Periorbital Hyperpigmentation: A Comprehensive Review

Rashmi Sarkar, MD, MNAMS; Rashmi Ranjan, MD; Shilpa Garg, DNB; Vijay K. Garg, MD, MNAMS; Sidharth Sonthalia, MD, DNB; Shivani Bansal, MD, DNB

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Abstract

Periorbital hyperpigmentation is a commonly encountered condition. There is very little scientific data available on the clinical profile and pathogenesis of periorbital hyperpigmentation. Periorbital hyperpigmentation is caused by various exogenous and endogenous factors. The causative factors include genetic or heredity, excessive pigmentation, postinflammatory hyperpigmentation secondary to atopic and allergic contact dermatitis, periorbital edema, excessive vascularity, shadowing due to skin laxity and tear trough associated with aging. There are a number of treatment options available for periorbital hyperpigmentation. Among the available alternatives to treat dark circles are topical depigmenting agents, such as hydroquinone, kojic acid, azelaic acid, and topical retinoic acid, and physical therapies, such as chemical peels, surgical corrections, and laser therapy, most of which are tried scientifically for melasma, another common condition of hyperpigmentation that occurs on the face. The aim of treatment should be to identify and treat the primary cause of hyperpigmentation as well as its contributing factors.

Introduction

Periorbital hyperpigmentation (POH), also known as periocular hyperpigmentation, periorbital melanosis, dark circles, infraorbital darkening, infraorbital discoloration, or idiopathic cutaneous hyperchromia of the orbital region, is a common condition encountered in dermatology practice.[1–4] It is an ill-defined entity that presents as bilateral round or semicircular homogenous brown or dark brown pigmented macules in the periocular region.[1,2] It can affect an individual's emotional well-being and influence quality of life.

There is scarcity of data regarding the incidence and prevalence of POH due to its transitory nature and lack of reasonable etiological explanation. In an Indian study, it was found that POH was most prevalent in the age group of 16 to 25 years (i.e., 95 out of 200 patients [47.50%]). Among the 200 patients studied, it was more prevalent in women (162 [81%]) than men and the majority of the affected women were housewives (91 45.50%]).[5]

Classification

Recently, Huang et al[6] performed a clinical analysis and proposed classification on the basis of clinical pattern of pigmentation and vasculature.[6] Periorbital hyperpigmentation was classified into pigmented (brown color), vascular (blue/pink/purple color), structural (skin color), and mixed type based on the clinical appearance assessed by the physician. The mixed type of dark eye circle included the following four subtypes: as pigmented-vascular (PV), pigmented-structural (PS), vascular-structural (VS), and a combination of the three.

Pigmented type (P) appears as infraorbital brown hue. Vascular (V) type appears as infraorbital blue, pink, or purple hue with or without periorbital puffiness. Structural type (S) appears as structural shadows formed by facial anatomic surface contours. It can be associated with infraorbital palpebral bags, blepharoptosis, and loss of fat with bony prominence. Mixed type (M) combines two or three of the above appearances. This classification can help in introducing the therapeutic modalities on the basis of POH type, as different types of POH respond to different types of treatment.

Clinical Features

Clinically, POH is characterized by light- to dark-colored, brownish-black pigmentation surrounding the eyelids. It gives a tired look to the patient. Diagnosis is mainly based on clinical examination. It is important to differentiate the dark eyelid skin with shadowing due to tear trough. Manual stretching of the lower eyelid skin can help to differentiate between true pigmentation and shadowing effect. Although the former retains its appearance with stretching, the latter improves or resolves entirely. An

increase in violaceous discoloration on manual stretching of the lower eyelids is due to thin eyelid skin or hypervascularity of lower eyelid.[7]

Wood's lamp examination can be done to differentiate between the epidermal and dermal pigmentation.[8] The variations in epidermal pigmentation become more apparent under Wood's light. For dermal pigmentation, this contrast is less pronounced. Ultrasonographic evaluation can help to differentiate the vascular cause from the periorbital puffiness.

