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C. Diehl
Universit Degli Studi Guglielmo Marconi, Rome, Italy

Dermo-cosmetic management of the periorbital complex

With the recent developments of highly technological dermo-cosmetics showing proofs of efficacy and safety, this category of products may be included in our recommendations to patients when they are concerned by skin aging and the appearance of their face. The periorbital complex is of particular relevance in this demand, as it is of major concern in the appearance of the whole face. Further, during the process of aging, the periorbital complex is often showing earlier signs of aging than other parts of the face. In this article, after a short summary about anatomy, we shall review the different signs of aging in this area, namely eyelid bags (EB), periorbital hyperpigmentation (POH), Crow's Feet (CF) and finally eye lashes. Eyelid bags may have different aetiologies, and this is not only important to know them, but also to know how to distinguish them, in order to be able to bring the most convenient treatment and recommendations for their management. About POH, it also constitutes a frequent complaint in dermatology and aesthetic medicine. It can also have different aetiologies and for this reason, a strict classification was established for POH, both of them leading to differentiated treatments based on these data. Crow's feet are also of importance, and often appear very early, being the first signs of face aging. To date exist efficient treatments for CF based on dermo-cosmetics, especially among the various bioactive peptides developed in the course of the last decade, but also vegetal active ingredients. Oral collagen may also be useful in this scope, when adequately prescribed. Finally, eye lashes, as they are considered an important aspect of the facial aesthetics, are the object of various beauty treatments to enhance them. They comprise the use of prostaglandins, efficient but accompanied by various side effects, and here also bioactive peptides, which represent a key stone in the dermo-cosmetic management of the periorbital complex.

Key words

Periorbital complex, aging, eyelid bags, periorbital hyperpigmentation, crow's feet, eyelashes, dermo-cosmetics, bioactive peptides.

1. INTRODUCTION

The periorbital complex is composed of bony structures surrounding the eye, upper and lower eyelids, eyelashes and eyebrows. This is a critical cosmetic unit, as it does interfere with the visual aspect of the face and may modify the aesthetics of one's facial presentation. For this reason, it constitutes an important dermatological and aesthetic concern for a long time. From the ancient times, the Egyptians were using dyes as a makeup for correcting the visual disorders in this area, and to date there are lots of invasive and non-invasive procedures aimed to this purpose. Among them dermo-cosmetic management of the periorbital complex is of importance and can help in the search for eternally young looking.

2. EYE-CONTOUR AGING

Eye contour aging may feature various symptoms at different anatomical levels.

In order to properly understand the phenomenon of eye contour aging, knowledge of the anatomical structures is necessary and understanding the causes of the symptoms are prerequisites for the aesthetic medical practitioner to select optimal treatment [1].

Anatomy design of the periorbital area

The face is classically divided into upper face, mid face and lower face (Fig. 1). The periorbital area is located at the limit of upper and mid face and also divided in three zones (Fig. 2).

The cheekbone, major osseous structure of the face, is constituted laterally by the zygomatic bone and in the front by the medial maxillary bone.

The whole periorbital area contains deep and superficial fat pockets. They are giving shape and volume to this area (Fig. 3).

The muscle orbicularis oculi is the most important muscle in the periorbital area and is divided into three parts: pars orbital, responsible of the

