Journal of Dermatology and Therapies (JDT)

HENDUN RESEARCH ACCESS

Research Article

News in the Treatment of Periorbital Hyperpigmentation

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Definition

Periorbital hyperpigmentation is a common complaint amongst men and women, young and elderly worldwide. It is known also as dark circles around eyes, periorbital dyschromia, periocular hyperpigmentation, periorbital melanosis, infraorbital darkening and infraorbital hyperpigmentation.

Due to the central localization of eyes in the face periorbital hyperpigmentation is most noticeable and a great percentage of patients seeking medical assistance.

Though not life threatening, POH has noticeable negative impact on the self-esteem of patients.

Causative Factors

Periorbital hyperpigmentation is multifactorial in etiology. It is caused by various endogenous and exogenous factors. Genetic factors are common causative factors. Anemia, stress, aging, dermal melanin deposition, post inflammatory hyperpigmentation due to atopic or contact dermatitis are other known causative factors [1]. Some systemic diseases and faulty habits can cause periorbital hyperpigmentation. Periorbital aedema and prominent superficial vasculature are other causes of periorbital hyperpigmentation.

Classification (Huang, et al.):

Periorbital hyperpigmentation is classified according to Huard et al to four types based on clinical pattern of hyperpigmentation and Vasculature;

1. Pigmented type (brownish color).
2. Vascular type (blue, pink or purple).
3. Mixed type.
4. Structural type (an anatomical shadowing, skin color) [2].

A scoring system with nine parameters, including brown hue, pigmented lesions, blue/pink/purple hue, periorbital puffiness, shadow hue, infraorbital palpebral bags, infraorbital grooves, blepharoptosis, and skin type, was used for clinical evaluation [2].

Classification (Ranu, et al.):

Periorbital hyperpigmentation is classified according to Ranu et al into five categories based on the causative factors [3];

1. Constitutional type: seen as typical brownish curved band on lower eyelid or both.

2. Postinflammatory type: irregular patches of brown or grey pigmentation on periorbital skin associated with features of lichenification or eczema. Family history may be positive.

3. Vascular type: erythema or prominent capillaries or telangectasia and sometimes bluish color.

4. Shadow effect type: tear trough and eye bags due to sagging skin around eyes.

5. Others: anemia, hormonal disturbances, nutritional deficiencies and chronic illnesses [3].

The commonest form of POH according to Ranu, et al. was the vascular type (41.8%), followed by constitutional (38.6%), postinflammatory hyperpigmentation (12%), and shadow effects (11.4%). The vascular type was seen predominantly in Chinese, whereas as the constitutional type was most common in Indians and Malays [3].

Epidemiology:

Constitutional type is the most commonly seen type (51.5% of patients) of which 42% are females and 9% males. Female predominance is evident in all types of POH [4].

Postinflammatory hyperpigmentation (PIH) is the second common type of POH (22.5% of patients) followed by the vascular type and the structural type (8% and 2.5% respectively) [4].

In another study, according to Huang et al classification, pigmented, vascular, structural, and mixed types of POH or dark eye circles (DEC) represented 5%, 14%, 3%, and 78% [2].

Lower eyelids hyperpigmentation is the most commonly seen form amongst patients in all four types of POH, constitutional (67%), Postinflammatory (64.4%), vascular (68.7%) and structural type (60%) [4].

Involvement of both eyelids, upper and lower, is the second common form seen (18.44- 31.25%); this form is more common in vascular type of POH (31.25%) [4].

The upper eyelid involvement alone is the least common of all types of POH and that is found only in constitutional type (2.9%) [4].

Demographic Features:

Periorbital hyperpigmentation is more commonly seen in females aged 16-25 years. 81 % of patients are females. POH is more common in housewives (45.5%), indoor workers (29% of patients) and students (19.5% of patients) [4].

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Received: August 06, 2017; **Accepted:** September 25, 2017; **Published:** September 29, 2017

Grading of POH:

POH is graded into four groups according to the severity of the case to be treated;

- Grade1: characterized by faint pigmentation of infraorbital region.
- Grade 2: pigmentation is more pronounced.
- Grade3: deep dark color, all four lids involved.
- Grade 4: grade 3 + pigmentation spreading beyond infraorbital fold.

