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THE RESULTS OF THE CLINICAL EFFECTIVENESS OF THE TREATMENT OF PATIENTS WITH VITILIGO AS A RESULT OF TREATMENT WITH THE DEVELOPED MODIFIED IMMUNOCORRECTIVE COMPLEX THERAPY.

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Abstract:

For the period from 2020 to 2023, 118 patients (Group I (main group) n=60, Group II (comparison group) n=58) from patients with two clinical forms of vitiligo were examined. The control group for immunological studies consisted of 20 healthy donors. The study included patients of both sexes: 66 women and 52 men, aged 18 to 75 years (mean age 38.5 ± 6.8 years). Complete clinical improvement (repigmentation ≥96%), complete clinical remission in Group I patients who used the modified immunocorrective complex therapy developed by us with the inclusion of pentaxophylline and dexamethasone was achieved in 53 patients (44.9%), and in Group II patients who did not use immunocorrective therapy, only 34 (28.8%) patients with vitiligo.

Keywords: vitiligo, immunocorrective complex therapy, excimer laser, UVB therapy

Vitiligo is an acquired skin disease of unknown origin, which is characterized by the loss of pigmentation due to the destruction of melanocytes in certain areas of the skin [1,4,11, 20, 23, 25, 28]. Vitiligo is characterized by acquired hypomelanosis, often symmetrical, with the appearance of white spots on the skin, which enlarge over time due to the dysfunction of epidermal melanocytes and, in turn, the dysfunction of hair follicles. According to the World Health Organization (WHO), vitiligo patients account for more than 2% of the world's population, and 3-4% in southern countries and regions [5, 13, 15, 4, 27]. The incidence of vitiligo is highest in Central Asia and reaches 10% in some regions [2,3].

The etiology and pathogenesis of vitiligo have not yet been fully established. The origin of the disease is multifactorial, and exogenous and endogenous factors play an important role in the development of vitiligo. External trigger factors include stress, mechanical damage and damage to the integrity of the skin (Koebner's phenomenon), exposure to excessively strong ultraviolet rays, and chemicals. From endogenous factors, especially from somatic and infectious diseases (autoimmune thyroiditis, lupus erythematosus, rheumatoid arthritis, acute and chronic liver diseases of infectious or toxic origin, helmentoses), taking drugs that often have a negative effect on the function of pigment-producing melanocytes is noted.

In response to melanocyte damage, natural killer cells and anti-inflammatory proteins are activated, especially heat shock proteins (HSP- heat shock proteins) , as well as anti-inflammatory cytokines, the main of which are IL-1b , IL-6 and IL-8 increase [6, 14,13]. The formation of an inflammatory environment around vitiligo foci is indicated by an increase in the level of local inflammatory cytokines TNF- a , IL-1, IL-6, IL-8 and indirectly - IFN- g , as well as by an increase in the level of IL-6 and IL-2 in the peripheral blood serum. [15, 27]. Keratinocytes through the secretion of cytokines (IL- 1, Deregulation of TNFα) and melanocytes (IL-1) can lead to local immune response.

Among the physiotherapeutic treatments in vitiligo, the main method chosen is narrow-band UVB phototherapy. The mechanism of action of the ultraviolet B spectrum with a wavelength of 311 nm is to stimulate the production of IL-10, which causes the differentiation of regulatory T-lymphocytes [14, 16, 12, 29].

Recently, excimer laser is one of the methods widely used in practice, and it is one of the innovative methods of treatment of vitiligo, which provides monochromatic radiation with a wavelength of 308 nm. The mechanism of occurrence of repigmentation during its use is related to the immunosuppressive effect of radiation on skin lymphocytes, as well as the proliferative increase of melanocytes and the stimulating effect of the transfer of mature melanosomes along the dendrites to the surrounding keratinocytes. Much experience has already been gathered on the effectiveness of the use of ultraviolet rays of the excimer laser in patients with vitiligo [17,18, 19, 21,24, 22, 26].

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Thus, in spite of all the different methods of treatment of vitiligo, their effectiveness varies greatly depending on the type and location of the disease, and therefore, it is necessary to develop new innovative methods of treatment of this disease and conduct tests in clinical practice. One of these methods consists in the selection of drugs that have a clear immunocorrective effect and also treatment with a drug of choice that has high activity in the range of therapeutic doses used and does not have toxic or other negative consequences. Pentaxofylline and dexamethasone, which are used as immunocorrectors in medical practice, meet these requirements today.

