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## EVALUATION OF EFFICACY OF MODERN APPROACHES IN THE TREATMENT OF VITILIGO

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(\* - in our country a two-stage system for obtaining academic degree has been adopted, i.e. Doctor of Science is the highest research degree, many scientists having D.Sc. are Professors; Ph.D degree is the equivalent to doctoral candidate)

### ABSTRACT

**Background.** Vitiligo is an acquired and most common pigmented disorder of polygenic multifactorial inheritance. To date it is the most frequent cause of depigmentation worldwide. Vitiligo mainly affects melanocytes from epidermis basal layer, and the typical presentation is a progressive depigmentation of the skin and mucous membranes due to melanocyte disappearance. Until now the pathogenesis of vitiligo has not been totally determined and many theories have been proposed. Of these, the autoimmune hypothesis is now the most studied and discussed among researches. Dysfunction in metabolic pathways, which could lead to production of toxic metabolites causing damage to melanocytes, has also been investigated. However vitiligo is easy to diagnose, but characterized by specificity in terms of the treatment complexity. This paper deals with modern approaches in the surgical treatment of vitiligo.

**Research objective:** to study and evaluate the efficacy of the vitiligo therapy based on the localization of the disease process.

**Materials and methods.** The research included 345 patients categorized by three age groups: 18 to 40 years old, 41 to 60 years old, and 60 years old and older. Clinically, 121 (35.1%) patients had segmental vitiligo (70 women and 51 men), and 224 (64.9%) patients were

with non-segmental vitiligo (124 women and 100 men). Vitiliginous depigmented patches were studied according to their location on the body areas: face, trunk, hands and arms and legs. A mixture of hair follicle cell suspension (*NCECS + NCORSHFS*), obtained from the scalp of a patient with vitiligo, was applied with the mixture of the suspension of non-cultivated epidermal cells (*NCECS*) and the suspension of non-cultivated epidermal cells. During the research we used the high-technology apparatus “Regenera” (Italy), the action of which was to extract the mesenchymal cells of the hair follicle and to transplant the obtained material together with functionally active melanocytes into the depigmented skin of vitiligo patients.

**Findings.** The study showed that both methods proposed in the research had a high efficacy in repigmentation process of facial area; the significantly higher level of repigmentation on arms and legs compared to *NCECS* was achieved when treated with *NCECS + NCORSHFS* method. The study established that a high repigmentation can be achieved by choosing the treatment method depending on the location of depigmented patches on the body areas. The performed method of surgical treatment of vitiligo is highly effective, which is confirmed by the absence of signs of depigmentation after the end of the course of treatment. The recommended course of treatment with this surgical method is 1-3 procedures, depending on the location and volume of the pathological process. Application of the *NCECS+NCORSHFS* method promotes faster repigmentation, eliminating cosmetic defects in patients, and improving their quality of life.

**Keywords:** vitiligo, melanocytes, repigmentation, cell suspension, transplantation.

## INTRODUCTION

Vitiligo is one of the most striking of all human disease phenotypes and the most common pigmentary disorder worldwide. Because of its visually evident cutaneous manifestations, vitiligo has been known for thousands of years. Vitiligo mainly affects melanocytes from epidermis basal layer, and the typical presentation is a progressive depigmentation of the skin and mucous membranes due to melanocyte disappearance. The striking visual contrast between the normal pigmented and lesional skin causes psychological and social stigma among all patients, which can be devastating on darker skin phototypes.

Although a few etiologically based approaches to the therapy have been developed over the past few years, vitiligo is a difficult problem for

dermatologists, since there is no clear treatment regimen. The etiology of vitiligo is still insufficiently understood, and, in addition to the main classical theories of the development of vitiligo, namely the destruction of melanocytes (autoimmune, neurogenic and redox status disorders), and inhibition of melanocytes or their defective adhesion, a new theory has emerged based on the depletion of melanocytes as the prime cause of the disease has been recently proposed [1,2]. Many researchers believe that vitiligo is a serious cosmetic defect that occurs in people with a genetic predisposition and, in most cases with emotional disorders [3,4].