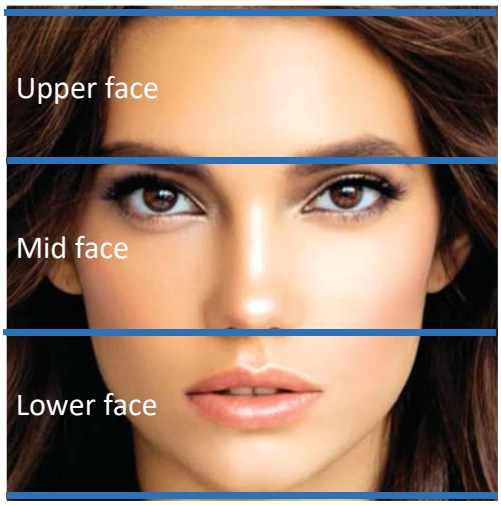

Fig. 1. **Zones of the face**

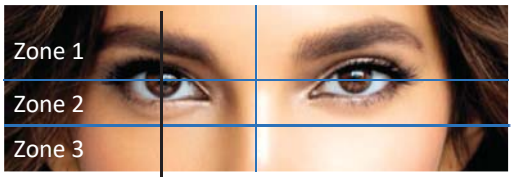

Fig. 2. **Zones of the periorbital complex**

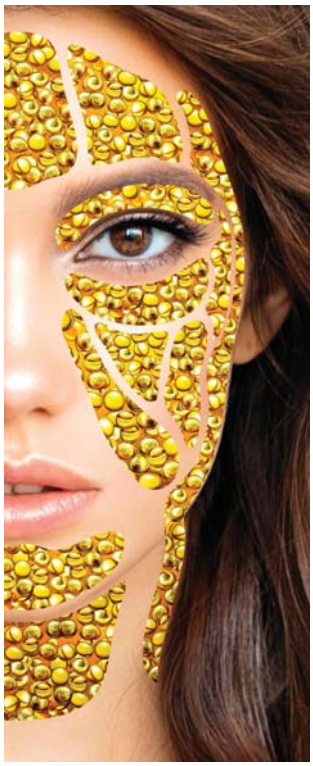

Fig. 3. **Fat compartments in the periorbital complex**

movements of the eyebrows, pars lacrimal compressing the sacculus lacrimal and pars palpebral permitting the movement of the eyelids (Fig. 4).

The aging process of periorbital area

The main causes of aging in the periorbital area are:

- First, there are significant changes in the bony structure of the periocular area.
  Shaw et al, by facial bone computed tomographic scans obtained from 60 female and 60 male Caucasian subjects, established that the orbital aperture width and orbital aperture area increased significantly with age for both sexes [2]. On the other hand, mandibular length and height both decreased significantly with aging for each sex. Bone resorption of frontal and zygomatic bones is also observed [1].

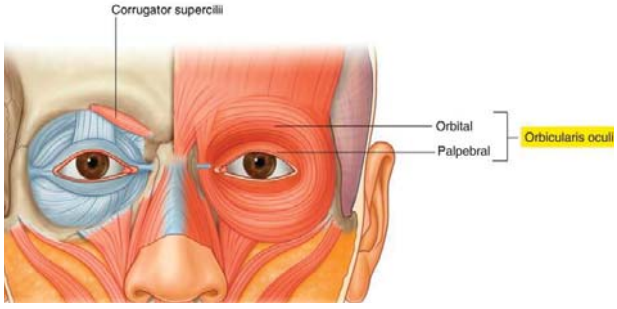

Fig. 4. **Musculature of the periorbital area**

- Significant changes in the soft tissue also occur. They manifest as loss of subcutaneous fat tissue to the forehead, brow, temple, and upper eyelid and atrophy of the temporal, frontal and periorbital fat compartments [1]. Overall eyebrow volume does not change with age, but the relative contribution of fat and soft tissue to the total volume does. As women age, the fat volume increases and the soft tissue volume decreases, whilst in men, the shift from soft tissue volume to fat volume is less pronounced [3].
- Pattern of muscles activity also dramatically changes from levators to depressors [1]. Hyperactivity of m. orbicularis, m. procerus, m. corrugator and m. depressor supercilii insupercilii are also noted in zone 1 [1].
- As a result, in many people, the brow descends with age and gets a flatter shape.
  The bony outline of the skull and supraorbital rims becomes more evident [1].
- Below (in zone 3) the superficial and deep fat pockets of the cheek get atrophic and slide to the mid face area [1]. Sagging of the periorbital fat causes tear through, although this can also be observed in younger subjects.
- Globally, the skin shows a decreased elasticity and hydration.

It must be noted that the chronologic aging process of the periorbital area may be aggravated by

both intrinsic and extrinsic factors. Among the first one, genetic predisposition is widely described. The most relevant extrinsic factor is the photodamage caused by excessive and/or prolonged sun exposure.

3. EYELID BAGS (EB)

Eye Bags (also named eye puffiness) are very common with aging and have different aetiologies.