In the foreign literature, there is also little information on the use of combined phototherapy - narrow-band UFB - therapy using an excimer laser with a wavelength of 311 nm and a wavelength of 308 nm with pentaxofylline, systemic minipulse therapy with dexamethasone and 0.1% ointment tacrolimus as a local treatment. This study sought to evaluate the efficacy and safety of modified immunocorrective complex therapy as a combination therapy for vitiligo patients.

THE PURPOSE OF THE STUDY: to develop a modified immunocorrective complex treatment method and evaluate its effectiveness in patients with various forms of vitiligo .

MATERIAL AND METHODS

In our study, from 2020 to 2023, 118 patients (group I (main group) n=60 , group II (comparison group) n=58) with various clinical forms of vitiligo were studied. All patients underwent general clinical and immunological examinations. Before and after the treatment, patients underwent a series of general clinical examinations to determine the combined pathology of various organs and systems, and the identified pathological conditions were consulted by relevant specialties. In order to rule out concomitant diseases and contraindications, the following examinations were performed: general clinical and biochemical analyzes of blood, general urinalysis, instrumental examinations (ultrasound examination of the thyroid gland, abdominal organs, kidneys, pelvic organs, electrocardiography (ECG), if necessary) if so, the patients were given advice by a therapist, endocrinologist, gynecologist (urologist) and other specialists.

Determination of the concentration of the three main classes of immunoglobulins in blood serum, immunoglobulin A, M and G, was carried out by the traditional radial immunodiffusion method according to Mancini (1963). The reaction was performed on a glass plate coated with an agar gel containing an antibody against a specific immunoglobulin plasma .

Cytokines involved in the inflammatory process were evaluated according to the content of TNF-α, IL-2, IL-6, IL-8, IL-10 in the blood plasma.

Patients in group 1 (main group) (n=60) received combined phototherapy - narrow-band UVB therapy with a wavelength of 311 nm and an excimer laser with a wavelength of 308 nm, and in addition, a daily dose of pentaxofylline 1200 mg (400 mg 3 times for 3 months) with minipulse corticosteroid therapy (dexamethasone 5 mg orally - 2 days a week from 3 to 6 months) local (3 to 6 months) treatment with ointment tacrolimus 0.1% was carried out.

In group 2 (comparison group) (n=58), patients received combined phototherapy - narrow-band UVB therapy with a wavelength of 311 nm and excimer laser with a wavelength of 308 nm and local treatment (from 3 to 6 months) with 0.1% tacrolimus ointment. The course of phototherapy received by patients in both groups did not last more than 20 weeks.

Phototherapy with 311 nm UVB rays was performed 3 times a week. Patients started phototherapy without a minimum erythematous dose. The initial dose was 0.05-0.1 J / cm2, then it was increased to 0.1 J / cm2 when erythema did not occur, depending on the reaction of the skin to ultraviolet light. For phototherapy, a general radiation booth (Kernel UV Phototherapy, MSLKN05 UVB/UVA 311 nm, China) equipped with fluorescent lamps operating in long and medium wavelength ranges was used. The structure of the cabin ensures an even distribution of UV rays (UVA, UVB, UVA + UVB, UVB 311 nm) over the entire surface of the skin. Sensors with monitors are installed on the outside of the cabin door, which allow you to monitor and take into account the intensity of UV radiation, as in any spectrum.

The excimer laser device is equipped with a convenient nozzle that creates a field radiation with an area of 3.2 cm2. The laser produces high-intensity radiation of 2-3 mJ/cm2 (radiation head size 2.3 x 2.3 mm). The pulse repetition rate is up to 200 Hz, the pulse duration is 30 ns. This type of phototherapy practice was carried out 2 times a week. It was started after determining the minimum erythematous dose (MED) to the skin outside the affected foci. To determine the MED test, 6 points are initially marked and evaluated 48 hours after irradiation with a 3 x 3 cm2 nozzle. The MED test is the area where the erythema is first detected, which is the individually determined dose for the patient.

