

Cumulative Effectiveness of Vitiligo Treatment Depending on the Stage of Clinical Course

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Abstract Vitiligo diagnosis and treatment are difficult. The advancement of vitiligo diagnostic procedures highlights the need to determine the severity of the disease, the extent of its progression, and the quality of life, all of which influence the volume of therapeutic measures. According to the World Health Organization, "the number of patients with vitiligo in the world is approximately 0,8-2,8% of the total population of the Earth; in recent years, there has been a tendency to increase the number of patients with vitiligo, and the frequency of this disease reaches 10% in various ethnic groups and populations". A large number of papers have been devoted to vitiligo research on a global scale, but the wide variety of methods of treating this pathology indicates a lack of a unified approach, which, in turn, indicates an unresolved pathogenesis of depigmentation in vitiligo. The study included 287 patients with non-segmental vitiligo, with an average age of $28,1 \pm 1,3$ years and a disease duration of $42,6 \pm 3,6$ months. All patients were examined and treated at the State Institution "RSNPMTSDVIK" between 2018 and 2022. In general, 161 (56,1%) of 287 patients received excellent results, 71 (24,7%) received good results, 42 (14,6%) received satisfactory results, 9 (3,1%) received unsatisfactory results, and 4 (1,4%) received progression. Excellent results were significantly more common with stable vitiligo - in 65% vs. 43% of cases ($p < 0,05$); good results were equally common - in 27% of cases, satisfactory - more common with unstable vitiligo - in 26% vs. 7% ($p < 0,05$).

Keywords Vitiligo, NB-UVB therapy, Provitilin, Vitiligo treatment, Fr: CO2 laser 10600 nm, YAG: Er laser 2940 nm

1. Introduction

Diagnosis and treatment of vitiligo present significant difficulties [1]. The improvement of diagnostic procedures for vitiligo indicates the need to determine the severity of the disease, the degree of its progression and the quality of life, on which the volume of therapeutic measures depends [2]. According to WHO, "the number of patients with vitiligo in the world is approximately 0,8–2,8% of the total population of the Earth; in recent years there has been a tendency to increase the number of patients with vitiligo, and in various ethnic groups and populations the frequency of this disease reaches 10% ..." [8]. In 2011, an initiative was launched to proclaim June 25 as World Vitiligo Day to include it in the UN calendar. Well-known entrepreneur Steve Hargadon organized a private social network Vitiligo Friends.org and the project "Uniquely beautiful", which is a powerful support for the social adaptation of people with vitiligo. All this once again proves the difficulties of treating vitiligo [7]. A large number of papers have been devoted to vitiligo research on a global scale, but the wide variety of methods of treating this pathology indicates the lack of a unified

approach, which, in turn, indicates the pathogenesis of depigmentation in vitiligo that has not been fully disclosed [3,4].

2. Materials and Methods

287 patients with non-segmental vitiligo were examined, average age = $28,1 \pm 1,3$ years, disease duration – $42,6 \pm 3,6$ months. All patients were examined and received treatment in the State Institution "RSNPMTSDVIK" in the period from 2018 to 2022. The ratio of men and women was 1,08, which shows an equal incidence of vitiligo in men and women. At the same time, 78,4% were persons under the age of 45. In our observations, Fitzpatrick skin types III and VI prevailed in persons with vitiligo: 51% and 38%, respectively, there were no persons with type V and VI. The degree of progression of the disease was determined by the presence of the following signs: 1) fuzzy borders of foci or the appearance of new point depigmented areas, 2) the Kebner phenomenon, 3) "trichromic" staining in foci, 4) signs of inflammation, hyperemia and itching in foci [4]. The severity of the disease (prevalence, degree of depigmentation + quality of life) was assessed according to our proposed M-VES scale. In the M-VES scale, we propose to summarize the scores on 2 scales: VES [4] and DIKJ for a full

assessment of the severity of vitiligo. Methods of treatment included UFO and laser therapy. PUVA, NB-UVB phototherapy was performed on the NEOLUX Series 3 installation ("Daavlin" USA), in the mode 3-5 times a week. Excimer light treatment was carried out on an Excilite μ 308nm unit (DEKA, Italy). Laser irradiation was carried out by two types of lasers. A fractional Fr:CO₂ laser with a wavelength of 10,600 nm was used, irradiation was carried out on a SmartXide installation with Punto technology

(DEKA, Italy) in a fractional mode of 10W, 800 ms, 10600 nm. An erbium laser was also used. Laser irradiation with YAG:Er erbium laser was carried out at the Harmony XL Pro installation (Alma Lasers, Israel), in ablation mode, with a 9*9 mm nozzle, at a wavelength of 2940 nm, 1800 J/cm². Provitilin cream was used locally. The distribution of patients depending on the type of treatment is presented in the table (Table 1).

