Periorbital Hyperpigmentation: Review of Etiology, Medical Evaluation, and Aesthetic Treatment

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ABSTRACT

Periorbital hyperpigmentation (POH) is a common worldwide problem. It is challenging to treat, complex in pathogenesis, and lacking straightforward and repeatable therapeutic options. It may occur in the young and old, however the development of dark circles under the eyes in any age is of great aesthetic concern because it may depict the individual as sad, tired, stressed, and old. While "dark circles" are seen in all skin types, POH is often more commonly seen in skin of color patients worldwide.[1] With a shifting US demographic characterized by growing number of aging patients as well as skin of color patients, we will encounter POH with greater frequency. As forecasted by the US Census, by 2030 1 in 5 Americans will be 65 plus years old and greater than 50% of the population will possess ethnic skin of color.[2] The disparity in the medical community's understanding of POH versus popular demand for treatment is best illustrated when you have only 65 cited articles to date indexed on PubMed line[3] compared to the 150,000,000 results on Google search engine.[4] Most importantly POH may be a final common pathway of dermatitis, allergy, systemic disorders, sleep disturbances, or nutritional deficiences that lends itself to medical, surgical, and cosmeceutical treatments. A complete medical history with ROS and physical examination is encouraged prior to treating the aesthetic component. Sun protection is a cornerstone of therapy. Safety issues are of utmost concern when embarking upon treatments such as chemical peeling, filler injection, and laser therapy as not to worsen the pigmentation. Without intervention, POH usually progresses over time so early intervention and management is encouraged. The objective of this study was to review the current body of knowledge on POH, provide the clinician with a guide to the evaluation and treatment of POH, and to present diverse clinical cases of POH that have responded to different therapies including non-ablative fractional photothermolysis in two skin of color patients.

J Drugs Dermatol. 2014;13(4):472-482.

INTRODUCTION AND CLINICAL OVERVIEW

Periorbital Hyperpigmentation (POH) is also known by the following names: periorbital melanosis, periorbital circles, dark circles, dark eye circle, underye circles, perioccular pigmentation, perioccular melanosis, infraorbital melanosis, and idiopathic cutaneous hyperchromia of the orbital region (ICHOR).[5,6] It is a common condition that occurs in both sexes with an increasing frequency in females. Globally, skin of color patients are affected more than Caucasians. POH is often a presenting cosmetic concern in our skin of color patients and may be considered to be normal variants of pigmentation.[7] There is most likely a familial component as it may be seen in family members over generations. Periorbital hypermelanosis is a complex entity with a multifactoral etiology and an expanding knowledge base. Clinical severity like the etiology may vary, however POH usually presents as bilaterally symmetric hyperpigmented patches around the eyes. One eye may be more involved than the other. It can affect either upper or lower eyelid or both upper and lower. It may extend to involve the glabella and upper nose. Periorbital hyperpigmentation may be seen in young and old[8] and with advancing age it is a significant cosmetic concern because it may make patients seem sad, tired, stressed, and feel older than they are.[9,10] The etiology of POH may be multifactorial with no one etiologic agent predominating.[10,11] However, importantly for clinicians, it may be a sign of an underlying systemic disease, skin disorder, allergic reaction, nutritional deficiency, or sleep disturbance. The patient should be medically evaluated as not to miss underlying systemic disease or lifestyle inadequacy that can be corrected (Table 1). POH may also be the earliest sign of periorbital aging, heralding skin, and musculo-ligamentous laxity. POH may also be the earliest sign of periorbital aging, heralding skin and musculo-ligamentous laxity.[12] Successful outcomes may be punctuated with chronic recurrences. With that in mind, there are promising treatments for POH on the horizon. Successful outcomes may be punctuated with chronic recurrences. With that in mind, there are promising treatments for POH on the horizon. Multimodality treatment will probably be the most efficacious and long lasting. In best hands multimodal treatment plan may take months to take effect. As this may be a chronic and relapsing condition, preventive and maintenance regimens that involve UV protection and patient education should be integrated into the treatment plan. A clinical approach to the treatment of POH should include identification and therapeutic targeting of each contributing etiologic factor for an individual patient. Medical treatments involve correcting the underlying condition. Aesthetic treatments include microdermabrasion, chemical peels, lasers, radiofrequency, injectable fillers, surgery, fat transfer, hydroquinone (HQ), non-HQ skin bleaching agents, topical retinoids, and

TABLE 1.

Evaluation of Periorbital Hyperpigmentation
Medical History
Family History- Possible extension of pigmentary demarcation lines (Futcher's lines)
Environment and Occupation: UV component, Contact Dermatitis
Medical History: ROS which includes history of allergy, atopy, thyroid disease, Addison's disease, anemia, nutritional status
Medications/Supplement History: Estrogens, NSAIDS, St Johns Wort
Topical Product History: Hydroquinone overuse, Mercury bleaching creams
Physical Examination *(circle positive findings)*
Fitzpatrick (I-VI) Roberts Skin Type Classification (hyperpigmentation and scarring risk)
Area of skin involvement (Upper eyelid- Lower eyelid- Both upper and lower eyelid)
Degree of hyperpigmentation (mild - moderate - severe)
Color of dyspigmentation (light brown- brown - violaceous)
Tear Trough deformity (none- present)
Mid Facial Descent (none- present-severe)
Sunken suborbital area (none -present)
Blood vessel prominence
Osteopenia (none- present- severe)
Periorbital edema (none- present)
Degree of skin laxity (none- present- severe)
Periorbital rhytides (suborbital, crowsfeet, nasalis)

cosmeceuticals. While there are many treatment possibilities for a specific case of POH, in this article, five cases are reviewed with a different aesthetic treatment modality. They include microdermabrasion, injectable filler, chemical peel, and fractional photothermolysis as monotherapy without topical HQ and fractional photothermolysis as combination therapy with topical HQ. A worksheet is offered to assist in the evaluation of POH.

Etiology

POH is a benign disorder that may have a heredity component. Goodman and Belcher reported many families with several family members with varying degrees of periorbital pigmentation. Some were mildly affected and some severely affected.[13]

