Maja Stanko-Nieniewska, Magdalena Rogóż

Faculty of Health Sciences and Physical Culture, University of Applied Sciences in Nysa, Ujejskiego 12 Steet, 48-300 Nysa
+48 794 035 500 *mnieniewska@gmail.com*

Sposób cytowania / Cite Stanko-Nieniewska M, Rogóż M. Micro-needle mesotherapy in anti-aging prevention and skin rejuvenation - the importance of inflammation, healing and skin regeneration after the procedure. *Aesth Cosmetol Med.* 2024;13(3):95-101. https://doi.org/10.52336/acm.2024.018

Micro-needle mesotherapy in anti-aging prevention and skin rejuvenation – the importance of inflammation, healing and skin regeneration after the procedure

Mezoterapia mikroigłowa w profilaktyce przeciwstarzeniowej oraz odmładzaniu skóry – znaczenie stanu zapalnego, gojenia i regeneracji skóry po zabiegu

ABSTRACT

The skin serves numerous vital roles in the human body, such as protecting against physical, chemical, and mechanical injuries. Although skin aging is a natural phenomenon, it is still the subject of research by scientists seeking methods to delay the process. One of the innovative treatments in this field is micro-needle mesotherapy, referred to as collagen-inducing therapy.

The study aimed to describe the features of the ageing skin, elucidate the alterations that occur with time, and investigate the reparative mechanisms triggered by micro-needle mesotherapy treatment.

Microneedle-induced skin inflammation is a desirable process. It leads to the healing of damage and can significantly contribute to wrinkle shallowing, improved hydration and skin remodeling.

Keywords: skin aging, micro-needle mesotherapy, micro-puncture, inflammation, healing, regeneration, wrinkles

STRESZCZENIE

Skóra pełni wiele istotnych funkcji w ludzkim organizmie, w tym również ochronną przed urazami fizycznymi, chemicznymi i mechanicznymi. Choć starzenie się skóry jest zjawiskiem naturalnym, wciąż pozostaje przedmiotem badań naukowców poszukujących metod opóźnienia tego procesu. Jednym z innowacyjnych zabiegów w tej dziedzinie jest mezoterapia mikroigłowa określana mianem terapii indukującej tworzenie kolagenu.

Celem pracy była charakterystyka starzejącej się skóry, zmian związanych z upływem czasu oraz mechanizmów naprawczych zachodzących podczas zabiegu mezoterapii mikroigłowej.

Zapalenie skóry wywołane mikronakłuwaniem jest pożądanym procesem. Prowadzi do gojenia uszkodzeń i może w znaczący sposób przyczynić się do spłycenia zmarszczek, poprawy nawilżenia oraz przebudowy skóry.

Słowa kluczowe: starzenie się skóry, mezoterapia mikroigłowa, mikronakłuwanie, stan zapalny, gojenie, regeneracja, zmarszczki

INTRODUCTION

The skin, which is one of the largest and heaviest organs of the body, consists of three essential layers: the epidermis (*epidermis*), the dermis (*cutis vera*) and the subcutaneous tissue (*tela subcutanea*) [1]. It protects against physical, chemical and mechanical trauma, and regulates heat and water-electrolyte balance. The skin secretes and absorbs many substances, is involved in the perception of external stimuli and participates in the metabolism of proteins, lipids, hormones, vitamins and carbohydrates. In addition, it plays an important role in immune reactions, ensuring the homeostasis of the body's internal organs [1, 2].

Skin ageing is a natural, biologically inevitable process that occurs in the human body over time and depends on many factors [3]. With age, the biological activity of cells decreases and regenerative processes slow down. The body's peak capacity is attained at the age of 25, after which there is a gradual decrease in performance throughout the rest of life.

Ageing can be classified into two categories: intrinsic ageing, which is caused by internal factors that are genetically determined changes in the human body, and extrinsic ageing, which is triggered by the influence of external environmental factors. Endogenous ageing is defined by a higher occurrence of atrophic processes, whereas exogenous ageing is characterised by a higher occurrence of hypertrophic mechanisms. The two types of ageing, intrinsic and extrinsic, are intricately interconnected and collectively contribute to the manifestation of ageing skin. The outcome of both processes is occasionally called true ageing [2-4].