Most experts believe that damage to melanocytes and disruption of melanogenesis processes in the skin of vitiligo patients are mainly caused by autoimmune mechanisms. Although the disease is not accompanied by a deterioration in physical well-being, but signs of affective-anxiety disorders are noted in all patients, which impair communication skills and reduce the quality of life.

Treatment of vitiligo is a monumental challenge, since the causes of its development are unknown, and mostly the depigmentation process may develop even in case of complete physical well-being. The therapy is aimed at eliminating cosmetic defects and restoring skin pigmentation. The choice of treatment method depends on the patient and factors such as the patient's skin phototype, age, somatic status, type and stability of the disease, as well as the size and location of depigmented areas [1,5,6,7]. Almost 80% of vitiligo patients receive ultraviolet radiation, often in combination with furocoumarin drugs.

Therapy for vitiligo is aimed at stabilization of the disease as well as the repigmentation of depigmented patches. Therapies that affect disease progression include systemic steroid medications, oral corticosteroid therapy, minocycline and methotrexate drugs. First-line therapies for repigmentation include topical corticosteroid medications, calcineurin inhibitors, and ultraviolet B phototherapy.

The most modern and effective methods include various types of phototherapy (PUVA therapy, UVA and UVB phototherapy, 311 nm, an excimer

laser - 308 nm) [7]. Insufficient treatment methods today (medium-wave ultraviolet therapy, PUVA therapy, treatment with local glucocorticosteroid drugs, local calcineurin inhibitors) increasingly aggravates the psychoemotional state of patients with vitiligo. In this regard, cell transplantation used to treat vitiligo is significantly superior to other treatments in terms of quality and the latest treatment approach. The methods of cell transplantation are based on the mechanical transfer of mature cells and undifferentiated precursor cells of melanocytes into the affected skin with the use of intermediate methods of re-cultivation, using a carrier base or without it. As a result the process of melanocyte regeneration is achieved.

The most important branch of regenerative medicine is a cell therapy, that is, the use of living cells of various origins, which, when introduced into the human body, are capable of actively functioning. This process leads to improvement and modification of existing tissue functions, or to recovery of functions lost by the tissue. Today it has become possible to use a cell transplantation for the treatment of vitiligo, which is characterized by the appearance of depigmented patches prone to peripheral location and developing as a result of melanocytes secretory dysfunctions.

### **RESEARCH OBJECTIVE**

The aim of the research is to study and evaluate the efficacy of vitiligo therapy based on the localization of the disease process.