Grade 2 is the most commonly seen type of periorbital hyperpigmentation (60.19% of constitutional type, 53.33% of PIH type, 68.75% of vascular type), while grade 1 POH is the most commonly seen type of structural type patients (60%) [3]. Grade 3 is the second commonly seen of all types of POH and grade 4 is the least seen [4].

Management and Treatment:

Classify to treat: Careful clinical examination and detailed history are the cornerstone of successful treatment.

Classification of the POH type is fundamental to optimal treatment for different types of POH respond to different types of treatment modalities.

"Classify to treat" is the piece of art in order to improve the treatment results.

Detailed classification of POH types will access physicians in the decision of appropriate therapeutic modalities [2].

Detailed history: Detailed history, family history, disease history and work history must be taken in details.

A good portion of patients have positive family history. 76.7% of patients of constitutional type and 62.5% of patients of vascular type have positive family history [4]. On the contrary, 71.1% of patients of PIG type and 100 % of patients of structural type have negative family history [4].

This constitutes a great help in classification of POH especially in mixed types and wherever physical examination alone does not help in differentiation.

Woods lamp & ultrasonographic examinations: Woods lamp examination is an essential part of good physical examination in POH patients. It is of great importance to determine the depth of the periorbital hyperpigmentation. Wood's lamp examination is done mainly to differentiate between epidermal and dermal hyperpigmentation. The variations of epidermal pigmentation become more apparent under wood's light whereas in dermal pigmentation this contrast is less pronounced [5]. No accentuation of pigment on wood's lamp examination means that the hyperpigmentation is dermal or vascular in origin [5]. Ultrasonographic evaluation can help differentiate between the vascular type of POH and periorbital aedema.

Skin stretch test: Manual stretching of the lower eyelid can help differentiate between true hyperpigmentation and shadowing effect due to tear trough. As the former retains its appearance with downward manual stretching, the problem improves or resolves entirely in tear trough. On the contrary, aggravated violaceous discoloration on manual stretching indicates that the hyperpigmentation is due to thin skin or subdermal hypervascularity of lower eyelid [6].

Histological Characteristics: One study was made on 100 patients, the aim of this study was to explore the nature of pigmentation in periorbital melanosis. Clinical examination, wood's lamp examination was done to all patients to determine the extent and depth of the periorbital hyperpigmentation. A 2-mm punch biopsy was carried out in 17 of 100 patients. In 92 (92%) patient's periorbital melanosis was an extension of pigmentary demarcation line over the face (PDL-F) [7]. Periorbital melanosis and pigmentary demarcation line of the face are not two different conditions; rather they are two different manifestations of the same disease [7]. Histological Characteristics of periorbital hyperpigmentation suggests that it can be both epidermal and dermal in nature [7].

Treatment:

1st line Treatment

Dew to multifactorial etiology of POH and the big role of many ophthalmic and systemic diseases in the occurance of dark circles around eyes, it is well established that successful treatment must irradicate known causative factors in the first place. Changing of one's lifestyle and faulty habits is considered to be relatively efficacious. Limitation of reading, computer use and TV watching to less than 8 hours a day is helpful. Sleeping well and cessation of smoking and alcohol consumption have positive effects. Ophthalmic disorders and errors of refraction (myopia…) must be corrected. Anemia and other systemic diseases must be treated.

Cosmetic use which is responsible for a great percentage of patients (36.9-60%) [4] must be illuminated to the minimum or changed to otherwise nonallergenic compounds. Eye rubbing must be minimized and dermatologic diseases like eczema, contact and atopic dermatitis must be treated. Stop causative drugs as some medicaments causes periorbital hyperpigmentation. Of these, Prostaglandins'analogues such as lanatoprost and bimatoprost, used as ocular hypotensive drops in patients with glaucoma can cause periorbital hyperpigmentation [8,9].