WRINKLES AS A SYMPTOM OF AGEING SKIN

Regardless of the causes of skin ageing, mature skin is characterized by several important features, most notably wrinkles. Among the factors leading to their formation are repetitive muscle movements that cause the facial skin to tighten and relax, known as myostasis, water loss associated with impaired synthesis of hyaluronic acid within the tissues, a decrease in the thickness of the dermis, weakening of the support function of collagen fibers and the elasticity of elastic fibers, and the action of gravitational forces on the skin. The formation of wrinkles is also influenced by external factors such as cigarette smoking and ultraviolet radiation [3, 5-7].

Regular contraction of facial muscles leads to constant tightening and relaxation of facial skin. Over time, furrows become more noticeable and deepen, resulting in early wrinkles. The repetitive contractions of the facial muscles cause mechanical damage to the structural fibres of the skin. These stresses are then transferred to fibroblasts, which, by increasing actin and myosin, transform into myofibroblasts and acquire the properties of a contractile cell. Contraction of fibroblasts causes the skin fold to be pulled into the skin, leading to the fixation of wrinkles [3, 6].

Depending on the etiology, there are different types of wrinkles. There are orthostatic wrinkles (visible from birth), facial, static, gravitational, atrophic (age-related), post-sun and elastic, sleep, and wrinkles resulting from dryness and improper skin care. Wrinkles can be divided into two types: superficial wrinkles, which are less than 0.05 mm deep, and deep wrinkles, which are more than 0.05 mm deep [3].

Facial wrinkles

The formation of facial wrinkles is the result of the continuous movement of the skin over the facial muscles. Facial wrinkles appear in a direction perpendicular to the line of muscle tension. The facial expressions characteristic for a person gradually leaves traces in the form of deepening wrinkles, which consolidate over time. This process is most evident in the area around the eyes, forehead, in the area between the eyebrows and at the level of the nose and mouth. Facial wrinkles occur mainly in young people and disappear after the cessation of muscle activity. The first wrinkles usually begin to be noticeable around the age of 20-25 [3, 5].

Of all the facial wrinkles, the earliest to appear are the transverse forehead wrinkles, which are the result of contraction of the frontalis muscle. Vertical wrinkles of the plains are formed as a result of the contraction of the brow crease muscle. They appear at different ages, in the area between the eyebrows, forming lines on the forehead smoothness between the eyebrow arches. Laughing wrinkles, commonly called "crow's feet," appear in the eye area as a result of contraction of the eye circular muscle. The horizontal wrinkles that occur around the root of the nose are the result of contraction of the longitudinal muscle of the nose. Horizontal wrinkles in the area of the base of the nasal skin septum occur due to contraction of the muscle that lowers the nasal septum. Wrinkles around the mouth usually appear around the age of 40-50 as a result of contraction of the circular muscle of the mouth [5].

Static wrinkles

Over time, lines of repetitive motion become noticeable, leading to static wrinkles. These wrinkles are mainly due to the fixation of existing facial wrinkles, which do not disappear even when the skin is straightened or the muscles stop moving, and deepen as the years go by. In addition, a slight discoloration of the epidermis can be seen in the area of the wrinkle formed. The shape of these wrinkles is often compared to the folds of a piece of paper, which, even when straightened, still remain visible. A variation of static wrinkles are structural wrinkles, also known as sun wrinkles, which occur in people who have experienced skin damage related to UV exposure. As a result of excessive sun exposure, the skin loses its firmness, and furrows and multiple wrinkles appear [2, 5, 7].

Gravity wrinkles

Gravity wrinkles manifest as a change in facial contours due to the action of gravity on skin with reduced elasticity. Deterioration of skin tone is associated with disturbances in the structure of collagen and elastic fibers and loss of natural facial fat padding. The effect of gravity is the formation of nasolabial furrows, sagging of the cheeks and sagging of the chin. Gravity wrinkles appear along the orbital rim lines, zygomatic protrusion and jawline. The process of gravity wrinkles is characterized by a gradual and slow progression [5, 7, 8]. Examples of gravity wrinkles include skin folds on both upper and lower eyelids, a drooping eyebrow arch, and sunken cheeks resulting from fat atrophy and the effects of gravity. The sagging of the cheeks exposes the lower edge of the bony orbit, leading to the formation of nasolabial furrows, known as the "valley of tears". In addition, the lowering of the cheeks below the bony edge of the mandible leads to the disappearance of the jawline and the appearance of so-called "hamsters". Facial expressions and smiles accentuate nasolabial furrows, which are linear depressions running from the wings of the nose to the corners of the mouth, formed at the border of the skin of the lip and cheek. Longitudinal folds are noticeable on the neck and around the chin [5, 6].

