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Original study article

Clinical and pathogenetic assessment of cyclosporine efficacy in the complex therapy of non-segmental vitiligo patients

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ABSTRACT

BACKGROUND: Vitiligo is a chronic disease of unknown etiology, characterized by the appearance of depigmented spots on various areas of the skin, rarely on mucous membranes, and discolored hair due to destruction and reduction of melanocytes. While not life-threatening, vitiligo significantly impacts the psychoemotional aspect. Studies assessing the quality of life of vitiligo patients reveal the presence of depression in these individuals. In addition to depression, a high susceptibility to anxiety, stigmatization, sleep disturbances, adaptation, and problems in personal relationships have been identified. The prevalence of depression and anxiety among vitiligo patients is comparable to other dermatological conditions such as atopic dermatitis, acne, psoriasis, and urticaria. This underscores the need to seek new means and methods for treating this condition.

AIM: Clinical assessment of the effectiveness of using cyclosporine in combination with UVB 311 nm and monotherapy with UVB 311 nm for vitiligo.

MATERIALS AND METHODS: The study involved 40 patients with progressive vitiligo. All patients were randomly divided into two groups. Group 1 (20 individuals) underwent a course of cyclosporine therapy in combination with UVB therapy, while Group 2 (20 individuals) received monotherapy with UVB 311 nm. The duration of the treatment was 6 months. The extent of the affected area relative to the body surface area was evaluated using the VES index (Vitiligo extent score) on a vitiligo calculator. The impact of the disease on the quality of life was assessed using the VitiQoL scale (vitiligo-specific quality-of-life instrument).

RESULTS: All patients included in the study completed the full course of treatment. Group 1 (20 individuals) underwent a course of cyclosporine therapy in combination with UVB therapy, while Group 2 (20 individuals) received monotherapy with UVB 311 nm. Patients in the combined therapy group experienced earlier stabilization of the skin process compared to those receiving monotherapy with UVB 311 nm. Additionally, Group 1 demonstrated more pronounced repigmentation of vitiligo lesions and significant improvement in quality of life compared to Group 2.

CONCLUSION: Cyclosporine in combination with narrowband phototherapy at 311 nm demonstrated good clinical efficacy and significant improvement in quality of life for non-segmental vitiligo patients. Cyclosporine is well-tolerated, has a low spectrum of side effects, and can be used long-term for patients with active vitiligo.

Keywords: vitiligo; vitiligo treatment; immunosuppressive drugs; cyclosporine.

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Оригинальное исследование

Клинико-патогенетическая оценка эффективности применения циклоспорина в комплексной терапии больных несегментарным витилиго

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АННОТАЦИЯ

Обоснование. Витилиго — хроническое заболевание неизвестной этиологии, характеризующееся появлением на различных участках кожи, редко на слизистых оболочках, депигментированных пятен и обесцвеченных волос вследствие разрушения и уменьшения количества меланоцитов. И хотя данное заболевание не представляет угрозу для жизни, оно оказывает большое влияние на психоэмоциональный статус пациента. Множество исследований, посвящённых оценке качества жизни пациентов с витилиго, демонстрируют наличие у них депрессии, нарушений сна, адаптации и проблем в личных отношениях, стигматизации, а также высокую подверженность тревоге. На данный момент распространённость депрессии и тревожных состояний среди пациентов с витилиго сравнима с такими дерматологическими проблемами, как атопический дерматит, акне, псориаз и крапивница, что в свою очередь доказывает необходимость поиска новых средств и методов лечения данного заболевания.

Цель исследования — клиническая оценка эффективности применения циклоспорина в сочетании с УФБ 311 нм и монотерапии УФБ 311 нм при витилиго.

Материалы и методы. Участники исследования с прогрессирующим витилиго (n=40) были разделены на две группы случайным образом: группа 1 (n=20) прошла курс терапии циклоспорином в комбинации с УФБ-терапией, группа 2 (n=20) получала монотерапию УФБ 311 нм. Продолжительность лечения составила 6 месяцев. Площадь поражения относительно площади поверхности тела оценивали с помощью индекса VES (оценка степени выраженности витилиго) на витилиго-калькуляторе. Влияние заболевания на качество жизни оценивали с помощью шкалы VitiQoL (оценка качества жизни больных витилиго).

Результаты. У пациентов, получавших комбинированную терапию, стабилизация кожного процесса наступила ранее, чем у пациентов на монотерапии УФБ 311 нм. Пациенты группы 1 также продемонстрировали более выраженную репигментацию очагов витилиго и значительное улучшение качества жизни по сравнению с пациентами группы 2.

