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## MORPHOLOGICAL AND FUNCTIONAL SUBSTANTIATION OF PREVENTION OF THE POSTOPERATIVE KELOIDAL SCARS OF THE FACE AND NECK

The development and improvement of methods of prevention of keloidal scars is an actual task. The effectiveness of existing methods of prevention of scars remains insufficient. Lipin solution and Dermofibrase cream applied for prevention in the patient with diagnosed polymorphism of the elastin gene g28197 A > G; the histological examination of biopsy were performed during the prevention every 3 month. In 12 months of observation of the skin structure at the site of operation, there was found that the structure of the skin matched the histological organization of mature hypertrophic scar, which confirmed the histological study. Considering above-mentioned, the use of Dermofibrase cream and Lipin liposome preparation would be appropriate for the purpose of prevention of pathological scarring already in the early stages of healing of postoperative wounds.

**Key words:** postoperative scar, pathological scar, prevention, microcirculation.

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The issues in prevention of formation of pathological scars are accompanied by solving of some problems. The numerous techniques and tools are applied for this purpose, such as enzyme therapy (as local injections and iontophoresis), hormone therapy, radiation therapy, Grenz rays therapy, beta therapy, therapy with biogenic stimulators, ultrasonic influence, Bernard currents, thermal treatment. These conservative measures aimed at preventing of the postoperative scars are not often sufficiently effective [1,4].

According to the literary sources of last decade on the issue in prevention of pathological scars, a growing interest to this problem at the level of ultrastructural mechanisms of pathogenesis should be noticed [3].

Analysis of the results of the prevention of formation of pathological scars presented in the literary sources shows that the relapse happened in 40-55% cases [23]. From the point of view of most experts, only comprehensive prevention helps to achieve the desired result [5].

**The purpose** of work was to establish the structural features of keloidal scars in patients inclined to formation of keloids and to study the biopsy during the prevention.

**Material and methods of research.** 60 patients ranged in age from 18 to 65 years with probable formation of postoperative keloids were under inpatient and outpatient treatment after the planned interventions because of various diseases and the primary surgical treatment of wounds. To all patients, with their written consent, before and during prevention conducting by Ліпін (Lipin) solution and Дермофібразе (Dermofibrase) cream was performed a genomic DNA from venous blood to define the elastin gene g28197 A > G; and to the patients with diagnosed polymorphism was performed the histological examination of biopsy.

**Results and its discussion.** In the histological study of keloids in patients inclined to formation of pathological scars, in the epidermis there was determined its thinning. Among the cells there were defined the atypical forms for different layers of the epidermis; the cells of basal layer were highly prismatic. The vacuolar degeneration, hypoplasia of keratinocytes and nucleus modified in kariopicnotic way were found in prickly layer. The thickness of granular layer reduced to 1 or 2 layers, the saturation with granules was low. The horny layer did not change.

In subepidermal zone of keloidal scars in patients with diagnosed polymorphism of elastin gene, we identified the flattening of epidermal appendages and dermal papilla, the mucoid swelling of collagen fibers. Epidermal derivatives (sebaceous glands, sweat glands, hair follicles) were not detected. In subepidermal layer there were identified the pockets of young connective tissue – “growth areas”. The concentric accumulations of fibroblasts were defined in their structure; in the heart of these accumulations there were localized the regressing capillaries. According to the literary sources capillary pericytes are stem cells for fibroblasts. Therefore, the accumulation of cells in growth areas consists of pericytes, which are transformed into fibroblasts [2]. Collagen fibers in the growth areas were visualized as unoriented friable bundles of immature collagen fibers in the mucoid swelling stage. There is some “lengthiness” of them and chaotic orientation due to increased tissue turgor because of edema. There are thin “communication fibers” together with thick ones. There are a large number of functionally active poorly differentiated young and pathological giant fibroblasts in keloidal scars. Their average number was  $87 \pm 4,29$  in sight.

In the middle sections of scar there was observed the variegated morphological picture caused by a combination of large regions of tissue with thick, randomly oriented collagen fibers with the areas of young connective tissue, localized in the thickness of the scar and the loci of degenerative changes and inflammatory reactions. Collagen bundles differ by the loose wrapping and disorientation. The thickness of collagen fibers is variable.