The sequence of wrinkle formation associated with skin ageing varies and occurs over the decades of life. At about age of 30, as a result of drooping of the excess skin of the upper eyelids, "crow's feet" in the lateral corners of the eyes begin to be marked. At the age of 40, the naso-cheek folds become clearly marked, the transverse wrinkles of the forehead and the vertical wrinkles between the eyebrows, the so-called "lion's wrinkles," become fixed. Around the age of 50, the jawline becomes much less pronounced, "hamsters" appear due to the drooping of the sides of the face, wrinkles appear on the neck and the end of the nose sinks. After the age of 60, the skin and subcutaneous tissue undergo further atrophy, which contributes to deepening wrinkles and skin flaccidity [5].

MICRO-NEEDLE MESOTHERAPY AS AN ANTI-AGEING TREATMENT

Micro-needle mesotherapy, also referred to as microneedling (MN), is a relatively new, minimally invasive procedure that involves controlled puncturing of the skin using thin needles. During the procedure, an area of skin is subjected to intensive, dense and appropriately deep puncturing, resulting in thousands of microneedles. Micropuncture is designed to stimulate the skin's natural potential for biostimulation, revitalization and reconstruction, as well as increase the absorption and effectiveness of therapeutic substances. The natural regenerative mechanisms created during the procedure lead to improved skin structure, tone and elasticity, thickening of the epidermis and improvement of its function, as well as an improved overall external appearance [9-12].

Micro-needle mesotherapy is used in a wide range of indications, which include anti-ageing prevention, skin rejuvenation, brightening of hyperpigmentation, levelling of dark circles under the eyes, stretch marks, acne lesions, atrophic and post-surgical scars, therapy of alopecia, as well as transepidermal delivery of active substances [9, 10].

Mechanism of action

The micro-needle mesotherapy procedure stimulates the formation of new collagen fibers in the dermis and renews and regenerates the entire epidermis. The microneedling procedure is also referred as collagen induction therapy (CIT) or percutaneous collagen induction (PCI) [10, 12].

Micro-needle mesotherapy is a procedure that uses two factors: a physical one, which is a prick that is a restorative signal, and a pharmacological one, so the deposition of active substances into the treated skin. The introduction of active substances into the bloodstream results in their distribution and direct effect on the cells of both the dermis and epidermis.

In turn, micro-damage to the skin stimulates natural repair mechanisms. As a result, the division of stem cells is activated and their metabolic activity is increased, leading to an increase in the synthesis of collagen, elastin and hyaluronic acid [3].

Physical factor

The micro-needle mesotherapy procedure involves controlled, mechanical damage to the skin through intensive puncturing with very thin needles of varying lengths. Due to the multiple micro-punctures, micro-bleeding occurs, leading to platelet activation and triggering a process comparable to wound healing. The healing process comprises three consecutive phases: inflammation, proliferation (the generation of new skin cells), and remodelling (the creation of new tissue [3, 12].

During the inflammation stage, which lasts about 72 hours after injury, clot formation and platelet activation occur. As a result, a number of cytokines and growth factors are released. These include transforming growth factor alpha (TGF-α), transforming growth factor beta (TGF-β), fibroblast growth factor 2 (FGF-2), epidermal growth factor (EGF), platelet-derived growth factor (PDGF) and connective tissue growth factor (CTGF). These factors accelerate the division, development and differentiation of skin cells and stimulate stem cells and fibroblasts to produce collagen, elastin and hyaluronic acid. They also exhibit a beneficial effect on improving microcirculation in the skin and the quality of intercellular connections. Neutrophils, leukocytes and macrophages released from blood vessels remove bacteria and damaged tissue fragments, cleansing the wound site [3, 10, 13] (Fig. 1).