The etiology of POH may be multifactorial however, importantly for clinicians it may be a sign of an underlying systemic disorder, allergic reaction, nutrition, or sleep disturbances. Gupta had evaluated the prevalence of dissatisfaction with skin appearance of 32 women with eating disorders compared with 34 healthy controls and found that 9% of those below 30 years of age were not satisfied with their under eye dark circles against 38% of women with eating disorders.[14] Periorbital dermatitis may be a precursor to PIH and POH. Landeck et al reported on a study that consisted of 266 patients affected by periorbital dermatitis. This entity showed significant predominance of female gender (87.6%) and of individuals aged 40 to 59 years (45.9%). Nickel (16.5%) and fragrance mix (13.2%) were the top-ranking sensitizers. Patch testing confirmed the likelihood of allergic contact dermatitis in 50.8% of the dermatitis patients tested.[15] Idiopathic cutaneous hyperchromia of the orbital region has been described as a subset of POH defined with no associated systemic or local disease such as PIH, contact dermatitis, or systemic component.[16] Using spectrophotometric intracutaneous analysis (SIA) Verschoore et al analyzed and quantified melanin and hemosiderin concentration in this disorder.[17] It has been proposed that idiopathic cutaneous idiopathic hyperpigmentation (ICHOR) is an extension of the pigmentary lines of demarcation also known as Futcher's lines.[18] In a study by Malakar et al, 100 Indian patients with a diagnosis of POH were evaluated. Their results showed that in 92% of study patient's periorbital melanosis was an extension of pigmentary demarcation line over the face. They concluded that in this population, periorbital melanosis and pigmentary demarcation lines of the face are not two different conditions, rather they are two different manifestations of the same disease.[18] In an effort to classify POH, Ranu et al examined 200 patients from Singapore with the diagnosis of POH. They were evaluated with medical history, clinical examination, mexameter reading, and physician assessment, by three dermatologists. The authors found 4 basic types: 41.8% was the vascular type (characterized by presence of erythema predominantly involving the inner aspect of the lower eyelids, with prominent capillaries or telangiectasia or the presence of bluish discoloration of the lower eyelid due to visible blue veins that became more prominent when the overlying skin is stretched; 38.6% were considered constitutional, which was characterized by the presence of a curved band of brownish to black hyperpigmentation of the lower eyelid skin along the shape of the orbital rim with velvety texture, often involving the upper eyelids; 12% were called post-inflammatory hyperpigmentation; and 11.4% characterized as shadow effects due to anatomical deformities such as tear trough deformity and fat herniation. There were other cases of POH that were deemed due to other causes like skin laxity, dry skin, hormonal disturbances, nutritional deficiencies, and other chronic systemic illnesses.[19] Most recently, in an effort to analyze and classify dark eye circles (DEC), Huang et al examined 65 cases of DEC and classified their results as pigmented, vascular, structural, and mixed types. In addition, they identified 33 cases with "periorbital puffiness" as patients with higher "pre-septal thickness" then the 20 controlled cases as determined by ultrasonagram and Wood's lamp.[20] POH may be the earliest sign of periorbital aging with concomitant skin and musculo-ligamentous laxity, increasing vascular show, and osteopenia of the periorbital osseous structures.[21] It must be differentiated from other benign disorders of hyperpigmentation

and the not so benign malignant that may arise in nevus of Ota and blue nevi. Without intervention, it worsens with advancing age and may be associated with other health disorders.[22] A medical workup is needed before embarking on aesthetic treatment. Table 1 illustrates a recommended work up of POH and focuses on the patient medical history and physical examination as a roadmap to successful treatment (Table 1).

"In our skin of color patients especially, this indentation, groove, or tear trough may be the only area of concavity visible in the face and thus may be the earliest sign of aging."

Anatomic Considerations for POH

POH has distinct anatomical features, which affect treatment decisions. In classic POH, when examining the lower eyelid component, the uppermost or proximal boundary is the tarsal plate of the lower eyelid. The most distal boundary is at the tear trough deformity. The tear trough is not exclusively the product of aging. Young people including children have a tear trough. It is the deepening of this groove that leads to indentation and becomes a visual deformity that affects facial appearance. To devise the optimal correction for the tear trough component of POH, understanding the anatomy of this area is critical. The nasojugal fold was defined initially by Duke-Elder, Wybar, and Loeb in 1961.[23] It was then in 1969 renamed the tear trough deformity by Flowers as the observation that tears will track along this groove.[23] The tear trough is the medial one-third of a periorbital sulcus. The sulcus starts at the lower eyelid inner canthus involving the thin loose eyelid skin and runs downward to the thicker skin of the cheek. The indentation that defines the tear trough deformity is at the junction of thin eyelid skin above and the thicker nasal and medial cheek skin below, marking the line along which the fascia is anchored to the periosteum.[12,21,22] Concave surfaces replacing convex surfaces is the hallmark of facial aging. Our facial aesthetic efforts are focused on restoring convex facial surfaces. In our skin of color patients especially, this indentation, groove, or tear trough may be the only area of concavity visible in the face and thus may be the earliest sign of aging.[7] The concave contour of the periorbital soft tissues results in a hollow area that creates a tired appearance. The shadow or dark halo created by this groove is commonly perceived as a dark circle or ring under the eye. Laxity of the lid-cheek junction with age accompanied with the herniation periorbital fat pads, involutional descent of the midface, and osseous and fat atrophy with aging may further contribute to the loss of soft tissue support and descent of the cheek that deepens the tear trough.[20]

Association With Aging

In addition to the anatomic changes described above for POH, photodamage has been demonstrated in cases of POH. Cumulative UVR damage results in a cascade of oxidative stress. Cytokine release with activation of matrix metalloproteinases results in collagen degradation, solar elastosis, and clinically rhytides. Loss of luminosity and progressive pigmentation results from UVR-induced activation of AP1 Complex and NF KB.[24] Without intervention, POH worsens for females and males with advancing age.

Histology

There is not a lot of literature on the histology of POH. Watanabe et al looked at biopsies from periorbital skin in 12 Japanese patients diagnosed with POH. Melanin pigment in was seen in upper dermal macrophages they found S100 and Fontana-Masson positive dermal melanosis.[25] Graziosi et al reported a histological evaluation of 28 cases with CIHOR. Twenty-eight adult patients who were diagnosed with CIHOR were elected for the study. Biopsy specimens were taken from the darkened skin of the eyelid. The control was uninvolved retro auricular skin. Their results were as follows: Hemosiderin was absent in all cases. The increase in melanin content in the papillary dermis was slight in mild clinical cases and moderate in both the moderate and severe clinical cases of CIHOR. Mild dilation of blood vessels were observed in the papillary dermis at the different clinical levels of CIHOR severity, while in the reticular dermis, blood vessels showed moderate dilation and few melanophages were found. The author concluded that an increase in melanin content was the most marked histological change in specimens of darkened skin. Dilation of dermal blood vessels may contribute to the severity of CIHOR.[26] These histologic findings are very important in our discussion of the POH with our patients. The fact that most of the melanin was dermal, as has been supported by Watanbe and Graziosi, clinically correlates with the difficulty in treating this disorder and the observed resistance of POH to respond to topical treatments.

Differential Diagnosis

There are many disorders that may mimic or be associated with POH. Because this may be a special opportunity to diagnose an underlying health issue prior to formulating a treatment plan, it is recommended rule out the following disorders (Table 2).

Aesthetic Treatments

Periorbital hyperpigmentation is often refractory to treatment. Aesthetic treatment modalities, both monotherapy and in combination, have been used for POH. They include microdermabrasion, chemical peels, lasers, radiofrequency, injectable fillers, surgery, fat transfer, hydroquinone (HQ) and non-HQ skin bleaching, and brightening agents, retinoids, ascorbic acid, botanicals, and other cosmeceuticals (Table 3).[29]

TABLE 2.

Differentiai Diagnosis of Periorbital Hyperpigmentation	
Differential Diagnosis of POH	**Distinguishing features from POH**
PIH	History of inflammation, post
Contact/ Hypersensitivity	Topical product, oral medication
Atopic Dermatitis	History of Atopy, pruritus
Bilateral Nevus of Ota [26]	Occurs at infancy and puberty
Acanthosis Nigricans	Primarily on neck, axillae and associated with insulin resistance
Melasma	Usually spares the upper eyelid and infraorbital area though commonly affects malar region
Erthema Dyschromicum Perstans [27]	Involvement of areas beyond face
Fixed Drug eruption	Offending drug
Ecchymosis	Presence of Hemosiderin vs Melanin
Amyloidosis	Edematous, Violaceous, Purpura
Dermatomyositis	Heliotrope dermatitis
Melanoma	Clinical presentation and supporting histology
Normal anatomic variant	Familial

TABLE 3.

