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SKIN PIGMENTATION CHANGES, CAUSES AND METHODS OF THEIR ELIMINATION

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Abstract

Skin is the largest organ of the human body, which performs many important functions. Skin colour is influenced by many factors, the most important of which is the melanin pigment. Skin pigmentation disorders may have exogenous or endogenous origin. They are divided into hyperpigmentation (darkening of skin), most often caused by an abnormally high amount of the skin pigment and hypopigmentation when there is abnormally Low amount of melanin. Increased melanin production leads to skin colour disorders. The formation of discoloration is influenced by many factors, such as: sunlight, hormonal and genetic factors, thyroid diseases, pregnancy and menopause, as well as mechanical damage, inflammation or the use of certain medications. The most common discolorations include freckles, chloasma and lentigines (age spots). A number of methods are available to reduce discoloration. The process of treatment is usually long and depends on the proper recognition of the changes, their causes, location and also the overall health of a person. Thanks to this, the therapy that gives the most effective results can be selected. Apart from whitening products and treatments, one of the most effective methods is laser therapy. Different types of lasers are used, such as Q - switched lasers (ruby, alexandrite) and IPL devices. Photoprotection is necessary during the therapy.

Key words: skin pigmentation, skin, hyperpigmentations, hypopigmentations

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Introduction

Pigmentation changes are one of the most common dermatological problems. They affect 35% of women over 35 and 90% over 50. They most often appear on skin exposed to solar radiation. The changes may be congenital or acquired and affect both the epidermis and dermis. They are caused by improper distribution and synthesis of pigment [1].

There are many methods available in modern cosmetology and aesthetic medicine to eliminate and reduce discoloration. In order to obtain satisfactory results, the treatment method should be selected appropriately [2].

Discoloration is a defect mainly of an aesthetic nature, but in addition to adversely affecting the external appearance, it may cause problems with self-esteem. This is a common problem that affects up to 90% of the population. Eliminating discoloration also improves the quality of life [2].

Pigmentation changes are limited as well as generalized changes in the normal skin colour. They may be congenital or acquired. They are divided into hyperpigmentation, also called discoloration, and hypopigmentation (discoloration). Discolorations are the result of increased melanin production, while discolorations result from partial or complete inhibition of pigment production [3, 4].

Intensified melanogenesis in a given area of the skin causes a significant increase in the amount of pigment produced relative to the surrounding tissues. Discolorations may be of exogenous origin (mainly injuries, irritations and UV radiation) or endogenous (caused by hormonal disorders or medications) [3]. The factors influencing the intensity of melanogenesis: (1) mechanical damage to the skin, which may lead to increased production; (2) melanin and hyperpigmentation, (3) chemicals that irritate the skin and lead to inflammation, which intensifies discoloration, (4) long-term exposure to heat on the skin may cause the development of temporary pigmentation changes, (5) in case of too frequent exposure to radiation, melanogenesis intensifies and the pigment is distributed unevenly, additionally, the use of photosensitizing preparations causes intensification of pigmentation and sun discoloration, (6) inflammation in the skin causes the process of melanogenesis in the skin to be intensified, melanocytic cells may also be destroyed and the large amount of stains [3].

Under physiological conditions, melanocytes produce more melanin when increased skin protection is needed, e.g. during sun exposure. However, sometimes the stain is distributed unevenly and the dark skin colour is not the result of an increased need for protection. This situation may occur as a result of inflammation, e.g. caused by skin eruption (post-inflammatory hyperpigmentation), as well as a result of age-related physiological processes occurring in the skin (age spots). Genetic conditions may also cause uneven distribution of pigment (freckles) [5, 6].

The causes of various types of discoloration:

1. genetic,
2. hormonal,
3. secondary:
   - increase in the amount of melanin as a result of an increase in the number of melanocytes,
   - the passage of melanin grains into the dermis as a result of inflammation causing the breakdown of melanocytes [7].