The proliferation phase begins immediately after micropunctures, resulting in the reproduction of new cells. Reepithelialization and granulation occurs in this phase. The stratum granulosum and stratum spinosum of the epidermis

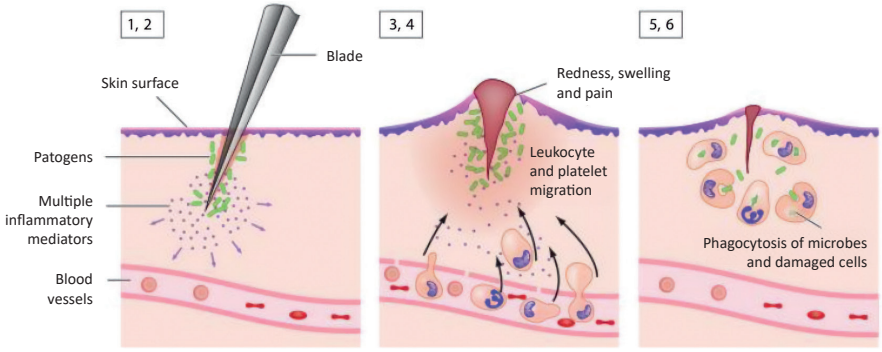

Fig. 1 Stages of the inflammatory process induced by skin damage **Source**: [14]

thicken, and epidermal icicles develop, leading to an increase in the integrity of the epidermis and dermis. Increased fibroblast activity affects the expansion of the extracellular matrix. The formation of elastin, collagen and new tissues and blood vessels also occurs. The proliferation of new cells continues for about 2-3 weeks [3, 13].

Granulation tissue, which is formed as a result of wound healing, consists mainly of fibroblasts, collagen and hyaluronic acid. Type III collagen predominates in granulation tissue, after which it is gradually transformed into type I collagen during a remodeling process. Through this process, the overall quantity of elastin in the skin is altered, leading to a transformation in its structure. When microneedling is applied, there is an observable increase in the quantity of well-aligned elastic fibres. Also, the angiogenesis is observed, or the formation of new blood vessels, which contributes to better oxygenation and blood supply to the skin. All the processes that occur during self-renewal result in an increase in the mechanical strength and elasticity of the tissues. The period of skin regeneration, restructuring and synthesis of new collagen lasts for several weeks after the procedure [3, 13, 14].

The research proved that micro-needle mesotherapy treatment is a safe method to promote regeneration without the risk of scarring. This is due to the increase in TGF-3 growth factor released during micro-puncture, which is responsible for scar-free healing. TGF-1 and TGF-2 factors are responsible for wound healing with scar formation [3].

Due to the processes discussed above, inducing microhemorrhage appears to be necessary to initiate the actual skin regeneration process associated with an increase in collagen and elastin production [10].

Pharmacological factor

Micro-needle mesotherapy can also exhibit additional pharmacological effects, which depend on the preparation used during the procedure. The intact epidermal barrier means that the active agents contained in cosmetics have limited ability to penetrate into the deeper layers of the intercellular space. Micropuncturing the epidermis significantly increases the penetration of active ingredients deep into the skin. As a result of numerous micropunctures, through the microchannels created during the procedure, there is an increase in the transepidermal penetration of active substances, depending on the preparation used. Studies have shown that the use of micropunctures before and after the application of cosmetics results in an increase in their absorption by up to 47%. In turn, the increase in transepidermal delivery lasts up to 72 hours after the treatment. Therefore, when performing skin microneedling, it is advisable to apply an appropriately selected product to the skin surface to enhance the intended effect. Special cocktails showing activity at the site of application are used for this type of treatment. The choice of the right preparation depends on the indications. The most common are preparations containing hyaluronic acid, proteins, minerals and antioxidant vitamins A, C, E. Substances used in micro-needle mesotherapy treatment should be sterile, water-soluble, well tolerated by the skin, biocompatible, isotonic, with a pH between 5 and 7, and chemically and physically stable. On the contrary, it is imperative that they are not oily or include any alcohol. Furthermore, it is essential that they possess the requisite certifications for parenteral administration and obtain the necessary approvals from the Ministry of Health [3, 10, 13, 15].