POH Example of Multifactoral Etiology/Multimodality Treatment of POH	
Cause	**Treatment**
Dark Circles	POH workup while using SPF, Camouflage with Cosmetic Concealer
Tear Trough Deformity	Injection of Hyaluronic Acid, Fat, Blepharoplasty
Lower Eyelid Skin Laxity	Co2Ablative and Non Ablative Laser
Lower eyelid hyperpigmentation	Microdermabrasion, Non Ablative Laser, Topical Skin Lighteners
Skeletonization / Osteopenia	PLLA, Hyaluronic Acid, Fat Transfer, vit D and Calcium, Rx by Primary Care
Fat herniation	Bepharoblasty, Camoflouge border with Filler/Fat
Vascular prominence	QS Alexandrite, Injectable filler in the dermis overlying vessels to reduce visibility
Periorbital edema	May occur from salt retention, thyroid dz Decrease salt intake, diuresis, facial massage
Post Inflammatory Hyperpigmentation	Occurs from rubbing. Treat underlying atopic, irritant or contact dermatitis. Microdermabrasion, Non Ablative Laser, Topical Skin Lighteners
Medications (estrogens, photosensitizers)	Discontinue consult with primary care regarding alternate medications
Supplements (photosensitizers)	Discontinue offending agent, SPF and antioxidants
Anemia	B12, Folate, Ferrous sulfate
Malnutrition	Balanced diet, Decrease alcohol
Increased Melanin Deposition	QS Ruby Laser (694nm),
Atopic Dermatitis	Treat underlying disorder , Barrier repair
Asthma	Treat underlying disorder
Loss of Sleep	8 Hours per night
Water	4-8 glasses per day
Thyroid disease	Screening thyroid panel
Pigmentary demarcation line	SPF, UV protective eyewear

Chemical Peeling

There is much anecdote regarding peeling of the periorbital region though there are few published articles. While chemical peeling has been used to treat a variety of facial pigmentary disorders, as of this publication, there are no randomized control studies on the efficacy of chemical peeling for the treatment of POH. The peeling agents removing melanin from the stratum corneum and epidermis, deep peels may remove melanin from the dermis but may lead to dyspigmentation and scarring and in this area of thin skin with minimal folliculosebaceous structures for repitheliazation, is not recommended.[30] Prepeel instructions should include discontinuance of retinoids or hydroxy acids that may potentiate the depth of the peel. Careful and gentle application of the wounding agent must be used to not traumatize the skin and inadvertantly increase the depth of the peel. With little published data specifically regarding treatment in POH, superfical, and medium depth peels utilizing salicylic, glycolic, lactic, hydroxy acids, retinoic, TCA, and mandelic acid have all been used on the face in the treatment of pigmentary disorders such as photodamage and melasma. A staged approach with the patient returning every 2-4 weeks for a peel is recommended for patient safety. C. Vavouli and A. Katsambas et al performed a use study of chemical peeling with TCA 3.75% and lactic acid 15% for infraorbital dark circles.[31] Thirty patients with periorbital dark circles and skin types II, III, or IV were included in the study. Chemical peeling was performed every week for a series of four treatments. The effect was photo-documented, and a patient's and physicians global assessment was evaluated. Almost all the patients showed significant improvement. Physicians assessed a fair, good, or excellent improvement in 93.3% of the patients. Patient's global assessment rated a fair, good, or excellent response in 96.7% of the patients. The procedure itself had expected temporary

adverse effects of erythema, edema, frosting, dryness, and telangiectasia. The authors reported the treatment results remained for at least 4-6 months in the majority of patients with appropriate sun protection.[31]

Laser and Device

This is becoming increasingly integrated into the treatment of POH, however, there is still a lot to be learned. While there are randomized controlled studies for periorbital rejuevenation with laser, there is a paucity of data for the treatment periorbital hyperpigmentation. Before embarking upon a laser treatment it is important to understand the skintype of your patient. This goes beyond Fitzpatrick skintype because your Caucasion patient (phenotypic Fitzpatrick I or II) may have a brown or dark complexioned parent and or grandparent. The patient's skin may respond like the darker skinned relative and result in dyschromia. Both hypo and hyperpigmentation have been seen as laser complications in ethnic skin of color. The Roberts Skin Type Classification System is an efficient way to document and communicate your patients ancestry, liklihood for dyschromia post laser procedure, and assist in the selection of safe laser settings (Table 4).[32,33] Laser safety is of utmost importance. Patient protective eyewear such as eyeshields should be used as necessary. Innappropriate use of laser in this area may result in eye problems including blindness, dryness and photophobia.[34] Importantly, IPL is not indicated for the treatment of POH. The pigmented iris absorbs light in the same wavelength range of IPL. The IPL when applied to the perioccular area is absorbed by the pigment of the iris and can result in severe eye damage that may include photophobia, pain, and anterior uveitis.[34,35] As we have histologic data showing that dermal melanosis is one of the etiological factors in POH, laser treatment used to target the melanin has been investigated.[25] An emerging practice is combination of device and topical product for the treatment of POH. One group recommends the use of topical hydroquinone and tretinoin in addition to Q-switched ruby laser sessions; they postulate that these topical treatments not only enhance treatment efficacy, but also lower the risk for PIH secondary to laser treatments.[35] Skin laxity has been sighted as a causative factor of POH and ablative and nonablative lasers and devices are being investigated.[36] In 1998 ,West and Alster conducted a study to determine the effectiveness of cutaneous CO_2 laser resurfacing in reducing infraorbital hyperpigmentation.

Twelve female patients (age range, 27–56 years; mean, 44 years) presented for either full-face or periorbital CO_2 laser resurfacing. It is an important laser safety tip to note all patients had skin types I, II, or III. There were no skintypes IV –VI in this study. Prior to the laser resurfacing procedure and at 3, 6, and 9 weeks after treatment, the average of three melanin measurements was obtained from the infraorbital regions using a handheld reflectance spectrometer (Dermaspectrometer; Cortex Technology, Haugland, Denmark). Photographs were taken using identical lighting and camera settings preoperatively and at each of the three scheduled follow-up visits. Simultaneous projection of pre- and posttreatment photographs (Mirror Image, Virtual Eyes, Inc., Kirkland, WA) were scored independently by two blinded assessors. Clinical improvement was rated on a 1–4 scale with <25% lightening = 1, 25–50%= 2, 51–75%= 3, and

TABLE 4.

Roberts Skin Type Classification System (Four elements (FZ/ H/ G/ S) in a serial series so the skin type reads as FZ/ H/ G/ S)	
FZ: Fitzpatrick Scale (measures skin phototype)	
Type FZ1	White skin. Always burns, never tans.
Type FZ2	White skin. Always burns, minimal tan.
Type FZ3	White skin. Burns minimally, tans moderately and gradually.
Type FZ4	Light brown skin. Burns minimally, tans well.
Type FZ5	Brown skin. Rarely burns, tans deeply.
Type FZ6	Dark brown/black skin. Never burns, tans deeply.
H: Roberts Hyperpigmentation Scale (propensity for pigmentation)	
Type H0	Hypopigmentation
Type H1	Minimal and transient (<1 year) hyperpigmentation.
Type H2	Minimal and permanent (>1 year) hyperpigmentation.
Type H3	Moderate and transient (<1 year) hyperpigmentation.
Type H4	Moderate and permanent (>1 year) hyperpigmentation.
Type H5	Severe and transient (<1 year) hyperpigmentation.
Type H6	Severe and permanent (>1 year) hyperpigmentation.
G: Glogau Scale (describes photoaging)	
Type G1	No wrinkles, early photoaging.
Type G2	Wrinkles in motion, early to moderate photoaging.
Type G3	Wrinkles at rest, advanced photoaging.
Type G4	Only wrinkles, severe photoaging.
S: Roberts Scarring Scale (scar morphology)	
Type S0	Atrophy.
Type S1	None.
Type S2	Macule.
Type S3	Plaque within scar boundaries.
Type S4	Keloid.
Type S5	Keloidal nodule.