Заключение. Циклоспорин в сочетании с узкополосной фототерапией 311 нм продемонстрировал хорошую клиническую эффективность, а также значительное улучшение качества жизни пациентов с несегментарным витилиго. Циклоспорин обладает хорошей переносимостью, имеет небольшой спектр побочных реакций, может быть использован в длительной перспективе у пациентов с активным витилиго.

Ключевые слова: витилиго; лечение витилиго; иммуносупрессивные препараты; циклоспорин.

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ЭКО•ВЕКТОР

BACKGROUND

Vitiligo is a chronic disease of unknown etiology characterized by the appearance of depigmented patches and discolored hairs on various skin surfaces, rarely on mucous membranes, because of the destruction and reduction in the number of melanocytes [1]. In the general population, the prevalence of vitiligo ranges from 0.5% to 2% [2, 3]. It has no sex predisposition and does not depend on race or age [4]. However, it is more commonly diagnosed in young people aged <30 years [5].

Vitiligo negatively affects the quality of life, reduces self-esteem, and causes significant psychological distress in patients [6, 7]. Vitiligo affects aspects of daily life such as the choice of clothing, social activities, and problems in intimate life. Moreover, >50% of people with vitiligo believe that their life has greatly changed after its onset [8]. Numerous studies have shown that the involvement of body parts such as the face, hands, and feet has the most adverse effect on the quality of life [9, 10]. Patients with darker skin phototypes are more susceptible to depression: some reports indicate that up to 90% of patients with vitiligo and ethnic dark skin suffer from depression. India's Prime Minister Jawaharlal Nehru listed vitiligo as one of the three most important medical problems in the country, which shows the importance of vitiligo in some regions [11].

Although the etiology and pathogenesis of vitiligo are not fully understood, melanocyte damage and disruption of melanogenesis in the skin is attributed to autoimmune mechanisms [12, 13], as evidenced by the prevalence and progression requiring the prescription of systemic immunosuppressive agents. According to Russian and European clinical recommendations, such immunosuppressive agents include systemic glucocorticoids. Vitiligo requires long-term treatment. Furthermore, long-term use of glucocorticoids can be associated with serious side effects. In addition, this drug group has a rather long list of contraindications [14, 15]. Therefore, alternative therapies that would serve as a safe and effective substitute for corticosteroids are needed. Evidence shows that Janus kinase inhibitors, genetically engineered drugs, azathioprine, and methotrexate may be effective immunosuppressants. Cyclosporine is a potential candidate for use as an immunosuppressive therapy for vitiligo.

Cyclosporine is a calcineurin inhibitor and a cyclic lipophilic polypeptide containing 11 amino acids. Its mechanism of action is the suppression of cell-mediated immune responses. The main target cells for cyclosporine are $CD4^+$ T-lymphocytes, and their activation underlies the development of immune responses. Because of its immunosuppressive effect, cyclosporine inhibits the synthesis of interleukin (IL) 2, which is necessary for the self-activation of T-lymphocytes and their differentiation. In addition, cyclosporine suppresses the secretion of ILs 3, 4, 6, 7, 8, 17, and 23 and other cytokines (interferon gamma, tumor necrosis factor alpha, etc.). Furthermore, it inhibits the release of histamine from mast cells and reduces the activity of various cell adhesion molecules. The mechanism of action of cyclosporine is referred to as "selective immunosuppression," which gives an advantage over other drugs with cytotoxic and immunosuppressive effects [16, 17].

In foreign literature, single studies have examined the efficacy of cyclosporine in vitiligo [18, 19]. According to the latest clinical guidelines, combined therapy is recommended for adult patients with vitiligo to increase its efficacy. In this regard, we aimed to compare the clinical efficacy of mid-wave narrowband ultraviolet B (UVB) 311 nm as monotherapy and that in combination with cyclosporine and to develop a safe and effective regimen for the use of cyclosporine in the combined therapy for vitiligo.

The aim of the study was to clinically evaluate the efficacy of cyclosporine in combination with UVB 311 nm and UVB 311 nm monotherapy in vitiligo.

MATERIAL AND METHODS

Study design

A randomized interventional prospective study was conducted.

Eligibility criteria

Inclusion criteria: male and female patients with nonsegmental vitiligo aged 18–70 years of age who provided written informed consent to participate in the study.

Non-inclusion criteria: persons aged <18 and >70 years of age; individuals with segmental, mixed, and nondeterminant vitiligo; pregnant or lactating women; individuals with active infection, congenital or acquired immunosuppression, history of malignancy, eye disease (glaucoma, cataract), and hypertension (grades II–III); history of using cyclosporine; use of phototherapy, systemic steroids, or immunosuppressants within 4 weeks before randomization; hypersensitivity to cyclosporine or other drug components; and concomitant use of cyclosporine and methotrexate, apremilast, other immunosuppressive drugs, nonsteroidal anti-inflammatory drugs, rifampicin, barbiturates, sulfonamides, corticosteroids, tetracyclines, trimethoprim, chloramphenicol, para-aminobenzoic and para-aminohippuric acids, and probenecid.