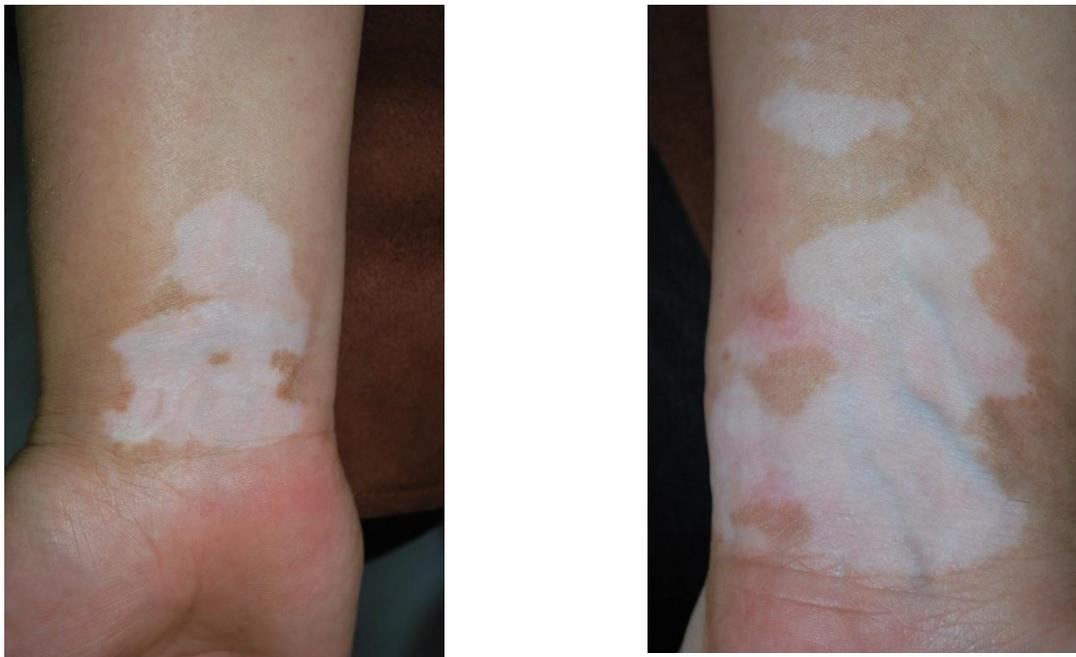
### **MATERIAL AND METHODS**

When studying the incidence of skin types in vitiligo patients in our work, vitiligo patches were observed in 3 skin types according to the Fitzpatrick classification scale. In total the study included 345 patients, of which 9 (2.6%) were classified as skin type II. Most of the patients - 266 (77.1%) had skin type III, while 70 (20.3%) patients were classified as skin type IV.

Vitiligo was clinically studied and analyzed in 2 large groups: segmental and non-segmental.



**Fig. 1. Segmental form of vitiligo (in the unilateral face-neck area)**



**Fig. 2. Non-segmental form of vitiligo (in the wrist areas of both hands).**

During the study, all patients were categorized by three age groups: from 18 to 40, from 41 to 60, and from 60 and older. Of the patients who underwent our observation, 194 patients (56.2%) were women, and 151 (43.8%) were men. Clinically 121 (35.1%) patients suffered from segmental vitiligo (70 were women, 51 were men), and 224 (64.9%) patients had non-segmental vitiligo (124 were women and 100 – men) (Table 1).

Table 1

<b>Age</b>	<b>18-40</b>	<b>41-60</b>	<b>60 and older</b>	<b>TOTAL</b>
Segmental	100	17	4	121
Non-segmental	171	36	17	224
	271	53	21	345

In the age aspect, 100 cases of segmental vitiligo were diagnosed in patients from 18 to 40 years old, and in 171 patients - non-segmental form of vitiligo. Among patients aged 41 to 60 years, 17 had segmental vitiligo and 36 had non-segmental vitiligo. Besides, there were 22 patients over the age of 60, of which 4 were segmental and 17 were non-segmental.

The distribution by age shows that a large proportion (78.6%) of patients with vitiligo are in the age group from 18 to 40 years. The contingent of this group, according to their active way of life compared to other patients, are considered to be patients requiring vitiligo treatment. Patients over 40 rarely seek medical advice and are often in state after a long-term treatment.

The applied method of transplantation of non-cultured epidermal cell suspension is carried out by obtaining a suspension of epidermal cells (keratinocytes and melanocytes) from small dermo-epidermal layers of the skin, which is transplanted into the depigmentation zone. During the research we used the high-technology apparatus Regenera (Italy), which extracts the hair follicle mesenchymal cells and, subsequently, transplants together with functionally active melanocytes into the depigmented skin of vitiligo patients. This technology has a highly specific effect on tissues requiring restoration and a targeted complex stimulating regeneration effect on the degrading complex of cellular and protein structures of the restored tissue.

## RESULTS AND DISCUSSION

As known one of the modern and advanced approaches in the treatment of vitiligo at present is the automelanocyte transplantation method. In our research, 113 vitiligo patients underwent surgical treatment of automelanocytes transplantation from the patients' healthy skin to depigmented patches in completely different body areas. The depigmentation areas were classified according to the development of patches on the body regions: face, trunk, hands and arms and legs (Table 2).

Table 2

TOTAL	Localization			
	Face	Trunk	Hands and arms	Legs
113	43	26	32	12
%	38,0	23,0	28,3	10,7

In 43 patients (38.0%) with vitiligo, depigmented patches were observed in the area of face, whereas 26 (23.0%) patients had depigmentation patches in distinctive body areas. 32 (28.3%) patients complained of depigmented patches on their hands and arms, 12 (10.7%) patients had depigmentation on legs and feet. Depigmented patches are of significant importance in repigmentation process on the body areas. Depigmented patches located in the distal and lower lateral zones of the body are recalcitrant, and repigmentation in these zones takes more time and effort.