TABLE 5.

Mechanism of Action of Skin Bleaching Agents	
Skin Lightener	**Gold Standard**
Skin turnover accelerator	Hydroxy acid, retinoic acid
Premelanin synthesis **Tyrosinase transcription**	Tretinoin
During melanin synthesis **Tyrosinase inhibition**	Hydroquinone, Azelaic, Kojic, Arbutin, Soy, Mushroom, Peptide
Postmelanin Synthesis **Tyrosinase degradation**	Linoleic acid
Postmelanin synthesis **Melanosome transfer inhibition**	Soy, Niacinamide
Antioxidants	Vit C interacts with copper ions to reduce dopaquinone

>75% clearance = 4. Clinical grades ranged from 1 to 4, with an average score of 2.5, corresponding to approximately 50% improvement 9 weeks after laser resurfacing Posttreatment melanin readings (mean value = 1.14) were not significantly different from those obtained preoperatively (mean value = 1.25), and thus did not correlate with the favorable clinical findings seen. Four patients experienced transient infraorbital hyperpigmentation postoperatively lasting 8 weeks.[37]

Another study used a CO_2 laser followed by a Q-switched alexandrite laser, effectively targeting pigmentation in the dermis and epidermis.[38] Several authors including Tierney, Hanke, and Moody have commented on the effectiveness of nonablative fractional photothermolysis (FP) for the treatment of POH.[36,38] The fractionated 1550nm erbium doped fiber laser creates microscopic, pixels of wounding in the dermis results in significant skin pigmentary and textural improvements without the adverse effects of prolonged wound healing and risks of dyspigmentation associated with traditional ablative resurfacing.[39] The nonablative fractionated 1550-nm erbium-doped fiber laser been proven to treat a variety of pigmented conditions effectively, including photoaging and melasma. The proposed mechanism of action is fractionated photothermolysis with preservation of the stratum corneum while creating microscopic treatment zones (MTZs) of thermal injury in the epidermis and dermis.[39,40] The laser functions to eliminate melanin pigment from the epidermis and dermis through a "melanin shuttle," which exudes the pigment from the skin through the MTZs.[40,41] Moody et al, reported one case of a Fitzpatrick II female diagnosed with POH who underwent four non ablative laser treatments spaced out at 4 week intervals with a 1550nm fractionated erbium-doped fiber laser over a 4 month period. They used a 15mm spot, energy fluency of 70 J/cm^2 treatment level of 10-11, 4 passes for a total surface area coverage of 29-32%. This was used in conjunction with a Zimmer chilling cryo system that kept the epidermis cool during the treatment. Two months after the last treatment the physician and patient noted significant improvement of the POH.[40] What must be stressed in this successful case report is the skin type of the patient and these settings must be readjusted in skin of color patients (Case 1 and Case 2). In 2010 a consensus panel of experts convened to communicate best practices for fractional photothermolysis[42] Ruiz Esparza examined the efficacy of nonablative radiofrequency (NARF) to tighten noninvasively the skin laxity of the lower eyelids by treating the periorbital area.[43] Nine patients with skin flaccidity of the lower eyelids had a single treatment session with NARF in a small area of skin in the periorbital region, specifically the zygomatic and/or temporal areas. His results indicated that all of the nine patients in the study achieved cosmetic improvement of the eyelids ostensibly through skin contraction. All patients were able to return to their normal routines immediately. Results were gradual and patient satisfaction was remarkable. No complications were seen in this study. He concluded that NARF was successful in providing a safe, noninvasive, cosmetic improvement in patients with excessive skin laxity of the lower eyelids. Similar findings for NARF were also seen in 2008 by Sukai.[44]

Injectable Filler

While there have been no randomized controlled studies analyzing the effectiveness of treating POH in isolation, there is evidence based medicine that dermal fillers have shown efficacy in repairing the tear trough deformity that may be an important contributing factor to some cases of POH especially in the skin of color patient. Carruthers, Sadick, and others have worked to classify this complex and multidynamic area.[45,46] The European and North and South American aesthetic experts convened at an academic workshop to develop keys to optimal outcomes.[47] The best practice guidelines recommended from the consensus group for midface and infraorbital hollow injections were the vertical supraperiosteal depot technique (VSDT) or linear threading for infraorbital hollow augmentation.[48] Sharad has recently done a comprehensive review of the tear trough anatomy, treatment techniques, and clinical outcomes. I recommend the reader to this article.[49]

Ten Clinical Pearls for Tear Trough Injection

1. It is an advanced technique not for novice injectors
2. The skin should be sanitized with antiseptic and gloves should be worn throughout the session.
3. Caution with injecting too quickly either with needle or cannula.
4. Low-viscosity HA can be safely injected to correct tear trough deformity. High-viscosity HA and permanent fillers should be avoided and only done in the hands of an experienced injector.

5. Injections must be at a supraperiosteal level of the orbital rim below the nasojugal defect. Caution however, to not harshly bounce the needle or cannula tip against the zygomatic periosteum as that can be traumatic to the bone, a superficial injection above the trough defect may result in a tyndall effect that makes the skin appear blue or blue-grey.

6. Identify the infraorbital foramen before you inject and while injecting use one hand to identify and protect the orbital rim.

7. If a patient expresses pain while injecting stop the injection immediately and observe for bleeding and blanching as you may be in proximity of the neurovascular bundle.

8. To decrease irregularities the HA should be gently massaged with hand or cotton tipped applicator for even distribution. Strong massage should be avoided.

9. Overcorrection should be avoided. HA is hydrophilic and may cause a swelling or beading this is temporary and will subside.[49] In addition HA may produce neocollagenesis so the area may continue to correct after initial treatment. A Staged treatment to avoid overcorrection is always advisable

10. If overcorrection does occur with HA then Hyaluronidase may be injected to remove excess product, 50-100 units per side depending on the amount of volume injected. You may want to lesionally inject hyaluronidase in two separate visits as not to remove all of the product. Contraindicated in patients who are allergic to bees.[50]

Autologous Fat Transfer

While there is much literature written on facial fat transfer there is little discussing autologous fat transfer and POH. Roh et al, reported on the results of a pilot study in 2009.[51] Ten patients diagnosed with infraorbital eye circles underwent successful autologous fat transplantation. The patients reported 78% improvement.