SKIN HEALING AND REGENERATION PROCESS IN ANTI-AGEING THERAPY

As defined by The Wound Healing Society, wound healing is "a complex, dynamic process that results in the restoration of continuity and anatomical function" [16]. The process of wound healing is associated with a defence mechanism that allows for the protection of the site of injury and the regeneration of damaged tissue to maintain homeostasis, since any damage to the skin poses a threat to the body. Repair of injured tissue involves the interaction of extracellular matrix elements, growth factors, cytokines and various cells that are involved in repairing the damage. Among the most important cells involved in wound healing are epidermal and connective tissue stem cells and cells of myeloid origin. Cell activity is regulated by the growth factors EGF, FGF, TGF, PDGF and VEGF [16-19].

Depending on the extent of the damage, there are two main modes of healing. In the case of shallow damage to the epidermis, involving only the outer layers of the epidermis, where there is no damage to the germ cells in the basal layer, healing involves simple tissue regeneration, associated with the renewal of successive layers of the epidermis. If the damage is deep, tissue repair is necessary, requiring filling the defect with connective tissue, resulting in a scar [17].

Inflammation

The first phase, inflammatory, begins very soon after the harmful agent is acted upon and lasts for several days. It is preceded by the mechanism of hemostasis, a process leading to the formation of a clot (in the case of the skin called a scab), which additionally serves as a reservoir of various cytokines and growth factors such as TGF-β , TGF-α , basic fibroblast growth factor (bFGF) and PDGF, released from activated platelets [16, 18, 20].

The developing inflammatory process in the connective tissue results in an influx of neutrophils, which are attracted to the wound within 24-48 hours of injury by chemotactic factors such as fibronectin, kinins and growth factors [16, 21]. Neutrophils accumulating in the wound environment cleanse the wound of external materials and bacteria, and provide a source of pro-inflammatory cytokines [16]. The developing inflammatory response is also triggered by the influx of other cells, such as lymphocytes and monocytes. Monocytes, after entering the damaged tissue, become macrophages, which release cytokines and growth factors, such as PDGF and VEGF, which help regenerate the damaged tissue [20, 21]. Other cells are also activated - myofibroblasts (connective tissue cells) that tighten the edges of the wound due to their ability to contract; angioblasts (vascular endothelial cells) that form new blood vessels in the wounded area; and fibroblasts that increase the synthesis of connective tissue fibers (especially collagen fibers) and extracellular matrix (ECM). In parallel with the stimulation of collagen production, its enzymatic degradation is inhibited [17]. Once the damaged structures are removed and possible pathogens are eradicated, the number of macrophages and inflammatory mediators is reduced, leading to a gradual extinction of inflammatory processes [22].

Proliferation

The proliferative phase begins after the first inflammatory stage and usually lasts 3-4 weeks after tissue damage. Several classes of cells proliferate in conjunction with the synthesis of connective tissue intercellular substance. Proliferation involves several processes simultaneously: granulation, angiogenesis (formation of new blood vessels) and epithelialization (epithelial regeneration) [20].

The first process is granulation leading to the formation of granulation tissue, which is newly formed, highly blood-starved connective tissue. The predominant cell type in granulation tissue are fibroblasts, whose proliferation is stimulated by the factor PDGF, as well as TGF-β 1 and TNF-α. As inflammation subsides, fibroblasts migrate to the damaged area, where they gradually multiply and begin to produce extracellular matrix components (hyaluronic acid, fibronectin, proteoglycans) and connective tissue fibers. The new granulation tissue that is formed at this stage is mainly type III collagen, the amount of which is 30% to 40%, while in the intact dermis it is about 20% [16, 18, 20].

The second, simultaneously occurring process, is neoangiogenesis, or the formation of new blood vessels, whose main task is to supply the newly formed tissue with oxygen. During this stage, chemotactic factors and growth factors are secreted, causing activation of endothelial cells of surrounding tissues. Metalloproteinases degrade the basement membrane of the endothelium, leading to the release of its cells. These cells, in response to chemotactic factors, migrate to the site where the formation of a new blood vessel is intended. The above processes occur under the influence of vasculotropin, integrins and proteinases. Exudate fluid containing growth factors that activate fibroblasts and keratinocytes escapes from the unsealed blood vessels. Once the tissue is supplied with oxygen, angiogenesis stops [17, 20].