Histopathology

Histological characteristics of periorbital hyperpigmentation suggest that it can be both epidermal and dermal in nature. Biopsy specimen must be stained with routine hematoxylin and eosin. Special stains can also be used. Fontana-Masson silver stain can be used to stain melanin. Hemosiderin deposits seen in few cases (resulting from extravasation and superficial location of vasculature) can be stained with Perl's potassium ferrcyanide.[9,10]

Etiology

There are very little scientific data available on the clinical profile and pathogenesis of POH. Various exogenous and endogenous factors are possibly implicated in its pathogenesis. The causative factors include genetic or heredity, excessive pigmentation, postinflammatory hyperpigmentation secondary to atopic and allergic contact dermatitis, periorbital edema, excessive vascularity, and shadowing due to skin laxity and tear trough associated with aging.

Genetics

Periorbital hyperpigmentation is considered to have a genetic basis. Goodman and Belcher[11] reported many families with pigmentation around the periorbital area in several members of the family. Some were mildly affected and some severely affected. Many of them recognized the pigmentation early in childhood and stated that pigmentation increased with age. They were also aware that stress made pigmentary changes more intense, while rest and good health seems to produce lessening of color.[11] Gellin et al reported a familial case in which 22 members were affected in six generations that had a genetically determined form of hyperpigmentation involving the periorbital area.[11]

Periorbital pigmentation due to dermal melanocytosis. Dermal melanocytosis is characterized by the presence of melanocytes in the dermis. Clinically, these lesions are recognizable by their distinctive grey or blue-grey appearance. Dermal melanocytosis causing periocular hyperperpigmentation can be due to congenital or acquired causes.[9,12,13] Dermal melanocytosis can be placed into the pigmentary class of Huang et al's classification.

Nevus of Ota, also known as oculodermal melanocytosis or nevus fuscocaeruleus ophthalmomaxillaris, is a type of congenital dermal melanocytosis that involves the areas innervated by the first and second divisions of the trigeminal nerve. It appears as speckled or mottled brown-grey to blue-black patches that may involve the skin, conjunctiva, sclera, tympanic membrane, or oral and nasal mucosa of the affected dermatomes. If it is located infraorbitally, it can be a cause of periorbital hyperpigmentation.

Nevus of Hori was first described in 1984 by Hori et al and is defined as acquired, bilateral nevus of Ota-like macules. Clinically, it presents with blue-brown to slate-grey mottled hyperpigmentation with a predilection for the malar region, which may extend to involve the periocular area causing dark circles. A distinct lack of ocular or mucosal involvement differentiates the nevus of Hori from other forms of dermal melanocytosis. Reports have linked sun exposure, hormonal changes in pregnancy, and chronic atopic dermatitis to occurrence of nevi of Hori.[12,13]

Postinflammatory hyperpigmentation. Excessive pigmentation can also be due to postinflammatory hyperpigmentation secondary to atopic and allergic contact dermatitis and other dermatological conditions (e.g., lichen planus pigmentosus) and can be drug induced, such as in the case of fixed drug eruptions and erythema dyschromium perstans (Figure 1).[14,15] Periorbital hyperpigmentation can be caused by rubbing and scratching of skin around the eyes and by accumulation of fluid due to allergy as in atopic dermatitis and allergic contact dermatitis.

Superficial location of vasculature. Superficial location of vasculature and thin skin overlying the orbicularis oculi muscle is another common cause of periorbital hyperpigmentation.[1–3] This condition usually involves the entire lower eyelids with a violaceous appearance due to prominent blood vessels covered by a thin layer of skin, more in the inner aspect of the eyelid, and is usually accentuated during menstruation. When the lower eyelid is manually stretched, the area of darkness spreads out without blanching or significant lightening and results in deepening of violaceous color, which could be used as a diagnostic test to confirm the vascularity.[2]

Tear trough depression. Tear troughs represent an anatomical location that becomes depressed with

age, centered over the inferio-medial orbital rim. It is an age-related change. It occurs mainly because of loss of subcutaneous fat and thinning of overlying skin of the orbital rim ligaments, combined with cheek descent, conferring hollowness to the orbital rim area. A combination of the hollowness and the overlying pseudoherniation of the infraorbital fat accentuate the shadowing in the tear trough causing dark circles, depending on the lighting condition (Figure 2).[1–3]