Blepharoplasty

Classical blepharoplasty or resection blepharoplasty is a surgical procedure, which requires skill and training to be successfully done to restore a natural appearance to the eye anatomy. Studies have shown that blepharoplasty by restoring normal anatomy and removing excess skin and fat may also affect eyelid pigmentation by decreasing a shadow effect. In addition to classical blepharoplasty, augmentative blepharoplasty has been described where autologous fat transplantation occurs at the same time as blepharoplasty. The authors report success in optimizing the periorbital complex.[52]

Topical Skin Bleaching Agents and Cosmeceuticals

A review of bleaching agents used for hyperpigmentation is beyond the scope of this chapter but there are overriding clinical practices used in rejuvenation of POH. The goal of using a skin-lightening agent is to reduce the amount of melanin in the skin as well as decrease the appearance of the darkness, shadow or pigmentation. Bleaching agents may be used as a monotherapy or combined with procedures to treat POH. A bleaching agent may be composed of one compound for example ascorbic acid or most popular now is the combination of many cosmeceutical agents into one formulation. These "cocktail bleaching agents" have increased in popularity and each one has unique proprietary ingredients. These ingredients target different portions of the melanin cascade.[53,54] While hydroquinone remains the gold standard for a bleaching agent in the US, the HQ free market is growing. With so many products to choose from it is often difficult for the patient to navigate their way for an optimal product. The melanin pathway is complex however the author recommends that with knowledge of the pathway each portion of the pathway be targeted for increasing successful outcomes, Table 4 reviews how this may be done with the gold standard bleaching agent in each category. The table is not meant to be a comprehensive listing of available agents but an example of an approach toward treatment. Skin bleaching agents and cosmeceuticals are discontinued one week prior to a procedural treatment and may be brought back one week after a successful outcome

Cosmetic Camouflage

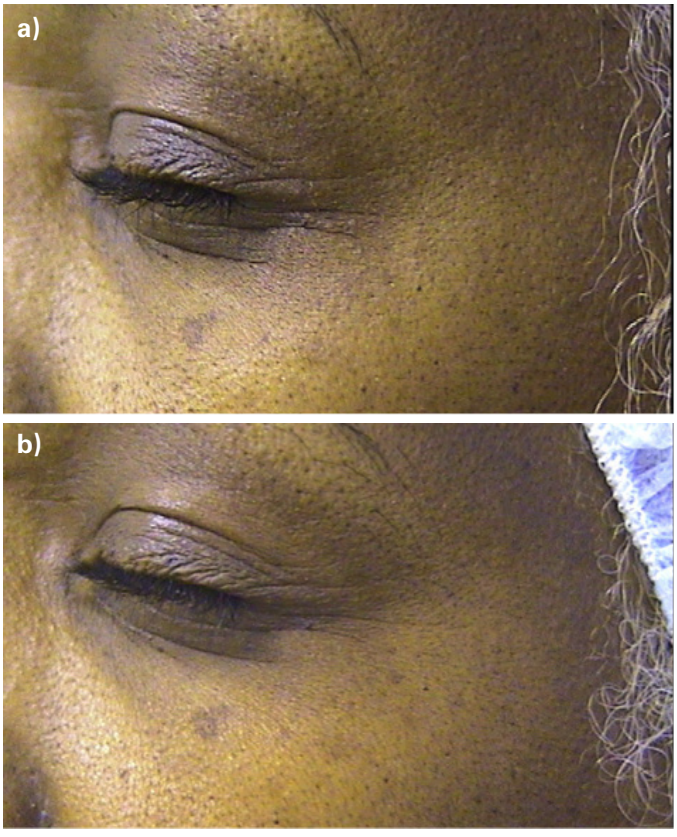
Cosmetic camouflage may be very useful while the patient is undergoing treatment of POH. As treatment may be prolonged the results seen after makeup application may give the patient an optimistic window to a future free of dyspigmentation and increase quality of life. Cosmetic camouflage comes in a variety of preparations it may include liquid, cream, stick or mineral based powders that are applied to cover the hyperpigmentation and blend the skin tone. Because most of these products contain zinc oxide and or titanium dioxide they also bring UV protection to the patient. For severe cases thick cream concealers that match the skin color or are lighter may be applied for camouflage (Dermablend-Quik Fix Concealer®, Cover/ Fx Concealer®). In cases with a highly vascularized component a green concealer may neutralize the red or violaceous discoloration (Physicians Formula Gentle Cover Concealer Stick®). A makeup expert can counsel your patient as to the optimal product and application techniques.

CASE 1

A 67-year-old African American female, Fitzpatrick skin type 5 (Roberts Skin Type F5/H2/G2/S0), reported progressive darkening of the skin around her eyes and had no significant past medical history other than a family history of eye darkening with aging. She reports having used a prescription 4% HQ product of and on for one year with no undereye improvement. On presentation, she had significant bilateral confluent brown patches periorbital patches that were bilateral and symmetrical. She had mild skin laxity and lateral eye rhytids. Tear

trough deformity was minimally present (Figures 1A and 1B). Because of her obvious increased suborbital melanization and failure to clear with topical bleaching as monotherapy, conservative fractional resurfacing was chosen as her first line treatment She underwent non ablative laser fractional photothermolysis with 1550-nm fractionated erbium-doped fiber laser (Fraxel Restore, Solta Medical, Haywood, CA). Settings used: 30 mJ/Treatment level (TL) 5/4 passes for a total of 3 sessions at 4 week intervals.

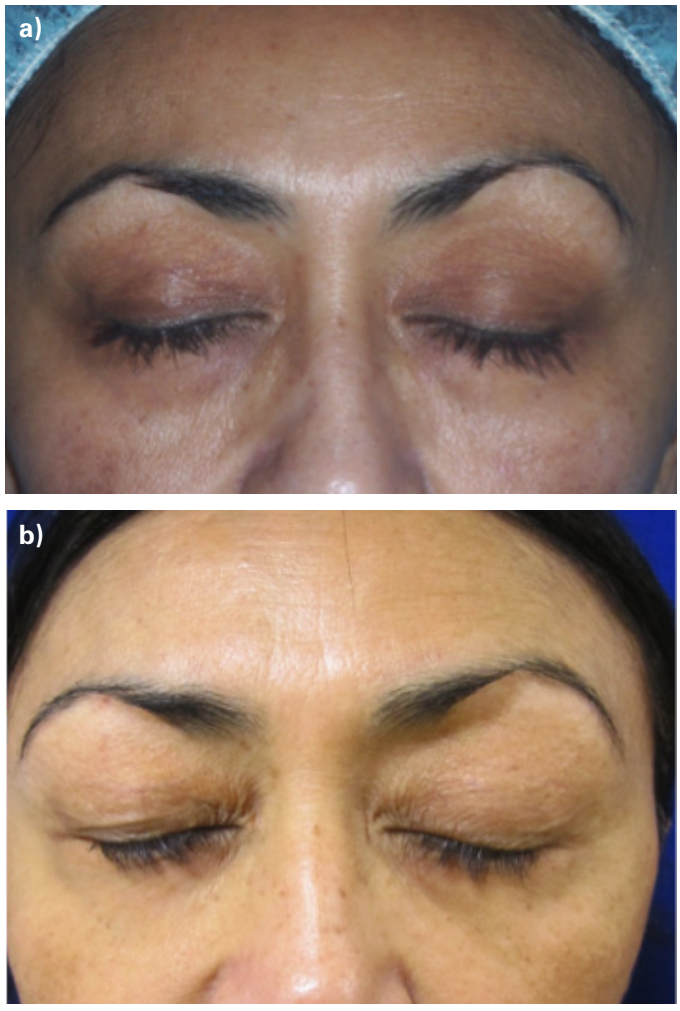
FIGURE 1. a) Patient at baseline with periorbital pigmentation; **b)** at 14 weeks after three treatments at 4 week intervals using a fractionated 1550-nm erbium-doped fiber laser. While not completely treated, there is a decreased darkness of both upper and lower eyelid. In addition she exhibits an observed decrease in suborbital skin laxity depth of her lateral rhytids.