The most massive bundles of collagen fibers are in the middle zone of colloid. Between the collagen fibers there were identified the different populations of fibroblasts, from the immature and giant ones to fibrocytes with typical elongated shape

and normal size; the swelling was found in the interstitial substance. In the middle and deep sections of scar there were a reduced number of cellular elements, and interstitial substance. There is an increasing the number of morphologically mature forms of collagen fibers. The most massive collagen bundles were identified in the middle zone of colloid.

In keloidal scars in patients with diagnosed elastin gene polymorphism, the exchange element of microcirculatory bed is presented by capillaries, consisting of two types - separative and functional. In subepidermal layer of keloidal scars there were determined 3 – 5 microvessels of capillary type in sight, in the growth areas there was 1 vessel for 1 – 3 fields of vision. In separative capillaries there were visualized the stasis, stagnation, diapedesis of erythrocytes into perivascular connective tissue, which is a morphological evidence of tissue hypoxia. The lumens of functional capillaries did not contain the formed elements; some of them were in the reduction (fig.1). Around the vessels there were defined sometimes the clusters of cells of lymphocytic-histiocytic series.

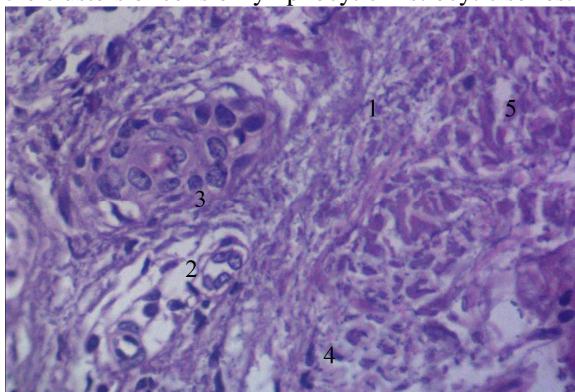


Fig. 1. The growth area of keloidal scar in patient with diagnosed elastin gene polymorphism. Hematoxylin-eosin stain; magnification: Ob.:x15; Ok.: x100.

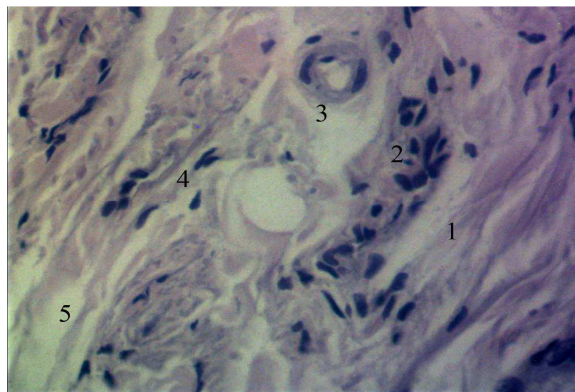


Fig. 2. Subepidermal zone in 9 months after the surgery to remove the keloids in patients with diagnosed elastin gene polymorphism, who received the proposed prevention. Hematoxylin-eosin stain; magnification: Ob.:x15; Ok.: x100.

In 3 months after the surgery to remove the keloids in patients with diagnosed elastin gene polymorphism, who received the proposed prevention, the study skin biopsies revealed that the epidermis was thinned. Layerwise structure was not determined. The cells and their nuclei showed the polymorphism, their size and shape were variable. The basement membrane on the border with connective tissue was absent. Under the epithelial layer there was found a young connective tissue that morphologically confirmed by the predominance of cellular component over the fibrous one. Most cells were young polymorphic fibroblasts, there were also the lymphocytes, plasma cells, macrophages and mast cells. Number of collagen fibrils was insignificant. The vast majority of intercellular substance was the amorphous component presented by glycoproteins and proteoglycans. In thin-walled vessels newly formed the formed elements of blood were not identified.

