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REVIEW ARTICLE

CICATRICIAL DEFORMITIES MANAGEMENT: A NARRATIVE REVIEW

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Abstract

Background: Treatment and prevention of the development of pathological scars (hypertrophic and keloid) is an important issue in modern dermatology and plastic surgery due to a violation of aesthetic perception (aesthetics), and in severe cases, the function of various areas of the human body.
The purpose of this systematic review of the literature was to analyze the proposed effective methods for treating scar deformities of the skin.
Methods: The systematic review included articles from Google Scholar, Medline, Scopus, Web of Sciences, PubMed. Search keywords terms included: pathological scar, therapy, botulinum toxin, laser, cryodestruction, hyaluronidase, skin scar prevention, new methods of wound treatment, wound and skin scarring, bioengineering surgery.
Results: Conducted a preliminary search and reviewed 132 titles and abstracts in this review and 50 full-text articles were selected of high methodological quality.
This review concluded the necessity of developing pre-surgical methods for preventing pathological scarring, which could potentially become a universal standard for any plastic and aesthetic surgery intervention. Treatment depends on the clinical and morphological characteristics of athological scars.
Conclusion: The current systematic review demonstrated the need to develop presurgical methods for the prevention of pathological scarring, which could in the future become a universal standard for any intervention in plastic surgery, since the issue of treating skin scars is sufficiently covered in the available world literature.

Keywords: *pathological scarring; therapy; botulinum toxin; laser; cryodestruction; hyaluronidase; prevention of scarring; new methods of wound treatment; wound and skin scarring; bioengineering surgery.*

Introduction

Facial scars are known for their unsightly appearance and are often associated with previous surgery or lacerations. Extensive cicatricial deformations of the face significantly disfigure the appearance, leaving both patients and surgeons dissatisfied with the treatment outcomes. Enlargement of the scar area is facilitated by the presence of opposing forces that separate the line of the postoperative suture, especially in the area of newly formed collagen until its maturation.[1] Particularly unfavorable may be scar formation on the face due to muscle tension, which stretches the skin edges and forms a scar under secondary tension.[2]

Opposing vectors in the scar area arise due to

muscle tension, elasticity of adjacent skin, and external pressure. Thus, the enlargement of cicatricial deformation is mainly the effect of mechanical impact on elastic and immature collagen. Also, overexpression of connective tissue growth factor (CTGF) is an important factor in hypertrophic scar formation.[3] Increased levels of melatonin also have a negative impact on skin healing and scar formation.[4]

Physiologically, wound healing is a synergistic process and consists of four interrelated phases, including hemostasis, inflammation, granulation tissue formation, and wound remodeling. In cases of unfavorable wound healing, there may be changes in the patients' (especially in children) psychosocial status. In such wounds, the inflammation phase is prolonged, leading to the formation of hypertrophic and keloid scars, which are thick areas of reddish skin that protrude above unaffected adjacent skin and can lead to aesthetic and functional impairments.[5] For this reason, most patients with facial scars strive to improve their appearance, even in minor changes.[6]

Although the etiology of pathological scar formation is still not fully understood. But it is widely accepted that excessive tension in the wound area is a negative factor for the normal healing process.[7]

It is important to note that pathological scarring is not uncommon and occurs in 40-70% of cases after various surgical interventions and up to 90% cases after burns. Pathological scarring causes a substantial portion of visits (25%) to dermatology and cosmetology clinics[8] It is estimated that approximately 100 million people worldwide develop scars for various reasons each year, with 15% of cases being pathological.[9] Moreover, in some regions the incidence pathologic scarring reaches 16%, which necessitates the need to control the wound healing process, treat keloid and hypertrophic scars and finding effective measures to prevent their development.[10]

In terms of areas of predominant formation of skin scars, the face and the upper half of the body prevail (about 90%). Kutsenko et al. (2010) noted that keloid scars are more likely form on chest (about 40% of cases), on the upper back (about 40% of cases), and less frequently on the face (about 1.5%), but quite often (about 10%) on the earlobes.[11]

Methods of pathologic scars treatment

All currently used strategies for pathological scarring management, except surgical methods, can be divided into several major groups: therapeutic, physical, physiotherapeutic, and alternative methods, including the use of botulinum toxin and tissue-engineering technologies.