CASE 2

A 58-year-old Asian female, Fitzpatrick skin type 4 (Roberts Skin Type F4/H2/G2/S2), reported progressive darkening of the skin around her eyes and cheeks. She had a significant past medical history for Melasma but reports eyelid darkening ten years prior. She was also on HRT. On presentation, she had significant bilateral confluent brown patches periorbital patches that were bilateral and symmetrical involving both upper and lower eyelid. She had mild skin laxity and a mild tear trough deformity (Figures 2A and 2B). In addition to discontinuing her HRT in consultation with her Primary care she was counseled about using SPF daily and she underwent 3 x 30% Salicylic acid peels at 3 week intervals.

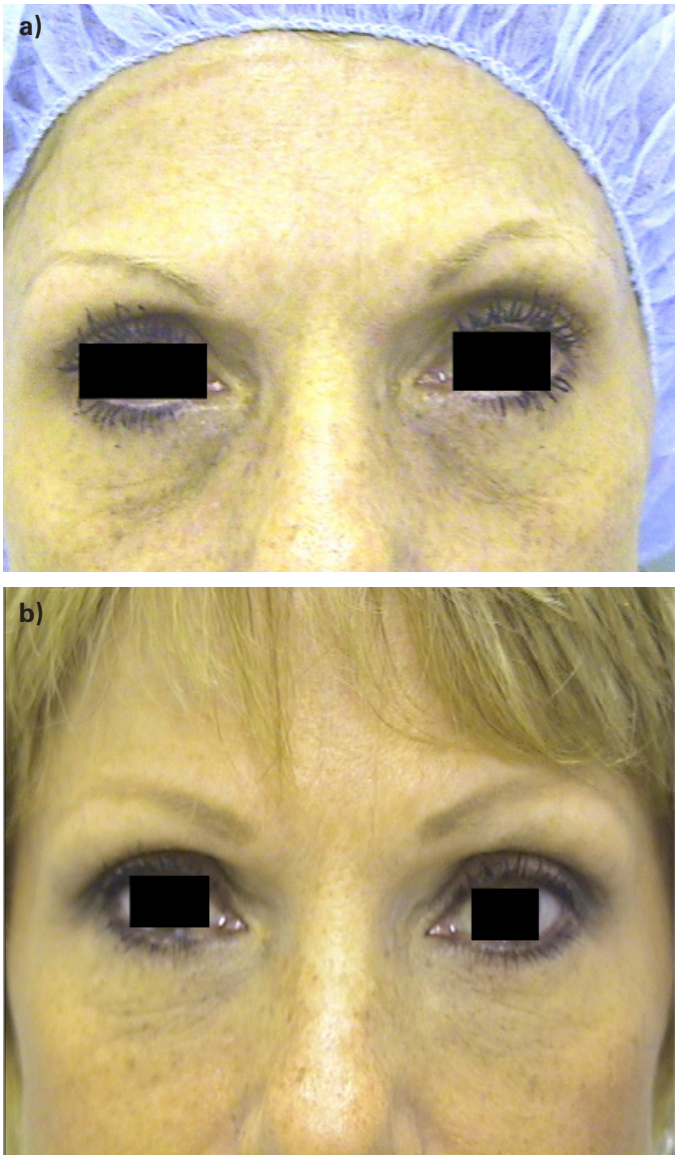
FIGURE 2. a) Patient at baseline with periorbital pigmentation; **b)** at 12 months after three Salicylic chemical peel one treatment every four weeks resulting in a significant decrease in pigmentation of both the upper and lower eyelid.



CASE 3

A 44-year-old Caucasian female, Fitzpatrick skin type 2 (Roberts Skin Type F2/H1/G2/S1), reported progressive darkening and sagging of her suborbital skin that was making her look drained and tired. She had no significant past medical history. She had used various undereye creams with no success. On presentation, she had significant mid facial descent, fat herniation skin laxity and suborbital hyperpigmentation. Tear trough deformity was present (Figure 3A). Because of the mid face aging poly-lactic acid 1 vial per session for 2 sessions at 4 week intervals. PLLA dilution with 6 cc of distilled water and 2ccs 1% Lidocaine for a total dilution of 8 cc was injected into the mid face.

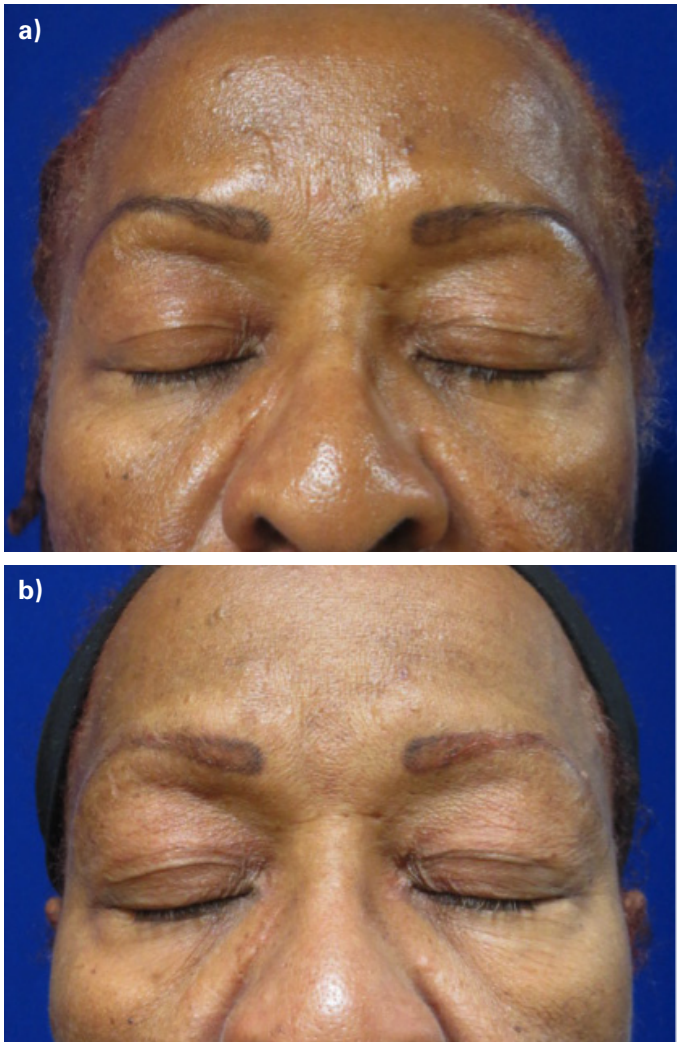
FIGURE 3. a) Patient at baseline with suborbital pigmentation; **b)** and at 4 months after two sessions of mid face PLL A injection 1 vial every every four weeks for a total of two vials resulting in a significant decrease in suborbital skin laxity and pigmentation.



CASE 4

A 58-year-old African American female, Fitzpatrick skin type 5 (Roberts Skin Type F5/H3/G3/S2), who presented with complaints of darkening skin globally but reporting she felt "especially tired around the eyes". Her occupation was in school transportation and she was outside every day with no sun protection. She also reported 5 hrs or less of sleep per night. On physical examination she had severe mid facial descent also with a significant tear trough deformity and suborbital shadowing.Though this patient would be an excellent candidate for mid face filling she was not amenable to this and just wanted to look more refreshed until the school year was out. Her first line treatment was microdermabrasion that gave her no downtime and did not pose a risk for her daily exposure to sun. She was also started on a routine daily SPF 30, foundation mineral makeup and counseled to get more sleep. At 2 months she noted an increased luminosity and eveness to her skin with decreased pigmentation of her face globally which included the undereye area. This case demonstrates how simple counseling in skin care may improve the appearance of some cases of POH.