Periorbital edema. The eyelid region has a spongy property, which can lead to fluid accumulation due to systemic and local causes. Diagnostic features that suggest edema includes worsening in morning or after eating salty meals. The history of variability in intensity and extension is important to determine the influence of edema on periorbital hyperpigmentation.[16] When compared with normal orbital fat, edema is still present in downward gaze and does not change much in upward gaze.[1,2]

Extension of pigmentary demarcation lines of face. Pigmentary demarcation lines (PDL) are borders of abrupt transition between hyperpigmented skin and lighter areas. According to the site, they have been labeled A to H lines. F and G types are present over the lateral side of orbit and present as V-shaped and W-shaped patches, respectively (Figure 3).[10,17] In a study by Malakar et al, 100 Indian patients with a diagnosis of POH were evaluated. Their results showed that in 92 percent of study patients, periorbital melanosis was an extension of the pigmentary demarcation line over the face.[10]

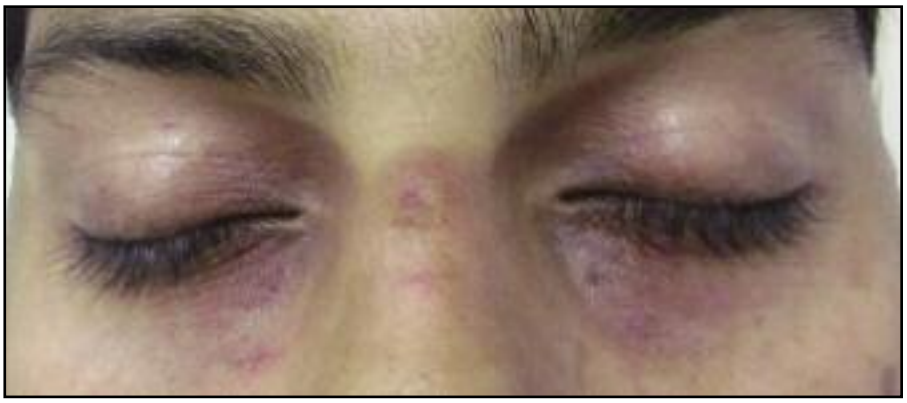

Figure 1. Periorbital hyperpigmentation due to postinflammatory hyperpigmentation

Figure 2. Tear trough deformity presenting as dark circles

Other Causes

Ocular hypotensive drugs. Prostaglandin analogues, such as latanoprost and bimatoprost, which are used as ocular hypotensive eye drops in patients with glaucoma, can also cause periorbital hyperpigmentation.[18,19] Patients develop periocular hyperpigmentation most frequently between 3 to 6 months of initiating bimatoprost therapy. Complete reversal of pigmentation occurs after discontinuation of bimatoprost.[19] It was reported that the increased melanogenesis in dermal melanocytes and increased transfer of melanin granules to basal epidermis is the likely mechanism of bimatoprost-induced hyperpigmentation.

Environmental Causes

Ultraviolet radiation aggravates POH,[20] and some lifestyle factors may contribute to developing POH, including lack of sleep, stress, alcohol overuse, and smoking, although not clinically substantiated.[3]

Treatment

There are a number of treatment options available for POH. Among the available treatment options for POH include topical depigmenting agents, such as hydroquinone, kojic acid, azelaic acid, topical retinoic acid, and physical therapies, including chemical peels, surgical corrections, and laser therapy, most of which are tried scientifically for melasma, another common condition of hyperpigmentation, which also occurs on the face.[1-3] The aim of treatment should be to identify and treat the