1) Therapeutic management (longidase, hormone therapy, cytostatics)

Therapeutic options for the management of hypertrophic scars are quite widely used in dermatology. They mainly include drugs with high enzymatic properties, for example, hyaluronidase derivatives. Despite the large number of similar substances, not all of them can be used due to high toxicity and insufficient effectiveness in breaking down excessively formed collagen, limiting the aesthetic and functional outcome of treatment.[12]

One of the most commonly used drugs with enzymatic activity is longidase, containing about 3000 IU of hyaluronidase on an azoximer bromide carrier. The introduction of longidase allows prolonging the action of hyaluronidase by increasing the stability of molecules and protecting them from inhibitors (up to 7 days). The therapeutic effect of longidase is associated with breaking down excess fibrotic tissue and inhibiting the synthesis of new collagen fibers by depolymerizing proteoglycans through inhibition of metalloproteinase-1.[13] The longidase also has anti-inflammatory, detoxifying, and antioxidant effects, allowing its use not only in dermatology but also in other areas of medicine.[14] The effectiveness of longidase depends on its administration route (parenteral, enteral, topical) and can reach up to 70% note a good clinical outcome from longidase injection directly into the pathological scar.[13,15] However, the injection is very painful for the patient, and undesirable reactions may develop in the long-term.

In recent decades, hormonal drugs (Diprospan, triamcinolone acetonide, and others) have been frequently used in the postoperative period for the prevention and management of pathological scars. Their injections reduce collagen synthesis of a newly formed scar, inhibiting the mitotic activity of fibroblasts and increasing collagenase content. Hormonal drugs suppress the active inflammatory process, which also affects the appearance of the scar. Hormonal agents can be used as monotherapy

for keloid scars management or in combination with surgery or during application of silicone agents for symptomatic therapy.[16,17]

Complications of glucocorticoids include skin atrophy and pigmentation.[18,19] In the past decade, several studies found the effectiveness of treating keloid scars during corticosteroid therapy in combination with cytostatics (5-fluorouracil, bleomycin, and others).[18]

2) Physical methods

Cryotherapy

One of the methods of treating keloid scars actively used in dermatology is their cryodestruction using liquid nitrogen. When cryogenic agent is applied at low temperatures, local necrosis of microvessels and fibroblasts is observed. However, Shafranov et al. note that such changes are very limited and do not always extend to the full depth of the keloid scar.[20] According to I.V. Kutsenko (2010), who treated 68 patients with keloid scars of the face and neck using «Cry-Ac Tracker», exposing the affected area with -40°C temperature for 2 minutes, complete resolution of scars with a limited size (no more than 10 cm) is achieved in 97% of cases within 3-8 weeks.[11] It is worth noting that in almost 80% of cases, the author had to perform not just one treatment session, but 2 or 3, depending on the size of the scars. Only in 2 patients, even after completing the entire course of therapy, a positive effect was not achieved. The biggest advantage of cryotherapy is the possibility to create a strictly controlled zone of tissue necrosis in the desired area of the face and body.

Brachytherapy

As an adjunctive method in practical dermatology, focused X-ray therapy (brachytherapy) is also used in combination with other techniques for preventing keloid scar formation and inhibiting their growth after surgical excision. S.G. Ananian and A.G. Stenko (2009) applied local treatment for small or massive scars with single-field or multi-field irradiation respectively using an X-ray machine.[21] Particular emphasis was paid to treating patients with scars larger than 10 cm2 according to the scheme recommended by K.F.Sibileva (1977), under certain physical conditions (current strength, distance between the radiation source and the surface, wavelength). The absorbed radiation dose per single exposure ranged between 1000 and 1500 Rad and depended on the health status of the patients, their age, the extent of scar, and their localization. The number of procedures ranged from 2 to 10, and absorbed does not exceed 10,000 Rad. Treatment was carried out in the postoperative period after complete wound healing with active monitoring of the effect or development of adverse reactions. In case of unpleasant reaction, it is recommended to discontinue brachytherapy sessions immediately. Also, the brachytherapy should not be performed in the presence of unfavorable factors, such as increased UV exposure in summer.

The effectiveness of the treatment was assessed based on changes in clinical parameters, such as: reduction of intensity of local symptoms (burning or itching) and discoloration, volume and height of scars, their density and mobility. The effectiveness of brachytherapy on the process of scar regression, the absence/presence of relapses and side effects from the treatment itself was also evaluated.

