COMPARATIVE EVALUATION OF THE EFFICIENCY OF BIOREVITALIZATION AND COLLAGEN THERAPY WITH COLLOST® GEL 7 % IN A PATIENT WITH CONNECTIVE TISSUE DYSPLASIA

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In aesthetic medicine, when working with patients, it is important for a cosmetologist not only to correctly perform various correction techniques, but also to conduct a full diagnosis beforehand. Recently, patients with connective tissue dysplasia have become quite common in cosmetology and dermatology appointments. And this is absolutely justified. One of the clinical manifestations of connective tissue dysplasia (CTD) is premature aging of the skin, manifested in an early decrease in its tone, the appearance of lacrimal, nasolabial and mid-cheek grooves [1].

Connective tissue dysplasia

The term “dysplasia” (from the Greek δυσ dys – disorder + πλαθω plaeo – I form), or dysgenesis (from the Greek δυσ dys – disorder + ancient Greek γενεσις – origin, occurrence) is the abnormal formation of one or another living tissue of the embryo, as well as the abnormal development of tissues, organs or body parts. This group of diseases includes genetically determined defects of fibrous structures and the main substance of connective tissue, leading to disruption of the formation of organs and systems [2]. Clinical manifestations of CTD can be varied and affect different organ systems in which connective tissue is present, but do not necessarily manifest in all of them [3].

A separate group of hereditary CTDs (Ehlers-Danlos syndrome, osteogenesis imperfecta, Marfan syndrome, etc.) is distinguished – monogenic hereditary diseases. As a rule, these diseases are quite severe, manifest early and are not very common. Cosmetologists and dermatologists may first encounter CTD as a multifactorial pathology during their appointments. The etiology of such diseases is based on many factors (internal and external), the sum of which can lead to pathology. Such diseases have a milder course, are much more common, are detected late, and sometimes it is cosmetologists who first diagnose CTD [2]. This is due to the fact that patients did not seek medical advice from other specialists, since they were most concerned about the purely external factor in the manifestation of pathology – premature aging.

Currently, diagnosis of CTD is possible only on the basis of clinical manifestations. The clinical manifestations of CTD are varied, depending on the organ systems involved. Thus, there may be changes in the bones and joints, changes in the skin and muscles, signs of CTD of the visual organ, cardiovascular system, bronchopulmonary system, upper urinary tract, gastrointestinal tract, blood system, nervous system, mental disorders and behavioral disorders.

Table 1. Phene signs in patients with CTD according to the phenotypic map of Glesby M.J. (1989) (3 or more) and the assessment table of Abbakumova L.N. (2008)

Phene signs in patients of the studied groups according to the phenotypic map of Glesby M.J., 1989	Signs of CTD and minor developmental anomalies according to the assessment table of Abbakumova L.N. (2008)
Asthenic type of constitution	Asthenic type of constitution
Arched palete	Arched palete
Hypermobility joint syndrome	Hypermobility joint syndrome
Scoliosis	Scoliosis
Flat feet	Flat feet
Myopia	Myopia
Funnel chest	Funnel chest
Sparrowy chest	Sparrowy chest
Increased skin elasticity	Increased skin elasticity
Multiple pigment spots on the skin	Multiple pigment spots on the skin
Loss of normal posture	Deviated septum
Arachnodactyly	Pronounced venousity of the skin
Positive wrist symptom	Transverse striation of the foot
Positive thumb sign	Clavi
Straight back	Hallux valgus
Ectopia lentis	Large foot stamping
	The presence of scars on the skin

Table 2. Characteristic changes in the skin and subcutaneous fat in CTD

Skin characteristics	Thin, easily damaged, translucent, dry, flaccid and loose skin structure, stretchable (painless skin retraction by 3 cm or more)
Regeneration	Violated (reduced)
Scarring	– Atrophic striae not associated with pregnancy or weight loss, keloid scars – Specific skin symptom – a special type of skin healing in the form of “tissue paper”
Involutional changes in the skin	Early appearance of wrinkles and folds, most pronounced nasolabial folds and nasolacrimal grooves, less often - wrinkles in the eye area and wrinkles in the forehead area
Additional signs	– Spherical subcutaneous formations in the area of the elbows and knees – Positive pinch, tourniquet, cuff tests (formation of bruises, petechiae, ecchymosis)

The diagnosis is based on the identification of three or more phenotypic characteristics according to the phenotypic map of Glesby M.J. (1989) (3 or more) and the assessment table of Abbakumova L.N. (2008) **(Table 1)** [3].

