Periocular Pigmentation: Overcoming the Difficulties

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Abstract
Periocular pigmentation is bilateral, round, homogeneous macules especially on the infraorbital regions. Despite its prevalence, there are few published studies about dark circles and its pathogenesis. Possible causative factors of the dark circles include excessive pigmentation, periorbital edema, thin-translucent lower eyelid skin overlying the orbicularis oculi muscle; and shadowing due to skin laxity and tear trough. A clinical approach to the treatment of periocular pigmentation should include identification and therapeutic targeting of each contributing etiologic factor for an individual patient. Treatment modalities, both monotherapy and in combination, have been used for periocular hyperpigmentation. They include bleaching creams, topical retinoic acid, chemical peels, laser therapies, injectable fillers, fat transfer and surgery.

Keywords: Periocular pigmentation; Monotherapy; Periorbital edema; Infraorbital regions

Introduction
Periocular pigmentation is also known as periorbital hyperpigmentation, dark circles and dark rings and defined as bilateral, homogeneous macules especially on the infraorbital regions. Dark circles give the patient a tired, sad or hangover look [1]. It is a common condition that occurs in both sexes with an increasing frequency in females [2]. The extent of the problem is reflected in the sheer number of products advertised to either lighten or cover the pigmentation [1]. Despite its prevalence, there are few published studies about dark circles and its pathogenesis [3].

Etiology
The etiology of periocular pigmentation may be multifactorial with no etiologic agent predominating. First, the patient should be medically evaluated not to miss underlying systemic disease or lifestyle incompetence that can be corrected (Table 1) [2].

Periocular pigmentation is more pronounced in certain ethnic groups and also frequently seen in multiple members of the same family [3]. Possible causative factors of the dark circles include excessive pigmentation, periorbital edema, thin-translucent lower eyelid skin overlying the orbicularis oculi muscle; and shadowing due to skin laxity and tear trough.

Excessive pigmentation is seen in such conditions as dermal melanocytosis and postinflammatory hyperpigmentation secondary to atopic or allergic contact dermatitis [1-3]. Atopic dermatitis and allergic contact dermatitis are frequent causes of chronic rubbing around the eyes. Chronic rubbing will lead to exuberative pigmentation and appearance of dark circles around the eyes [1].

Dermal melanocytosis is due to congenital and environmental causes, including several benign pigmented lesions that are histologically characterized by the presence of melanocytes in the dermis. Of the dermal melanocytic lesions that can appear on the face, nevus Ota usually present at birth. Clinically, dermal melanocytoses are gray or blue-gray in color as a consequence of the color transmission of black pigment through the dermis. If they are located infraorbitally, they can be cause of dark circles under the eyes [4]. Watabane et al., studied periorbital biopsies of 12 Japanese patients with dark circles and found that all patients had dermal melanosis in the history. According to study, the melanosis can be interpreted as dermal melanocytosis based on the findings of anti-S100 protein and Masson-Fontana silver staining’s. Differentiation of dermal melanostasis relies on clinical features because the histopathologic findings are similar in most forms [5]. Environmental causes that result in dermal melanocytosis include excessive sun exposure and drug ingestion [4].

The eyelid region seems to have a ‘sponge’ property that helps the accumulation of fluid in systemic or local edema situations. Diagnostic features that suggest eyelid fluid deposit include its worsening in the morning or after a salty meal, the purplish color, and the undefined contours of the regional fat complements [6].

Another common cause of infraorbital dark circles can be thin, translucent lower eyelid skin overlying the orbicularis oculi muscle. The orbicularis oculi muscle lies right beneath the skin, with little or no subcutaneous fat, and the darkness may be due to the visible prominence of the subcutaneous vascularplexus or vasculature contained within the muscle. This condition usually involves the entire lower eyelids, with a violaceous appearance consistent with prominent blood vessels covered by a thin layer of skin. The violaceous appearance is more prominent in the inner aspect of the lower eyelids and is usually accentuated during menstruation [4].

Another cause of infraorbital dark circles is shadowing due to skin laxity and tear trough associated with aging [4]. Skin laxity due to phagocytic imparts a shadowing appearance on the lower eyelids that results in infraorbital dark circles. Tear trough is a depression centered over the medial side of the inferior orbital rim. It is also an age-related change due to the loss of subcutaneous fat with thinning of the skin over the orbital rim ligament that confers hollowness to the orbital rim

| Family history | Possible extension of pigmentary demarcation lines |
|----------------|---------------------------------------------------|
| Environment and occupation | UV component, Contact dermatitis |
| Medical history | History of allergy, atopy, thyroid disease, Addison’s disease, anemia, nutritional status |
| Medications/supplement history | Estrogens, NSAID |
| Topical product history | Hydroquinone overuse |

Table 1: Evaluation of Periorbital Hyperpigmentation [2].