The patients included in the research underwent the surgery of automelanocyte transplantation. The surgical treatment was performed in two groups. In the first group, a transplantation of non-cultured epidermal cell suspension (autokeratinositomelanocytes) (NCECS) was performed with material taken from the healthy skin to the depigmentation area. In the second group, the

method of transplantation of non-cultured epidermal cell suspension to the patient with vitiligo was carried out with the mixing of hair follicles from the patient's scalp to the prepared suspension (NCECS+NCORSHFS).

Transplantation of non-cultured epidermal cell suspension (NCECS) is a modern surgical method in the treatment of vitiligo. After dermabrasion of the upper epidermal depigmentation layer by mechanical or laser method, the automelanocyte suspension is transplanted and fixed with special collagen for 5-7 days. Re-pigmentation is observed 2-6 months after the treatment, depending on the recovery of the transplanted automelanocytes function.

Non-cultivated Outer Root Sheath Hair Follicle Cell Suspension (NCORSHFS) is a suspension made from healthy human hair follicles rich in stem cells and growth factors in the follicles.

Transplantation method using a combination of hair follicle cell suspension (NCECS + NCORSHFS) obtained from the scalp of a patient with vitiligo with the mixture of a suspension of uncultivated epidermal cells (NCECS) was carried out in 50 patients. The prepared suspension before transplantation was introduced into the depigment patches using the method of mesotherapy.

63 patients with vitiligo treated with the NCECS method accounted for 55.8% of the total number of patients, of which 41 (33.3%) had non-segmental vitiligo and 22 (19.5%) were segmental. NCECS + NCORSHFS method was performed in 50 patients, of whom 40 (80.0%) had non-segmental vitiligo and 10 (20.0%) - segmental vitiligo (Table 5).

Table 5

Treatment method	NCECS n=63		NCECS+NCORSHFS n=50	
	Non-segmental	segmental	Non-segmental	segmental
<b>Clinical forms of vitiligo</b>				
<b>Total n=113</b>	41	22	40	10
<b>%</b>	65,1%	34,9%	80,0%	20,0%

Pathological depigmented patches in patients treated with NCECS method were as follows according to their location in the body:

Table 6

NCECS n=63	According to the location area			
	Face	Trunk	Hands and arms	Legs
	24	13	17	9

24 (38.1%) patients receiving NCECS method of treatment had depigmented patches on the area of face. Depigmented patches in the area of trunk were observed in 13 patients (20.6%), on hands and arms - in 17 patients (27.0%) and on legs in 9 patients (14.3%) (Table 6).

From patients receiving the NCECS + NCORSHFS method, to 19 (38.0%) a transplantation was performed in the area of face, to 13 (26.0%) patients - in the area of trunk, 15 (30.0%) - on the hands and arms and to 3 (6, 0%) patients automelanocytes were transplanted on depigmented patches located on legs and feet in the form of the suspension prepared from hair follicles (Table 7).

Table 7

NCECS + NCORSHFS n=50	According to the location of patches			
	Face	Trunk	Hands and arms	Legs
	19	13	15	3

Patients who underwent both methods of treatments were observed during 3 months, and after this period the efficacy of treatment and repigmentation indicators were evaluated.

Table 8

	Treatment method	
	NCECS n=63	NCECS+NCORSHFS n=50
<b>Repigmentation indicator</b>	63,17±2,47%	85,88±1,82%
P<0,001		

According to the Table 8, the overall repigmentation indicator in patients treated with NCECS method averaged 63.17±2.47%, while NCECS+NCORSHFS was statistically significant at 85.88 ± 1.82% after the treatment (P<0.001).