In the practice of aesthetic medicine, skin changes in CTD are of greater interest. They are separately identified in the symptom complex “skin manifestations of CTD” **(Table 2)** .

But what are the most common issues that cosmetologists encounter?

Most often, such patients complain of an early decrease in skin tone, thin, loose skin, pastosity or swelling of the skin, a decrease in the reparative capacity of the skin after injuries, and easy bruising. During the examination, the degree of severity of age-related changes in the skin is determined, the extensibility of the skin (usually over the lateral part of the clavicle), venousity of the skin, skin tone are assessed, and the presence of hypermobility syndrome and arachnodactyly is additionally assessed.

Based on such a full examination of the patient and diagnostic research, a complete diagnosis is established and, in accordance with it, the tactics of patient handling in cosmetology.

Management of patients with CTD

Comprehensive management of patients with CTD includes home recommendations and cosmetic procedures in the doctor's office **(Table 3).**

Among injection procedures, as a rule, the first place is occupied by working with the quality of the skin, then correction of individual aesthetic defects (contour plastic surgery of the tear trough, nasolabial fold, mid face, etc.).

Classically, we can work with the quality of the skin with the help of biorevitalizers and collagen therapy.

It is important to understand the difference in the use of preparations based on unstabilized hyaluronic acid (HA) and collagen-based preparations.

When using biorevitalizants based on non-reticulated HA (also with the addition of amino acids, antioxidants, peptides, vitamins and other components), we create conditions for fibroblasts activation. As a result, we see the clinical effect (increased hydration, turgor and tone of the skin) primarily due to the availability of the necessary components for the synthetic activity of fibroblasts [4].

When collagen-based preparations are used, collagen chains are incorporated into the extracellular matrix of the skin [5]. These chains have specific sites that interact with fibroblast cell adhesion molecules, as a result of contacts with which fibroblasts adhere to them, acquiring an elongated “synthetically active” phenotype due to the activation of intracellular signaling pathways.

Table 3. Recommendations for patients with signs of CTD

Physical activity	Adequate, without excessive effort and prolonged static stress
Nutrition	- Various – Food enriched with proteins, chondroitin sulfates – Food products enriched with substances involved in the connective tissue metabolism: vitamins (C, E, B_6, D, P) and microelements (magnesium, copper, manganese, zinc, calcium, selenium, sulfur)
Nutritional supplement	Supplementation with carnitine and coenzyme Q10, ascorbic acid, vitamin D, melatonin, vitamin E, B-complex, vitamin K, glucosamine, chondroitin, gamma-linolenic acid, pycnogenol, magnesium, zinc, methylsulfonylmethane and silicon dioxide
Additionally	– Consultations with other specialists – Correction of anxiety-depressive disorders (rational psychotherapy or drug correction)
Treatment that a cosmetologist can offer to a patient	– Improvement of microcirculation and tissue trophism – massage and microcurrent therapy – Correction of glycosaminoglycan synthesis and collagen formation – intradermal injections of 1 % hyaluronic acid with amino acids (proline, lysine, glycine, cysteine), with vitamin C, glutathione and succinic acid – Before surgical interventions: restoration of the skin's reparative capacity: Vitamin D prescription

Therefore, we expect a greater clinical effect in improving skin quality precisely when skin tone is reduced.