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area [7]. The condition aggravates with the eyelid and midface aging because of the loss of subcutaneous fat with thinning of the skin over the orbital rim ligaments that, combined with cheek descent, confer a hollowness aspect to orbital rim area. Combination of the hollowness and the overlying pseudoherniation of the infraorbital fat accentuate the shadow in the tear trough depending on the lighting conditions [4].

There are many disorders that may mimic or be associated with periorcular pigmentation (such as Acanthosis nigricans, melasma, Erythema dyschromicum perstans, fixed drug eruption, ecchymosis, amyloidosis, dermatomyositis). Because this may be a special opportunity to diagnose an underlying health issue prior to formulating a treatment plan [2].

**Treatment Options**

A clinical approach to the treatment of periorcular pigmentation should include identification and therapeutic targeting of each contributing etiologic factor for an individual patient [2]. Periorcular pigmentation is often refractory to treatment. Treatment modalities, both monotherapy and in combination, have been used for periorcular hyperpigmentation. They include bleaching creams, topical retinoic acid, chemical peels, laser therapies, injectable fillers, fat transfer and surgery.

**Topical Applications**

Topically applied products are by far the most convenient way to start with for the majority of patients [1]. Despite the great number of available topical medications and creams, there are no evidence-based studies to support their use [3]. These cosmetics have thus generally been designed to improve blood circulation and/or reduce melanin. 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. 'Cocktail bleaching agents' have increased in popularity and each one has unique ingredients. These ingredients target different portions of the melanin cascade (Table 2) [2].

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 [2].

Vitamin C and derivatives (such as magnesium ascorbyl phosphate and sodium ascorbate) have a long history as topical lightening agents. They inhibit melanogenesis in human melanocytes, regulate collagen production and conceal the color of blood stasis. Ohshima et al., studied 14 subjects with dark circles of the lower eyelids and applied sodium ascorbate or ascorbic acid glucoside lotion for 6 months. They conclude that sodium ascorbate may improve dark circles by thickening the eyelid dermis and concealing dark coloration due to congested blood and there was no change in the melanin index [8]. In another study 57 patients with dark circles vascular and/or pigmentation applied gel formulation (2% phytosodium, 0.1% retinol, 0.1% vitamin C and E) twice a day for 8 weeks. The gel was fairly or moderately effective (47%), especially in hemostasis. Treatment also decreased wrinkles but pigmentation was not clearly removed [9].

Sahni ve Kassir presented a case of a 48-year-old man (skin phototype IV) with significant idiopathic periorbital melanosis had good response with combination micro-needling and serum containing active ingredients (12 sessions, every 2 weeks). There was 50–75% improvement in periorbital melanosis after 4 sittings and 75–90% improvement after 12 sittings, as assessed by 2 independent physicians [10].

**Chemical Peels**

While chemical peeling has been used to treat a variety of facial pigmented disorders, there are no randomized-control studies on the efficacy of chemical peeling for the treatment of periorcular hyperpigmentation. The peeling agents remove melanin from the stratum corneum and epidermis. Deep peels may remove melanin from dermis but may lead to dyspigmentation and scarring. In this area the skin is thin, so deep peels are not recommended [2]. Vavouli and Katsambas applied chemical peeling with TCA and LA to 30 patients with periorcular pigmentation (and skin types III, IV and V). Chemical peeling (TCA 3.75% and lactic acid 15%) was performed every week for four treatments, four layers of the peel were applied to each infraorbital area in the same session and total time for a single session was 8–11 minutes. Almost all the patients showed significant improvement (23.3% excellent improvement, 46.7% good, 26.7% fair, 3.3% poor) [11].

**Lasers**

In recent decades, lasers have increasingly been used in cosmetic dermatology. Periorcular pigmentation due to excessive pigmentation have been successfully treated with various pigment lasers, including the Q-Switch ruby (694-nm) laser, Q-Switch alexandrite (755-nm) laser and Nd:YAG (1,064) laser [3]. Watabane et al., treated 5 cases, who have dermal melanosis histologically, with Q-Switch ruby laser (694 nm) with a pulse width of 30 ns and fluences of 6.0 to 7.0 j/m² 1 to 5 treatments and 4 patients showed good response [5]. Lowe et al. treated 17 patients with 1 to 2 sessions Q-switch (694 nm) laser with a pulse width of 28 nanosecond and fluences of 7.5 J/cm². The result is 23.5% of those treated once achieved a response greater than 50%, of those treated twice, 88.9% achieved a response greater than 50% [12]. Mamossawa et al., performed a study on periorcular pigmentation with combination treatment using a Q-switch ruby laser and bleaching agents. 18 patients underwent initial topical bleaching treatment with tretinoin aqueous gel and hydroquinone ointment for 6 weeks, followed by a Q-switch ruby laser. After the treatment seven of 19 patients (38.9%) showed excellent clearing, and eight (44.4%) were rated as good [13].