PIn terms of the depth of their occurrence in the skin, in the histological picture, pigmentation changes are divided into:

1. epidermal,
2. cutaneous,
3. dermal-epidermal [8].

Determining the depth of discoloration is very important in selecting the most effective treatment method. For this purpose, Wood's lamp examination is used. In the case of surface (epidermal) discoloration, there is a clear contrast between the lesion and healthy skin. Deeper discolorations do not become more visible in lamp light [7],

Due to clinical disorders, hyperpigmentation is divided into:

1. diffuse - accompanying systemic diseases,
2. local [9].

The most common discolorations include: freckles, chloasma (melasma), lentigines, post-inflammatory and drug-induced discolorations, cafe au lait spots (coffee with milk) and Ot's nevi [10].

Freckles

These are small lesions that are light brown or brown in colour. They are usually located on the face and arms, i.e. areas that are particularly exposed to solar radiation. Histologically, they are located in the basal layer of the epidermis [11].

Freckles are a genetically inherited disorder (autosomal dominant), so they are often found among members of the same family. Most often in people with fair skin and red hair. The changes persist throughout life, but are less severe in old age and in winter [12].

Chloasma

Chloasma is also called melasma, pregnancy mask or chloasma. It is a common skin lesion that affects women more often than men. It is characterized by the presence of symmetrically placed, irregular yellow-brown or dark brown lesions, located mainly on the face (Fig. 6), but may also occur on the neck, chest, and also the skin of the arms and forearms [13].

Changes can occur in three patterns. The most common pattern, occurring in as many as 50-80% of cases, is a pattern where discoloration is located on the nose, forehead and above the upper lip (mid-facial pattern). The malar pattern is characterized by lesions on the cheeks, while the mandibular pattern is characterized by lesions on the mandible and chin [13, 14].

The aetiology of melasma is not single-factor and is influenced by several elements. The main contributor is solar radiation, which intensifies symptoms and causes relapses. Other factors include oestrogen and some progestogens, as well as genetic predisposition. Due to the significant influence of hormones, melasma occurs more often in women during pregnancy and when taking oral contraceptives [13].

Coffee-with-milk stains

These changes may occur throughout the skin and are not dependent on exposure to light. These are light brown discolorations with an oval shape, demarcated from the skin with a delicate contour. They are located in the basal layer and their number and size may vary. In 10 - 15% of healthy people, they appear as single lesions, but in larger numbers (over 5) and with a diameter of over 5 mm, they are usually a symptom of neurofibromatosis [15].

Lentigines

Lentigines are called age spots or sun spots. The lesions range in colour from light brown to black. They have various shapes and sizes, usually from approx. 3 mm to 12 mm, but they can also be larger. Lentigines are located in the basal layer of the epidermis. They are permanent changes and do not tend to disappear spontaneously [16].

They most often appear after the age of 40-50, becoming larger and more numerous as the years go by. They may appear earlier in people who excessively use solariums. Most often, they are located on the skin that has been exposed to solar radiation for many years. Characteristic places of occurrence are the backs of the hands, forearms, as well as the face and forehead. In men, the characteristic location is the head, in the area of the senile bald spot, and also around the neck. They are mainly an aesthetic problem, but attention should be paid to the diagnosis of malignant lentigines or melanoma [4, 16].

Secondary discoloration

Post-inflammatory discoloration

This type of discoloration comes in various shapes and sizes. These are dark spots that appear after the inflammation, acute or chronic, has subsided. They can occur regardless of age or race, but people with darker skin are more susceptible to these changes [4].

Post-inflammatory discoloration occurs as a result of the increased production of melanin, which is a response to inflammation and skin trauma. They are located on the surface of the dermis. One of the most common causes of post-inflammatory discoloration is acne. Other causes include: lichen planus, atopic dermatitis, allergic contact dermatitis, UV and ionizing radiation. In most cases, they tend to fade over time. It is important in the treatment to take into account the elimination of the disease factor that causes the discoloration [17].

