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EVALUATING THE EFFECTIVENESS OF GLUCOCORTICOSTEROID MONOTHERAPY FOR THE TREATMENT OF KELOID AND HYPERTROPHIC SCARS

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ОЦЕНКА ЭФФЕКТИВНОСТИ ПРИМЕНЕНИЯ МОНОТЕРАПИИ ГЛЮКОКОРТИКОСТЕРОИДОМ ГИПЕРТРОФИЧЕСКИХ И КЕЛОИДНЫХ РУБЦОВ

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Treatment of pathological excess scars is one of the urgent problems in rehabilitating patients after injuries and operations. A comparative analysis of the treatment results of 260 patients who developed pathological scars after injuries using glucocorticosteroid hormone (triamcinolone acetonide) was carried out. Stable remission in all patients with keloid scars was achieved. Monotherapy with triamcinolone in patients with hypertrophic scars did not show high efficiency. A good but short-term effect was conducted, including a reduction in connective tissue and scar size with a noticeable analgesic and antipruritic effect. However, later hyperplasia of the scar was noted. Thus, the analysis of the data obtained indicates a greater pathognomonic and expediency of monotherapy with triamcinolone for the treatment of keloid scars. In contrast, its use in hypertrophic scars is possible only as part of combined anti-scar therapy.

Keywords: keloid scar, hypertrophic scar, triamcinolone acetonide, treatment

Лечение патологических избыточных рубцов является одной из актуальных проблем реабилитации пациентов после травм и операций. Проведён сравнительный анализ результатов лечения 260 пациентов, у которых после травм развились патологические рубцы, с применением глюкокортикостероидного гормона (ацетонид триамцинолона). Стойкая ремиссия была достигнута у всех пациентов с келоидными рубцами. Монотерапия триамцинолоном у пациентов с гипертрофическими рубцами не показала высокой эффективности. Был достигнут хороший, но краткосрочный эффект, включающий уменьшение соединительной ткани и размеров рубца с заметным обезболивающим и противовоспалительным эффектом. Однако в дальнейшем отмечалась гиперплазия рубца. Таким образом, анализ полученных данных свидетельствует о большей патогомоничности и целесообразности монотерапии триамцинолоном для лечения келоидных рубцов, в то время как его применение при гипертрофических рубцах возможно только в составе комбинированной противорубцовой терапии.

Ключевые слова: келоидный рубец, гипертрофический рубец, триамцинолона ацетонид, лечение

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COX – cyclooxygenase
TA – triamcinolone acetonide

TGF- β – transforming growth factor- β

The prevention and treatment of excessive abnormal scarring are now of great importance in the rehabilitation of patients after injuries and operations and require an interdisciplinary approach, including dermatology, surgery and rehabilitation medicine, and immunology, as detailed research and thorough understanding of the processes involved in the development of scar tissue, allows influencing its growth. Interdisciplinary teams usually participate in this process [1–3].

Over the past decade, it has been the pathological hypertrophic and keloid scars that an increasing number of patients have sought medical treatment for injuries and surgeries. These are mainly pediatric patients and young patients of working age [4]. Coarse deforming scars caused by tissue damage cause both physical and psychological discomfort, which undermines the patient's quality of life and leads to incapacity. Statistics obtained by the WHO Data Analysis Division indicate that surgical procedures of varying complexity are performed annually for more than 100 million people, of which 4–10 % are affected by keloid and hypertrophic scarring, while 10–15 % of burned patients show excessive growth of connective tissue in the area of damage [5]. Currently, there is no agreed standard of treatment and prevention for the treatment of pathological scars, which contribute to various therapeutic regimens, and medicines that are not always pathogenically justified. There are, however, some groups of drugs that demonstrate efficacy that is justified by their specific effects either on inflammatory factors or on the formation of collagen and immune responses of tissues in the area of damage [1, 6, 7].