The study and evaluation of the repigmentation indicators of pathological depigmented patches depending on their location on body areas, established that the repigmentation indicator after NCECS averaged 75.20±3.38% in 24 patients who underwent transplantation in the area of face. Repigmentation indicator in the area of trunk amounted to 58.85±4.43%, on hands and arms - 51.47±5.39%, on the legs - 50.55 ± 5.29% (Table 9).

Table 9

NCECS n=63	According to the location area			
	Face	Trunk	Hands and arms	Legs
	24	13	17	9
<b>Repigmentation indicator</b>	75,20±3,38%	58,85±4,43%	51,47±5,39%	50,55±5,29%

Repigmentation indicators showed high repigmentation process in the depigmented patches in the area of face and low repigmentation on hands and arms and legs.

In patients who underwent NCECS+NCORSHFS, repigmentation of depigmented patches in the area of face was 86.84±4.61%, in the area of trunk -

85.0±5.68%, on the hands and arms - 85.6±5.29%, and on legs - 85.0 ± 9.79% (Table 10).

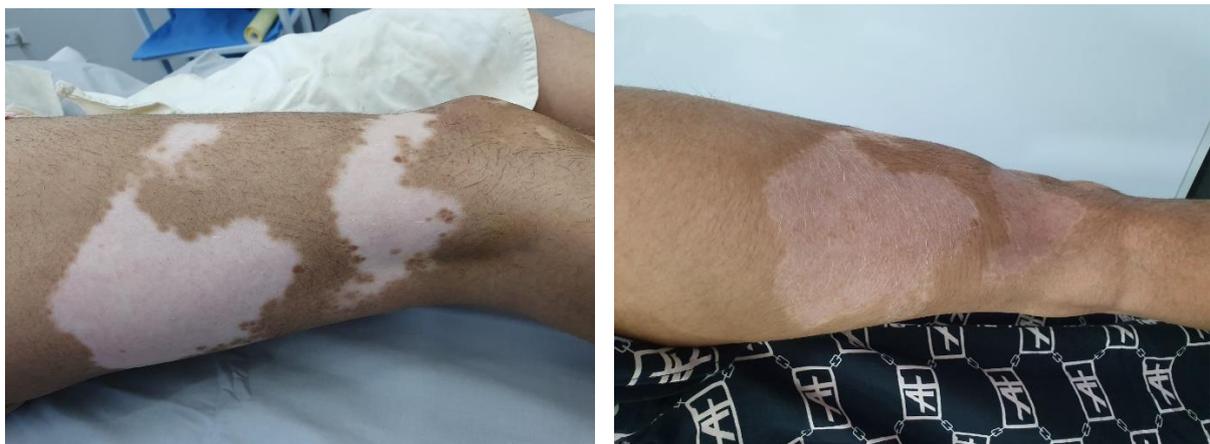
Table 10

NCECS + NCORSHFS n=50	According to the location area			
	Face	Trunk	Hands and arms	Legs
	19	13	15	3
Repigmentation indicator	86,84±4,61%	85,0±5,68%	85,6±5,29%	85,0±9,79%

As the table shows, high repigmentation indicators were established in all areas of the body of vitiligo patients who underwent NCECS+NCORSHFS.



**Fig. 4. Pre- and post-treatment condition after the NCECS+NCORSHFS method in the area of hands**



**Fig. 5. Pre- and post-treatment condition after the NCECS+NCORSHFS method in the area of legs.**

It would also be appropriate to mark the contribution of Professor U.Yu. Sabirov and Dr. B.A. Toirov who evaluated the efficacy and safety of non-cultured epidermal suspension application as a surgical treatment for patients with vitiligo. They retrospectively analyzed the treatment outcomes of 537 patients (308 women and 229 men) who underwent the surgery of transplantation of non-cultivated epidermal suspension. Repigmentation has started in 3 weeks after treatment in 10% of cases, in 4 weeks – in 25%, and in 8 weeks in 80% of cases. In general, 89.7% of cases (482/537) were successful in the treatment. The authors concluded that non-cultivated epidermal cell suspension is a reliable surgical method for vitiligo patients, refractory to nonsurgical treatment, especially in the case of large areas of depigmentation that can be corrected with non-cultivated epidermal cells [8].