Aetiology

First, EB may be the result of fluid retention, basically caused by impaired lymphatic drainage. Lifestyle factors also have a strong influence on their occurrence: stress, excess alcoholic intake, chronic lack of sleep, or insufficient moisture of the periorbital area. In addition, repeated treatments with Botulinum toxin A in the caudal part of the m. orbicularis oculi may lead to eye puffiness through reduction of the pump function of the orbicularis oculi together with underlying lymphatic network [1]. Excessive crosslinked hyaluronic acid injections in the malar are also susceptible of compressing the lymph pass, provoking the occurrence of eye puffiness [1]. EB may also occur due to sagging of the periorbital fat pockets caused by a weaker m. orbicularis oculus. This phenomenon may be observed at any age and is well known as tear through, giving a tired look and making the face seeming much older.

Dermo-cosmetic management of EB

The goal of a dermo-cosmetic treatment will be:

- Improving the blood microcirculation and the lymphatic drainage.
- Strengthen the blood capillaries.
- Prevent the degradation of haemoglobin (antioxidants).
- Strengthen and protect the supportive tissues in order to reduce the laxity and lack of elasticity of the skin.

Many active ingredients may enter in the composition of these dermo-cosmetic products [1]:

- Flavonoids: Troxerutin, Rutin, Naringin, Hesperidin Methyl Chalcone, Hesperidin.
- Saponins: Ruscogenin, Neoruscogenin, Escin.
- Polyphenols: Resveratrol, Viniferin, Coumarin.
- Trace element: Organic Silicium.
- Antioxidants: Vit C, Naringin, Resveratrol, Viniferin etc...
- Peptides: DipeptideVW, Peptide Pal-GQPR, Acetyl Tetrapeptide-5.

When these dermo-cosmetics are adequately formulated, they can give excellent and rapid results, as shown in Fig. 5 with a cream containing Acetyl Tetrapeptide-5 10 % applied during 14 days.

All the dermo-cosmetics used on the eye contour must be submitted by the company in charge of their marketing not only to skin tolerance tests, but also to ocular tolerance tests in order to avoid any side effect on the eyes.

4. PERIORBITAL HYPERPIGMENTATION (POH)

Also known as Dark Eye Circles (DEC) this is a very frequent complaint in dermatology and aesthetic medicine. It affects both genders and appears to be more frequent in certain ethnic groups. On the other hand, there is an evidence of a family character, with dominant autosomal inheritance and variable expression of the genes involved [4]. In 1962, Hunzinker2 described a family in which 10 of its members were affected by POH, including an 8-year-old girl [4]. Goodman et al [5] reported 22 individuals with POH, spanning six generations of a single family. Subsequently, they described three families, one with 11 members with POH, across two generations. In 1969, Maruri et al [6] described 20 affected individuals in three generations in another family. There are studies indicating a greater incidence of POH complaint among individuals with darker hair, eyes, and skin [7]. POH features bilateral round or semi-circular homogenous brown or dark brown pigmented macules in the periorbital region, with usually one periorbital region more affected than the other. It can affect either the upper or lower eyelid or both upper and lower [8].

Aetiology of POH

Multiple intrinsic and external factors may take part to the aetiology of POH, and no factor is predominating. Besides genetic predisposition which was already previously described, it was also observed that higher pigmentation was a predisposing factor for POH [7]. Others causes can be post-inflammatory hyperpigmentation following atopic and allergic contact dermatitis, periorbital swelling, excessive vascularity, shadowing secondary to skin laxity, and tear trough related to aging [8].

Classification of POH

When considering a treatment for POH, classification of the same is important to consider. Three authors [8—10] are coinciding on a classification based on 4 types.

For Ranu et al [9] are namely vascular, pigmented, constitutional and shadow effects.

Huang et al [10] described vascular, pigmented, structural, and mixed types, introducing subtypes in the latter. Finally, Fatin et al [8] coincided with Ranu's classification. Another interest of these

three studies was to establish the proportion of each type in cohorts of patients affected by POH. Twice [8, 9] the commonest type was the vascular one (respectively 51 and 41.8%) with only 14% in Huang's cohort, but this result was biased by the addition of subtypes (mixed types) where pigmented-vascular and three-combined (pigmented-vascular-structural) types accounted respectively for 37 and 26%. In any case, the last type is the pigmented one.