Mechanical discoloration

They arise as a result of long-term action of a factor causing mechanical trauma. There is an overproduction of melanin and the release of pigment from melanocytes as a result of their injury [18].

Drug-induced discoloration

It is a heterogeneous group of discolorations that differ in colour, location and intensity of changes. The factor causing drug-induced discoloration is not always only due to the increased amount of melanin. Additionally, various drug metabolites accumulate in the skin. Solar radiation also plays an important role, as changes occur most often in areas more often exposed to radiation when using photosensitizing drugs [4].

Chemical peels used to remove discolorations

One of the popular methods used to reduce discoloration are chemical peels. It is a treatment involving controlled exfoliation and damage to the epidermis as a result of a chemical substance. This damage leads to the stimulation of repair processes and remodelling of the dermis [19].

Chemical peels are divided into three groups depending on the depth of skin penetration. Surface peels only work on the epidermis, while medium-deep peels reach the papillary layer of the dermis. Deep peels damage tissues up to the reticular layer. The factors affecting the depth of peeling action are: the duration of action on the skin, the concentration and strength of the acid, the amount of the preparation applied, and the condition of the skin [19].

Hydroxy acids

AHA (alpha hydroxy acids)

Glycolic acid

Glycolic acid is the most popular and most frequently used α-hydroxy acid. It is highly soluble in water, and the small size of the molecule allows it to easily penetrate the layers of the epidermis, up to the basal layer. Its effect depends on the concentration and pH of the solution. In low concentrations, it has a moisturizing effect. In surface peelings, it is used in concentrations ranging from 20 - 70%, while in concentrations above 50% it causes strong exfoliation. It loosens the cohesion of the stratum corneum cells and leads to their exfoliation. Its action also includes stimulating collagen production, improving skin elasticity and reducing wrinkles. It helps in eliminating freckles, lentigines and chloasma [20, 21].

Lactic acid

The size of the lactic acid molecule is slightly larger compared to glycolic acid. Due to this, it does not reach the deeper layers of the skin and its action is limited only to the epidermis. When used in concentrations higher than 10%, it has a keratolytic effect - it weakens the adhesion of corneocytes to each other. In lower concentrations, it has a moisturizing effect. It has a brightening effect on discolorations by superficial exfoliation of the epidermis. Moreover, it reduces the time that cells need to regenerate and increases the penetration of additional substances with a brightening effect [22].

Almond acid

The molecule of mandelic acid is larger than that of glycolic acid and therefore penetrates the epidermis more shallowly; therefore, it does not cause skin irritation. It is suitable for use on sensitive and vascular skin prone to telangiectasia. Mandelic acid loosens intercellular connections in the epidermis, and additionally has bacteriostatic, sebostatic and keratolytic effects. It is used primarily in acne. It has a brightening effect and works well in combination with other substances such as lactic acid, thioglycolic acid and vitamin C. It works well in lightening molasses, freckles, lentigines and post-inflammatory discolorations. It does not cause sun sensitivity, so it is believed that it can be used all year round [23].

BHA (beta hydroxy acids)

Salicylic acid

BHA acids are also used in skin depigmentation treatments. However, their molecule is much larger, and therefore they penetrate the skin to a much deeper depth than AHA acids [24].

Salicylic acid is a component of Jessner's solution, used, among others, in the treatment of discolorations, which additionally includes lactic acid and resorcinol. However, due to its antibacterial properties, salicylic acid is most often used to treat acne and effectively removes blackheads [23].

Carboxylic acids: TCA acid (trichloroacetic acid)

Trichloroacetic acid is a very strong acid whose action is exceptionally effective due to the small size of the molecule, which allows rapid penetration of the epidermis and dermis. In exfoliation treatments, it is used in various concentrations depending on the depth of the peel to be performed. Surface peels are performed at a concentration of 15 - 20%, and at a concentration of 35 - 50% it is used to perform medium-deep peels. The action of TCA acid is to coagulate proteins and damage living epidermal cells. Exfoliation occurs as a result of necrosis in the epidermis and superficial layer of the dermis. Damaged cells are replaced with new ones, and collagen production is additionally stimulated. Surface peels using TCA are used to treat melasma. In concentrations above 40%, it is mainly used to remove lentigines, but when using lower concentrations, the treatment may not give lasting results. The use of high concentrations of TCA carries the risk of numerous complications, which include: post-inflammatory discoloration, irritation, persistent erythema, scars, and increased skin sensitivity [25, 26].

