CONSERVATIVE TREATMENT OF PATIENTS WITH CICATRICIAL SKIN CHANGES WITH ELECTRODE PHARMAPHORESIS

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The problem of treatment of patients with hypertrophic and keloid scars is one of the most topical problems in modern dermatocosmetology. Extensive cicatricial deformities, especially on the face or other exposed parts of the body, significantly reduce the quality of life, and in some cases leads to anatomic functional disorders and disability, development of neuropsychiatric disorders [1]. The existing methods allow patients to customize a comprehensive approach to correction of cicatricial lesions by choosing the principal or main method of treatment – first-line therapy and several adjuvant methods, the combination of which will shorten rehabilitation of patients and prevent the recurrence of pathological scars.

Selection of the main method of treatment depends primarily on how long the cicatricial lesions exists, its localization, size, presence of anatomical and functional disorders, and other factors. Physiotherapy is efficient at the stage of development of a pathological scar, which is clinically manifested by hardening of cicatrical tissue, increasing of the colour intensity, the presence of subjective sensations such as pain, itching, tingling. Conservative therapy using different devices shortly after injuries or surgical interventions allows to reduce both the degree of subjective discomfort and the volume of scar tissue, prevent recurrence of pathological cicatricial lesions. Sonic phoresis or ultrasound (US) with Longidaza or electrophoresis with Fermenkol. These drugs facilitate resorption of collagen, which is the main protein in the cicatrical tissue. Fermenkol is a unique natural complex of collagenase isoenzymes with a molecular weight of 23 to 36 kD that can break down the triple helical collagen molecule. The complex exhibits both collagenolytic and general proteolytic activity. This means that the action of the enzyme complex is not limited to hydrolysis of the triple helix of native collagen; collagen fragments are destructed to individual amino acids. Scar reduction is due to the hydrolysis of collagen. Currently, there are new methods of physiotherapeutic action facilitating penetration of drugs through the skin barrier, that have collagenolytic activity and thereby destroying excessive collagen in the scar tissue. One of these methods is the electrode pharmaphoresis with Fermenkol using a medical device for transdermal drug administration of Farmateb. Farmateb generates complex electrical signals having different characteristics depending on the depth or type of damaged tissue or affected organ requiring the maximum drug concentration. The method is based on transdermal movement of the drug through the natural barrier of the human body consisting of skin. Farmateb device uses electrical signals that allow even drugs with high molecular weight to penetrate directly deep into lesions, i.e. into the nucleus of tissue cells of the lesion with positive results for almost all types of defects or localized pathologies. Under the influence of signals of Farmateb device, active substances cause temporary changes in the tissues, increase permeability of the horny layer and facilitate the opening of ion channels of the tissue cells requiring active substances from outside for regeneration. After that, the receptors are activated in a shorter time, with a higher concentration and without the systemic circulation. Increased permeability is achieved by using various forms of electrical current modulated by frequency and amplitude and/or combinations thereof. Application of evolutionary electronic components has allowed to create special complex waveforms that allow to very selectively vary the permeability of cell membranes, analysing the reaction in order to automatically optimize the intensity of the electrical signal and transfer of the matter. Electrode pharmaphoresis uses additional transport paths and is the more effective way of extracellular and intracellular transfer, acting directionally on the carrying capacity of ion channels, using the "pump effect" of cell membranes that expand and contract under the influence of an alternating electric field. This phenomenon is described as a kind of reversible elongation or stretching of molecules, which occur under the influence of modulated electric current and controlled mechanical compression/relaxation of cell membranes. This way, it is possible to move large molecules (not only ions or ion particles).

Passage of the drug through the horny layer is possible through:

- the intracellular path through the corneocytes;
- the intercellular path through the extracellular matrix;

● a subordinate path through the hair follicles, sweat and sebaceous glands.

The subordinate path is preferred for water-soluble drugs as the pores have polar characteristics. Only in some special circumstances, such as the use of ionophoresis, the subordinate path is preferred. Thus the transepidermal path, comprising the intra- and intercellular paths, allows for the greatest possible penetration, while the passage is conducted by passive diffusion. The intracellular pathway involves passage through the extracellular matrix and is preferred for fat-soluble drugs. The importance of the intracellular penetration is confirmed by the existence of the relationship between the fat-soluble property of matter and its coefficient of permeability through the skin. Therefore, the phase restricting the permeability of the substance is presented by a barrier of hydrophobic nature, such as extracellular matrix of fat. Excessive fat-solubility of the drug, on the one hand, contributes to its concentration in the horny layer, but on the other hand, prevents its penetration into the deeper layers of a more polar nature. Lastly, the intracellular path involves passage of molecules through the cell wall of corneocytes, and after passing the membrane, polar molecules are directed to the water-based layers of corneocytes, while fat-soluble molecules are located in areas with a high fat content. After passing through the horny layer, the molecules rapidly distribute through the layers of the epidermis and into the dermis, where absorption, deactivation of agents and, in case of drugs, activation are possible.