Classification of POH is not an easy task and needs adequate history taking, serious clinical examinations and proper investigations in order to propose the most suitable treatment to the patient [8].

Treatment of POH

Obviously, the treatment of POH will depend on its aetiology and classification.

For pigmented POH, treatment will be based on depigmenting agents such are Hydroquinone, arbutin, kojic acid, azelaic acid or vitamin C, In our practice, we had excellent results with topical tranexamic acid, because besides its depigmenting action, it also works on the vascular component of POH. This is the ideal therapy for mixed pigmented-vascular POH. Besides vascular lasers and intense pulsed light, vascular type can be successfully treated with topical vitamin K, but also vegetal active ingredients such as Troxerutin, Rutin, Naringin, Hesperidin Methyl Chalcone, Hesperidin, Ruscogenin, Neoruscogenin or Escin. All these molecules strengthen capillary blood vessels, avoid their extravasation and facilitate blood flow. Organic silicon may also be useful as a protector of vascular tissues. We have also noted good results with creams containing Acetyl Tetrapeptide-5, an inhibitor of vascular permeability.

Mixed types of POH will need combined treatments containing both depigmenting agents and vascular-oriented active ingredients, and topical tranexamic acid is a first line therapy in such case. For structural type and tear through, there is no dermo-cosmetic approach available, and the best treatment probably consists in injections of hyaluronic fillers.

As we can see, dermo-cosmetics are bringing lots of opportunities in the treatment of POH, but one must be careful on that they are accompanied by enough credible evidence-based or significant studies to ultimately justify their use.

5. PERIORBITAL RHYTIDS (CROW'S FEET – CF)

Periorbital rhytids, also named crow's feet, are one of the most common complaints of aging patients. For this reason, this is one of the areas in the upper face that is most frequently considered for rejuvenating treatment. CF designs the lines that radiate outward from the lateral canthus during smiling. With aging, these transitory expression lines tend to become permanent. Histology shows a deterioration of the elastic tissue network, especially of collagen fibres.

Aetiology of CF

Intrinsic factors such as skin thickness or amount of subcutaneous fat are crucial in the development of CF [11].

Extrinsic factors, namely sun exposure, smoking history and amount of contraction of the lateral orbicularis oculi muscle during smiling or squinting are also of importance in their occurrence [12]. Compared with skin with less sun exposure (postauricular skin), crow's feet skin demonstrates reduced epidermal thickness, a more compact stratum corneum, increased granular layer thickness, increased perifollicular fibrosis, and increased solar elastosis [11].

Clinical patterns of CF

Various patterns may be observed in crow's feet (Fig. 6). According to Kane [12] the most common pattern (47%) is the full fan pattern. These patients exhibit crinkling of their lateral canthal skin from the lower lateral brow across the upper eyelid, through the lateral canthus, and across the lower eyelid/upper cheek junction. The second most common pattern (25%) involves wrinkling of the lower lid/upper cheek area alone. Follows (18% of cases) a pattern in which the patients primarily exhibit wrinkles only in the upper eyelid skin, down to the lateral canthus. In the last pattern (10% of patients), only the skin immediately surrounding the lateral canthus is severely wrinkled.

Treatment of CF

The last trend in terms of treatment of facial wrinkles are probably bioactive peptides. Among them, wound healing peptides such as Palmitoyl pentapeptide-3, derived from procollagen and stimulating production of collagens I and III in addition to fibronectin [13]. In the same category, oligopeptide is an elastin sequence and stimulates the growth of fibroblasts and accelerates angiogenesis [14]. Palmitoyl tripeptide-38 and palmitoyl tripeptide-5 have also been shown to be highly effective at stimulating the production of collagen and hyaluronic acid and promoting dermal thickening [15]. Another category of peptides is worth of interest in the dermo-cosmetic management of CF: peptides as an alternative to Botulinum neurotoxin.