Alpha - keto acids: pyruvic acid

Pyruvorous acid causes superficial exfoliation of the epidermis, and its action is quick and may cause irritation. It has brightening, anti-blackhead and bacteriostatic properties. It quickly penetrates the skin, so one can achieve effects similar to medium-depth peels in a relatively short time. It reduces the adhesion of corneocytes to each other, which loosens the connections between cells. At a concentration of 40%, it is used to remove post-inflammatory discolorations, and at 60% it is used to treat post-inflammatory scars [25].

Retinoids have a strong brightening effect, similar to hydroquinone. Tretinoin, unlike hydroquinone, does not affect skin discoloration of phototypes V and VI. The mechanism

of action is based on a direct effect on melanocytes. Topical retinoids inhibit tyrosinase, which in turn inhibits melanogenesis. They also have an exfoliating effect by accelerating the maturation of epidermal cells and reducing their adhesion. As a result of the exfoliation process, the skin becomes brighter and other active substances penetrate better. Additionally, they stimulate the synthesis of collagen and normalize the processes of maturation and differentiation of keratinocytes. Retinoids used externally are: isotretinoin, tretinoin, tazarotene and adapalene. They work well on melasma and lentigines, and the treatment results are visible after at least 3 months of therapy. In the first month, side effects such as erythema, dryness, irritation, itching and skin peeling are very common. Over time, when the skin gets used to retinoids, these symptoms disappear [27].

Vitamin C

Vitamin C is a naturally occurring antioxidant. It is used in skin lightening products. It is one of the agents that interrupt key stages of melanogenesis. It interacts with copper ions in the active site of tyrosinase and inhibits the action of the enzyme, thereby reducing the formation of melanin. Ascorbic acid is an unstable compound, so it is often replaced with more stable derivatives. The most popular of them are sodium acorbic acid monophosphate (SAP), ascorbic acid phosphoric ester (MAP), and ascorbyl palmitate. Additionally, to obtain a better effect, they are combined with other decolourizing agents. MAP penetrates the stratum corneum well because it is lipoid. It has been found that 10% MAP cream has a significant skin brightening effect, but most care products contain concentrations of up to 1% [28, 29].

Vitamin E

Vitamin E is a lipophilic antioxidant that provides protection against UV radiation. In nature, it occurs in the form of eight molecules (four tocopherols and four tocotrienols). Alpha-tocopherol is the most abundant in humans, followed by gamma tocopherol. Vitamin E causes depigmentation of discolorations by interfering with lipid peroxidation in melanocyte membranes, increasing intracellular glutathione content and inhibiting tyrosinase. In cosmetic products, vitamin E is used in concentrations not exceeding 5%, most often in combination with vitamins A and C [30, 31].

Azelaic acid

Azelaic acid is obtained from yeast-like mushrooms (Pityrosporum ovale). It affects the inhibition of tyrosinase (a key enzyme of melanogenesis). It has a beneficial effect on eliminating post-inflammatory discolorations, discolorations after phototoxic reactions, and melasma. It does not have a brightening effect on freckles and lentigines because it does not affect melanocytes, which are in the resting phase. It is used primarily in creams and gels in concentrations of 15 - 20% and also as an addition to chemical peels. Acid therapy should last at least 4 weeks and not longer than half a year [32].