RESULTS

We conducted complex treatment in 118 patients with various forms of vitiligo. All patients in the study were divided into two groups:

Group I (main group) (n =60) patients with vitiligo received combined phototherapy - narrow-band 311

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nm UVB therapy and 308 nm excimer laser therapy and additionally daily dose of pentoxifylline 1200 mg, minipulse corticosteroid therapy (dexamethasone 5 mg - weekly 2 days to 3 months to 6 months) and topical 0.1% tacrolimus ointment treatments were performed.

Group II (comparison group) (n =58) patients received combined phototherapy - narrow-band UVB therapy at a wavelength of 311 nm and excimer laser therapy at a wavelength of 308 nm and topical application of 0.1% tacrolimus ointment.

We estimated the effectiveness of the treatment in percentages depending on the dynamic change of the regeneration-repigmentation level across the area of the affected areas. We considered clinical improvement when the degree of repigmentation in affected areas was at least 25–50%, significant clinical improvement when the efficacy was 51–95%, and complete clinical recovery when 96–100% repigmentation. Failure to observe the effectiveness of the treatment was noted only when recovery-repigmentation occurred on the surface of less than 15% of the area of the initial lesion. The clinical efficacy results of the modified immunocorrective complex treatment developed for the treatment of vitiligo patients are presented in Table 1.

Table 1
Results of clinical efficacy of modified immunocorrective complex treatment for patients with vitiligo.

Clinical form	Complete clinical improvement (≥ 96 % repigmentation)		Significant clinical improvement (up to 75% repigmentation)		Clinical improvement (repigmentation 25-50%)		Ineffective (less than 15% repigmentation)	
	Gr I	Gr II	Gr I	Gr II	Gr I	Gr II	Gr I	Gr II
Segmentary	23	16		5		4		
Focal	10	5	1	2				
Vulgar	8	4	2	2		3		
Acrofascial	12	9	3	1	1	3		4
Total	53-44.9%	34-2 8.8 %	6-5 , 1 % _	10-8 , 5%	1-0 , 85 %	10 - 8.5 % _		4-3, 4 %

I - 23 patients with segmental form and 37 patients with non-segmental form: 16 acrofacial, 10 vulgar and 11 - focal form. Group II vitiligo consisted of 25 segmental and 33 non-segmental patients: 7 focal, 9 vulgar and 17 acrofascial forms.

I , 4 months after the start of treatment, complete clinical improvement (repigmentation above 96%) was observed. Of 25 patients with segmental vitiligo in group II, only 16 (64%) patients had complete clinical improvement (>96% repigmentation), significant clinical improvement (up to 75% repigmentation) in 5 (20%) patients, and 4 (16%) patients had clinical improvement . improvement (repigmentation 25-50%) was noted.

Of 11 patients with focal vitiligo of group I , 10 had complete clinical improvement (>96% repigmentation) and 1 patient had significant improvement (up to 75% repigmentation). At the same time, only 5 (71.4%) of 7 patients with focal form of vitiligo in group II had complete clinical improvement (>96% repigmentation) and significant improvement (up to 75% repigmentation) in 2 (28.6%) patients.

(>96% repigmentation) was achieved in 8 (80%) of 10 patients with vitiligo vulgaris in group I , and 2 (20%) of these patients had significant improvement (up to 75% repigmentation). Also, vitiligo vulgaris in group II out of 9 patients with the form, only 4 (44.4%) patients had complete clinical improvement (96% repigmentation), significant improvement (up to 75% repigmentation) in 2 (22.2%) patients and improvement in 3 (33.3%) patients (repigmentation 25-50%) was observed.

I , we can observe a complete clinical improvement (100% repigmentation) in 12 (75%) and significant improvement (up to 75% repigmentation) in 3 (18.8%) patients. Also, from 17 patients with acrofascial form of vitiligo in group II , only 9 (52.9%) patients had complete clinical improvement (>96%

