spots and patches appear on the surface of the skin, and tyrosinase is the key enzyme in the synthesis of melanin.²² Whitening products contain arbutin, licorice flavone, tranexamic acid, vitamin C, green tea extract, and so on which can whiten, anti-freckle and reduce pigmentation by inhibiting tyrosinase and other functions.³ Niacinamide (NAM), the water-soluble, active form of vitamin B₃, can inhibit the transfer of melanosomes to keratinocytes by regulating protease activated receptor-2 (par-2).²³ Vitamin C, a natural antioxidant, interacts with copper ions to inhibit tyrosinase activity, which also plays a significant role in collagen synthesis and possess photoprotection effect.²⁴ Vitamin E has been proved to interfere lipid peroxidation of melanocyte membranes, increase intracellular glutathione content, and inhibit tyrosinase activity.²³ A double-blind, randomized, parallel-group clinical trial conducted by Bronzina et al²⁵ have showed that the experimental group received the combination of cosmetic products: Neotone® serum and Neotone® Radiance SPF 50+ (ISISPHARMA, Lyon, France) improve the severity of melasma more effectively and with less side effects compared with the control group only received 4% HQ cream (same formulation as Neotone® serum but the active ingredient is replaced by 4% HQ) and an SPF 50+ cream (same formulation as Neotone® Radiance, with the same UV filters but without the actives). To sum up, adding nicotinamide, vitamin C, vitamin E and other whitening ingredients to skin care products can reduce the production of melanin, thus improve the skin lesions of patients with melasma and prevent post-inflammatory hyperpigmentation, which is an important auxiliary means for the treatment of melasma.

Moisturizing Products

Moisturizing skin care products are effective which can increase the moisture content of the epidermis, help restore barrier function of the skin, reduce the dryness and peeling of the skin, and make skin smooth.²⁶ Moisturizing skin care products are mainly divided into four categories: occlusives, humectants, emollients and rejuvenators. 1) Occlusives can form a hydrophobic layer on the surface of the skin to avoid the loss of water, such as petrolatum, dimethicone. 2) Humectants are able to increase the moisture content of the skin by attracting water from the dermis and the environment, such as hydroxy acids, propylene glycol(glycerin), and urea. 3) Emollients can improve the look and texture of skin by filling in the crevices between keratinocytes. Most of this skin care products are essential fatty acids in natural oils, such as linoleic acid. 4) Rejuvenators are used to supplement essential proteins in the skin, such as collagen, keratin and elastin.²⁷ A study conducted by Kang et al showed that the skin barrier function of melasma was disrupted and the transdermal epidermal water loss (TEWL) of the melasma was not different from that of the surrounding (13.5 ± 4.0 vs 15.6 ± 4.6 , $P = 0.210$), but the recovery rate of barrier at the lesional skins was significantly delayed ($76.3 \pm 12.3\%$ vs $62.5 \pm 22.8\%$, $P = 0.043$).⁹ Once the skin barrier is destroyed, the moisturizing capabilities will decrease, therefore a vicious circle forms.²⁸ Peter et al²⁹ proposed that dryness and destruction of skin barrier will lead to skin pigmentation. At the same time, the routine treatment of melasma, like laser therapy, local application, will also disrupt the skin barrier function.⁵ Therefore, using moisturizing products daily can help restore skin barrier function and improve the skin lesions of patients with melasma. Xiaofeng Huang et al²⁸ have found that TEWL decreased, the skin water content increased, and the skin became whitened after using Vaseline moisturizing lotion (Unilever company) alone for 2 months in chloasma patients.