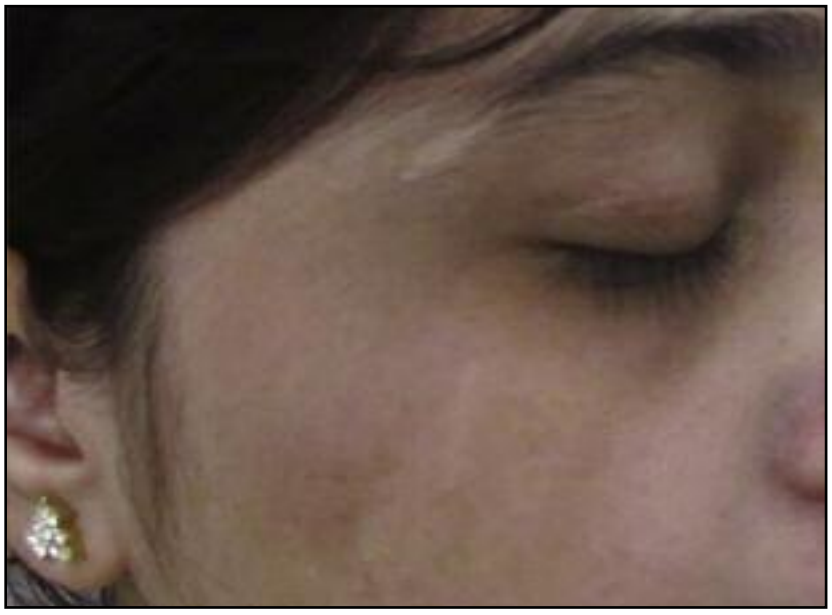

Figure 3. Periorbital hyperpigmentation with pigmentary demarcation line (G type)

primary cause of hyperpigmentation as well as its contributing factors. Also different modalities are used according to cause of POH.

Topical agents. Topical phenolic or nonphenolic bleaching agents are used in the treatment of hyperpigmentation, particularly hydroquinone and tretinoin. The mechanism of action of most bleaching agents is inhibition of tyrosinase enzyme, which inhibits the conversion of dopa to melanin, hence leading to a reduction of the melanin content of the epidermis.

Hydroquinone. Also known as 1,4 dihydrobenzene, hydroquinone is the most prescribed bleaching agent worldwide. It is used in strengths of 2 to 6%. The effect of treatment generally becomes evident after 5 to 7 months of therapy, hence the treatment should be given for at least three months.[21,22]

Frequently observed acute side effects include mild skin irritation, itching, postinflammatory hyperpigmentation, and transient hypochromia. Long-term use can lead to exogenous ochronosis, leukomelanoderma en confetti, nail discoloration, and colloid millium.[23,24]

Hydroquinone was reported to cause cancer in rodents, yet human carcinogenicity has not been established. A number of studies have shown that hydroquinone is safe and no cases of skin cancer or internal malignancy have been reported with topical application of hydroquinone, which has been used for more than 50 years.[25] Hydroquinone has also been used safely in the periocular area.[26]

Triple combinations. The United States Food and Drug Administration (FDA) has approved a modified combination of the Kligman's formula, containing 4% hydroquinone, 0.05% tretinoin, and 0.01% fluocinolone acetonide for use in melasma and various other pigmentary disorders,[27] but its long-term use in the periorbital area is a concern since it contains a topical steroid.

Kojic acid. Kojic acid is a naturally occurring fungal derivative produced by *Aspergillus* species and *Penicillium* species. It acts by inhibiting tyrosinase, and is used in a concentration ranging from 1 to 4%.[28,29]

In a study conducted by Lim et al,[28] it was found that the addition of kojic acid to a gel containing 10% glycolic acid and 2% hydroquinone further improves pigmentation in melasma. Although there are no studies, kojic acid has been tried anecdotally in the treatment of periorbital hyperpigmentation and has been found to be effective. Side effects of kojic acid include erythema and contact dermatitis.[28]

Azelaic acid (AzA). Azelaic acid (1,7- heptanedicarboxylic acid) was initially developed as a topical anti-acne agent, but because of its effect on tyrosinase, it has also been used in the treatment of hyperpigmentary disorders such as melasma. Its mechanism of action includes the inhibition of DNA synthesis and mitochondrial enzymes, thereby inducing direct cytotoxic effects on the melanocyte.[30,31]

In vitro studies show that AzA interferes with DNA synthesis and mitochondrial enzymes in abnormal melanocytes and fibroblasts,[32] thus neither leukoderma nor exogenous ochronosis are associated with its use. It can be used safely for prolonged periods of time. Since it was found to be effective for facial postinflammatory hyperpigmentation, it is a potentially promising agent for periocular hyperpigmentation due to postinflammatory hyperpigmentation.