The third process that occurs simultaneously with the previous ones is epithelialization, or epidermination. The epithelialization process involves the filling of cells of the basal layer of the epidermis into the area of damage in order to initiate proliferation and formation of a new basement membrane [20]. These processes are stimulated by the local release of growth factors such as EGF, TGF-α and keratinocyte growth factor (KGF) [21]. They also vary depending on the extent of tissue damage. If the damage is not too extensive, the source of cells is the wound edges and epithelial proliferative cells, such as matrix from hair follicles or skin glands. With extensive damage, in which glands and hair follicles have been destroyed, stem cells only crawl from the edges of the wound. The process of epithelialization occurs toward the centre, starting from the edges of the wound, and stops when the filling cells meet from opposite edges. Parallel to epithelialization, wound contraction occurs. This happens thanks to myofibroblasts, which are differentiated from fibroblasts, and by contracting they cause the edges of the wound to move closer together [20].

Redevelopment

The remodeling phase is the final stage of healing. It begins a few weeks after injury and can last for several years. As a result of the rapid reconstitution of tissue from newly synthesized collagen fibers and fibroblasts, a scar is formed and transformed. Remodeling of collagen fibers occurs - type I collagen displaces the initially formed type III collagen, the course of the fibers is reorganized by dissolution and re-synthesis. During this phase, fibronectin, hyaluronic acid

and other glycosaminoglycans play an important role in regulating remodeling processes. During the late phase of wound healing, there is a reduction in the number of already redundant fibroblasts and in the number of blood vessels that are required to supply the tissues being rebuilt. The reduction in the number of blood vessels is visible as a fading of the scar. The healing process ends with shrinking of the scar [16, 17, 20].

MEDIATORS OF INFLAMMATION - CYTOKINES AND GROWTH FACTORS

Regeneration of damaged skin is a complex physiological process that requires the coordinated action of many factors, including those secreted by various cell types - cytokines and growth factors belonging to the inflammatory mediators group. Mediators play key roles in the process of inflammation, which is the body's complex immune response to various types of harmful agents, such as infection, tissue damage or trauma. Mediators of inflammation cause four characteristic symptoms of inflammation, which include redness (*color*), swelling (*tumor*), warming (*calor*) and pain (*dolor*). Inflammation is a desirable process because it ultimately leads to healing of the damage [23-25].

Cytokines

Cytokines are a large group of polypeptides that play a key role in the processes of skin cell proliferation and differentiation. Cytokines are secreted by various cell types, including skin cells. In the dermis, they are produced by fibroblasts, endothelial cells, dendritic cells, macrophages, mast cells, lymphocytes and other inflammatory cells. In contrast, keratinocytes, Langerhans cells and melanocytes are primarily responsible for their production in the epidermis. Cytokines regulate various physiological processes - they play a crucial role in immune, inflammatory reactions, as well as in the processes of tissue regeneration and development. There are cytokines with opposing activities - pro- and anti-inflammatory [20, 23, 24].

Pro-inflammatory cytokines include interleukin IL-1 (α and β), tumor necrosis factor TNF-α, IL-2, IL-4, IL-5, IL-6, IL-8. IL-12. Interleukin IL-1 (α and β) induces keratinocyte differentiation, stimulates the proliferation of B lymphocytes, activates neurophils and macrophages, and affects the secretion of other pro-inflammatory cytokines. IL-1 is secreted continuously, in small amounts by the epidermis, and once its barrier is damaged, the secretion process increases significantly. Similar in scope to IL-1 is TNF-α. This cytokine has strong pro-inflammatory properties and affects early collagen synthesis. Both IL-1 and TNF-α are secreted by keratinocytes and Langerhans cells. In turn, IL-6, produced by the aforementioned cells and skin-settled immune cells, acts synergistically with other cytokines and enhances the activity of IL-1 and TNF-α. Anti-inflammatory cytokines include IL-10. This cytokine inhibits the immune response and the expression of the major tissue compatibility complex. IL-10 interrupts cytokine synthesis and also inhibits the release of reactive oxygen species [17, 24, 26].

Growth factors

Growth factors are a group of proteins that control cell proliferation and differentiation and regulate many physiological processes. Some cytokines can also be classified as growth factors, while others do not meet this criterion. There are many families of growth factors that include PDGF, EGF, FGF and the TGF-β [24].