It is necessary to recall that two phenotypes of fibroblasts are distinguished in the aspect of skin aging. The first phenotype is “young” – fibroblasts of an elongated shape (they have maximum stretch due to the fibrous component of the extracellular matrix), such fibroblasts are maximally synthetically active and produce HA, collagen fibers and other components of the extracellular matrix of the skin. The second fibroblast phenotype, the “aged” (in a state of replicative senescence), is smaller, round fibroblasts that form as a result of loss of contact (and tension) with the fibrous component of the skin’s extracellular matrix (which degrades and fragments with age). Such fibroblasts have reduced synthetic activity, but if the “aged” cells are placed in a full-fledged extracellular matrix of the skin, they restore their synthetic activity.

In this work, we conducted a pilot comparative study of the effectiveness of the indicated injection methods aimed at improving skin quality in a patient with CTD.

Clinical example

Patient D., 40 years old, visited us with complaints of decreased tone and dry skin, fine wrinkles, enlarged pores **(Fig. 1)** .

On examination: The patient has an asthenic body type and has a mild soft tissue deficit in the mid face. The skin is pale, with a bluish tint in the suborbital region, with small foci

Fig. 1. Patient D., 40 years old, before aesthetic correction

hyperpigmentation all over the face, a large number of enlarged pores are observed. Palpation revealed a decrease in skin tone, and a rotational compression test revealed the formation of numerous fine wrinkles. Lower eyelid elasticity test (pinch test) – straightening the fold with a delay of 2–3 seconds.

Additionally, the patient's signs of CTD were assessed: skin extensibility (above the lateral edge of the clavicle) 2 cm, multiple pigment spots, grade 1 scoliosis, increased venousity of the skin, hypermobility syndrome (in addition to asthenic physique). In addition, the patient has a pathology of the dental system and minor developmental anomalies: fused earlobe, bluish sclera, wide gap between the upper incisors.

Diagnosis: Senile skin atrophy (L 57.4). Connective tissue dysplasia with cutaneous and osteoarticular manifestations.

During the work, it was decided to compare the effect of biorevitalization with native 1.8 % HA and collagen therapy with the product Collost® gel 7 %.

The product Collost® gel 7 % contains collagen fibrils in a concentration of 7 %. When administered intradermally, collagen fibrils serve as an additional source of cellular adhesion sites for fibroblasts in the extracellular matrix of the skin. As a result, additional tension is created for fibroblasts, they become more elongated, due to which their synthetic activity increases.

Study Design

The patient gave written consent for the study.

To evaluate the effectiveness of the procedure, photographs before and after the procedures, ultrasound sonography of the soft tissues of the face before and after the procedures, and questionnaires on the procedures results were used.

During an ultrasound examination of the soft tissues of the face, the thickness of the epidermis and dermis was assessed at two points on the face on the left and right sides.

Table 4. Global Aesthetic Improvement Scale (GAIS)

Assessment	Degree of satisfaction	Description
1	Marked improvement	Excellent correction result
2	Very good improvement.	Improvement in appearance was noted, but not completely satisfactory.
3	Improvement	Improvement in condition compared to the previous one, but additional correction is necessary
4	No change	The appearance remained the same as the previous one.
5	Deterioration of the patient's condition	The appearance has deteriorated compared to the previous one.

Table 5. Skin changes after the procedure

Characteristics	There were no violations	No changes	The improvements are noticeable	Apparent improvements
Skin color	0	1	2	3
Skin vibrancy	0	1	2	3
Skin hydration	0	1	2	3
Softness (pleasant texture) of the skin	0	1	2	3
Enlarged pores	0	1	2	3
Skin tone	0	1	2	3
Fine wrinkles	0	1	2	3

The first point is the center of the zygomatic arch, the second point is above the projection of the lower jaw body.

The standard Global Improvement Questionnaire (GAIS) was used as a post-procedure questionnaire (assessment was carried out by both the physician and the patient) **(Table 4)** , as well as a questionnaire developed by the author **(Table 5)** . The development of our own questionnaire was related to the fact that when assessing the results of biorevitalization, patients do not quite clearly understand what exactly needs to be assessed, and assess the changes that have occurred in the area of expression wrinkles, volume restoration, the evidence of folds, which is more correctly assessed after contour plastics/botulinum therapy procedures.