Arbutin. Arbutin is an extract of leaves of the bearberry shrub and the cranberry, pear, or blueberry plants. It inhibits tyrosinase activity, but also inhibits melanosome maturation. Its effects are dose-dependent, but high concentrations of arbutin can cause hyperpigmentation. It is available in a concentration of 3%.[33]

A randomized open study by Ertam et al[33] found that gel containing topical arbutin was effective in reducing pigmentation in melasma patients. Arbutin can also be used in other facial hyperpigmentation including POH.

Topical vitamin C. Vitamin C, an antioxidant, has also been used for the treatment of hyperpigmentation. Because ascorbic acid is unstable in many topical preparations, esterified derivatives, such as L-ascorbic acid 6-palmitate and magnesium ascorbyl phosphate are used in compounds.

L-ascorbic acid is the predominant cutaneous antioxidant. It scavenges the free oxygen radicals in the aqueous compartment which trigger melanogenesis. Vitamin C promotes collagen production and conceals color of blood stasis, which could improve appearance of dark circles under the lower eye lid.[34]

Ohshima et al[34] showed that vitamin C and its derivatives, such as magnesium ascorbyl phosphate and ascorbic acid glucoside, inhibit melanogenesis in human melanocytes. They used two types of 10% vitamin C lotion, sodium ascorbate and ascorbic acid glucoside for six months in a split-faced manner for dark circles. Melanin index, erythema index, thickness, and echogenecity of the dermis of the bilateral eyelid was measured and it was found that there was lightening of pigmentation owing to an increase in dermal thickness due to concealment of dark discoloration from congested blood. However, they did not find any significant difference in melanin index.

Sunscreens. Hyperpigmentation can be improved with sunscreen alone as reported by Guevara and Pandya in a study conducted in patients with melasma.[35] Patients should be cautious while using chemical sunscreen in the delicate eye area. Similarly, broad spectrum sunscreen and ultraviolet (UV) coated sunglasses are considered to be beneficial in POH.

Chemical peels. Chemical peels may be used alone or in combination with treatments such as topical bleaching agents. Glycolic acid is the most widely used alpha hydroxy acid for chemical peeling. Glycolic acid 20% can also be used for periocular hyperpigmentation. Lactic acid 15% has been used in periorbital hyperpigmentation in combination with trichloroacetic acid (TCA) 3.75% by Vavouli et al[36] and it was found that almost all the patients showed significant esthetic improvement.For treatment of POH in medium to darker skin, it is best to extend the peel to the entire face to avoid post-peel demarcation. For optimal outcome, pretreatment with a tretinoin and hydroquinone bleaching agent for 2 to 4 weeks is recommended before undergoing a chemical peel. The most disturbing side effect of chemical peels can be postinflammatory hyperpigmentation. This may be minimized with the help of priming agents, such as hydroquinone and tretinoin.

Lasers. In recent time, lasers have been used increasingly in cosmetic dermatology. Periorbital hyperpigmentation has been successfully treated with various noninvasive lasers that target pigment and vascularity. Various lasers that have been used for treating dark circles are: Q switched ruby laser (694 nm), Q switched alexanderite laser, and Nd:Yag laser (1064nm).[1,2]

In a study conducted by Watanabe et al,[12] patients with homogenous bilateral pigmented macules in the periorbital region were selected for study of dark circles. Five patients with infraorbital dark circles received 1 to 5 treatments with the Q switched ruby laser (694nm); four patients showed good response and two patients showed excellent results.[8]