FIGURE 4. a) Patient at baseline with suborbital pigmentation with prominent tear trough deformity; **b)** at 2 months after four microdermabrasion sessions, increasing her sleep to 7 hours per night instead of 5 hours.

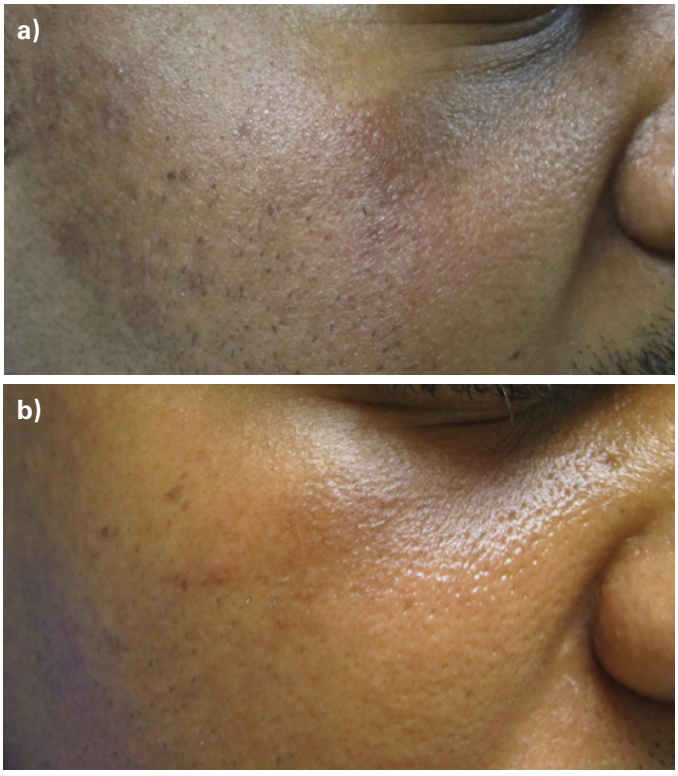


CASE 5

A 27-year-old African American Male, Fitzpatrick skin type 5 (Roberts Skin Type F5/ H 1/ G1/ S3) presents with an unknown history of increasing hyperpigmentation of the right suborbital area. He had a positive history for atopy and had used a variety of unknown products to treat the hyperpigmenta-

tion. He presented with a dark blue/grey patch involving the right suborbital area. The etiology of his infraorbital pigmentation was diagnosed as PIH. His first line treatment was two treatments with fractional photothermolysis with 1550-nm fractionated erbium-doped fiber laser (Fraxel Restore, Solta Medical, Haywood, CA). This was followed by four weeks of once nightly application of triple combination bleaching agent containing Fluocinolone acetonide 0.01% , 4% Hydroquinone, .05% Tretinoin (Triluma, Galderma, Houston Texas).

FIGURE 5. a) Patient at baseline with Right cheek infraorbital pigmentation; **b)** at 12 weeks after two fractional laser sessions and 2 weeks of Triluma.



DISCUSSION

Treatment Options

POH remains a complex entity. While we have excellent randomized controlled studies looking at treatments for periorbital rejuvenation primarily for the elimination of rhytids and facial hyperpigmentation; there is a lack of evidence based studies for the treatment of POH. We do have excellent case reports, use studies, large global patient studies and anecdote to guide us in making safe and efficacious clinical treatment plans.

CONCLUSION

Periorbital Hypermelanosis is a complex entity with a multifactoral etiology and an expanding knowledge base. It is most often observed in darker races and may be considered to be normal variants of pigmentation. There is most likely a familial component as it may be seen in family members over generations. Though patients are distressed and usually seek medical attention because of their appearance it is not strictly a cosmetic issue and may be a sign for underlying health issues. POH has specific histology and may be a final common clinical pathway of dermatitis, allergy, sleep disturbances or nutritional deficiences that lend itself to medical, surgical and cosmeceutical treatments. A complete medical history with ROS and Physical Examination is encouraged prior to treating the aesthetic component. Sun protection is a cornerstone of therapy. Cosmetic camouflage may be used during treatment. Procedural and surgical treatments may improve the appearance of POH. Safety issues are of utmost concern when embarking upon treatments such as chemical peeling, filler injection, and laser therapy as not to worsen the pigmentation. Without intervention POH usually progresses over time so early intervention and management is encouraged.

DISCLOSURES

The author has not disclosed any relevant conflicts. Wendy E. Roberts is a consultant/speaker/advisor for the following companies for Allergan, Kythera, La Roche Posay, L'Oreal, MelaScience, Neostrata, SkinMedica, Top MD, Theraplex, and Valeant.

REFERENCES

1. Epstein JS. Management of infraorbital dark circles. *Arch Facial Plast Surg.* 1999;1:303–9.
2. www.census.gov
3. PubMed Central® www.ncbi.nlm.nih.gov/pubmed
4. http://search.aol.com/aol/search?enabled_terms=&s_it=client97_searchbox&s_chn=tt_unauth&q=treatment+periorbital+pigmentation
5. Maruri CA, Diaz LA, Dark Circles around the eyes. Cutis 1969;5:979
6. Cestari T, Freitag FM, Cestari TF. What causes dark circles under the eyes? *J Cosmet Dermatol.* 2007;6:211–5.
7. Grimes, PE. Aesthetic and Cosmetic Surgery for Darker Skin Types. 2007 Lippincott.
8. Mashood AA. Treatment of hyperpigmentation disorders. *J Pakistan Assoc Dermatol.* 2006;16-65.
9. Gendler EC Treatment of Periorbital hyperpigmentation. *Aesth Surg J.* 2005;25:618.
10. Gathers RC Dermatology For Skin of Color p.341-343 McGraw Hill-2009
11. Alsaad S, Mikhail M Perioccular Hyperpigmentation: A Review of Etiology and Current Treatment Options. *J Drugs Dermatol.* 2013;12(2):154-157
12. Hirmand H. Anatomy and nonsurgical correction of the tear trough deformity. *Plast Reconstr Surg.* 2010;125(2):699-708.
13. Goodman RM, Belcher RW. Periorbital hyperpigmentation. An overlooked genetic disorder of pigmentation. *Arch Dermatol.* 1969 Aug;100(2):169-74.
14. Gupta MA, Gupta AK. Dissatisfaction with skin appearance among patients with eating disorders and non-clinical controls. *Br J Dermatol.* 2001;145:110-3.
15. Landeck L, Schalock PC, Baden LA, Gonzalez E. Periorbital contact sensitization Am J Ophthalmol. 2010 Sep;150(3):366-370
16. Sarkar R. Idiopathic cutaneous hyperchromia at the orbital region or periorbital hyperpigmentation. *J Cutan Aesthet Surg.* 2012 Jul;5(3):183-4.
17. Verschoore M, Gupta S, Sharma V, Ortonne JP. Determination of Melanin and Haemoglobin in the Skin of Idiopathic Cutaneous Hyperchromia of the Orbital region (ICHOR): A Study of Indian Patients. *J Cutan Aesthet Surg.* 2012 Jul-Sep; 5(3): 176–182.
18. Malakar S, Lahiri K, Banerjee U, Mondal S, Sarangal S. Periorbital melanosis is an extension of pigmentary demarcation line-F on face. *Indian J Dermatol Venereol Leprol.* 2007;73:323–5.
19. Ranu H, Thng S, Goh BK, Burger A, Goh CL. Periorbital hyperpigmentation in Asians: an epidemiologic study and a proposed classification. *Dermatol Surg.* 2011 Sep;37(9):1297-303.
20. Huang YL, Chang SL, Ma L, Lee MC, Hu S. Clinical analysis and Classification of dark eye circle. *Int J Dermatol.* 2014 Feb 53(2) 164-70.