PDGF factor is one of the most important and potent stimulators in wound healing and tissue regeneration. PDGF is the most important chemotactic factor for fibroblasts. The main sources of this protein are macrophages and platelets, as well as keratinocytes, fibroblasts and endothelial cells. PDGF stimulates the proliferation of fibroblasts and influences the production of extracellular matrix components by these cells in the later stages of the healing process. PDGF also induces the transformation of fibroblasts into myofibroblasts, which enables wound contraction [18, 19].

The EGF family includes a number of mitogens, including those crucial to the healing process: EGF, TGF-α , HB-EGF, epiregulin, amphiregulin and neuregulin. The main regulators of keratinocyte proliferation are EGF, TGF-α and HB-EGF. Growth factors belonging to the EGF family are mainly produced by macrophages and neutrophils migrating to the wound site. Moreover, keratinocytes located at the wound edges are an additional source of TGF-α. The action of EGF increases the thickness of the epidermis, stimulates an increase in the differentiation and proliferation of epidermal cells, and influences the activity of fibroblasts, which are involved in skin regeneration and wound healing [19, 24].

The FGF also plays an important role in the regeneration processes of damaged skin. The factors that primarily affect keratinocytes include FGF-7 (also called keratinocyte growth factor KGF-1), which, along with other proteins in its family, FGF-10 (KGF-2) and FGF-22, stimulate keratinocyte proliferation. A main role in the healing process of damaged skin is played by FGF-2 (also known as bFGF), which is secreted by macrophages and damaged endothelial cells. It initiates the process of angiogenesis (formation of new blood vessels) and exhibits the ability to proliferate and migrate epidermal cells [18, 19].

The TGF-β growth factor superfamily has many functions, the effects of which may vary depending on the dose and type of cells. In the process of wound healing, TGF-β is responsible for attracting monocytes, neutrophils and fibroblasts to the wound. At higher concentrations of TGF-β , monocytes are activated to secrete a variety of growth factors and fibroblasts are activated for increased production of cellular matrix. TGF-β exhibits dual effect on keratinocytes depending on the concentrations. It can stimulate the migration of keratinocytes and inhibit their

proliferation. TGF-β stimulates the production of extracellular matrix for procollagen production, and also acts as a growth factor for collagen production by fibroblasts [24].

SUMMARY

Skin ageing is a natural and inevitable process. Over time, the skin develops wrinkles, becomes dehydrated, thins out, and experiences a loss of firmness and elasticity. Micro-needle mesotherapy is a natural, relatively non-invasive treatment to delay this process. The key aspect of the treatment is the controlled damage to the skin caused by performing numerous micro-punctures at the appropriate depth. This results in microhemorrhage, which activates platelets and initiates a process similar to that which occurs during wound healing, contributing to skin remodeling. The healing process consists of three successive phases: inflammation, which activates platelets to release a number of cytokines and growth factors; proliferation, which is the multiplication of new skin cells; and remodeling, which is the formation of new tissue. These processes lead to, among other things, thickening of the stratum granulosum and squamous layer in the epidermis, increased synthesis of collagen and elastic fibers, and hyaluronic acid in the dermis. The aforementioned processes of micro-needle mesotherapy result in the stimulation of skin regeneration, leading to enhanced structural integrity, increased thickness of the living layers of the epidermis, improved hydration, and enhanced tension and elasticity. Micro-needling treatment is utilised for both anti-aging prevention and skin rejuvenation, rendering it a highly effective tool in skincare.