Pathological scars are diverse, while hypertrophic and keloid scars are the most notable. Given that the surgical treatment of keloid scars (the most complex variant of pathological scarring) contributes to more severe relapses in 50–100 % of cases, pharmaceutical approaches have become particularly important [8].

Hypertrophic scars, as well as keloids, are caused by thermal damage, cuts, surgical interventions, piercing and exposure to other traumatic agents. Still, hypertrophic scars commonly develop at the site of thermal and mechanical injuries, especially if deep layers of the dermis

are involved and high levels of β -transforming growth factor (TGF- β) are expressed. Unlike keloids, hypertrophic scars contain nerves and blood vessels. However, symptoms like pain or itching are more characteristic of keloid scars [9, 10]. A specific role in the development of hypertrophic scars belongs to abnormal fibroblasts (HS-subtype) and impaired chemical signaling. A great number of mast cells and their excessive activity are associated with moderate synthesis of TGF- β and enhanced synthesis of HIF-1 α (hypoxia-inducible factor-1 α), VEGF (vascular endothelial growth factor), plasminogen activator inhibitor-1 (PAI-1) and other known promoters of fibrosis induce chronic fibronectin sedimentation and neovascularization.

The study aimed to compare the results of local treatment of triamcinolone (TA) acetonide in patients with pathological scarring.

Material and Methods. A comparison of treatment and clinical trials involving patients with hypertrophic and keloid scars of varying maturity was conducted to obtain data on the feasibility of TA injections for treating hypertrophic and keloid scars in monotherapy.

Two hundred and sixty patients between the ages of 16 and 54 were under observation at various points in time, corresponding to their physical condition and lack of comorbidity, which could affect the scarring process; with comparable results for the severity of trauma and operations that have developed excessive pathological scars from injuries. Notably, keloids were 1.7 times less common than hypertrophic scars – 141 (68 %) patients with hypertrophy and 79 (32 %) with keloid scars. All patients were divided into two groups depending on the type of scar tissue. Group 1 (keloid scars) included 79 patients with keloid scars, which were additionally divided into two subgroups: 1A (main subgroup) – 54 patients; 1B (control subgroup) – 25 patients. Group 2 (hypertrophic scars) included 141 patients with hypertrophic scars; all patients were also divided into two subgroups – 2A (the main subgroup) – 75 patients and 2B (the control subgroup) – 66. The monitoring was performed as a clinical examination over 6 to 18 months.

All patients in major groups (subgroups 1A and subgroups 2A) received monotherapy with TA. The agent

was injected into the scar tissue one time with an interval of 7 to 9 with treatment mode no. 5 using radial infiltration into the scar tissue. During the free intervals from treatment, patients independently used TA ointment, applying it to the scar. The final evaluation of the effectiveness was carried out by clinical data analysis, ultrasonography, histochemical analysis of scar tissue (selectively), and an analysis of the history of the disease filled by the patient once a week with an assessment of the subjective sensations and parameters of the scar.

It should be noted that there is no «recommended» period for the use of TP for treating keloid scars since collagen contained in keloids does not evolve into mature forms, and the related processes are mainly of intensity and not of the stage, unlike hypertrophic scarring. In patients with hypertrophic scars, IEDs were used at various stages of scarring maturation and had a less significant effect.

In control groups (Subgroup 1B and Subgroup 2B), patients received combined anti-loss therapy similar to keloids and hypertrophic scars, which included compression of the scar area with cohesive tapes or bandages, multi-component anti-scarring scars gels and physiotherapy procedures.

Statistical processing was performed in Statistica 10.0 (Statsoft, USA). The comparison was made using the Mann – Whitney U-test and Student's t-test. The value $p < 0.05$ was chosen as the critical level of statistical significance of differences.

Results and Discussion. Considering the fact that intramuscular TA inhibits the release of COX-2 and fibroblast activity, as well as slowing the migration of leukocytes, the release of IL-1 macrophages and the synthesis of type 1 collagen in pathological keloid fibroblasts, TP can be used to treat this specific pathological excessive scar. With TA infusion, the scar loses its density, decreases in size and ceases to cause physical discomfort to the patient (itching, pain, pressure, and tension sensations are significantly reduced).