In the histological examination of skin biopsies in 6 months after the surgery to remove the keloids in patients with diagnosed elastin gene polymorphism, who received the proposed prevention, the identification of cell layers in the epidermis was not difficult, even the horny layer was formed by 1 or 2 layers of scales. However, there was found a violation of keratinization in the form of vacuolar degeneration of cells of basal and prickly layers. In the connective tissue, compared with the previous period of observation, the relative number of cells component decreased. Among the cells there were mainly identified fibroblasts and macrophages, sometimes there were determined the lymphocytes and plasmocytes. The wall of most formed vessels had a three-layer structure and was formed from the endothelial cells, basal membrane and adventitial fibroblasts. In the lumen of venules and veins manifested the hyperemia and stasis.

In 9 months after the surgery to remove the keloids in patients with diagnosed elastin gene polymorphism, who received the proposed prevention, the smoothing of epidermal appendages and the acanthosis were determined in the epidermis. Mitotic figures were visualized in the basal and prickly layers.

The normal hair follicles, sweat and sebaceous glands were determined together with distorted ones in the scar. In subepidermal zone, the thin collagen fibers formed a loose grid, in the intercellular substance dominated the chondroitin sulfates. The number of fibroblasts was significant, young forms were dominated among them. There were found also the lymphocytes, mast cells, plasma cells, macrophages (fig.2).

In the middle sections of scar, the scar tissue consisted of horizontally oriented collagen fibers, blood vessels, interstitial substance and cellular elements, whose number is reduced in comparison with the upper sections of the scar. In the vessel lumens there were defined sometimes the stasis phenomena, occasionally it was the desolation. In the lower sections, the collagen fibers formed the bundles oriented parallel to the skin surface, the density of bundles was high. The immature giant forms of fibroblasts were not identified. In subepidermal layer of scar there were determined the infiltrates, forming by clusters of lymphocytes and plasma cells that were in the connective tissue surrounding the microvessels.

In 12 months after the surgery to remove the keloids in patients with diagnosed elastin gene polymorphism, who received the proposed prevention, the histological examination of biopsies established that the skin structure at the surgery place matched the histological organization of mature hypertrophic scar.

### Conclusions

The histological study of skin after the surgical removal of scars and the proposed prevention in patients with keloids, inclined to the formation of pathological scars, was found that the structure of the skin at the site of operation

matched the histological organization of mature hypertrophic scar. The received data determine the relevance of preventive measures already in the early stages of healing of postoperative wounds for prevention of pathological scars.

#### References

1. Неклюдов А.Д. Коллаген: получение, свойства и применение: монография / А.Д. Неклюдов, А.Н. Иванкин. М.: Изд-во Моск. гос. ун-та леса, 2007. - 334 с.
2. Озерская О.С. Рубцы кожи и их дерматокосметологическая коррекция / Озерская О.С. – СПб. : ОАО «ИскусствоРоссии», 2007.–224с.
3. Brudnik U. Therapeutic problems connected with keloid treatment-new treatment possibilities. [Article in Polish]. / U. Brudnik, M. Podolec-Rubis, A. Wojas-Pelc // Przegł Lek.- 2006.-Vol.63, № 9.-P. 803-806.
4. España A. Bleomycin in the treatment of keloids and hypertrophic scars by multiple needle punctures / A. España, T. Solano, E. Quintanilla // Dermatol. Surg.- 2001.- Vol.27, № 1.-P. 23-27.
5. Reid R. R. Inhibition of procollagen C-proteinase reduces scar hypertrophy in a rabbit model of cutaneous scarring / R.R. Reid, J.E. Mogford, R. Butt // Wound Repair Regen. -2006.-Vol.14, № 2.-P. 138-141.

#### Реферати

##### МОРФОФУНКЦИОНАЛЬНЕ ОБГРУНТУВАННЯ ПРОФІЛАКТИКИ ПІСЛЯОПЕРАЦІЙНИХ КЕЛОЇДНИХ РУБЦІВ ОБЛИЧЧЯ ТА ШИЇ

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Розробка та вдосконалення методів профілактики келоїдних рубців шкіри, є актуальним завданням. Ефективність існуючих методів профілактики рубців залишається недостатньою. Для профілактики застосовували розчин «Ліпін» та крем «Дермофібразе» у хворим з виявленим поліморфізмом гена еластина g28197 A>G та гістологічне дослідження біоптату в період профілактики через кожні 3 міс. Через 12 місяців спотереження структура шкіри на місці операції встановило, що структура шкіри на місці операції відповідала гістологічній організації зрілого гіпертрофічного рубця, що підтвердило гістологічне дослідження. Враховуючи вищезазначене доцільним було б використання крему «Дермофібразе» та ліпосомального препарату «Ліпін» з метою профілактики патологічного рубцювання вже на ранніх стадіях загоєння післяопераційних ран.