Fig. 5. **Reduction of eyelid bags after 14 days using a cream with 10 % Acetyl Tetrapeptide-5**

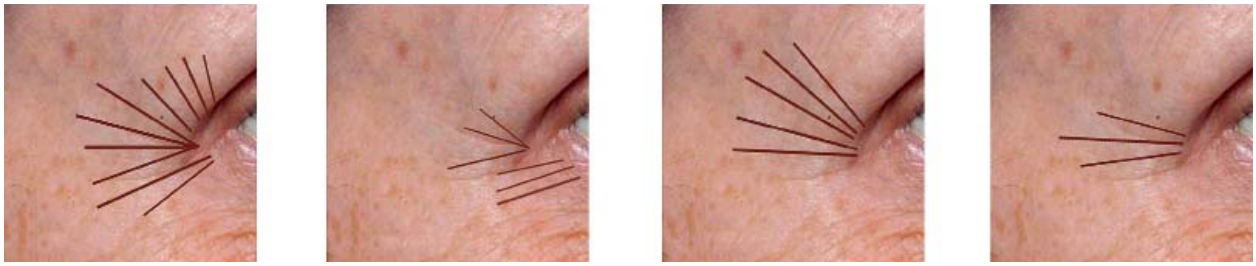

Fig. 6. **Different patterns of crow's feet**

Fig. 7. **Crow's feet before and after application of a cream with 2 % Spilanthes acmella extract**

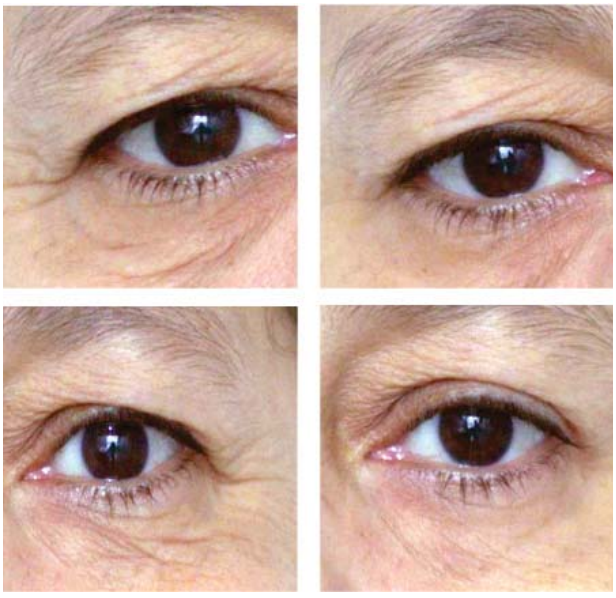

Fig. 8. **At D0 and D14 after intake of oral collagen 10 g/day**

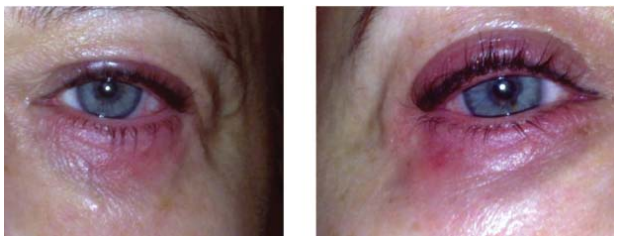

Fig. 9. **Side effects observed after using topical bimatoprost for eyelash entenhancement**

In this category we can mention Acetyl hexapeptide-3, a six-amino-acid peptide derived from SNAP-25 which has been shown to produce the desired interference with the neurosecretion [16]. A clinical study reported that acetyl hexapeptide-3 at a 10 % concentration reduces the depth of wrinkles up to 30 % after 30 days of use [17]. Diaminobutyroyl Benzylamide Diacetate, synthesized for reducing wrinkles by inhibiting muscle contractions and Pentapeptide-3, an oligopeptide exhibiting curare-like activity, as it is a competitive antagonist at the acetylcholine postsynaptic membrane receptor, are also of interest in our indication.

Various vegetal active ingredients are also proposed for the improvement of CF. Among them, Spilanthes acmella (paracress), a plant, which mainly grows in subtropical regions, deserves a special attention. It permits a clear stimulation of

the contractile power of the fibroblasts, and this result is observed from the first application (Fig. 7).