This hyperpigmentation is completely reversible on cessation of the drug [9].

Topical creams

A wide range of topical medicaments and cosmeceuticals are available worldwide with newer and newer versions every day promising miracles in the treatment of POH without any scientific evidence.

Topical depigmenting agents like hydroquinone 2-6 %, kojic acid 1-4%, azelaic acid, topical retinoic acid and vitamin C re used widely. Hydroquinone 4% is the most prescribed bleaching agent worldwide. Hydroquinone is unavailable now in Europe and Asia due to possible carcinogenicity. It is not admitted yet that hydroquinone is cancerogen in human beings, although large amounts of oral hydroquinone was reported to cause cancer in rodents [10]. It's important to know that the effect of treatment will need 5-6 months to become evident hence hydroquinone should be prescribed for at least 3 months [11].

Arbutin and kojic acid are effective alternatives. The mechanism of action of all bleaching agents is inhibition of tyrosinase enzyme, which inhibits the conversion of dopa to melanin thus leading to the reduction of melanin content in the epidermis.

Triple Combination Therapy

Triple Combination Therapy with fluocinolone acetonide 0.01%, hydroquinone (HQ) 4% and tretinoin 0.05%, has been shown to be safe and more effective for the treatment of melasma than the treatment with hydroquinone alone. Efficacy in Asians and patient satisfaction were superior with the fixed TC than with HQ 4% alone [11].

This triple combination therapy has been approved by the United States Food and Drug Administration as an effective treatment of melasma and other pigmentary disorders [12], however its long-term

use in the periorbital region is not allowed since it contains a topical steroid.

Is hydroquinone and tretinoin safe to use in the periorbital area?

This question is probably the most common question patients ask in the clinic. And the answer is yes.

Especially in the treatment of POH, it is one of the major components of a good treatment modality.

Hydroquinone has been used in many studies to enlighten the periorbital skin area alone or in combination therapy with lasers or peelings [13,14].

4% Hydroquinone versus 30% Salycilic acid

In a study done on 50 dermatologic outpatients with clinically evident POH, the patients were divided in to two groups one of which were treated with hydroquinone 4% and the other with Salyclic acid 30%.

Assesment with visual analogue scale (VAS) was done at 4,6 and 12 weeks. On VAS most of the patients showed mild improvement (10-30%) at 12 weeks of treatment in both groups. Separately, both treatments significantly improved the dermatological life quality index of the patients although there was no significant difference found between the two groups [13].

Chemical Peelings

Chemical peelings could be used alone or in combination therapy with topical treatments.

Glycolic acid 20% is the most commonly used peeling in the treatment of POH. Lactic acid 15% + TCA 3.75% combination was shown to be very effective in the treatment of POH [14]. This combination peeling therapy had only mild and temporary adverse effects, such as erythema, edema, frosting, dryness, and telangiectasias. The effects of treatment remained for at least 4-6 months in the majority of patients with appropriate sun protection [14].

Postinflammatory hyperpigmentation (PIH) is the most commonly seen side effect after most chemical peelings. PIH is minimized by the optimal pretreatment by tretinoin and hydroquinone for 2-4 weeks before peeling.

For optimum results it is advisable to extend the peeling to the entire face in medium to darker skin to avoid post-peel demarcation.

Combination Therapy: TCA10%+ microneedling

In one study, thirteen patients were treated with automatic Microneedle Therapy System-Handhold and topical application of 10% TCA solution to each infraorbital area for five minutes. Assessment rated a fair, good or excellent response in 92.3%. Microneedling and 10% TCA constitute an innovative combination treatment for DC with encouraging results and minor side effects [15].

Lasers:

Ablative Laser Resurfacing

1- Treats POH + skin laxity effectively.

2- mechanism of action: controlled tissue injury with resultant reparative

process.

3- Fractionated and nonfractionated CO2 and Erb: YAG lasers [16].

Q-switched ruby laser

1- Q-switched ruby laser (694 nm) (Fitzpatrick's skin types1-3).

