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Review Article

A Comprehensive Review of Topical and Systemic Therapies for Melasma Treatment

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Abstract

Mostly affecting women, melasma is a common acquired hyperpigmentation condition that is characterized by brown to grayish-brown spots on the face, especially where the skin has been exposed to the sun. Genetics, hormone changes (particularly during pregnancy or while using oral contraceptives), and environmental factors—UV radiation being the primary trigger—all play a role in its development. Although melasma is not dangerous, many people find it to be a major cosmetic problem, which has increased demand for efficient treatments. The goals of current melasma treatment strategies are to decrease pigment production, increase skin turnover, and stop more UV damage. To lighten the afflicted skin, topical medications such hydroquinone, tretinoin, azelaic acid, niacinamide, and vitamin C are frequently used, either alone or in combination. Prescription medications such as azelaic acid (20%), hydroquinone (4%), and Tri-Luma (a combination of hydroquinone, tretinoin, and fluocinolone acetonide) have demonstrated effectiveness; however, extended usage may result in ochronotic or skin irritation. Despite the advancements, melasma is still difficult to treat since it recurs frequently and doesn't respond to some treatments. To improve long-term results for those with this illness, a combination of early intervention, sunscreen use, customized treatment regimens, and new technology advancements in laser and topical therapies are essential.

Keywords: Hyperpigmentation; Melasma; Ochronotic; Topical Therapies

Introduction

Brown or gray-brown spots on the skin, usually on the face, are the hallmark of melasma, a common skin disorder. Although it can affect anybody, it is most frequently observed in women, particularly those who have Asian, African, and Brazilian heritage. Although the precise etiology of melasma is unknown, hormone fluctuations, UV exposure, and hereditary factors are frequently implicated. Treatment for melasma, which usually affects the cheekbones, forehead, upper lips, and chin, can be difficult. Melasma, formerly called chloasma, is an acquired pigmentary disorder that mostly affects the face. UV exposure and hormonal factors are the main causes of this illness, which is more common in women and those with darker skin tones. Centro facial, malar, and mandibular symmetric reticulated hyper melanosis are the three main facial patterns that comprise melasma, which is often diagnosed clinically. The mandibular melasma is seen on the chin and jawline, whereas the malar motif is limited to the facial malar cheeks. The latter is believed to affect elderly people and might be more closely linked to severe photodamage. Despite being widespread, the therapy of this condition is still difficult since the pathophysiology, chronicity, and recurrence rates are not well understood. There are promising novel treatments for melanomas in addition to conventional ones, such as topical, oral, and procedures therapy. The latest research on melasma, including clinical diagnosis, pathophysiology, and treatments—including a discussion of novel topical, oral, and procedural therapies—will be reviewed in this review.

The authors' new research on humans or animals is not included in this article; rather, it is based on earlier research. Dark brown or grayish-brown spots are the consequence of melasma, a common acquired hyperpigmentation disease of the skin. Usually, the cheekbones, forehead while upper lip, nose, and jawline are where these patches show up on the face. Even while melasma is not a fatal disorder, it can cause serious cosmetic concerns, especially for people with darker skin colors. Although men can also be affected, women are more likely to have the illness, particularly those who are in their reproductive years.

Figure 1: Melasma.

Types of melasma

Based on the level of pigmentation, melasma can be categorized as follows:

- **Epidermal melasma:** Under a Wood's light, epidermal melasma, which affects the skin's outer layers, frequently appears darker.
- **Dermal melasma:** More deeply layers beneath the skin are affected by dermal melasma, which is less treatable.
- **Mixed melasma:** A mixture of dermal and epidermal involvement is known as mixed melasma.

Figure 2: Types of Melasma.

Pathophysiology

Melasma is caused by melanocytes that the skin cells that produce color, producing too much melanin. Three primary elements are linked to the condition:

- **Exposure to ultraviolet (UV) radiation:** One of the most important environmental risk factors for melasma is exposure to the sun.
- **Hormonal changes:** During pregnancy, the use of contraceptive medications, or testosterone replacement therapy (HRT), melasma frequently appears (commonly referred to as "the disguise of pregnancy").
- **Genetic predisposition:** Melasma frequently has a family history, indicating a genetic component.

Melasma is caused by an overexpression of melanogenesis and a surge in the total amount of melanocytes. Hormonal variables (such as progesterone and estrogen), UV radiation, and other environmental elements also have an impact.

Clinical presentation

Melasma usually manifests as brown to grayish stained macules that but patches that are symmetrical and clearly defined. The region's most frequently impacted are:

- Forehead and Cheeks
- The nose chin
- Upper lip (commonly referred to by the term "mustache" region in women)
- Jawline and temples (less common).