The effect of pain relief was seen on average 2.1 ± 0.3 days after the first injection and showed no reductions for the entire treatment period. Recurrent pain and itching developed in 40 % (22 patients) cases on average after three months and were much less severe on a pain assessment scale that could be stabilized by injecting 1 TA into scar tissue. In case of repeated pain and discomfort, the injection course is once a month for the first four months, followed by one injection every three months during the year for sustainable remission. Stable remission was achieved in all cases. Scar density was reduced. It's restructuring, reduced volume, length and width were recorded in 46 patients (85 %) 4 days after the first TA injection (Figure). There has not been a complete reduction of keloid through TP injections, and all patients rate their scar as a «slight increase over the skin» in the questionnaire.

A comparison of the results with subgroup 1B showed higher TA efficacy. The combination anti-scar treatment in 17 (68 %) patients produced no significant effect and reported perpetual itching and scar sensitivity. No significant changes of either density or scar displaceability were seen during the examination; height, width and length showed no significant differences. The ultrasound scan was unremarkable. Five patients (20 %) reported moderate subjective improvement, including itch and pain of lesser intensity and visibly reduced scar during three months of follow-up. Reduced density and mass of the scar tissue were objectively noted. The effect was considered positive in three patients (12 %), as evidenced by examination results when assessed subjectively and

objectively. A positive outcome was noted in 51 (94 %) subgroup 1B. However, we did not obtain a significant ($p > 0.05$) result for treatment between subgroups.



Fig. Keloid scar that developed after surgery of benign skin neoplasm: A) type of scar before treatment; B) the appearance of the scar after 1 month of treatment with TA

Comparative analysis of the use of TA in monotherapy in a subgroup of studies of patients with hypertrophic scars showed the effectiveness of combined therapy much higher throughout the maturation of the hypertrophic scar. Reduced pain and itching and a feeling of pressure in the scar area were observed in all patients during the examination for two weeks of treatment in both subgroups; two weeks later, 57 patients (76 %) reported frequent itching and feeling of pressure during the study, while only 7 (11 %) Subgroup 2B had itching, sensitivity and limited skin mobility in the scar area. Subsequent monitoring by ultrasound and histology of scar tissue showed higher efficacy of combination therapy for hypertrophic scarring. Three months later, 61 patients (92 %) of Subgroup 2B showed a positive trend that was clinically significant and confirmed by subjective (re-interview) and objective changes, including changes in the height and width of the scar, reduced density, structured scar tissue fibers, and collagen ripening according to minimum age. However, 69 2A patients showed no significant alteration to the scar tissue. The density, height and width of scar tissue, subjective symptoms, and scar tissue swelling were obtained. The effect is positive in six patients who did not report itching and sensitivity; the study found a decrease in scar tissue density, a reduction in edema, a change in the length and width of the scar tissue, and a decrease in scar tissue maturation.

Monotherapy with TA in patients with hypertrophic scars did not bring the expected effect. Based on the results of the study, a good but transient effect, including reduced connective tissue, reduced scarring, Prominent pain-relief and antipruritic action of TA was demonstrated when used during the first three months after damaging with hypertrophy development, but followed by (on average 2.2 ± 0.5 weeks) progression of scar active pathological hyperplasia.

The use of TA in patients with hypertrophic scars did not have an effect comparable ($p < 0.01$) to that observed in TA in the treatment of keloids. This is probably due to a different formulation and specificity of the development and maturation of scar tissue. The use of TA in subgroup 2A caused the growth of connective tissue. In addition, no continuous (more than seven days) pain relief and itching were found in the scar area. All patients voluntarily switched to combined scar therapy, with the subsequent remarkable positive effect.