Exclusion criteria: pregnancy that occurred during the study, occurrence of adverse effects during therapy, refusal of the patient to continue participation in the study, and other circumstances that prevented compliance with the treatment protocol (prolonged absence of the patient, relocation, inability to attend consultations at the scheduled time, etc.).

Settings

The study was conducted at the Rakhmanov Department of Skin and Venereal Diseases of the N.V. Sklifosovsky Institute

of Clinical Medicine of the I.M. Sechenov First Moscow State Medical University, Ministry of Health of Russia (Sechenov University).

Duration of the study

The study was conducted between December 2021 and October 2023.

Description of the medical intervention

The study participants (*n*=40, including 17 men and 23 women) diagnosed with nonsegmental vitiligo were randomly divided into two groups. Group 1 (*n*=20) received cyclosporine at a dose of 3 mg/kg in two daily receptions in combination with UVB 311 nm phototherapy three times a week. The initial dose of UVB rays was 0.1 J/cm^2, with a gradual increase of the UVB dose by 0.1 J/cm^2 in each subsequent procedure. Group 2 (*n*=20) received UVB 311 nm monotherapy (three times a week) according to a similar scheme. The treatment was administered in a Herbert Waldmann UV 7002 K ultraviolet cabin (Germany). All patients were treated for 6 months. The lesion area relative to the body surface area was evaluated using the vitiligo extent score (VES) on a vitiligo calculator. The effect of the disease on the quality of life was assessed using the vitiligo-specific quality-of-life (VitiQoL) instrument. All patients completed the self-administered questionnaires comprising 15 main questions and one additional question. The scale ranged from 0 to 6, with 0 indicating no severity and 6 indicating severe and frequent symptoms. The additional question focused on individual self-assessment of vitiligo severity. The maximum possible score for this question was 90+6. The interpretation of the summarized scores is presented in Table 1.

Table 1. VitiQoL (vitiligo-specific quality-of-life instrument)
Таблица 1. VitiQoL (vitiligo-specific quality-of-life шкала)

Total score	Explanation
0–5	No effect on the patient's life
6–20	Minor effect on the patient's life
21–38	Moderate effect on the patient's life
⩾39	Very strong effect on the patient's life

Methods of recording outcomes

The results of the study were recorded before and after the treatment using photofixation under both natural and artificial light.

Ethical review

The study was approved by the Local Ethical Committee of Sechenov University (Protocol No. 01-22 dated January 20, 2022). All patients included provided informed voluntary consent to participate in the study. Patients were fully informed about the study, therapy courses, possible outcomes, and side effects of the therapy.

Statistical analysis

To analyze the presented quantitative and categorical data, advanced universal nonparametric (randomization–reversal) algorithms for constructing confidence intervals (CIs) and statistical comparisons based on bootstrap and Monte Carlo methods were used. A statistical description of quantitative features typically entails the estimation of mean and median values with 95% CIs, calculation of indicators of variation around the mean value — standard deviation and coefficient of variation — and assessment of the observed distribution's agreement with the normal (Gaussian) law to select criteria for further comparison of groups. The chi-square test (χ^2) was employed to assess the uniformity of distributions of categorical features. For the statistical comparison of quantitative traits, parametric criteria were used, including Student's/Welch's t-test (for unequal variance) for independent samples (comparison of groups 1 and 2), Student's t-test for paired samples (before–after comparison), and the nonparametric Mann–Whitney U-test (comparison of groups 1 and 2). Linear regression analysis (least squares method) with Box–Cox transformation for the response was used to plot the relationship between VES score and disease duration.

RESULTS

Study objects (participants)

The study included 40 patients (17 men and 23 women) suffering from progressive vitiligo. Disease progression was manifested by an increase in the size of vitiligo foci and the appearance of new spots. All patients were randomly divided into two groups using a random number generator. Group 1 (n = 20) was treated with cyclosporine in combination with UVB therapy, and group 2 (*n* = 20) received monotherapy with UVB 311 nm.

Disease progression was observed within 4–6 months in 18 patients, 2–4 months in 13 patients, and <2 months in 9. The average disease duration at the time of treatment was 9.8 years (group 1, 8.95 years; group 2, 10.7 years).

In 13 patients, the disease manifested before the age of 20 years, in 10 patients between the ages of 20 and 30 years, and in 17 patients after the age of 30 years. Vitiligo was presented in close relatives of 12 out of 40 patients.