2- 2- Q-switched Alexendrite laser (755 nm) (Fitzpatrick's skin types 4&5).

3- 3- Q-switched Nd Yag laser (1064 nm) (Fitzpatrick's skin types 5&6) [17,18].

In a histotological study done on Japanese people, all 12 patients (100%) were confirmed to be dermal melanocytosis using the Masson Fontana silver stain and that can be successfully treated by Q-switched ruby laser [19].

Low fluence or subthermolytic Q-switched treatment (1064 nm), is with less side-effects compared to traditional Q-switched lasers [20].

Lutronic dual pulsed Q-switched Nd YAG laser spectra is the first and only FDA approved one [20].

Low fluence Nd Yag laser (Lutronic)

- First and only FDA approved Q-switched Nd Yag laser for the treatment of melasma.
- Requires multiple treatments on weekly intervals.
- Requires more sessions compared to other lasers.
- High 3-month recurrence rate (64-81%).
- Combining low-fluence Q-switched lasers with long-pulsed Nd Yag laser or IPL may reduce recurrence rate [20,21].

Other Lasers:

1- Pulsed Dye Laser

2- Diode laser.

3- 1064 nm Nd: YAG laser.

4- 1320 nm Nd: YAG laser

5- 1540 erbium glass Laser.

6- Intensed Pulsed Light [21,22].

Combination therapy:

Multimodal therapy is used frequently to treat periorbital hyperpigmentation and known to be the best treatment method with best results and less side effects [23]. The new treatment protocol combining Q-switched ruby laser and topical bleaching treatment using tretinoin and hydroquinone is considered effective for improvement of periorbital skin hyperpigmentation, with a low incidence of postinflammatory hyperpigmentation [24].

Pusled dye laser

1- treatment of dark circles with vascular etiology.

2- Fitzpatrick skin types 1-3.

3- needs 3 or more sessions at 4-6 weeks interval [25].

Nonablative fractionated laser resurfacing

- Four NAFL wavelengths are used: 1330nm, 1540 nm, 1550 nm, 1927 nm [26].
- 1440 nm and 1550 nm penetrate to the mid-reticular dermis induce neocollagenesis [26].
- 1440nm is used to treat Nevus of Ota.
- Treats a wide range of skin types "including Fitzpatrick III to VI".
- Side effects: erythema, swelling and pain (3 -10 days).
- 4-6 sessions needed.
- 1927-nm NAFL laser, provides superficial resurfacing (depth:

200 microns) [27].

1927-nm NAFL laser

- First introduced in 2009.
- Maximum depth penetration 200 microns.
- Less side effects compared with other NAFL treatments.
- Long term efficacy.
- May offer good clearance of POH in a single treatment [27].

Ablating fractionating resurfacing lasers

- CO2 lasers (10,600 nm) and Er: YAG lasers (2940nm) commonly used ablative lasers.
- A fractionated approach decreases epidermal injury resulting in fewer side effects.
- Combined therapy of CO2 laser with long term topical lighting cream showed the greatest improvement.
- Er: YAG laser allows for more superficial ablation with minimal thermal damage.
- Used to treat POH, skin laxity, and wrinkling [28].

Hyaluronic Acid Injection:

Hyaloronic acid injections help to ree - dimensional reshaping of periodontal region.

1- Excellent tear trough contour improvement.

2- Under- eye dark circle improvement.

3- Treat prominent nasojunctial groove.

4- Patient satisfaction is high.

5- Side effects: minor erythema, bruising, Tendall effect, overcorrection [29,30].

Radiofrequency device:

1- Tightens the periorbital skin.

2- Collagen contraction and neocollagenesis due to RF thermal effect.

3- Treat dark circles due to shadowing and loose PO skin.

4- desirable choice if mild effects are desired with low risk profile [31].

Autologous Fat Transplantation

Treat hyperpigmentation due to thin and translucent lower eyelid skin with high satisfaction rate [32].

Blepharoplasty:

1 - Surgical correction of fat deposits or excess skin or both.

2- Transconjunctival or transdermal.

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