Clinical diagnosis of melasma is usually made using the distinctive pigmentation pattern and distribution. The level of hyperpigmentation (epidermal vs. dermal) may occasionally be ascertained by a Wood's lamp examination as this might affect the choice of therapy.

Risk factor

Sun exposure

Melasma is made worse by UV light, which causes melanocytes to create more melanin. One of the most prevalent external triggers is UV light.

Hormonal changes

Melasma is closely associated with pregnancy (sometimes referred to as chloasma or the "cover up of pregnancy"), birth control pill use, and hormone replacement treatment.

Genetics

The chance of getting melasma is increased if there is a family background of the disorder.

Skin type

People have dark complexions, such as people of Southeast Asian, African, or Hispanic heritage, are more likely to develop melasma.

Cosmetics

Irritating ingredients in some skincare products can exacerbate melasma or make treatment more challenging.

Figure 3: Causes of Melasma.

Diagnosis

Melasma is often diagnosed clinically based on the distribution and characteristic appearance of hyperpigmented patches. Differentiating amongst epidermal, superficial, or mixed forms of melasma can be aided using Wood's lamp:

- **Epidermal melasma:** Under the Wood's light, epidermal melasma appears darker, signifying the pigmentation's superficial location.
- **Dermal melasma**: Under the Wood's lamp, dermal melasma appears less strong or unaltered, indicating deeper pigmentation.

Management and treatment

Melasma treatment can be difficult, and a mix of strategies is frequently needed for success. Lightening the hyperpigmented regions, preventing recurrence, and managing any contributory variables, such as hormonal imbalances, are the major objectives of therapy.

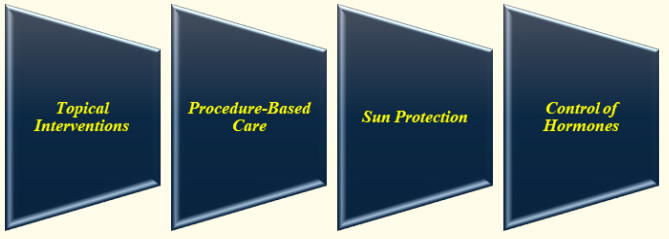

Figure 4: Treatment of Melasma.

Topical interventions

The mainstay of melasma treatment is topical therapy. By preventing melanogenesis, or the synthesis of melanin, or encouraging skin turnover, these seek to lessen the pigmentation.

- **Hydroquinone**: Tyrosinase, the enzyme that produces melanin, is inhibited by hydroquinone, a strong skin-lightening agent. It comes in both prescription and free of charge formulations and is regarded as the first-line therapy for melasma.
- **(Retinoids) Tretinoin:** Retinoids encourage the turnover of skin cells, which aids in the removal of pigmented skin and encourages the development of new skin. They frequently work in tandem with hydroquinone.
- **Corticosteroid:** In order to decrease inflammation and improve the efficacy of hydroquinone, mild topical steroid applications are occasionally utilized. Long-term usage, however, may result in adverse consequences such skin thinning.
- **Azelaic Acid:** This organically generated acid possesses anti-inflammatory and melanin-inhibiting qualities. It is helpful for people with sensitive skin or people who cannot handle hydroquinone.
- **Vitamin C:** By preventing the creation of melanin and encouraging the manufacture of collagen, vitamin C, an antioxidant, helps lessen hyperpigmentation.
- **Niacinamide:** A kind of vitamin B3, folic acid prevents melanin from moving from melanocytes that to skin cells, therefore reducing pigmentation.

Procedure-based care

Procedural therapies may be taken into consideration for situations that are chronic or that do not respond to topical treatments:

- **Chemical peels:** To enhance skin texture and remove pigmented skin layers, exfoliating acids such as glycolic acid, salicylic acid, or trichloroacetic acid for short are used.
- **Microneedling:** This technique stimulates the formation of collagen and improves the absorption of topical therapies by making small punctures in the skin using needles.
- **Laser therapy:** To break up pigmentation, lasers like Q-switched lasers and fractional lasers (like Fraxel) target the skin's melanin. Laser beams should be used carefully, though, as misuse can exacerbate melasma, particularly in those with darker skin.
- Pigment is the target of intense pulsed light (IPL), a non-ablative light treatment. Although it is less intrusive than lasers, vigilance is still necessary to prevent pigmentation from getting worse.

Sun protection

Sun protection is essential for both preventing and treating melasma since exposure to the sun is one of its main triggers:

- **Broad-spectrum marijuana sunburn (SPF 30 or higher):** To shield the skin from UVA and UVB radiation, sunscreen should be used every day, even on overcast days.
- **Physical sunscreen:** Broad-spectrum protection is better and delicate skin is less likely to be irritated by sunscreens that contain magnesium oxide or titanium dioxide.
- **Sun protection gear:** It's crucial to wear sunglasses, wide-brimmed hats, and to limit your exposure to the sun between 10 AM and 4 PM.