Research protocol

1. Filling out informed consent, taking photographs, performing an ultrasound examination of the face, application anesthesia, performing biorevitalization with a product based on 1.8% HA.
2. In 2 weeks: application anesthesia, biorevitalization with a product based on 1.8% hyaluronic acid.

Fig. 2. Patient D., 40 years old, after a course of biorevitalization

3. In 2 weeks: application anesthesia, biorevitalization with a product based on 1.8% hyaluronic acid.
4. After 1 month: filling out questionnaires, taking photographs, conducting an ultrasound examination of the face, conducting an intradermal test of the product Collost® gel.
5. After 1 month: application anesthesia, collagen therapy with the product Collost® gel 7 %.
6. In 2 weeks: application anesthesia, collagen therapy with the product Collost® gel 7 %.
7. In 2 weeks: application anesthesia, collagen therapy with the product Collost® gel 7 %.
8. After 1 month: filling out questionnaires, taking photographs, conducting an ultrasound examination of the face.

Results

After a course of biorevitalization with HA, the patient noted a slight general improvement in the condition of her skin: increased moisture, improved color **(Table 6, 7)**. No changes in skin tone, fine wrinkles or enlarged pores were noted. The doctor did not note any external changes in the condition of the facial skin **(Fig. 2)**.

After a course of collagen therapy with Collost® gel 7%

Fig. 3. Patient D., 40 years old, after a course of collagen therapy with Collost® gel 7 %

Table 6. Global Aesthetic Improvement Scale (GAIS) after biorevitalization and collagen therapy with Collost® gel 7 % (the rating given is highlighted in color)

Assessment after biorevitalization		Degree of satisfaction	After collagen therapy	
Patient	Doctor		Patient	Doctor
1	1	Marked improvement		
2	2	Very good improvement.	2	2
	3	Improvement	3	3
4		No change	4	4
5	5	Deterioration of the patient's condition	5	5

Table 7. Skin changes after biorevitalization procedure and collagen therapy with Collost® gel 7 %

Characteristics	After biorevitalization	After collagen therapy
Skin color	2	3
Skin vibrancy	1	3
Skin hydration	2	3
Softness (pleasant texture) of the skin	2	3
Enlarged pores	1	3
Skin tone	1	3
Fine wrinkles	1	3

the patient noted a significant improvement: significant increase in skin tone, reduction in severity of fine wrinkles, narrowing of pores, improvement of skin color and smoothness **(table 6, 7)**.

The doctor also noted a significant improvement in the skin quality **(Fig. 3)**.

Ultrasound examination of the skin also confirms clinical changes: An increase in skin thickness was noted after a course of collagen therapy with Collost® gel 7 % from 12.5 % to 57.2 % **(Table 8)**.

And in conclusion

Patients with CTD tend to respond more poorly to standard cosmetic procedures. Therefore, it is initially necessary to actively identify patients with CTD, prescribe them complex correction and take a more differentiated approach to the choice of drugs for biorevitalization. Preparations based on non-reticulated HA are excellent for moisturizing the skin, giving it freshness, and have results in cases of decreased tone, but not in all patients [4]. This clinical example shows the difference in the clinical effect of using a HA-based biorevitalizer and a preparation based on collagen, Collost® gel 7 %.

Table 8. Dynamics of changes in skin thickness in the mid and lower face according to ultrasound scanning data

Skin thickness (epidermis and dermis)	Left part, before procedure (mm)	Left part, after the procedure with 1.8% HA (mm)	Left part, after the procedure with Collost® gel 7 % (mm)	Right part, before procedure (mm)	Right part, after the procedure with 1.8% HA (mm)	Right part, after the procedure with Collost® gel 7 % (mm)
In the mid face area	1.9	1.8	2.4	2.1	2.0	
In the lower face area	1.6	1.4	2.2	1.5	1.6	

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