Among the factors that could potentially provoke vitiligo, 9 patients (group 1, *n*=4; group 2, *n*=5) reported exposure to the sun, 4 (2 in each group) reported skin trauma, and 4 (group 1, *n*=1; group 2, *n*=3) reported acute respiratory viral infections. Two patients (one in each group) exhibited respiratory viral infections, whereas three patients (group 1, *n*=2; and group 2, *n*=1) exhibited COVID-19. Eight patients

could not identify any provoking factors associated with the onset of vitiligo.

Of the 40 patients, 9 exhibited concomitant endocrine system diseases, including hypothyroidism, diffuse thyroid changes, autoimmune thyroiditis, pancreatitis, benign pituitary cysts, and operated adrenal adenomas. These conditions were in remission at the time of the study. In addition, 14 participants exhibited other comorbidities, including chronic gastritis, chronic rhinitis and rhinosinusitis, chronic tonsillitis, chronic cholecystitis, cholelithiasis, urolithiasis, cervical erosion, and grade I hypertension.

In the review of the patients' medical histories, the majority had received standard therapy for vitiligo, including external therapy with topical glucocorticoids and topical calcineurin inhibitors. Seven patients had received systemic corticosteroids in the form of low-dose pulse therapy; however, the effect of the therapy was weakly positive and short-lived or absent altogether, with the disease continuing to progress. Phototherapy was administered to 19 patients throughout their illness. However, the observed positive dynamics were either not sustained or were transient, resulting in relapse. The patients had not received any treatment for 3 months before the commencement of this study. After their enrollment in the study, they were required to adhere to the therapeutic regimens that were recommended by the investigators.

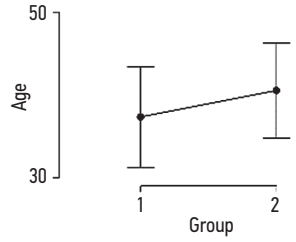
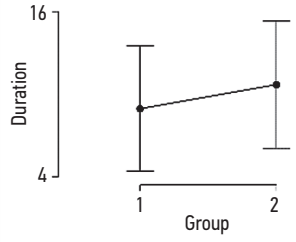
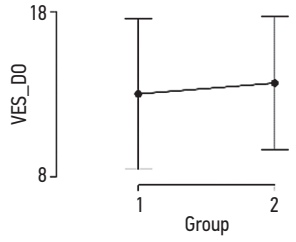
Main results of the study

The results of this study are based on the examination of two groups of patients with progressive vitiligo. As shown in Table 2, no statistically significant differences in age, disease duration, or prevalence of skin processes were found between the two groups. Furthermore, the *p*-value of the χ2 exact comparison criterion with a uniform distribution corresponded to 0.824 and 0.503, indicating that no statistically significant differences in the distribution of patients in groups 1 and 2 by sex.

A 6-month course of therapy in group 1 resulted in the cessation of the progression of depigmentation, stabilization, and absence of new foci or enlargement of existing ones in 95% of the patients (20/20). In 15 of the 20 patients, repigmentation of the vitiligo foci was

Table 2. Descriptive statistics of patients in study groups

Таблица 2. Описательная статистика пациентов групп исследования

Category	Statistical analysis, 95% CI				*p*-value permutable/ VS-MPR	Mean values in groups with 95% CI
	Mean/median* subgroup value		Difference in mean medians/Hodges–Lehman medians*	Standardized effect according to Cohen		
	Group 1	Group 2				
Age, years	$_{32}$ 37 $_{43}$	$_{35}$ 41 $_{46}$	$_{-11}$ -4 $_{5}$	$_{-0.9}$ -0.3 $_{0.4}$	0.442	
Disease duration, years	$_{5}$ 9 $_{13}$	$_{7}$ 11 $_{15}$	$_{-8}$ -2 $_{4}$	$_{-0.8}$ -0.2 $_{0.4}$	0.588	
Disease duration*, years	$_{2}$ 4 $_{14}$	$_{5}$ 8 $_{15}$	$_{-7}$ -2 $_{2}$	-	0.303	
VES_Before	$_{9.05}$ 13.02 $_{17.14}$	$_{10.21}$ 13.68 $_{17.28}$	$_{-6·21}$ -0.66 $_{4.93}$	$_{-0.7}$ -0.1 $_{0.5}$	0.830	
VES_Before*	$_{7.38}$ 10.22 $_{16.31}$	$_{9.44}$ 12.22 $_{15.00}$	$_{-5.61}$ -1.30 $_{3.35}$	-	0.608	

Note. * Denotes comparison of median values performed for indicators with significant asymmetry.