We must also keep an eye on the intake of oral collagen, as its best results can be observed on the improvement of CF (see Fig. 8). The dose for an ideal result is 10 g/day.

6. EYELASHES

Eyelashes are considered an important aspect of the facial aesthetic and are the object of various beauty treatments to enhance them. The human lower lid contains 75—80 lashes dispersed in three to four rows, whereas the upper lid has 90—160 lashes scattered on five to six rows [18]. The anatomy of the lash and hair has some similar characteristics. Both have a hair shaft (the visible part) that extends outside the skin, a root that is under the skin and a bulb, which is the enlarged terminal portion [19]. The lash itself is made up of three structures that fit into one another. The innermost structure, the medulla, consists of loose cells. A thicker cortex surrounds the medulla to ensure its strength and stability. The pigmentation of either the lash or hair is the result of the melanin contained in the cortex. Finally, the cuticle, composed of several cell layers, forms the outermost portion, offering protection to the internal structures by its impermeability [18]. However, the anatomy and physiology of the lash follicle are distinctive from other hair follicles.

Similar to other hair follicles, lashes have a life cycle consisting of three phases: the growth phase (anagen), the degradation phase (catagen) and the resting phase (telogen). The daily growth rate of a lash is 0.12—0.14 mm, the anagen phase duration varies from four to ten weeks and the complete life cycle is from four to eleven months [20]. The lash length rarely exceeds 12 mm, as the growth rate and anagen phase duration are shorter than the ones observed in scalp hair [20]. The morphology of the eyelashes is such that they are curved in all individuals, regardless of ethnicity [19], and this makes their morphology different from that of scalp hair.

Aging of eyelashes

There is no comprehensive study about the aging of lashes. By analysis of photographs of the upper natural eyelashes of 179 subjects, it could be observed that advancing age among an ethnically diverse population of healthy women is associated with significant decreases in eyelash length, thickness, and darkness [21].

Another study focusing on the curvature of the lower eyelashes in different age groups identified that lashes in the lateral portion of lower eyelid tend to maintain the same angular position throughout life, whilst on the central and medial portions it tends to approach a 90° angle with age [22].

Dermo-cosmetic management of lashes aging

Due to their importance in the global appearance of facial aesthetic, lashes are the object of more and more concern by our patients. Long lashes are considered a sign of femininity in most cultures, and women intend to increase the length and volume of their lashes. For a few years, prostaglandins started to be used in this indication.

Analogues of the prostaglandin F2α (PGF2α), bimatoprost and latanoprost, have been discussed exhaustively in relation to enhancing eyelash growth [23]. Satisfactory results may be observed, although their mechanism of action is not well known. However, side effects can be observed during their use in this indication, such as stinging and pruritus (quite common), darkening of the eyelid skin, ocular irritation, eye dryness or inflammation of eyelids (Fig. 9).

Alternative topical treatments exist, based on bioactive peptides. Myristoyl Hexapeptide-16 and Myristoyl Pentapeptide-17 were shown to stimulate in a significant manner the keratin genes. It was demonstrated in human keratinocytes that Myristoyl Tetrapeptide-12 was able to directly activate SMAD 2 and induce SMAD 3 to link to DNA [24]. SMAD 2 and SMAD 3 act as activators of stem cells of the hair follicle in order they turn from the telogen to anagen phase [25]. Such peptides show good results when used in association, and do not present side effects.

7. CONCLUSION

In summary, the periorbital complex is of major concern in the appearance of the whole face, and aging is particularly affecting this area. Its various features, eyelid bags, periorbital hyperpigmentation, crow's feet and eyelash aging must be adequately diagnosed as per their aetiology and classification in order to allow bringing to the patient the most accurate treatment, active dermo-cosmetics being part of it.

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К. Діл

Університет Гульєльмо Марконі, Рим, Італія

Дермокосметичне лікування періорбітального комплексу

Завдяки недавнім високотехнологічним розробкам ефективних і безпечних продуктів, що застосовують у дермокосметології, їх можна включати в рекомендації для пацієнтів, стурбованих старінням шкіри і зовнішнім виглядом свого обличчя. Періорбітальний комплекс має особливе значення в цьому процесі, оскільки справляє значний вплив на зовнішній вигляд усього обличчя.