Some authors claim [11–13] that the hyperproduction of TGF- β in combination with interleukin-6 (IL-6), PDGF (growth factor derived from platelets), $\alpha 1\beta 1$ -integrin, and IgA, G and M are involved in the formation of keloids. In addition, the appearance of keloids is closely related to the immune transformation of the sebaceous glands and increased androgenic receptor expression with increased secretion and lipid metabolism alteration, decreased cell apoptosis and neurogenic inflammatory reactions.

The humoral and cellular immune component in the formation of keloids is represented in various studies by increased IL-4, IL-5, IL-6, IL-13 and IL-21 with simultaneous reductions of IL-12 and interferon- γ (IFN- γ) [14–16].

There is a clear difference in histochemical characteristics. Overexpression of cyclooxygenase type 1 (COX-1) is observed in hypertrophic scars, while cyclooxygenase type 2 (COX-2) is observed in keloids. It is known that a large number of pigments (melanin) present in the skin are predictors of keloid formation [16, 17]. When injected into tissue, TA suppresses leukocyte and macrophage function, restricting leukocyte migration into the inflammatory node, impairs the ability of macrophages to produce interleukin-1; suppresses fibroblast and collagen formation; inhibits the activity of A2 phospholipase resulting in inhibition of prostaglandin and leukotriene synthesis. It suppresses the release of COX (COX-2 mainly). The report suggests the ability to activate cell apoptosis [18]. Due to this mechanism, TA is used to treat excessive pathological scars.

Conclusions. Based on the analysis of subsequent data, it was concluded that the use of TP is very effective when it is used as a monotherapy for the treatment of keloids, regardless of the age of the scars. In addition, this remedy may be a component of combined conservative therapy for treating hypertrophic scars. Still, from our point of view, it does not produce any significant independent long-term effect when used as a single treatment for hypertrophic scars.

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IMPROVEMENT OF SURGICAL CARE FOR CHILDREN WITH FOREIGN BODIES IN THE AIRWAYS

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СОВЕРШЕНСТВОВАНИЕ ХИРУРГИЧЕСКОЙ ПОМОЩИ ДЕТЯМ С ИНОРОДНЫМИ ТЕЛАМИ ДЫХАТЕЛЬНЫХ ПУТЕЙ

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An analysis was made of 1355 children with a suspected foreign body of the respiratory tract (FB RT), treated in the 2nd clinic of the Samarkand Medical Institute over the past 20 years. Of these patients, 948 patients were diagnosed and were divided into two subgroups according to the method of treatment. In the first subgroup of 478 patients with FB RT, from 2000 to 2009, the removal of FB was performed using rigid bronchoscopy. In the second subgroup of 470 patients treated from 2010 to 2019, the removal of FB was conducted by video bronchoscopy. The use of video bronchoscopy contributed to a clear visualization of all departments of the AP RT, made it possible to easily and quickly remove the latter, significantly improved the course of the post-bronchoscopy period, and reduced the development of late complications.

Keywords: foreign body, respiratory tract, children, video bronchoscopy

Произведен анализ 1355 детей с подозрением на инородное тело дыхательных путей (ИТ ДП), пролеченных во 2-й клинике Самаркандского медицинского института за последние 20 лет. Из этих больных у 948 пациентов диагноз был подтвержден, и по методу лечения они были разделены на две подгруппы. В первой подгруппе – 478 пациентов с ИТ ДП, в период с 2000 по 2009 год, удаление ИТ проводилось при помощи жесткой бронхоскопии. Во второй подгруппе 470 пациентов, пролеченных в период с 2010 по 2019 год, удаление ИТ проводилось методом видеобронхоскопии. Применение видеобронхоскопии способствовало четкой визуализации всех отделов ДП и ИТ, позволило легко и быстро проводить удаление последнего, значительно улучшило течение постбронхоскопического периода и уменьшило развитие поздних осложнений.

Ключевые слова: инородное тело, дыхательные пути, дети, видеобронхоскопия

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