In another study on POH, Momosawa et al[26] combined Q switched ruby laser with a bleaching agent containing 0.1% tretinoin and 5% hydoquinone. The bleaching agent was applied for six weeks before the laser treatment. The purpose of this treatment was to improve epidermal pigmentation by accelerated discharge of epidermal melanin by tretinion and suppressing new epidermal melanogenesis by hydroquinone ointment. Fifteen out of 18 patients showed excellent or good results after 3 to 4 laser treatments with no complications. Thus, it was concluded that in treating POH, the Q switched ruby laser should be considered as first-line treatment and it was found effective in both dermal and epidermal pigmentation.[26] The Nd:Yag laser (1064nm) is also effective in reducing the pigmentation and vascular component of infraorbital dark circles.

Skin laxity and tear trough deformity are age-related changes that they can be treated with lasers. Alster and Bellew[37] treated 67 patients with dermatochalasia and periorbital rhytides using CO_2 laser resurfacing and found significant improvement.

Although ablative laser resurfacing is a well-accepted treatment modality for improving the appearance of photo-induced rhytides coexisting with periocular hyperpigmentation, but due to untoward side effects such as prolonged erythema, pigmentation, and infection, and in some cases scarring, great interest has been shown toward less invasive methods to treat photo-induced rhytides effectively. These include the pulsed dye laser, diode laser, 1064nm Nd:YAG laser, 1320nm Nd:YAG laser, 1540nm erbium glass laser, and intensed pulsed light laser sources.

Autologous fat transplantation. Autologous fat transplantation is used to treat periorbital hyperpigmentation

due to thin and translucent lower eyelid skin overlying the orbicularis oculi muscle.

Fillers. Hyaluronic acid gel is used as a filler for three-dimensional reshaping of periorbital complex. Patient satisfaction is high, but some patients with dark circles noted darker pigmentation after hyaluronic acid gel. Bosniak et al[38] treated 12 patients with POH, tear trough deformity, or prominent nasojugal groove with the hyaluronic acid push technique. All patients experienced immediate improvement after the procedure. Excellent tear trough contour improvement was achieved in all patients and under eye dark circle improved. Minor post-injection erythema and edema were observed, which resolved within 72 hours.

Platelet-rich plasma. Recently, platelet-rich plasma has been used in treating dark circles due to tear trough deformity and wrinkles. A single session with intradermal injections of 1.5mL platelet-rich plasma was given into the tear trough area and wrinkles of crow's feet. Effect was compared three months after treatment with baseline. The improvement in infraorbital color homogeneity was statistically significant.[39]

Surgery. *Blepharoplasty.* Blepharoplasty helps in eliminating dark circles caused by shadows that are cast by fat deposits or excess skin.[40] Transconjunctival blepharoplasty is a better approach than transcutaneous blepharoplasty so that no external visible scar is created. Epstein used transconjunctival blepharoplasty and deep depth phenol peel simultaneously to treat hyperpigmentaion of skin and pseudoherniation of orbital fat, which is a contributing cause for infraorbital dark circles.[40]

Carboxytherapy. Paolo et al[41] used subcutaneous injections of CO_2 once a week for seven weeks in the periorbital area and found significant improvement in fine lines and POH.

Conclusion

Periorbital hyperpigmentation is a commonly encountered condition. It is less responsive to standard therapies due to its multifactorial etiology and deposition of melanin in both dermis and epidermis. However, even a mild-to-moderate improvement in appearance can cause an improvement in the quality of life of the patient, hence topical therapies and simple physical therapies such as chemical peels can be used to treat the patients who want to improve the cosmetic appearance of their face.

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Drs. Sarkar, Ranjan, Garg V, and Bansal are from the Department of Dermatology, Maulana Azad Medical College and LokNayak Hospital, New Delhi, India. Dr. Garg S is from the Department of Dermatology, Army College of Medical Sciences, Base Hopsital, Delhi Cantt-10, India. Dr. Sonthalia is from Skinnocence Clinic, Gurgaon, Haryana, India. ***Disclosure: The authors report no relevant conflicts of interest in the preparation or content of this manuscript.***