Medical Skin Care Product

Medical skin care product, also called cosmeceutical, is active product with drug or similar drug characteristics sold as cosmetics, and is a special cosmetic between traditional cosmetics and medicine. Compared with traditional cosmetics, it has better safety, stability, comfort and effectiveness which main mechanism is to increase the water content and lipid composition of the stratum corneum to repair epidermis, rebuild skin barrier and anti-inflammation.³ A variety of components in medical skin care product play an auxiliary role in the treatment of melasma. For example, tranexamic

acid has anti-inflammation and anti-angiogenic effect.³⁰ Resveratrol possesses a large number of pharmacological activities, including inhibition of tyrosinase activity, anti-inflammatory, anti-oxidant and UV Protectant.³¹ The extracts from orchid (phenolic compounds) possess antioxidant properties.³² Arbutin is a hydroquinone glycoside with great capacity to reduce tyrosinase activity.³³ Soybean extract possess antioxidant properties and can suppress melanosome metastasis.³⁴ Extracts of Aloe (aloin et al) are known to exhibit moisturizing, anti-inflammatory, and antioxidant properties. They can also promote wound healing and inhibit tyrosine convert into DOPA.^{35,36} The extract of *Camellia sinensis* has the effects of moisturizing, anti-inflammation, anti-oxidation and inhibiting tyrosinase activity.³⁷ Cysteamine has the effects of anti-oxidation and inhibition of tyrosinase and peroxidase activity.³⁸ Wenli Lu³⁹ conducted a 12-week clinical trial in China which proved that the whitening cream contain some new whitening extract of *prinsepia utilis*, *Portulaca oleracea*, China camellia, sanchi can effectively improve melasma with no obvious adverse reaction in clinic. In summary, the rational use of medical skin care products for patients with melasma not only can increase skin moisture content, restore skin barrier function, but also help to reduce pigmentation with less side effects. Medical skin care product is expected to become a new choice for maintenance treatment for patients with melasma. There are some of the active ingredients for melasma treatment and their functions in Table 1.

Combination of Skin Care Products and Conventional Treatment

Skin care products can not only be used alone but also combine with other therapy for melasma patients. Skin care products have the effect of repairing the damaged skin barrier, and also can reduce the adverse reactions of routine therapeutic approaches, so as to improve the tolerance and compliance of melasma patients. This may improve the success rate of melasma treatment. Meanwhile, skin care products can also be used as maintenance treatment to avoid the recurrence of melasma.

Combination of Skin Care Products and Drug Therapy

Oral medication is generally not the first choice for the treatment of melasma, in most cases, it is used for over-indication.⁵ Topical drug application is the preferred treatment option for melasma, however, the adverse

Table 1 Active Ingredients and Functions of Skin Care Product

Active Ingredient	Function	References
Titanium dioxide	Sunscreening properties	[20]
Niacinamide	Inhibiting melanogenesis through interfering with the interaction between keratinocytes and melanocytes, inhibiting melanin transferring by modulating the protease-activated receptor (PAR-2), antioxidant by increasing NADPH, improving the skin barrier function by upregulating the synthesis of ceramides and stimulating keratinocyte differentiation	[23,34]
Vitamin C	Antioxidant, inhibiting tyrosinase through interaction with copper ions at tyrosinase active sites, decreasing melanogenesis, UV-protective by neutralizing free radicals	[24]
Vaseline	Moisturizing and recovering the skin barrier through AHR pathway	[28,40]
Tranexamic acid	Anti-inflammatory and anti-angiogenic by suppressing of ET-I	[30]
Resveratrol	Direct and indirect tyrosinase inhibitor by decreasing transcription and post-transcriptional regulation, anti-inflammatory by activating PTEN/PI3K/AKT pathways, regulating inflammatory mediators and affecting arachidonic acid metabolism, UV Protectant through direct antioxidant effects and activation of the nuclear factor erythroid 2-related factor (Nrf2) pathway	[31]
Orchid extracts	Phenolic compounds have antioxidant activities	[32]
Arbutin	Reduces tyrosinase activity	[33]
Soybean extract	Antioxidant through raising cellular glutathione content and glutathione S-transferase activity, preventing antioxidant enzyme depletion, decreasing H ₂ O ₂ formation, and preventing ornithine decarboxylase induction and DNA degradation, suppressing melanosome metastasis by inhibiting the protease-activated receptor (PAR-2)	[34]
Aloe extracts	Moisturizing, anti-inflammatory by inhibiting cytokines, ROS production, and JAK1-STAT1/3 signaling pathway, antioxidant through free radical scavenging, metal chelation, and enzyme regulation, reducing the production of melanin by inhibiting the hydroxylation of tyrosine to DOPA and oxidation of DOPA, promoting wound healing by increasing cell migration via phosphorylation of Cdc42 and Ral1, cytokines, and growth factors	[35,36]
Extract of Camellia sinensis	Moisturizing by reducing TEWL value, anti-inflammation by inhibiting the production of NO, PGE (2) and TNF- α and reducing the expression of COX and iNOS gene, anti-oxidation by scavenging reactive oxygen species and enhancing the activity of oxidase in keratinocytes, and tyrosinase inhibitor	[37]
Cysteamine	Anti-oxidation and inhibition of tyrosinase and peroxidase activity	[38]
Glycerol	Moisturizing by increasing the water content in the superficial and reducing TEWL value	[41]
Hyaluronic acid	Moisturizing and anti-inflammatory	[42]
Fruit acid (alpha hydroxy acids)	Accelerating the exfoliation of keratinocytes, moisturizing, repair skin barrier and antioxidant	[43]