Kojic acid

Kojic acid chelates iron ions, preventing the formation of free radicals, and additionally has antibacterial properties. Moreover, it affects the shortening of melanocyte dendrites. It has a brightening effect, similar to hydroquinone, but unlike it, it does not cause secondary discoloration. It can be used as an alternative to hydroquinone. It is part of the popular Cosmelan peeling [12].

Microdermabrasion

Microdermabrasion is a treatment of mechanical, controlled abrasion of the epidermis. During the treatment, the stratum corneum is exfoliated, and the depth of exfoliation is controlled by visual assessment. There are three basic types of this treatment: diamond microdermabrasion, corundum microdermabrasion and water-oxygen microdermabrasion, i.e. oxybrasion [16].

Diamond microdermabrasion is a treatment using heads equipped with an abrasive ring made from diamonds. The diamond head can have different gradations and diameters, and its size is selected depending on the place of treatment. The greater the gradation, the more delicate the treatment. Diamond microdermabrasion is effective in removing superficial discolorations [16].

Corundum microdermabrasion uses aluminium oxide (corundum) crystals. Microcrystals are thrown out of the head under pressure and then sucked in along with the abraded epidermis. It is more intense than diamond microdermabrasion and is not suitable for delicate skin [33].

Oxybrasion is the gentlest type of microdermabrasion. The treatment involves the use of a stream of compressed air and a saline solution. During oxybrasion, the skin is gently exfoliated and oxygenated [32].

The intensity of microdermabrasion treatments depends on the duration of the treatment, the vacuum used, the gradation of the head (diamond microdermabrasion), the size of the grains of the abrasive material (corundum microdermabrasion) and, in oxybrasion, on the distance of the nozzle from the skin [33].

Mechanical exfoliation stimulates skin reconstruction, which in turn contributes to brightening and smoothing. The epidermis, deprived of dead cells, regains its smoothness and uniform colour, but positive changes also occur in the dermis. As a result of abrasion of the stratum corneum, the epidermal barrier decreases, which results in increased penetration of active ingredients into the skin. The use of more intense abrasion leads to the stimulation of the activation of inflammatory processes, the amount of pro-inflammatory cytokines increases, resulting in skin regeneration, the mechanism of which is similar to the healing processes [34, 35].

Lasers used to remove discolorations

Laser therapy is an effective method of reducing discoloration. The effect of radiation on the skin depends on: laser power, pulse duration, wavelength, exposure time, and the surface area

of the head. The light energy emitted by lasers is absorbed by chromophores. The chromophores of the skin are water, collagen, haemoglobin and melanin. The most important chromophore in eliminating pigmented lesions is melanin, which absorbs light in the range of 250 - 1200 nm. In the treatment of discoloration, it is important to select a laser that emits radiation selectively absorbed by melanin. Absorption of radiation causes heat generation and, consequently, destruction of the absorbing molecules [10, 16].

Copper-bromide laser

The copper-bromide laser emits radiation with a wavelength of 511 nm. This is a green light. Devices operating in the green light range are the most effective in eliminating discoloration. Short-wave green light is the most selective towards melanocytes, which heat up and are destroyed under its influence. Additionally, the effect on other tissues is minor. The copper-bromide laser also emits yellow light, which is absorbed by the red colour, which is helpful in the treatment of vascular melasma. Using this laser, lentigines, post-inflammatory and post-traumatic discolorations are removed [10].

Q-switch lasers

Q-switch lasers are often used to remove pigmented lesions. They produce high-energy pulses with a very short pulse time, which is measured in nanoseconds. The most commonly used lasers are alexandrite, ruby and Nd-Yag [36].

The Q-switch ruby laser is one of the most frequently used methods for removing discoloration. It produces red light with a wavelength of 694 nm. This light penetrates the skin to a depth of 1 mm and is selectively absorbed by melanin, and to a small extent by haemoglobin. The length of the generated pulse is within the thermal relaxation time of the melanosome. Using this type of laser, changes easily remove epidermal spots, such as freckles, as well as lentigines. Post-inflammatory hyperpigmentation and melasma do not respond as well to ruby laser treatments [36].