Примечание. * Сравнение медианных значений, выполненное для показателей с существенной асимметрией.

observed. Six patients demonstrated a pronounced positive effect, nine demonstrated a moderate positive effect, and one exhibited a weak positive effect. One patient did not respond to the conducted therapy.

Among the 20 patients in group 2, stabilization of the skin process was observed in 15 (75%). Repigmentation was observed in 10 patients, of whom 2 exhibited a pronounced positive effect, 5 exhibited a moderate positive effect, and 3 exhibited a weak positive effect. In five patients, new depigmentation foci and/or an increase in the size of existing ones were observed during the treatment (Fig. 1).

Assessment of vitiligo severity

The lesion area relative to the body surface area before and after therapy was assessed using the VES index on a vitiligo calculator.

Before therapy, the lesion area ranged from 2.36% to 38.08% (mean, 13.02%) in group 1 and from 2.64% to 39.96% (mean, 13.68%) in group 2. After the treatment, the lesion area ranged from 1.14% to 32.86% (mean, 9.83%) and 1.31% to 40.84% (mean, 12.51%) in groups 1 and 2, respectively. A strong direct correlation between VES and disease duration was observed in both groups (Fig. 2).

Assessment of the quality of life of patients with vitiligo

The effect of the disease on quality of life was assessed using the VitiQoL scale. The mean VitiQoL score in both groups before therapy was 41 (range, 9–80 in group 1 and 12–77 in group 2). The maximum scores were observed in items 1 (concern about skin appearance), 10 (influence of the skin condition on the emotional state), and 15 (concern about disease progression), even after a pronounced positive result was achieved. Item 11 (effect of the skin condition on physical health in general) exhibited the lowest score. After 3 months of treatment (week 12), the mean VitiQoL scores were 30 in group 1 and 35 in group 2. After the treatment, the VitiQoL scores were on average 23 (3–51) points in group 1 and 30 (7–54) points in group 2.

Before treatment, the mean score of the additional VitiQoL question in both groups was 4.5. After 3 months of treatment (week 12), the mean scores of the additional VitiQoL question were 3.4 in group 1 and 3.8 in group 2. After treatment, the additional VitiQoL question scores were on

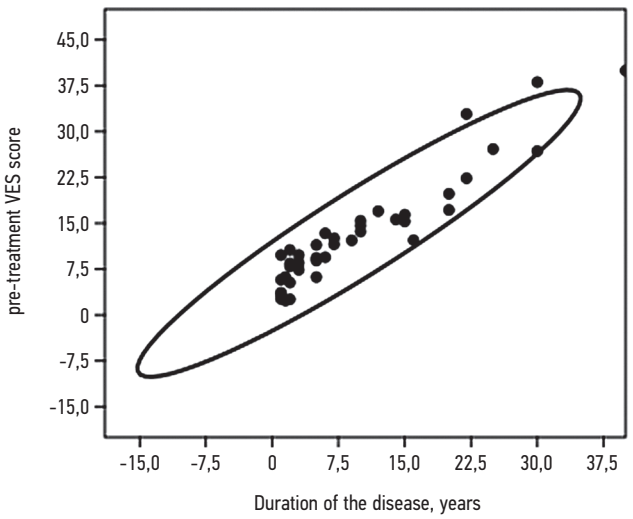


Fig. 2. Scatter plot with ellipses of patient disease duration and pre-treatment VES score.
Рис. 2. Эллипс рассеяния продолжительности заболевания пациента и показателя VES до лечения.