Table 1. Distribution of patients depending on the type of combination therapy

Type of irradiation	In its pure form, n	+Provitilin, n	+Provitilin +Fr:CO ₂ laser 10600 nm, n	+Provitilin + YAG: Er laser 2940 nm, n	Total, n
NB-UVB	50	35	45	58	188
Eximer Light	19	24	16	18	77
PUVA	22	-	-	-	22
Total	91	59	61	76	287

The regression of initial scores on the M-VES scale by 0-50% according to the method of Kawakami, 2011 was taken as a criterion for the effectiveness of treatment (Table 2.)

Table 2. Evaluation of the result of vitiligo treatment

Decrease in MOVES points, %	Evaluation of the result
50%	Excellent result
25-50%	Good
10-25%	Satisfactory
0-10%	unsatisfactory
Progress by 10%	Slight deterioration
Progress 10-25%	Decline
25-50%	Severe deterioration
More than 50%	Very severe deterioration

The combination of excellent and good results was considered an effective treatment (overall effectiveness); the combination of unsatisfactory results (regression of M-VES less than 10%) and cases of vitiligo progression was considered as a bad result; satisfactory results (regression of M-VES less than 25%-10%) were considered low treatment effectiveness.

3. Results and Discussion

Unstable vitiligo was detected in 122 (42.5%) patients. The activity of the process (unstable course) was characterized by the presence of all 3 signs: "scalped" vitiligo, tricolor vitiligo, the presence of the Kebner phenomenon in 85 (29.6%) patients, an increase in the area of existing foci and the appearance of new ones during the last 3 months was in 33 (11.5%) patients, in 4 (1.4%) cases there was the process of inflammation in the foci was revealed. Stable vitiligo – in 165 (57.5%).

In our studies, NB-UVB therapy was given to patients with an initially severe course, progressive-unstable vitiligo. Thus, 37 out of 103 patients who received NB-UVB in combination with lasers had progressive vitiligo, which in the first 4-6 months was treated only with narrow-band UVB, and subsequently, laser therapy was connected.

When analyzing the results of treatment in patients with stable vitiligo in the general subgroup of combined treatment with NB-UVB+lasers+Provitilin showed mostly good and excellent results. Thus, out of 67 patients with excellent results, 49 (73.1%) had stable vitiligo, 18 (26.9%) had unstable vitiligo. Of the 18 patients with a good result, 15 (83%) had stable vitiligo, 3 (17%) had unstable vitiligo at the beginning of treatment.

In the general subgroup NB-UVB+lasers+Provitilin out of 37 patients with unstable vitiligo, only 17 (45.9%) had an excellent result, 3 (8.1%) had a good result, 14 (37.8%) had a satisfactory result, and 3 (8.1%) had an unsatisfactory result. Out of 66 patients with stable vitiligo, 49 (74%) had an excellent result, 15 (22.7%) had a good result, and only 2 (3%) patients had a satisfactory result.

In general, out of 287 patients, 161 (56.1%) had excellent results, 71 (24.7%) had good results, 42 (14.6%) had satisfactory results, 9 (3.1%) had unsatisfactory results, and 4 (1.4%) had progression (Table 3).

When analyzing the results of treatment in patients with stable and unstable vitiligo, it was revealed that excellent results were in 65% and 43% of cases, respectively ($p < 0.05$); good results were equally common in 27% of cases, satisfactory – 7 and 26%, i.e. statistically significant in unstable vitiligo ($p < 0.05$) (fig.1).

An unsatisfactory result of treatment with all types of combined phototherapy was observed in carriers of unfavorable alleles of the TNFAIP and REL genes, which proves the contribution of autoimmune diseases during vitiligo and its resistance to treatment.

Table 3. Distribution of patients depending on the result of treatment

	PUVA	NB-UVB	Ex. light	NB-UVB+ провिति-лин	Ex.light + hold-lin	NB-UVB+ CO2-лаз.+ провिति-лин	NB-UVB+Y AG:Er-лаз+ провителин	Ex.light++CO 2-manhole.+ rulers	X.light+ YAG:Er-eye+ draw-line	Total
Great	10	17	10	18	12	33	34	12	15	161
Good	6	16	7	8	10	5	13	3	3	71
Satisfactory	4	11	2	7	2	7	8	1	0	42
Unsatisfactory	2	2	0	2	0	0	3	0	0	9
-	0	4	0	0	0	0	0	0	0	4