Advantages of transdermal drug transfer

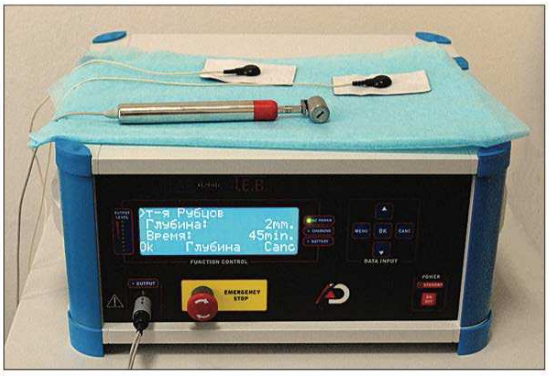
● drug therapy with a short biological half-life;
● painless conduct of the procedure;
● reduction of the amount of drug needed for therapy;
● high local concentration of the drug;
● selectivity of action;
● increase in the speed of action;
● absence of adverse reactions.

Transdermal administration method solves a lot of problems as it allows molecules polarized by a pulse (coated with electron sphere) move under the action of the electric force and instantly reach specific receptor cells of the damaged tissue.

Drug administered by electrode Pharmaphoresis does not get into the digestive tract and plasma, thus avoiding the biotransformations induced by gastrointestinal hydrolysis, is not fermented on the intestinal walls and in the liver, and reaches its target organs almost exclusively in its free form. It also allows to avoid saturation of the whole body with drugs, which might lead to side effects. Method of electrode pharmaphoresis with Fermenkol using a medical device for transdermal drug administration Farmateb was tried on 28 patients with keloid and hypertrophic cicatricial lesions of the face and body in the department of cosmetology of the CJSC Active Longevity Clinic “Beauty Institute on Arbat” for treatment and prevention of pathological scarring. The age of patients ranged from 6 to 64 years, duration of existence of cicatricial lesions – from 4 months to 7.5 years. Prior to treatment, the patients underwent ultrasound scans of scar tissue at fixed locations.

Based on the clinical form, age, area and depth of the scar, Fermenkol solutions of different concentrations were used. The recommended concentration for correction of keloid scars is 0.5-1 mg/ml, for hypertrophic scars – 0.1-0.2 mg/ml. After cleansing the surface of the cicatricial lesion with an antiseptic solution, an active substance is applied to the skin. Electrode pen is placed at a 45 degree angle relative to the surface of the skin, with smooth motions administer the drug using a rotating roll, without putting pressure on the skin and without losing contact between the roll and the surface of the skin. A treatment program is selected individually for each patient in accordance with the diagnosis. For treatment of hypertrophic and keloid scars, the “scars” mode is used, for atrophic scars, the “stretch marks” mode is used. For each session of the selected therapy, the device offers certain parameters of the depth and the duration of the procedure. If necessary, they may be changed. Duration of the course is 10-15 procedures, every other day. If necessary, the course can be repeated. Interval between courses is 7-10 days.

Fig. 1.



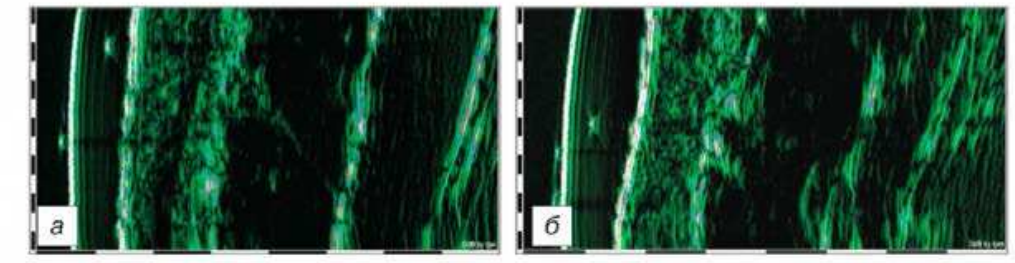
Farmateb device for electrode pharmaphoresis – transdermal drug administration.

Evaluation of treatment outcome. Compared with healthy skin, the pathological scar tissue is dehydrated, the amount of water in the extracellular matrix is reduced. Without corrective measures, only 30-40 days after the beginning of the formation of scar, the hydration of the scar tissue begins to rise gradually, but it never reaches the initial level. The hydration process of scar tissue goes quite slowly. As a result of introduction of Fermenkol by electrophoresis, in 15-20 days the ratio of the total and the structured water in the scar tissue begins to approach the indicators of healthy skin, as evidenced by the method of EHF-dielectrometry. Good results were observed in 21 (75%) patients, which included suspension of the active growth, full or partial regression of scar tissue, disappearance of local unpleasant subjective sensations (itching, burning, soreness), difference in colour between the scar and surrounding tissues. Satisfactory results of treatment were obtained in 7 (25%) patients. All patients reported settling and softening, reduction of local unpleasant subjective sensations (itching, burning), reduction in the severity of parameters characterizing the appearance of cicatricial lesions (height of protrusion). The used system is capable to independently and simultaneously control pulses and frequency of administration of therapeutic active substances through the dermis with a significant increase in absorbing capacity. Due to a built-in safety system, the device can constantly assess the change in resistance of tissues of interest and adjust the allocation of energy in real time, thus automatically optimizing the biostimulation of tissues and ensuring maximum clinical efficacy, which has never been achieved before using the existing traditional methods (Fig. 2, 3).