Крім того, в процесі старіння періорбітальний комплекс часто виявляє більш ранні ознаки старіння, ніж інші частини обличчя. У статті після короткого огляду анатомічних особливостей розглянуто різні ознаки старіння в цій ділянці, а саме: мішки на повіках, періорбітальну гіперпігментацію, «гусячі лапки» і стан вій. Мішки на повіках можуть мати різну етіологію, тому важливо не тільки знати її, а й вміти розрізняти, щоб запропонувати найбільш адекватне лікування і рекомендації щодо усунення. Періорбітальна гіперпігментація також є частою скаргою в дерматології та естетичній медицині. Вона має різну етіологію, і тому було розроблено її чітку класифікацію, на основі якої запропоновано диференційоване лікування. «Гусячі лапки» часто виникають досить рано і є першими ознаками старіння обличчя. Сьогодні, завдяки досягненням дермокосметології, існують ефективні методи лікування цього стану. Серед них доцільно виділити різні біоактивні пептиди, розроблені протягом останнього десятиліття, а також активні рослинні інгредієнти. За умови правильного призначення колаген для перорального застосування також може бути корисний для цих цілей. Вії як важливий аспект естетики обличчя є об'єктом різних косметичних процедур для поліпшення їхнього стану. Вони включають простагландини, які визнані ефективним засобом, але водночас викликають різні побічні ефекти, а також біоактивні пептиди, що відіграють ключову роль у дермокосметичному лікуванні періорбітального комплексу.

Ключові слова: періорбітальний комплекс, старіння, мішки на повіках, періорбітальна гіперпігментація, «гусячі лапки», вії, дермокосметика, біоактивні пептиди.

К. Дил

Университет Гульельмо Маркони, Рим, Италия

Дермокосметическое лечение периорбитального комплекса

Благодаря недавним высокотехнологичным разработкам эффективных и безопасных продуктов, применяемых в дермокосметологии, их можно включать в рекомендации для пациентов, которые обеспокоены старением кожи и внешним видом своего лица. Периорбитальный комплекс имеет особое значение в этом процессе, поскольку оказывает большое влияние на внешний вид всего лица.

Кроме того, в процессе старения периорбитальный комплекс часто проявляет более ранние признаки старения, чем другие части лица. В статье после краткого обзора анатомических особенностей рассмотрены различные признаки старения в этой области, а именно: мешки на веках, периорбитальную гиперпигментацию, «гусиные лапки» и состояние ресниц. Мешки на веках могут иметь разную этиологию, поэтому важно не только знать ее, но и уметь различать, чтобы предложить наиболее адекватное лечение и рекомендации по устранению. Периорбитальная гиперпигментация тоже является частой жалобой в дерматологии и эстетической медицине. Она имеет различную этиологию, и поэтому была разработана ее четкая классификация, на основе которой предложено дифференцированное лечение. «Гусиные лапки» часто появляются достаточно рано, являясь первыми признаками старения лица. Сегодня, благодаря достижениям дермокосметологии, существуют эффективные методы лечения этого состояния кожи. Среди них следует выделить различные биоактивные пептиды, разработанные в течение последнего десятилетия, а также активные растительные ингредиенты. При условии правильного назначения коллаген для перорального применения также может быть полезен для этих целей. Ресницы, считающиеся важным аспектом эстетики лица, являются объектом различных косметических процедур для улучшения их состояния. Они включают простагландины, которые признаны эффективным средством, но одновременно вызывают различные побочные эффекты, а также биоактивные пептиды, играющие ключевую роль в дермокосметическом лечении периорбитального комплекса.

Ключевые слова: периорбитальный комплекс, старение, мешки на веках, периорбитальная гиперпигментация, «гусиные лапки», ресницы, дермокосметика, биоактивные пептиды.

Дані про автора:

Dr. Christian Diehl, Department of Dermatology, Universit Degli Studi Guglielmo Marconi
Via Plinio, 44, 00193, Rome, Italy. E-mail: chdiehl@hotmail.com