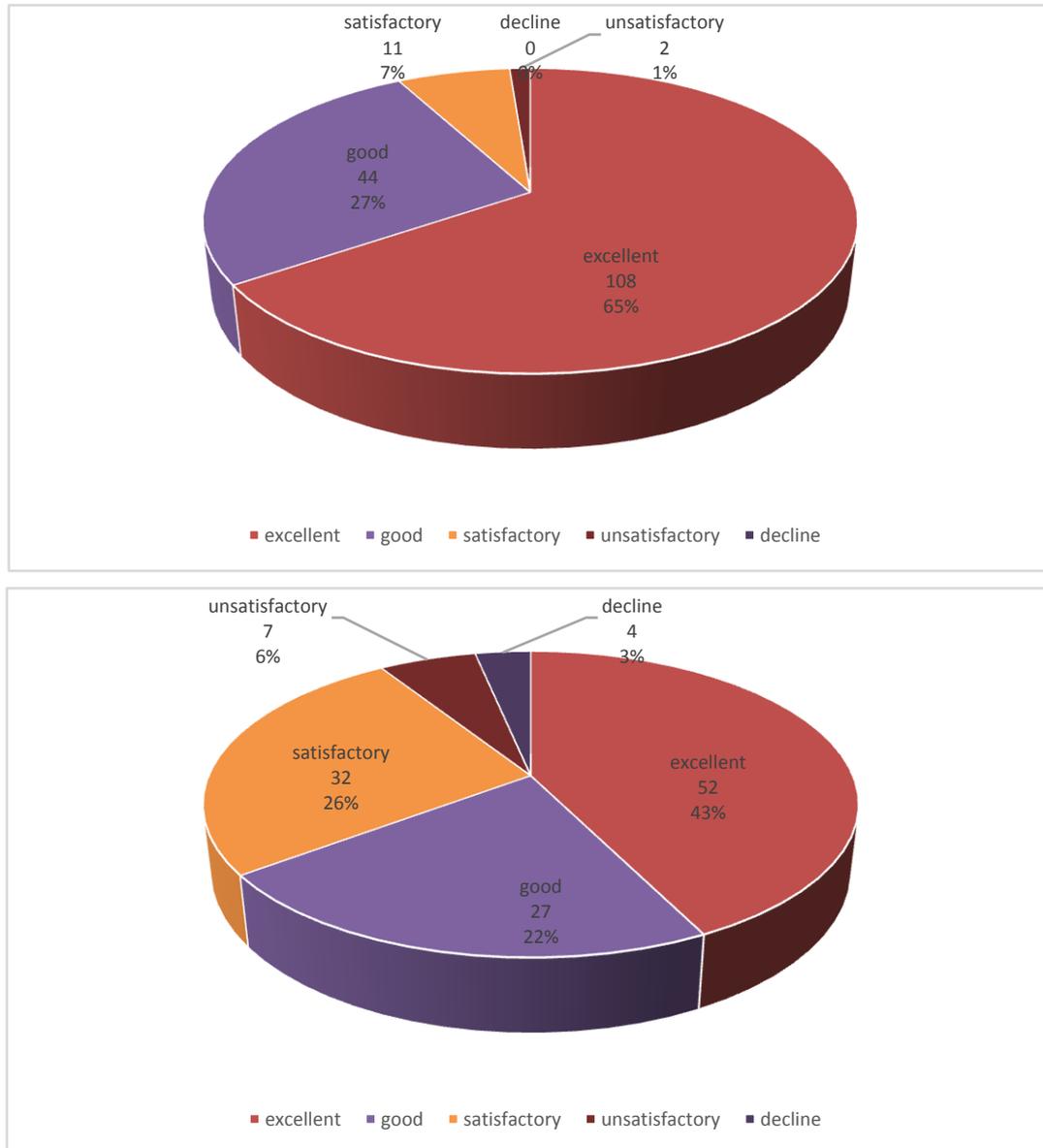


Figure 1. Results of treatment of stable and unstable vitiligo

Evaluation of the relationship of the treatment result with the reserve for repigmentation- the content of residual melanocytes according to the data of the MEX showed that good and excellent results were observed in patients with an initial IP of more than 7UE and NIP of more than 2.0, as

evidenced by the data of the ROC analysis. The cut-off thresholds for predicting good and excellent repigmentation results were $IP > 7$ for IP with 100% sensitivity and 90% specificity; for $NIP > 2$ with 100% sensitivity and 95% specificity (Fig.2).