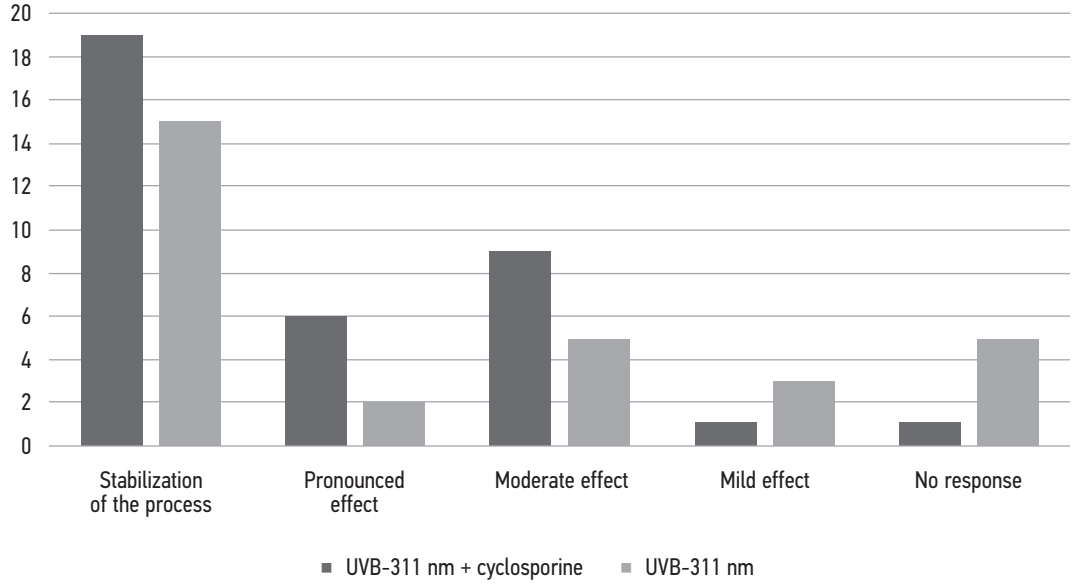


Fig. 1. Response to therapy in patients in the study groups, *n*.
Рис. 1. Ответ на проводимую терапию у пациентов групп исследования, *n*.

average 2.2 and 3.15 points in groups 1 and 2, respectively. Typically, the presence of this disease caused greater emotional distress to young people, particularly girls, than to older individuals.

Table 3 demonstrates that the absolute changes in disease severity measures AFTER treatment compared to BEFORE treatment differ between groups. At the 0.05 significance level, the decrease in VES was more pronounced in group 1 than in group 2. At the 0.05 significance level, the decrease in VitiQoL was more pronounced in group 1 than in group 2. Similarly, at the 0.005 significance level, the decrease in VitiQoL_additional question was more pronounced in group 1 than in group 2.

Clinical observations of patients receiving complex therapy (cyclosporine + UVB 311 nm) before and after treatment

Figs. 3 and 4 show a photographic report of patients who received cyclosporine therapy combined with UVB 311 nm.

DISCUSSION

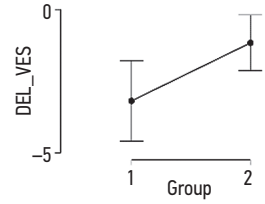
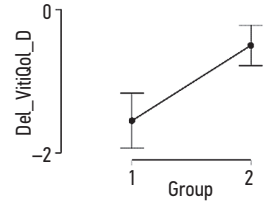
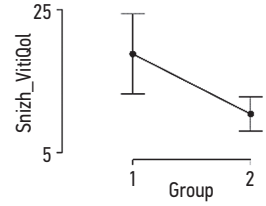
At present, owing to the more demanding attitude of society toward appearance, interest in the problems of diseases such as vitiligo is rapidly growing. The gold standard of therapy for this disease is UVB 311 nm. However, according to the latest clinical guidelines in patients with vitiligo, the effectiveness of recommended combination therapy must be improved; therefore, the search for new additional means and methods of treatment is necessary. Although the etiology and pathogenesis of vitiligo are not fully understood, the autoimmune theory of development is crucial. The mechanism of action of a drug such as cyclosporine is called selective immunosuppression, which gives it an advantage over other drugs with cytotoxic and immunosuppressive effects. This study shows that the combination protocol is the most effective in halting disease progression. Cyclosporine in combination with UVB 311 nm enhances repigmentation of nonsegmental vitiligo lesions compared with UVB 311 nm monotherapy, thus shortening the recovery time of patients. Good tolerability and significant improvement in patients' quality of life were observed.

CONCLUSIONS

In this study, the use of cyclosporine with 311 nm narrowband phototherapy promotes progression arrest and faster repigmentation compared with 311 nm

Table 3. Absolute changes in disease severity indicators before and after therapy in study groups

Таблица 3. Абсолютные изменения показателей тяжести заболевания до и после терапии в группах исследования

Category	Statistical analysis, 95% CI				*p*-value permutable/ VS-MPR	Mean values in groups with 95% CI
	Mean/median* subgroup value		Difference in mean medians/ Hodges–Lehman medians*	Standardized effect according to Cohen		
	Group 1	Group 2				
Absolute After-Before_VES	-4.44 **-3.19** -1.89	-2.05 **-1.16** -0.29	0.48 **2.03** 3.56	0.1 **0.8** 1.4	0.019/5.0	
Absolute After-Before_VES*	-5.56 **-2.22** 0.00	-1.47 **-0.50** 0.15	0.00 **1.79** 4.06	-	0.026/3.6	
Absolute After-Before_VitiQol_ Additional Question	-2 **-1.6** -1.2	-0.5 **-0.8** -0.3	0.6 **0.8** 1.5	0.7 **1.4** 2.1	0.0001	
Absolute change_VitiQol	14 **19** 24	8 **10** 13	3 **9** 14	0.2 **0.9** 1.6	0.0053/11.5	

Note. * Denotes comparison of median values performed for indicators with significant asymmetry.