Safety should be emphasized when treating periorcular pigmentation with lasers, because the eye is particularly vulnerable to laser injury. Therefore, use of proper eyewear (such as eyeshields) is crucial [4]. Inappropriate use of laser in this area may result in eye problems including blindness, dryness and photophobia. Importantly IPL is not indicated for the treatment of periorcular pigmentation. The pigmented iris absorbs light in the same wavelength range of IPL. The IPL when applied to the periorcular area is absorbed by the pigment of the iris and can result in severe eye damage that may include photophobia, pain, and anterior uveitis [14].

| Skin Lightener                          | Gold standard         |
|----------------------------------------|-----------------------|
| Skin turnover accelerator              | Hydroxy acid, retinoic acid |
| Premelanin synthesis                   | Tretinoin             |
| Tyrosinase transcription               |                       |
| During melanin synthesis               | Hydroquinone, Azelaic, Kojic, Arbutin, Soy, Mushroom, Peptide |
| Tyrosinase inhibition                  |                       |
| Postmelanin synthesis                  | Linoleic acid         |
| Tyrosinase degradation                 |                       |
| Postmelanin synthesis                  | Soy, Niacinamide      |
| Melanosome transfer inhibition         |                       |
| Antioxidants                           | Vit C interacts with copper ions to reduce dopaquinone |

Table 2: Mechanism of Action of Skin Bleaching Agents [2].

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Skin laxity and tear trough are age-related changes, and these changes can be treated with ablative/non-ablative lasers and surgical methods (injection hyaluronic acid/fat or blepharoplasty) [4]. West et al., treated 12 patients with Carbon dioxide Laser Resurfacing. Clinical grades ranged from 1 to 4, with an average score of 2.5, corresponding to approximately 50% improvement and no melanin correlation [15]. Moody et al., reported one case of Fitzpatrick II female diagnosed with periocular pigmentation who underwent four nonablative laser treatments spaced out at 4 week intervals with 1550 nm fractionated erbium-doped fiber laser (15 mm spot, 70 J/cm²) over a 4 month period. Two months after the last treatment the physician and patient noted significant improvement [16].

**Autologous Fat Transplantation and Injectable Filler**

The therapeutic modality for violaceous appearance (little or no subcutaneous fat) is to restore the volume underneath for eyelid using autologous fat transplantation or soft tissue fillers. Roh et al., treated 10 patients with infraorbital dark circles due to increased vascularity and translucency of the skin. They received at least one autologous fat transplantation, and follow-up evaluations were conducted at least 3 months after the last treatment. An average of 1.6 autologous fat transplantation were done in both infraorbital areas. Patients showed an average of 78% improvement [17].

Hyaluronic acid gel has been used with success as filler for three-dimensional reshaping of the periorbital complex [18-20]. Steinsapir et al., reported a 2 year experience of treating the naso-jugal groove with injectable hyaluronic acid gel. 164 patients received 303 sessions hyaluronic acid gel filler to address the naso-jugal groove. The mean dose of filler per session was 1.53 ± 0.8 ml, with 0.84 ± 0.38 ml divided between the two lower eyelids. Average improvement was rated 2.8 ± 0.7 out of 4 by a blinded observer [21].

**Conclusion**

Periorbital pigmentation is a complex entity with multifactorial etiology. There is a lack of evidence based studies for the treatment. It is important to identify the specific anatomic problem of each patient in order to tailor treatment. If periorcular pigmentation is mainly due to excessive pigmentation, the dermal pigmentation should be removed with treatment such as topical bleaching agent, chemical peels and laser. Periorcular pigmentation mainly due to the skin laxity and tear trough can be treated with ablative/non-ablative lasers and surgical methods (injection hyaluronic acid/fat or blepharoplasty). The therapeutic modality for violaceous appearance is to restore the volume underneath for eyelid using autologous fat transplantation or soft tissue fillers. Sun protection is a cornerstone of therapy. Cosmetic camouflage may be used during treatment.

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