Along with the above mentioned researchers, the work of Parul Thakur et.al. is also of great importance. He studied the efficacy of Follicular Unit Transplant (FUT) in cases of segmental/stabilized vitiligo as the treatment method for leukotrichia. They performed surgeries on 50 patients with 63 depigmented patches located superficially, using a transplantation of follicular unit grafts. Subjective and objective evaluation of treatment outcomes showed a reduction in vitiligo patches sizes, as well improvement in associated leukotrichia. Results were obtained by all 63 patches, with good or excellent indicators in 39 (61.9%) cases, satisfactory - in 16 (25.4%) and poor - in 8 (12.7%) cases. Only in two (4.8%) vitiligo patches no repigmentation process was observed. The average improvement of lesion areas was 61.17%. Excellent color matching was noted in 44 cases (69.8%), depigmented hair repigmentation was noted in 11 of 46 patients with leukotrichia. The authors concluded that FUT is a fairly safe and effective treatment method for localized and segmental vitiligo, especially on hairy skin areas [9].

## CONCLUSION

Thus, we can conclude that the NCECS+ NCORSHFS method for the treatment of vitiligo is significantly superior to the NCECS method, which was confirmed based on the above data. The correct choice of treatment, depending on the severity of the disease, contributes to faster and more effective repigmentation process. It was established that stem cells and developmental components of hair follicles increased the efficacy of dynamic melanocytes taken from the patient's healthy skin and transplanted to the depigmented patches for a more efficient pigmentation recovery process compared to the transplantation without hair follicles suspension. The performed method of surgical treatment of vitiligo is highly effective, which is confirmed by the absence of signs of depigmentation after the end of the treatment course. The recommended treatment course is 1-3 procedures, depending on the location and scope of the pathological process. Application of the NCECS+NCORSHFS method promotes faster repigmentation, eliminating cosmetic defects in patients, and improving their quality of life.

## REFERENCE

1. Diel K., Kolyadenko E.V., Kravchenko A.V. Vitiligo: current state of the problem. New etiologically grounded approaches to therapy // Ukrainian Journal of Dermatology, Venereology and Cosmetology. 2005. - No. 3. - P. 25–32.
2. Usovetskiy I.A., Sharova N.M., Korotkiy N.G. A modern view on the problem of vitiligo treatment. // Clinical Dermatology and Venereology. 2012. - No. 2. - P. 118-123.
3. Alkhateeb A., Fain P.R., Thody A. Epidemiology of vitiligo and associated autoimmune diseases in Caucasian probands and their relatives // Pigment. Cell. Res. 2003. -Vol.16. - P.208–216.
4. Belkheir N.H., Duweb G.H., El-Berghath A. Vitiligo: epidemiology and manifestations // JEADV. 2008. Vol. 37. P. 281–288.

5. Kuzmina T.S., Tkachenko S.B., Potekaev N.N. Vitiligo: pathogenetic substantiation of laser use // *Experimental and Clinical Dermatocosmetology*. 2005. - No. 4. - P.14-16.
6. Olisova O.Yu., Garanyan L.G., Kotelnikova L.A. Modern methods of vitiligo treatment // *Experimental and clinical dermatocosmetology*. 2013. - No. 2. - P.30–38.
7. Proshutinskaya D.V., Volnukhin V.A., Zhilova M.B., Borovaya O.V. The efficacy of treatment of patients with vitiligo with an ultraviolet excimer laser // *Bulletin of Dermatology*. 2009. - No. 4. - P.68–73.
8. Sabirov U.Yu, Toirov B.A. Transplantation of non-cultured epidermal cell suspension in vitiligo // *Scientific and practical journal "Dermatovenereology and Aesthetic Medicine"*, Collection of the Conference, 2019. - No. 3. – P. 160.
9. Parul Thakur, Sacchidanand S, Nataraj HV, Savitha AS. A Study of Hair Follicular Transplantation as a Treatment Option for Vitiligo. *Journal of Cutaneous and Aesthetic Surgery*, 2015, P211-217.