Примечание. * Сравнение медианных значений. выполненное для показателей с существенной асимметрией.

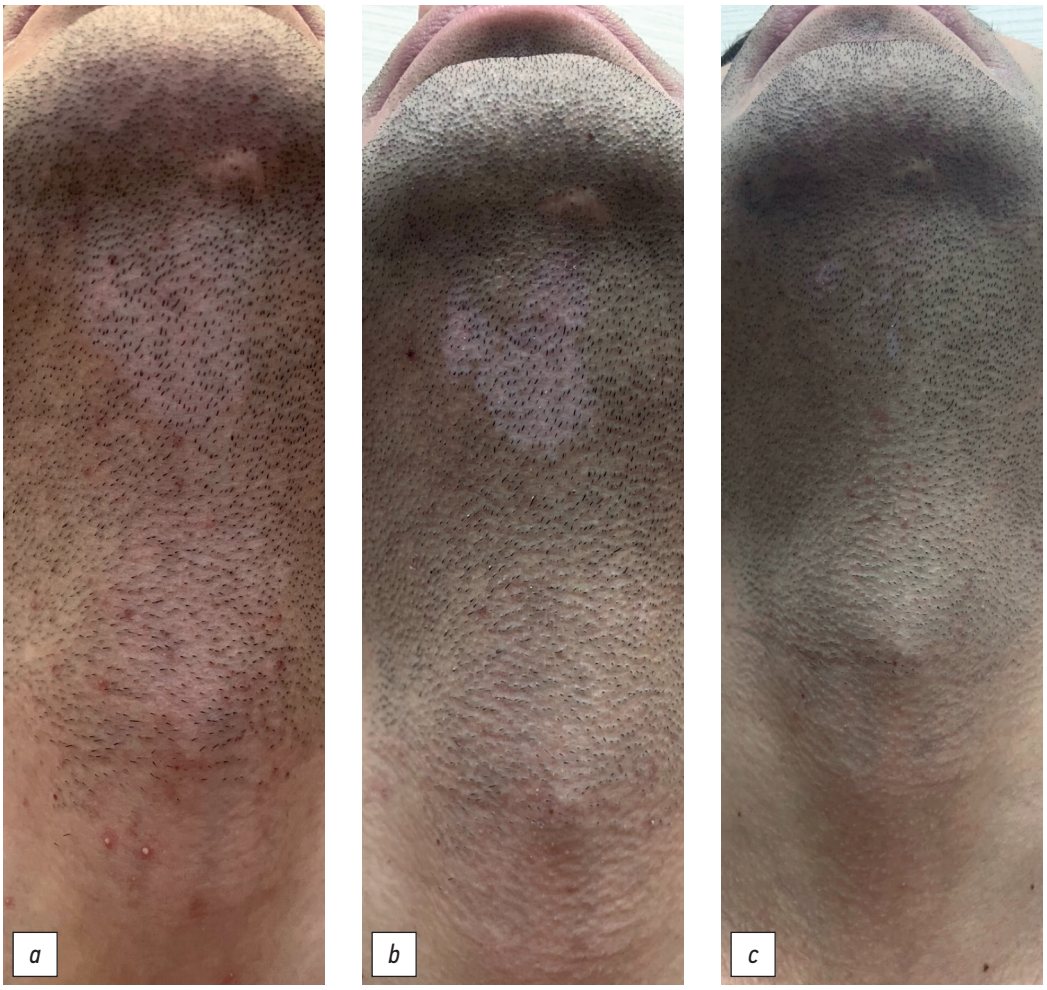


Fig. 3. Photoregistration of patients: *a* — progressive vitiligo before therapy; *b* — during the course of therapy (cyclosporine + UVB-311 nm); *c* — after the course of therapy.
Рис. 3. Фоторегистрация пациентов: *a* — прогрессирующее витилиго до терапии; *b* — во время курса терапии (циклоспорин + УФБ 311 нм); *c* — после проведённого курса терапии.

UVB monotherapy and may be used as an alternative immunosuppressive therapy in the treatment of nonsegmental vitiligo.

ADDITIONAL INFORMATION

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Authors' contribution. All authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work. K.M. Lomonosov — research concept, editing; A.S. Nikulina — collection and processing of material preparation and writing of the article.
Consent for publication. Written consent was obtained from patients for publication of relevant medical information and all associated images in the manuscript.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при подготовке рукописи.
Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.
Вклад авторов. Все авторы подтверждают соответствие своего авторства международным критериям ICMJE (все авторы внесли существенный вклад в разработку концепции, проведение поисково-аналитической работы и подготовку статьи, прочли и одобрили финальную версию перед публикацией). Наибольший вклад распределён следующим образом: К.М. Ломоносов — концепция исследования, научное редактирование текста; А.С. Никулина — сбор и обработка материала, подготовка и написание статьи.
Информированное согласие на публикацию. Пациенты подписали добровольное информированное согласие на публикацию персональной медицинской информации в обезличенной форме для медицинского журнала «Российский журнал кожных и венерических болезней».