The Q-switch neodymium-yag (Nd-Yag) laser is also an effective method of removing pigmented lesions. The pulse duration is very short, approximately 10-20 ns. Thanks to such short impulses, damage to the surrounding tissues is minimized. The laser emits infrared light with a wavelength of 1064 nm. Currently, methods are also used to increase the range of radiation produced. For this purpose, non-linear crystals are placed in the radiation path, which allows obtaining a wavelength of 532 nm (green). Light with a wavelength of 1064 nm penetrates the skin to a depth of 4-6 mm, which allows one to effectively eliminate skin pigment lesions, while green light is more selective and is absorbed by pigment cells (haemoglobin and melanin). Lentigines, cafe-au-lait spots, as well as deep-seated melasma respond well to treatment with this laser [16, 37].

The alexandrite laser is another treatment method using Q-switch lasers that emit light with a wavelength of 755 nm. Its operation and effectiveness in the fight against pigmentation changes is comparable to the ruby laser, but the alexandrite laser penetrates the skin slightly deeper. It is used to remove lentigines, but it is not effective in the treatment of melasma and post-inflammatory hyperpigmentation [38].

Pulsed dye laser

PDL, i.e. pulsed dye laser, is considered a relatively safe device that does not cause side effects. It emits light with a wavelength of 510 nm (green light). The pulsed dye laser induces selective photothermolysis of melanin in the epidermis. It has good results in eliminating freckles and lentigines. It is less effective against skin and post-inflammatory discolorations [39].

IPL devices

IPL devices emit an incoherent beam of high-energy light. Intense pulsed light is a popular method used to reduce discoloration and even out skin colour. As in the case of a laser, the energy is absorbed by the skin's chromophores, and more precisely by melanin. The energy is then converted into heat, which leads to partial or complete destruction of cells. It is important to select the appropriate wavelength and pulse intensity. IPL devices emit light in the range of 400 - 1200 nm. In the treatment of discoloration, heads emitting light in the range of 510 - 980 nm are used. Longer wavelength ranges stimulate collagen synthesis and even out the skin structure [40].

Cryotherapy

Cryotherapy is rarely used and is mainly used to remove single lentigines. It involves the destruction of cells as a result of low temperature. Melanocytes are temperature-sensitive cells, which is why they disintegrate at low temperatures (already at 4-7 ° C). When removing discolorations, liquid nitrogen is most often used. The procedure carries the risk of scarring. It should be performed by an experienced person in a gentle manner to reduce the risk of complications [12, 38].

Sun protection

Appropriate sun protection is a very important element of discoloration therapy. One should avoid excessive exposure to the sun and additionally use sunscreens with a high SPF (sun protection index) [30].

Protective sunscreens are divided into two groups in terms of chemical composition: chemical and physical sunscreens. The best protection is provided by a combination of different chemical and physical sunscreens. The strength of the sunscreen is determined by the SPF index. It informs how long one can stay in the sun before blushing occurs when using the preparation in relation to the exposure time without a protective preparation. SPF only applies to UVB radiation. During therapy, sunscreens with a minimum of SPF 30 should be used. The amount of preparation applied is also important, as too little may result in its lower effectiveness. Sunscreens should be applied every 1.5 hours during exposure to UV radiation [30, 41].

Conclusions

1. Pigmentation lesions are one of the most common dermatological problems. Most often, they arise as a result of UV radiation, but hormonal and genetic factors, as well as pregnancy and aging, are also important.
2. There are many methods of eliminating pigmentation lesions available on the market. In addition to brightening substances, chemical and mechanical peels, therapies based on modern technologies are available (laser therapy and IPL therapy).
3. The elimination of discolorations is usually a multi-stage process, because the changes are not always completely removed and may be recurrent.
4. The effectiveness of treatments is influenced by: the appropriate identification of the basis of changes, elimination or normalization of factors causing their development, and selection of appropriate treatment. Treatments should be combined with appropriate photoprotection.

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