Laser therapy

In the last few decades, various types of laser therapy (fractional non-ablative laser with a wavelength of 1540 nm, carbon dioxide laser with a wavelength of 10600 nm, neodymium-yttrium-aluminum-garnet laser with a wavelength of 532 nm, erbium laser with a wavelength of 2940 nm) have been intensively used for the treatment of pathological scars with a good clinical outcome in reducing scar density and collagen fiber content. However, the level of evidence is limited and requires further evaluation of the effectiveness of this treatment method[9,22,23,25;26,50] examined and treated 218 patients with pathological scars using a carbon dioxide laser. The evaluation of treatment results was based on the POSAS scale (Patient and Observer Scar Assessment Scale) and ultrasound examination using a linear probe.[27,28] The POSAS scale is composed of both subjective (pain in the scar area, itching, burning) and objective (scar color, its thickness and height, mobility) criteria. Carbon dioxide laser with a wavelength of 10600 nm with CPG and Deep FX scanners was used to treat patients with pathological scars. The Laser therapy was divided into 3 stages: deep fractional ablation (60-140 mJ), surface ablation (50-70 mJ, 350Hz), entire surface ablation (100 mJ,125-150 Hz). The authors concluded that carbon dioxide laser is not

sufficiently effective in cases of scar deformities alongside with functional impairments, where surgical treatment may be more appropriate. Thus, laser therapy is effective at the early stage of scar formation.

It should also be noted that laser therapy is less dependent on the cause of pathological scarring and its localization.

3) Physiotherapy

Physiotherapy can be used as a stand-alone treatment or in conjunction with other therapies. In the case of multicomponent treatment, using laser, ultrasound, electric or magnetic field as a physical factor, a general method drug phoresis is implemented, in which the additive effect of such treatment is noted, exceeding the result of each individual components.

O.S. Ozerskaya (2007) noted good clinical outcome of using drugs with enzymatic activity (such as collagenase). But in conjunction with physiotherapy (various phoresis techniques, microcurrents, mesotherapy), no side effects or tissue adaptation to the exposure method were noted, especially in the case of using a magnetic field.[29]

The literature highlights the clear advantage of complex approach compared to monotherapy with enzymatic medication, based on the summation and enhancement of the therapeutic effect of each component of treatment. Multicomponent therapy prolongs the activity of drugs and avoids additional trauma to surrounding tissues during targeted delivery of the active substance to the pathological focus.[8,30]

N.N. Potekaev et al. (2017) treated 50 patients with skin scar deformities at various sites and stages of healing using a magnetic field, which was applied to the affected areas in a pulsed mode with (Tp - 1.5-2.5 milliseconds).[8] The treatment consisted of 10 procedures for hypertrophic scars, and 15 - for keloid scars. The magnetic therapy was conducted in combination with 3000 IU of hyaluronidase administration. The authors noted a substantial reduction of the area of scar deformation by 75% in most patients (94%) at the end of the treatment period.

4) Alternative methods of treatment (BTA, new experimental modalities)

The onion extract is actively used in clinical dermatology for the treatment of hypertrophic scars and showed its effectiveness in improving the quality of the scar and reducing symptoms in patients.[31,32] However, in several randomized controlled trials, the results of its use were comparable to those with standard therapy using petrolatum emollient.[33] Moreover, no additional positive effect was found when compared to products containing silicone. However, the data may be insufficient due to the treatment of patients with burn pathological scarring rather than postoperative or post-traumatic cicatricial deformity.[34]

In the last decade, botulinum toxin has been actively used not only for correcting aesthetic and age-related aesthetic issues but also for management and prevention of the development of pathological scars.

Botulinum toxin A (BTA) is a neurotoxic protein that causes reversible muscle paralysis by affecting the neuromuscular junction and reducing the release of the neurotransmitter acetylcholine.[35]

According to recently published articles, this effect of botulinum toxin-induced paralysis, known as “chemoimmobilization,” has shown good clinical outcomes in hypertrophic scar prevention, wound healing, and management of existing hypertrophic and keloid scar.[36,37,38,39,40,4,42,43,44] Although randomized clinical trials have not yet been conducted.[7]

Among the latest experimental methods of pathological scarring management, the use of stem-cell technologies has become very promising due to their high biological potential through the production of active proteins, such as cytokines, cell growth and migration factors and others, which directly modulate the activity of fibroblasts.[45] It is well-known that during trauma caused by surgical instruments or laser exposure in various areas of the human body, skin cells are restored by stem cells, which further differentiate into fibroblasts. Newly arrived cells actively produce collagen and elastin fibers, glycosaminoglycans, and other substances, improving the quality of skin at microlevel. This technique is called "neurofibrolifting" and is proposed for the treatment of pathological scars and skin aging using a single monthly injection.[46,47,48] This technique creates optimal conditions for newly formed cells, inducing the formation of collagen fibers and extracellular matrix. Disadvantages of stem cell therapy include the need for thorough

cosmetic care of the area in which the injections were performed, and the scarcity of clinical data to assess long-term treatment outcomes.[18]

Prevention of pathological scars development

It is worth noting that a significant amount of research today is focused on achieving excellent clinical outcomes in the management of pathological scars, rather than on their prevention. Taking into account the polyethiological nature of keloids and hypertrophic scars, it is difficult to develop a unified approach to prevent pathological scars formation.