Fig. 2.

Patient P. with a diagnosis of a developing hypertrophic deformation in the pubic area, right inguinal fold, post-burn cicatrical lesions of front and inner surface of the upper third of the right and left hips.
a – before treatment;
b – after 10 sessions with the Pharmaphoresis with Fermenkol using the medical device for transdermal drug administration Farmateb

Fig. 3.



Patient P. Results of the ultrasound examination of the developing keloid post-burn scars on the right inguinal fold.
a – before treatment;
b – after treatment.

Patient P., age 7, was observed in the cosmetology department regarding post-burn cicatricial lesions of the skin of the pubic and inguinal areas, right and left hips. From the medical history: boiling water burn 1.5 years ago (30/09/2012), primary surgical treatment was conducted locally, on 17/10/2012 transplantation of a free skin part from the gluteal area was performed. 3 months after epithelialization of the wound surface of the cicatricial lesion in certain areas, mainly due to tension associated with motor activity, pronounced redness, induration, itching, burning, pain in the scars, especially on palpation and on contact with clothing appeared. Along the periphery of scar deformities, on the border with the surrounding non-damaged tissues, expressed hyperpigmentation is observed. Surgical correction with free skip part transplantation was performed. Compression clothes and external drug therapy was insufficient; along with hypertrophy, growth of cicatrical tissue was observed beyond the original lesion. In the right inguinal region, formation of contracture was observed, accompanied by strong unpleasant subjective sensations. Given the vastness, localization and the period of existence of the cicatricial lesion, the first stage of treatment consisted of the Bucky therapy in pubic area and physiotherapy by Pharmaphoresis with Fermenkol for the entire area of the cicatricial lesion.

Examination methods

The ultrasound scan was performed using a digital ultrasound imaging system Skinscanner DUB. The scanning was performed with a 22 MHz linear sensor (applicators) with a scanning depth of 10 mm. Axial resolution was 72 microns for 22 MHz. A and B imaging modes were used, in the A mode the amplitude spectrum of the reflected signals at each scan point was obtained, in the B mode two-dimensional image of the scanned area to a depth of 10 mm was obtained, the length of the scanned area was 12.8 mm (the size of the active sensor window). The cumulative two-dimensional image in the B mode was created from 384 scans with an interval of 33 microns. As the contact medium for ultrasound conductivity, ultrasound gel was used.

Using a frequency of 22 MHz, we visualized the epidermis, dermis, subcutaneous fat, muscle fascia, hair follicles, lumen of skin vessels.

Measurement of acoustic density of the dermis was performed in the scar area, the acoustic density of the dermis on the contralateral healthy skin area was used as a reference; the acoustic density of the dermis in the scar area immediately after exposure to Pharmaphoresis and after completion of the course of treatment was measured.

Before treatment, there was quite smooth contour of the surface of epidermis, sometimes intermittent. There is a clear border between the epidermis and dermis. The distribution of echo signals in the dermis is even, differentiation into layers is present. In the deep parts of the dermis, there was an increase in echogenicity in tenia (connective tissue). There is a clear border between the dermis and subcutaneous fat. The distribution of echo signals in the subcutaneous fat is even, streaking is present.

After the course of the electrode Pharmaphoresis with Fermenkol, a decrease in the thickness of hyperechogenic tenia in deep parts of the dermis with areas of normal echogenicity was observed. There is a

clear border between the dermis and subcutaneous fat. The distribution of echosignals in the subcutaneous fat is even, streaking is present.

Thus, the method of the electrode pharmaphoresis with Fermenkol using the medical device for transdermal drug administration Farmateb in patients with cicatricial lesions showed high clinical efficacy. Good results were noted in 21 (75 %) patients, including cessation of active growth, full or partial regression of scar tissue, disappearance of local unpleasant subjective sensations (itching, burning, soreness) and restoration of the colour of the scar deformation to shades of the surrounding tissues.

Increase in the average acoustic density and the average thickness of the dermis identified during ultrasonic examination in also associated with an increase in the synthesis of fibrous components and an increase in the amount of the extracellular matrix.

As a result of the treatment and preventive measures, the appearance of cicatricial lesion improved and the tension of tissues decreased.

By interaction with biological tissues, our method allows for outpatient treatment without anaesthesia by performing a non-painful and non-invasive procedure of lesion treatment without side effects and complications of cicatrical lesions. Utilization of this method should not be underestimated for patients of any age, including use in paediatrics without limitations on exposure to UV rays, which allows to apply this method without seasonal restrictions. It is reasonable to make a conclusion regarding possibility of using this method as a new and effective alternative in the treatment of pathological scars, which has proved to be a very effective, non-invasive, safe procedure, which gives fast results and is simple in use