Control of hormones

Hormonal changes are intimately associated with melasma, especially during pregnancy and when using oral contraceptives. If melasma is caused by hormones, it may become better if hormonal therapy is stopped or changed. This isn't always feasible, though, especially during pregnancy when melasma may go away after giving birth.

Modality	Treatment	Mechanism of action	Adverse effects (AE)
Topical	Iron oxide Hydroquinone (HQ) Azelaic acid, Ascorbic acid, Kojic acid	Block visible and ultraviolet light Tyrosinase inhibitor	Irritation Irritation, exogenous ochronosis (with HQ)
Oral	Tranexamic acid	Inhibition of melanin synthesis	Abdominal bloating, Menstrual irregularities, Headache, Deep venous thrombosis
Procedural	Q-switch ruby laser, Non-ablative fractional lasers Chemical peels Microneedling	Melanosome destruction Increased keratinocyte turnover Transdermal drug delivery Extrusion of melanosomes	Burn, PIPA Erythema, edema, tram-track marks, PIPA

Table 1

Marketed formulation

S. no	Marketed Product	Formulation	Features
01	Eldoquin Forte Cream (4% hydroquinone) Melquin Cream (4% hydroquinone) Obagi Nu-Derm Clear Fx Ambi Fade Cream (2% hydroquinone)	Hydroquinone-Based Formulations	Treating hyperpigmentation Reducing inflammation
02	Retin-A Cream Renova Cream Tri-Luma Cream	Tretinoin (Retinoid)-Based Formulations	Treatment of melasma
03	Azelex Cream (20% azelaic acid) Finacea Gel (15% azelaic acid) Azelaic Acid Suspension (10%)	Azelaic Acid-Based Formulations	Effective for hyperpigmentation disorders like melasma Reduce discoloration while calming the skin
04	Skinceuticals C E Ferulic La Roche-Posay Pure Vitamin C Face Serum	Vitamin C-Based Formulations	Reduce oxidative stress Reducing dark spots and brightening the skin

05	Paula's Choice 10% Niacinamide Booster The Ordinary Niacinamide 10% + Zinc 1%	Niacinamide-Based Formulations	Helps lighten hyperpigmentation Brighten the skin and improve pigmentation issues
06	Tri-Luma Cream Lustra MD Cream	Corticosteroid-Based Formulations	Reduce inflammation and pigmentation
07	Lysteda Mela-Release™ by Skinceuticals	Tranexamic Acid-Based Formulations	Inhibiting the activation of melanocytes
08	Glycolic Acid 7% Toning Solution Glycolic Acid Peels Skin Perfecting 2% BHA Liquid Exfoliant	Chemical Peels and Exfoliants	Fade hyperpigmentation Treat melasma.
09	Kligman's Formula Pigment Correcting Creams	Other Combinations and Formulations	Melasma treatment

Table 2

Future prospective

Despite many people find success with existing therapies for melasma, which is a complicated skin disorder with numerous contributing variables, there is still much space for improvement. Treatment for melasma will advance with the creation of more specialized medications, a deeper comprehension of the pathophysiology of the ailment, and cutting-edge technology. Thanks to developments in technology, novel medicine formulations, and genetic research, there are great prospects for the treatment of melasma in the future. The management of melasma is expected to improve dramatically in the upcoming years by emphasizing safer and more effective medicines, preventative measures, and more individualized treatment methods. Together, these developments provide a more focused, comprehensive, and less intrusive method of treating this persistent and frequently annoying skin disorder [1-31].

Conclusion

Melasma is a difficult illness that has to be treated with a multifaceted strategy. A blend of topical remedies (hydroquinone, retinoids, the substance known as acid), administrative programs (chemical peels, lasers), and rigorous sun protection can greatly reduce pigmentation and enhance the cosmetic appearance of those who are impacted, even though no single treatment is always successful. Early management, regular therapy, and permanent sun avoidance are essential for controlling melasma. Since a number of variables might affect the illness, a dermatologist's individualized treatment is necessary for the best results. Melasma has serious psychological ramifications and is still a difficult illness to treat. Numerous factors, including as differences in clinical appearance and response to therapy across genders, skin phototypes, and ethnic groups, might affect how effective a treatment is. A multimodal therapy strategy that tackles aspects including photoprotection, inflammation, vascularity, discoloration, and hormonal effects is crucial given the complex etiology of melasma. We are still learning more about melasma and the best ways to treat it thanks to new research.

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