reactions like skin irritation and contact dermatitis are easy to occur after the use of topical drugs such as hydroquinone, retinoic acid and azelaic acid.⁵ Many of these discomforts can be relieved with the use of skin care products. A placebo-controlled, single-blind trial conducted by Ibrahim et al⁴² has found that the subjects with hyaluronic acid(HA) had fewer side effects and the recurrence rate was lower than that of

hydroquinone or glycolic acid alone after 12-week treatment of melasma patients. The author believes that this is related to the moisturizing and anti-inflammatory effects of HA. Skin care products have the functions of moisturizing, anti-inflammation, repairing skin barrier and so on. Rational use of skin care products can increase the tolerance of patients, reduce the recurrence rate, and improve patient satisfaction.

Skin Care Products Combined with Laser Therapy

Laser therapy, one of the important methods for the treatment of melasma, explodes and reduces facial melanophores through photoelectric effect. However, phototherapy can also cause various degrees of damage to the skin barrier, resulting in adverse reactions such as erythema, burning sensation, post-inflammatory pigmentation, hypopigmentation, aggravation of primary skin lesions and even scars.⁵ Skin care products with whitening ingredients can reduce the formation and diffusion of melanin.³ A prospective study conducted by Polnikorn et al⁴⁴ showed that laser therapy combined with whitening products can effectively improve the skin lesions of patients with melasma with low recurrence rate (5.71%). Moisturizing products are the mainstay of treatment for xerosis and pruritus.⁴⁵ Skin care products for promoting wound healing can promote wound healing after laser and minimally invasive surgery by adding aloe, polypeptide, amino acid, hyaluronic acid and other ingredients.³ Therefore, laser therapy combined with skin care products can effectively relieve discomfort of patients, repair skin barrier and prevent post-inflammatory pigmentation and hypopigmentation.

Skin Care Products Combined with Chemotherapy

Chemical peeling acts on the surface of the skin by chemicals, resulting in controllable destruction and exfoliation of the skin and promoting new skin regeneration, so as to reduce spots.⁵ A clinical comparative study shows that the combined use of trichloroacetic acid and ascorbate can improve pigmentation and mMASI score of patients with melasma better than trichloroacetic acid alone.⁴⁶ Another clinical trial confirmed that the use of moisturizing cream (Winona special care cream) after fruit acid skin revitalizing procedure can significantly improve the discomfort and plays a good auxiliary role for melasma in increasing the stratum corneum water content and sebum content and restoring the skin barrier.⁴⁷ In summary, chemical peeling combined with skin care products containing whitening, moisturizing, anti-inflammatory and anti-allergic ingredients can help improve the skin lesions of patients with melasma, alleviate post-operative discomfort and improve patient satisfaction.

Conclusion

At present, medical skin care products have become an important part of the administration of melasma. These above studies demonstrated that various types of medical

skin care products have played different roles in the prevention and treatment of melasma, but there still lack of large sample, multicenter, randomized, double-blind, controlled experiment, and the evaluation criteria are not completely unified. Therefore, more relevant clinical observation and basic research are needed. Cosmetic dermatologists are supposed to choose appropriate skin care products and treatment programs according to the skin type, condition and expectation of patient. In the future, with the further study of the effective components and biological activities of skin care product, it is expected to bring better prospects for the treatment of melasma.

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