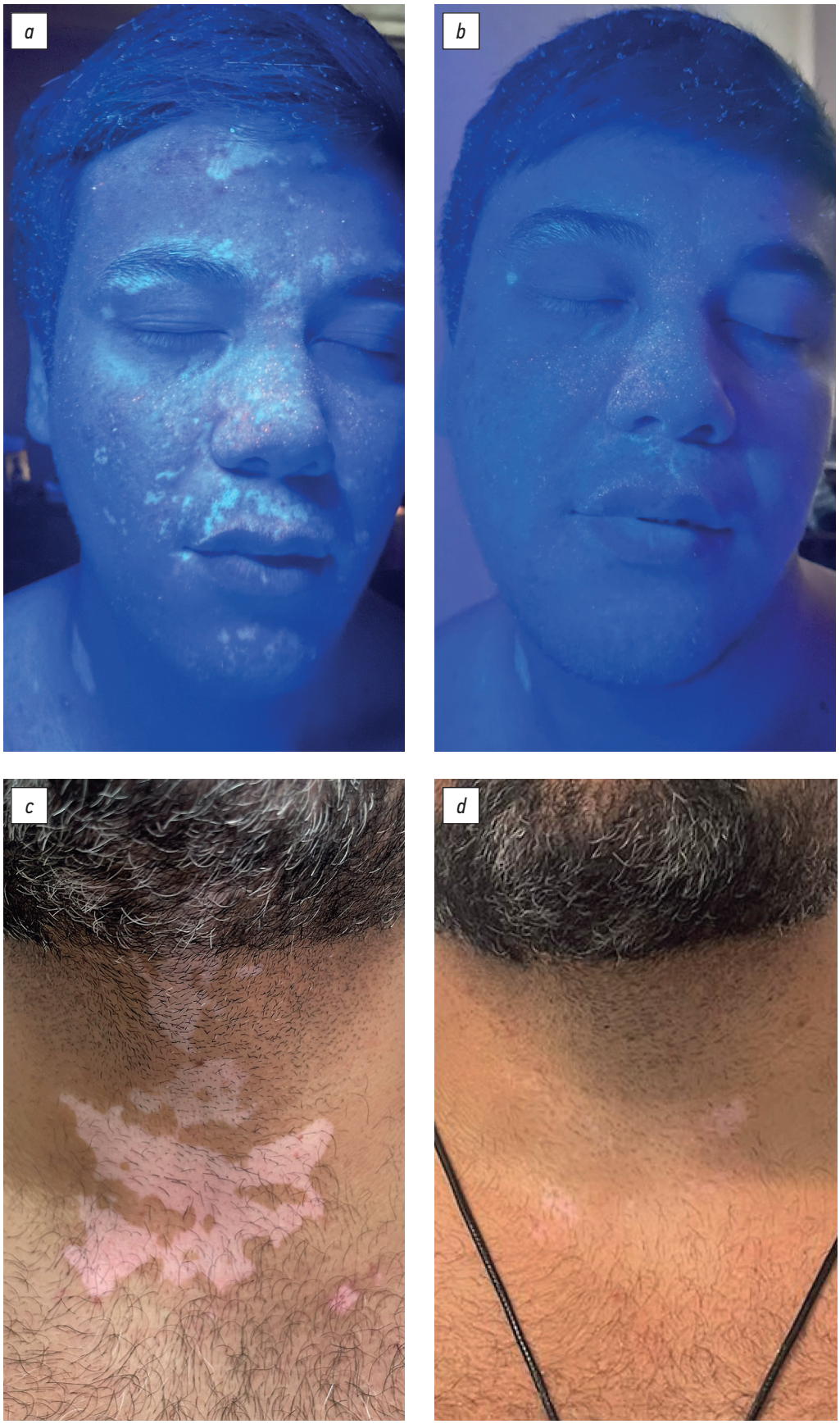

Fig. 4. Photoregistration of patients: *a*, *c* — progressive vitiligo before therapy; *b*, *d* — after the course of therapy (cyclosporine + UVB-311 nm).
Рис. 4. Фоторегистрация пациентов: *a*, *c* — прогрессирующее витилиго до терапии; *b*, *d* — после проведённого курса терапии (циклоспорин + УФБ 311 нм).

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