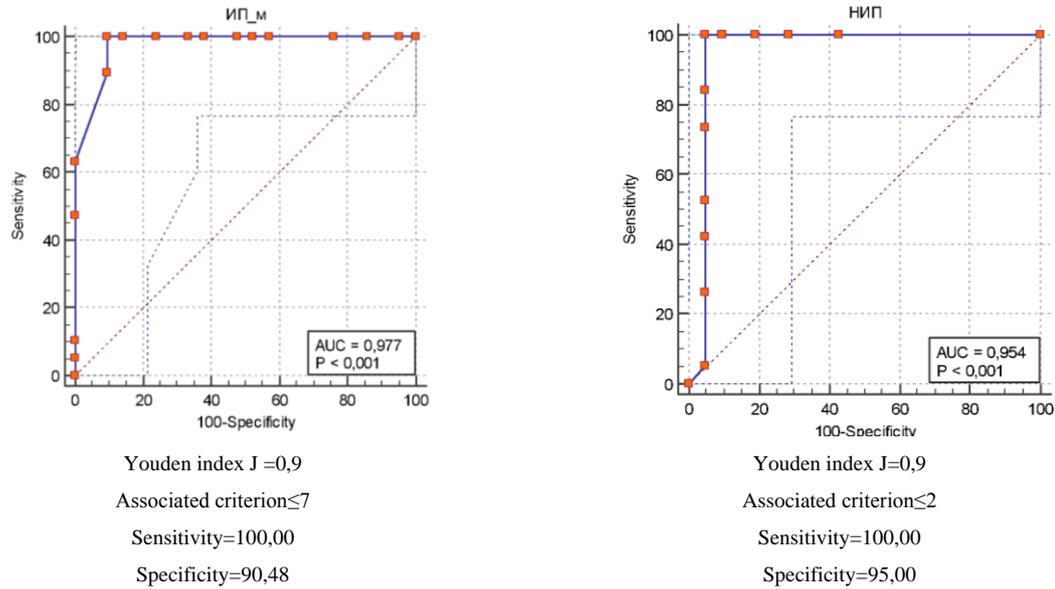


Figure 2. ROC curve for the diagnostic efficiency of IP and IM according to the data of mex

Table 4. Results of mexametry in patients with vitiligo

Form of the disease	IP on healthy skin before treatment	IP of the focus of depigmentation before treatment	IP in the depigmentation zone after treatment	NIP before treatment	NIP after treatment
Generalized	22,5±0,5	4,3±0,5	16,6 ± 1,1*	5,2±0,2	1,35 0,3*
Acrofacial	21,7±0,4	4,6±1,0	12,6 ± 0,3*	4,7±0,5	1,8 0,2*
Universal	22,5±0,3	5,2±1,1	15,6± 0,4*	4,3±0,2	1,53 0,2*
Mixed	22,6±0,3	4,4±0,7	14,7 ± 0,3*	5,1±0,4	1,6 0,2*
Vitiligo of the mucous membranes	21,2±0,2	4,4±0,6	11,5± 0,2*	5,1±0,3	1,8 0,1*
Total	22,8±0,7	4,5±0,7	14,8± 0,4*	5,1±0,4	1,5 0,3*

*-statistically significant from the indicator before treatment at p<0.05; ** - statistically significant from generalized vitiligo – not revealed.

As our studies have shown, in individuals with a good and excellent result of repigmentation, the indicators of IP in the depigmentation zone are more than 7, and the NIP is less than 2, also in some patients with a good result, the NIP was more than 2, and the IP was less than 7, but their treatment was still effective. Therefore, the specificity of the NIP and IP indicator was 95% and 90.5%, respectively.

The evaluation according to the data of mexometry after treatment showed that IP and NIP increased, the differences in the index of IP and NIP before and after treatment were statistically significant in all cases, but we did not detect differences in IP and IP depending on the form of vitiligo, in all groups p>0.05 (Table 4).

Our data are consistent with the literature, because IP and skin phototype are considered by a number of researchers to be prognostic important signs in vitiligo: with dark phototypes, the effect is more significant; the effect strongly depends on the localization of the process [5]. Many authors point out that the face, excluding the perioral, periauricular and behind-the-ear areas and non-oral areas of the skin, is easier to treat, which is associated with the reservoir of

melanocytes and the density of hair follicles [6]. There is a certain paradox – localization of foci on the face and IV, V phototypes of the skin, on the one hand, are factors causing an obvious clinic of vitiligo and poor quality of life, and on the other hand, the effectiveness of treatment is better.

4. Conclusions

1. Excellent results were significantly more common with stable vitiligo - in 65% vs. 43% of cases, respectively (p<0.05); good results were equally common – in 27% of cases, satisfactory – more common with unstable vitiligo - 26% vs. 7% (p<0.05).
2. Mex is an objective way to assess the reserve depigmentation in vitiligo, because the specificity of the normalized pigmentation index of NIP and IP was 95% and 90.5%, respectively.
3. The cut-off thresholds for the prediction of a good and excellent repigmentation result were for IP> 7 for IP with 100% sensitivity and 90% specificity; for NIP>2 with 100% sensitivity and 95% specificity.

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