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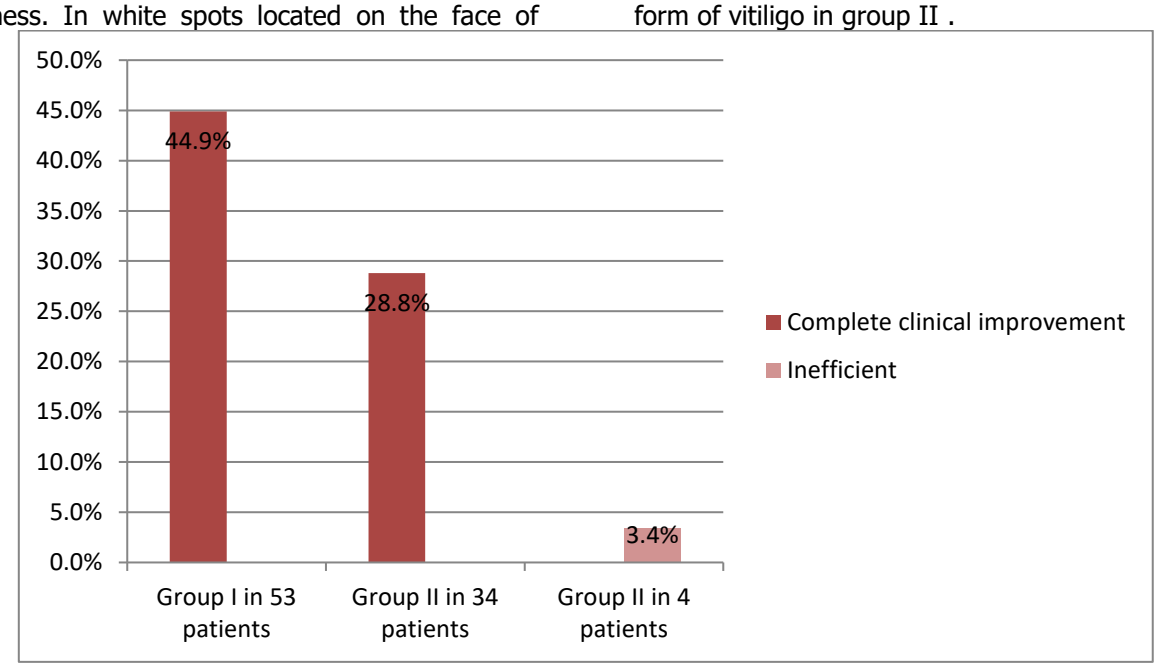
repigmentation), 1 (5.9%) patient had significant improvement (up to 75% repigmentation), Improvement (repigmentation 25-50%) was observed in 3 (17.6%) patients and no positive clinical outcome (repigmentation less than 15%) was observed in 4 (23.5%) patients (Table 10).

When we analyze the effectiveness of local treatment depending on the clinical form of the disease, we can conclude that patients with focal and segmental forms of vitiligo can achieve the best clinical effectiveness. In white spots located on the face of patients with acrofascial form of vitiligo, we can note that in almost all cases, effective complete or partial regeneration-repigmentation, and the treatment method chosen by us is not effective when located on the phalanges of the fingers and toes.

Complete clinical remission (repigmentation 100%) was achieved in 53 patients (44.9%) out of a total of 118 studied patients in group I, and only 34 (28.8%) out of all 118 studied patients in group II . No effect was observed in 4 (3.4%) patients with acrofascial form of vitiligo in group II .



The immunocorrective complex treatment developed in our study with the help of combined phototherapy - 311 nm narrow-band UVB therapy and 308 nm excimer laser therapy and additionally a daily dose of 1200 mg of pentoxifylline, minipulse corticosteroid therapy (dexamethasone 5 mg - 2 days per week from 3 to 6 months) and topical 0.1% tacrolimus ointment has clearly shown its advantage.

All patients responded well to treatment, with no adverse effects, complications, or rejection.

During the course of the treatment, it was possible to assess whether the patients changed their attitudes towards their disease and towards the treatment process. Against the background of active repigmentation of depigment foci, immunological indicators were normalized and symptoms of depressive disorders were reduced. Thus, our results show that vitiligo contains the possibility of reasonable, effective and safe treatment.

CONCLUSION

(>96% repigmentation) was achieved in 8 (80%) of 10 patients with vitiligo vulgaris in group I, and 2 (20%) of these patients had significant improvement (up to 75% repigmentation). Also, vitiligo vulgaris in group II out of 9 patients with the form, only 4 (44.4%) patients had complete clinical improvement (96% repigmentation), significant improvement (up to 75% repigmentation) in 2 (22.2%) patients and improvement in 3 (33.3%) patients (repigmentation 25-50%) was observed.

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