21. Roh MR, Chung KY. Infraorbital dark circles: definition, causes and treatment options. *Dermatol Surg.* 2009;35(8) 1163-1171.
22. Haddock NT, Saadeh PB, Boutros S, Thorne CH. The tear trough and lid/cheek junction:anatomy and implications for surgical correction. *Plastic Reconstr Surg.* 2009;123(4): 1332-1340.
23. Espinoza GM, Holds JB. Evaluation and treatment of the tear trough deformity in lower blepharoplasty. *Semin Plast Surg.* 2007 February; 21(1): 57–64.
24. Bickers DR, Athar M. Oxidative stress in the pathogenesis of skin disease. *J Invest Dermatol.* 126:2565-75 2006.
25. Watanabe S, Nakai K, Ohnishi T. Condition known as "dark rings under the eyes" in the Japanese population is a kind of dermal melanocytosis which can be successfully treated by Q-switched ruby laser. *Dermatol Surg.* 2006; 32:785–9.
26. Graziosi AC, Quaresma MR, Michalany NS, Ferreira LM.Cutaneous idiopathic hyperchromia of the orbital region (CIHOR): a histopathological study. *Aesthetic Plast Surg.* 2013 Apr;37(2):434-8. doi: 10.1007/s00266-012-0048-2.
27. Kolde G, Schmollack KP, Sterry W. Periorbital hyperpigmentation. Bilateral nevus of Ota. *Hautarzt.* 2001 May; 52(5):460-3.
28. Ing EB, Buncic JR, Weiser BA et al. Periorbital hyperpigmentation and erythema dyschromicum perstans. *Can J Ophthalmol.* 1992 Dec;27(7):353-5.
29. Manaloto RM, Alster TS. Periorbital rejuvenation: a review of dermatologic treatments. *Dermatol Surg.* 1999;25:1–9.
30. Berson DS, Cohen JL, Rendon MI, Roberts WE, Starker I, Wang B. Clinical role and application of superficial chemical peels in today's practice. *J Drugs Dermatol.* 2009 Sep;8(9):803-11.
31. Vavouli C, Katsambas A, Chemical peeling with trichloroacetic acid and lactic acid for infraorbital dark circles. J Cosmet Dermatol. 2013 Sep;12(3):204-9.
32. Roberts WE. The Roberts Skin Type Classification System. *J Drugs Dermatol.* 2008 May;7(5):452-6.
33. Roberts WE Skin type classification systems old and new. *Dermatol Clin.* 2009 Oct;27(4):529-33.
34. Trelles MA Sight lost after lower lid laser blepharoplasty. *Ann Plast Surg.* 2000 Dec;45(6):678-9.
35. Lee WW, Murdock J, Albini TA et al. Ocular damage secondary to intense pulse light therapy to the face. *Ophthal Plast Reconstr Surg.* 2011 Jul-Aug;27(4):263-5.
36. Momosawa A, Kurita M, Ozaki M, Miyamoto S, et al. Combined therapy using Q-switched ruby laser and bleaching treatment with tretinoin and hydroquinone for periorbital skin hyperpigmentation in Asians. *Plast Reconstr Surg.* 2008;121:282–8.
37. West TB, Alster TS. Improvement of infraorbital hyperpigmentation following carbon dioxide laser resurfacing. *Dermatol Surg.* 1998 Jun 24 (6) 615-6.
38. Tierney EP, Hanke CW. Review of the literature: Treatment of dyspigmentation with fractionated resurfacing. *Dermatol Surg.* 2010 Oct;36(10):1499-508.
39. Mansukiatri W, Fitzpatrick RE, Goldman MP treatment of Facial skin using combinations of Co2, Q-switched alexandrite, flash-pumped pulde dye, and Er:YAG lasers in the same treatment session. *Dermatol Surg.* 2000; 26: 114-20.
40. Moody MN, Landau JM, Goldberg LH, Friedman PM. Fractionated 1550-nm erbium-doped fiber laser for the treatment of periorbital hyperpigmentation. *Dermatol Surg.* 2012 Jan;38(1):139-42.
41. Manstein, D, Herron GS, Sink RK, Tanner et al. Fractional phothermolysis: a new concept for cutaneous remodeling using microscopic patterns of thermal injury. *Lasers Surg Med.* 2004;34:426-38.
42. Sherling M, Friedman PM, Adrian R, Burns AJ et al. Consensus recommendations on the use of an erbium-doped 1,550 nm fractionated laser and its applications in dermatologic laser surgery. *Dermatol Surg.* 2010;36:461-9.
43. Ruiz- Esparza J. Noninvasive lower eyelid blepharoplasty: a new technique using nonablative radiofrequency on periorbital skin. *Dermatol Surg.* 2004 Feb;30(2 Pt 1):125-9.
44. Sukal SA, Geronemus RG. Thermage: the nonablative radiofrequency for rejuvenation. *Clin Dermatol.* 2008 Nov-Dec;26(6):602-7.
45. Carruthers J, Rzany B, Sattler G, Carruthers A. Anatomic guidelines for midface volumetric augmentation. *Dermatol Surg.* 2012;38:1223–33.
46. Sadick NS, Bosniak SL, Cantisano-Zilkha M, Glavas IP, Roy D. Definition of the tear trough and the tear trough rating scale. *J Cosmet Dermatol.* 2007;6:218–22.
47. Matarasso SL, Carruthers J, Jewell ML, Restylane Consensus Group. Consensus recommendation for soft-tissue augmentation with nonanimal stabilized hyaluronic acid (Restylane). *Plast Reconstr Surg.* 2006;117:3S-34S.
48. Sattler G. The tower technique and vertical supraperiosteal depot technique: Novel vertical injection techniques for volume-efficient subcutaneous tissue support and volumetric augmentation. *J Drugs Dermatol.* 2012;11:45-7.
49. Sharad J. Dermal fillers for the treatment of tear trough deformity: a review of anatomy, treatment techniques, and their outcomes. *J Cutan Aesthet Surg.* 2012;5(4): 229–238.
50. Rzany B, Becker-Wegerich P, Bachmann F, Erdmann R, Wollina U. Hyaluronidase in the correction of hyaluronic acid-based fillers: a review and a recommendation for use. *J Cosmet Dermatol.* 2009 Dec;8(4):317-23.
51. Ciuci PM, Obagi S. Rejuvenation of the periorbital complex with autologous fat transfer: current therapy. *J Oral Maxillofac Surg.* 2008 Aug;66(8):1686-93.
52. Tonnard PL, Verpaele AM, Zeltzer AA. Augmentation blepharoplasty: a review of 500 consecutive patients. *Aesthet Surg J.* 2013 Mar;33(3):341-52.
53. SBruce Safety and efficacy of a novel multimodality hydroquinone-free skin brightener over six months. J Drugs Dermatol. 2013 Mar;12(3):S27-31
54. Fabi SG, Goldman MP. Comparative study of hydroquinone-free and hydroquinone-based hyperpigmentation regimens in treating facial hyperpigmentation and photoaging. *J Drugs Dermatol.* 2013 Mar;12(3):S32-7.

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