The prevention strategies are mainly taken after surgical interventions to avoid pathologic scar development. They involve the use of various methods of corticosteroid administration, silicone dressings, and other aforementioned techniques in different combinations.[4,7]

Discussion

Currently, there is a wide range of methods and medications for pathological scars management. Despite diversity of treatment options, there is no universal approach of treatment of keloids and hypertrophic scars, as well as pre-surgical prevention of their development.

Particularly little attention is currently paid to the prevention and slowing down the processes of pathological scarring, although this could significantly improve the quality of life of patients in the early stages of rehabilitation and reduce the time and costs of management of scars maturation[4]. Over the past 10 years there has been a fairly analysis extensive of various methods of pathological scars treatment. But the most successful, in our view, is the summary on pathologic scars treatment modalities, their success rates and adverse effects given by (Table 1).[18]

Table 1. *The clinical outcomes of pathologic scars treatment modalities*

Treatment	Outcomes	Side effects
Corticosteroid injections	50-100% response 9-50% recurrence	Injection pain, skin atrophy, hypopigmentation
Laser (PDL 585)	57-85% response	Painful
Contact cryotherapy	51-76% response	Painful, hypo- and hyperpigmentation, skin atrophy
Surgery	45-100% recurrence	Recurrences often bigger than original scar
Surgery followed by pressure therapy	0-10% recurrence	6-24 months treatment duration, high treatment adherence needed, not applicable on all body areas, depends on good pressure garment manufacturing
Surgery followed by corticosteroid injections	0-100% recurrence	Injection pain, skin atrophy, hypopigmentation, recurrences often bigger than original scar
Radiation	10-94% response	Stochastic carcinogenic effects, growth interference in children
Surgery followed by radiation	1-35% recurrence	Stochastic carcinogenic effects, growth interference in children, wound healing problems

As can be seen from the summary table, there is no 100% effective method or combination of methods for pathological scars treatment without side effects or adverse reactions.[49] In our opinion, it may be related to the lack of a unified approach of treatment outcomes evaluation. In clinical practice and research, a variety of scales (POSAS, Skindex-29, SF-36, EuroQol 5D) are used to describe the effect of treatment and to analyze the overall health status of patients and their pathologic scars perception. The objective indicators in clinical studies include gender, age of patients, the Fitzpatrick skin type, localization and visibility of pathological scars, their number, causes of its development, previous treatment, and comorbidities.[50]

Conclusion

Considering the various methodologies described above with different mechanisms of action and effectiveness, we believe that the treatment of pathological scars has already been widely studied and described in the literature. Currently, the most relevant issue is the development of new and improvement of existing modalities for preventing the keloids and hypertrophic scars formation, especially when planning surgical interventions. Further experimental and randomized controlled studies are necessary in order to identify more effective methods of pathological scars management.

Declarations

Conflicts of interest and financial disclosures

The author declares that he has no conflict percent and there was no external source of funding for the research in question.

Ethical approval

The study was approved by the University ethics committee and was conducted in accordance with the Declaration of the World Medical Association.

Source of funding

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Data Availability Statement

Not applicable.

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ՄԱՇԿԻ ՍՊԻԱԿԱՆ ԴԵՖՈՐՄԱՑԻԱՆԵՐԻ ԲՈՒԺՄԱՆ ՄԵԹՈԴՆԵՐԻ ԱԿՆԱՐԿ

Օլգա Դանիշչուկ,[1] Ելենա Կարպովա[2]