REFERENCES / LITERATURA

1. Zawadzki M, Szafraniec R, Murawska-Ciałowicz E. *Fizjologia człowieka. Podręcznik dla studentów wydziałów kosmetologii*. Wrocław: Górnicki Wydawnictwo Medyczne; 2017.
2. Padlewska K. *Medycyna estetyczna i kosmetologia*. Warszawa: Wyd. PZWL; 2022.
3. Kołodziejczak A. *Kosmetologia 1*. Warszawa: Wyd. PZWL; 2019.
4. Resich-Kozieł L, Niemyska K. Rodzaje oraz przyczyny starzenia się skóry. *Kosmetologia Estetyczna*. 2020;1(9):17-22.
5. Galicka E. Starzenie się skóry – Zmiany anatomiczne twarzy. In: Przypilak A, ed. *Medycyna estetyczna*. Warszawa: Wyd. PZWL; 2022:10-19.
6. Grządziel P, Goździalska A. Etiologia oraz możliwości spowalniania procesów starzenia się skóry. *Aesth Cosmetol Med*. 2022;11(1):3-10. https://doi.org/10.52336/acm.2022.001
7. Galicka E. Starzenie się skóry – Zmiany anatomiczne twarzy. In: Przypilak A, ed. *Podstawy medycyny estetycznej*. Białystok: Uniwersytet Medyczny w Białymstoku; 2014:14-18.
8. Donejko M. Zmiany mikroskopowe i metaboliczne w tkance. In: Przypilak A, ed. *Podstawy medycyny estetycznej*. Białystok: Uniwersytet Medyczny w Białymstoku; 2014:11-14.
9. Singh A, Yadav S. Microneedling: Advances and widening horizons. *Indian Dermatology Online Journal*. 2016;7(4):244-254. https://doi.org/10.4103/2229-5178.185468
10. Styczeń P. Mikronakłuwanie. In: Przypilak A, ed. *Medycyna estetyczna*. Warszawa: Wyd. PZWL; 2022:465-477.
11. Glenc-Ambroży M, Piejko L. Zastosowanie mezoterapii mikroigłowej w biorewitalizacji skóry twarzy – opis przypadków. *Polish Journal of Cosmetology*. 2020;23(2):125-131.
12. Osika A, Wesołowska A. Niechirurgiczne metody opóźniające procesy starzenia się skóry. *Farmacja Polska*. 2020;76(2):110-117. https://doi.org/10.32383/farmpol/119054
13. Gaweł E, Urtnowska-Joppek K. Mezoterapia mikroigłowa – aparatura oraz wskazania. *Kosmetologia Estetyczna*. 2019;8(5):607-611.
14. Drobnik A, Słodka A. *Kosmetologia z immunologią skóry*. Warszawa: Wyd. PZWL; 2021.
15. Glenc-Ambroży M, Bednarek J, Piejko L. Dermarollery i ich wykorzystanie w kosmetyce – opis przypadków. *Polish Journal of Cosmetology*. 2019;22(4):316-321.
16. Majewska I, Gendaszewska-Darmach E. Proangiogenic activity of plant extracts in accelerating wound healing – a new face of old phytomedicines. *Acta Biochimica Polonica*. 2011;58(4):449-460.
17. Błaszczyk M. *Histologia dla kosmetologów*. Nysa: Oficyna Wydawnicza PWSZ; 2013.
18. Jurzak M, Antończak P, Adamczyk K. Białko aktywujące fibroblasty α (FAPα) – udział w gojeniu tkanek i kancerogenezie. *Postępy Biologii Komórki*. 2011;38(4):597-612.
19. Pikuła M, Langa P, Kosikowska P, et al. Komórki macierzyste i czynniki wzrostu w gojeniu ran. *Postępy Higieny i Medycyny Doświadczalnej*. 2015;69:874-885.
20. Błaszczyk M. Skóra w ujęciu fizjologicznym. In: Kołodziejczak A, ed. *Kosmetologia 1*. Warszawa: Wyd. PZWL; 2019.
21. Fornalski J. Gojenie się ran z bliznowaceniem – metody terapeutyczne. *Borgis – Nowa Medycyna*. 2006;4:66-70.
22. Błaszczyk M. Skóra w ujęciu histologicznym. In: Kołodziejczak A, ed. *Kosmetologia 1*. Warszawa: Wyd. PZWL; 2019.
23. Chechlińska M. Rola cytokin w procesach nowotworzenia. Nowotwory. *Journal of Oncology*. 2003;53(6):648-659.
24. Ray Jalian H, Kim J. Immunologia skóry. In: Baumann L, ed. *Dermatologia estetyczna*. Warszawa: Wyd. PZWL; 2021.
25. Sawicki W, Malejczyk J. *Histologia*. Warszawa: Wyd. PZWL; 2012.
26. Kocik J. Udział cytokin i innych mediatorów w procesie gojenia rany. *Postępy biologii komórki*. 1996;23(1):63-82.

otrzymano / received: 04.01.2024 | poprawiono / corrected: 10.01.2024 | zaakceptowano / accepted: 16.01.2024