**Ключові слова:** післяопераційний рубець, патологічний рубець, профілактика, мікроциркуляція.

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##### МОРФОФУНКЦИОНАЛЬНОЕ ОБОСНОВАНИЕ ПРОФИЛАКТИКИ ПОСЛЕОПЕРАЦИОННЫХ КЕЛОЇДНИХ РУБЦОВ ЛИЦА И ШЕИ

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Разработка и совершенствование методов профилактики келоїдних рубцов кожи, является актуальной задачей. Эффективность существующих методов профилактики рубцов остается недостаточной. Для профилактики применяли раствор «Липина» и крем «Дермофибразе» в больным с выявленным полиморфизмом гена эластина g28197 A> G и гистологическое исследование биоптата, в период профилактики через каждые 3 мес. Через 12 месяцев спотережения структура кожи на месте операции установило, что структура кожи отвечала организации зрелого гипертрофического рубца, что подтвердило гистологическое исследование. Учитывая вышеупомянутое целесообразным было бы использование крема «Дермофибразе» и липосомального препарата «Липин» с целью профилактики патологического рубцевания уже на ранних стадиях заживления послеоперационных ран.

**Ключевые слова:** послеоперационный рубец, патологический рубец, профилактика, микроциркуляция.

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##### ДИФЕРЕНЦІЙНА ДІАГНОСТИКА НОРМОТРОФІЧНИХ ТА ПАТОЛОГІЧНИХ РУБЦІВ ГОЛОВИ ТА ШИЇ

##### DIFFERENTIAL DIAGNOSTICS OF NORMOTROPHIC AND PATHOLOGICAL SCARS OF HEAD AND NECK

Визначені відмінності морфологічної будови рубцеваних тканин різних типів. Під спостереженням знаходились 118 пацієнтів із нормотрофічними, гіпертрофічними та келоїдними рубцями голови та ший. Були визначені аномалії васкуляризації та іннервації різних типів тканин. Суттєво відрізняється кількісний та якісний показник основних клітинних диферонів та волоконних структур. Саме ці умови, на наш погляд, визначають основу диференціального підходу та в майбутньому можуть визначити об'єктивність підходу до лікування та профілактики рубцевих змін шкіри голови та ший.

**Ключові слова:** патологічні рубці, діагностика.

The differences of morphological structure of scurvy tissues of different types are determined. 118 patients with normotrophic, hypertrophic and keloid scars of head and neck were observed. Anomalies of vascularization and innervation of different types of tissues were determined. The quantitative and high-quality indexes of basic cellular diferones and fibrous structures differed substantially. Exactly these terms, in our opinion, determine basis of differential approach and in the future can determine the objectivity of treatment and prophylaxis of cicatricial changes of skin of head and neck.

**Key words:** pathological scars, diagnostics.

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*This work is the fragment of research work “Optimization of conservative and surgical treatment of patients which have defects and deformations of tissues of maxillofacial area” (number of state registration 0110U004629).*

Будь-яке порушення цілісності шкірного покриву людського тіла призводить до виникнення рубцевої тканини. Регуляція даного процесу залежить від багатьох, як ятрогенних, так і загальносоматичних факторів. Ятрогенні фактори обумовлені глибиною та площею пошкодження, терміном перебігу ранового процесу, видом

Any violation of integrity of a skin of human body makes the origin of cicatricial tissues. Regulation of this process depends on many paratherapeutic and general somatic factors. Paratherapeutic factors are conditioned by depth and area of damage, by the term of motion of healing process, kind and activity of traumatic agent.