1. Պլաստիկ վիրաբույժ, «Դանիշչուկ կլինիկա» ՍՊԸ-ի գլխավոր բժիշկ, Ռուսաստանի Դաշնության APO FMBA-ի պլաստիկ և էսթետիկ վիրաբուժության բաժանմունքի ասիստենտ, Մոսկվա, ՌԴ
2. Պլաստիկ վիրաբույժ, Ռուսաստանի ազգային գիտահետազոտական բժշկական համալսարանի մաշկային հիվանդությունների և կոսմետոլոգիայի ամբիոնի պրոֆեսոր, Ն.Ի. Պիրոգովի ան. Դաշնային հետբուհական ուսումնական հաստատություն, Մոսկվա, ՌԴ

Նախապատմություն. Պաթոլոգիական սպիների (հիպերտրոֆիկ և կելոիդային) առաջացման բուժումը և կանխարգելումը ժամանակակից մաշկաբանության և պլաստիկ վիրաբուժության կարևոր խնդիր է, որը պայմանավորված է էսթետիկ ընկալման (էսթետիկ) խախտմամբ, իսկ ծանր դեպքերում՝ մարդու մարմնի տարբեր հատվածների ֆունկցիաներով:

Նպատակ. Գրականության համակարգված վերանայման նպատակն էր վերլուծել առաջարկվող արդյունավետ մեթոդները մաշկի կիկատրիկ դեֆորմացիաների բուժման համար:

Մեթոդներ. Համակարգված ակնարկը ներառում էր հոդվածներ Google Scholar-ից, Medline-ից, Scopus-ից, Web of Sciences-ից, PubMed-ից: Որոնման տերմինները ներառում են՝ պաթոլոգիական սպի, թերապիա, բոտուլինումային տոքսին, լազեր, կրիոդեստրուկցիա, հիալուրոնիդազ, մաշկի սպիների կանխարգելում, վերքերի բուժման նոր մեթոդներ, վերքերի և մաշկի սպիներ, բիոինժեներական վիրաբուժություն:

Արդյունքներ. իրականացրել է նախնական որոնում 132 հոդված և համառոտագիր՝ ընտրելով բարձր մեթոդաբանական որակի 50 ամբողջական տեքստային հոդված:

Այս ակնարկը եզրակացնում է, որ անհրաժեշտ է մշակել պաթոլոգիական սպիների կանխարգելման նախավիրահատական մեթոդներ, որոնք կարող են դառնալ ցանկացած պլաստիկ և էսթետիկ վիրաբուժական միջամտության համընդհանուր չափանիշ: Բուժումը կախված է պաթոլոգիական սպիների կլինիկական և մորֆոլոգիական բնութագրերից:

Եզրակացություն. համակարգված վերանայումը ցույց տվեց պաթոլոգիական սպիների կանխարգելման նախավիրահատական մեթոդների մշակման անհրաժեշտությունը, որոնք ապագայում կարող են դառնալ պլաստիկ վիրաբուժության ցանկացած միջամտության համընդհանուր չափանիշ, քանի որ մաշկային սպիների բուժման հարցը բավականաչափ լուսաբանված է ժամանակակից աշխարհում:

ОБЗОР МЕТОДОВ ЛЕЧЕНИЙ РУБЦОВЫХ ДЕФОРМАЦИЙ КОЖНЫХ ПОКРОВОВ

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Актуальность: Лечение и профилактика развития патологических рубцов (гипертрофических и келоидных) является важной проблемой современной дерматологии и пластической хирургии в связи с нарушением эстетического восприятия (эстетики), а в тяжелых случаях и функции различных областей организма человека.

Целью систематического обзора литературы был анализ предлагаемых эффективных методов лечения рубцовых деформаций кожи.

Методы: В систематический обзор были включены статьи из Google Scholar, Medline, Scopus, Web Of Sciences, PubMed. Ключевые слова для поиска включали: патологический рубец, терапия, ботулотоксин, лазер, криодеструкция, гиалуронидаза, профилактика рубцов кожи, новые методы лечения ран, рубцевание ран и кожи, биоинженерная хирургия.

Результаты: В обзоре проведен предварительный поиск и рассмотрено 132 наименования и аннотации, отобрано 50 полнотекстовых статей высокого методологического качества.

В этом обзоре сделан вывод о необходимости разработки дооперационных методов профилактики патологических рубцов, которые потенциально могут стать универсальным стандартом любого пластического и эстетического хирургического вмешательства. Лечение зависит от клинико-морфологических особенностей патологических рубцов.

Заключение: Проведенный систематический обзор продемонстрировал необходимость разработки дооперационных методов профилактики патологических рубцов, которые могли бы в будущем стать универсальным стандартом любого вмешательства в пластической хирургии, поскольку вопрос лечения рубцов кожи достаточно освещен в современном мире.