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## SKIN MICROBIAL LANDSCAPE AND IMMUNE-ENDOCRINE PARAMETERS IN PATIENTS WITH PSORIASIS BY USING NARROWBAND UVB PHOTOTHERAPY

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Hennadiy Ye. Astsaturov<sup>1</sup>, Orysa O. Syzon<sup>1</sup>, Yuriy V. Andrashko<sup>2</sup><sup>1</sup>DANYLO HALYTSKY LVIV NATIONAL MEDICAL UNIVERSITY, LVIV, UKRAINE<sup>2</sup>UZHGOROD NATIONAL UNIVERSITY, UZHGOROD, UKRAINE

### ABSTRACT

**The aim:** The study of skin microbial landscape and immune-endocrine parameters as well as improvement of treatment efficiency in patients with different clinical course of psoriasis by using narrowband UVB phototherapy.

**Materials and methods:** We examined 89 patients with psoriasis (51 men and 38 women) aged 18–60. The comparison group consisted of 43 psoriasis patients comparable by age, sex and clinical course with those from the main group (46 patients). Cytokine levels IL-4, IL-8, IL-10, TNFα, thyroid peroxidase (TPO) and thyroglobulin (Tg) autoantibodies and microbial flora of skin were determined in patients with psoriasis.

**Results:** The study finds that conventional therapy does not have sufficient corrective impact on immune-endocrine disorders and the use of narrow-band light therapy has shown that it has a focused corrective impact on cytokine production and modulating effect on the level of TPO and Tg autoantibodies and the state of skin automicroflora of lesions in patients suffering from psoriasis.

**Conclusions:** Using UVB (311 nm) therapy in patients with psoriasis allows improving efficiency of treatment and limiting clinical signs in the form of achieving remission and significant improvement in patients' health without any negative dynamic changes.

**KEY WORDS:** psoriasis, etiopathogenesis, skin microbial landscape, immune-endocrine disorders, phototherapy

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### INTRODUCTION

Psoriasis is a systemic disease characterized by a complex of mutually conditioned pathogenetic links, i.e. immune, neuroendocrine, infectious etc. One of the main factors of morphological changes is accelerated epidermis proliferation, which occurs due to the reduction of cell cycle of epidermocytes [1,2].

An inherent pathogenetic mechanism of psoriatic disease is its mediated changes in the cytokine profile [3,4]. It should be noted that despite numerous studies of the interleukin cascade in psoriasis patients the results obtained and their interpretation are often quite controversial [5,6,7,8]. Therefore, we consider that it is necessary to focus on a more in-depth study of the relationship between individual cytokines, the association of their levels with the clinical psoriasis course and the state of other systems and organs in such patients. In such a perspective, based on the world and domestic scientific sources, according to the above subject, as well as based on our own clinical experience and studies of immunological parameters in psoriasis patients, we believe, the study of levels of IL-4, IL-8, IL-10, TNFα, which have both antiinflammatory and pro-inflammatory activity, is the most expedient except for pathogenetic IL-17 and IL-23.

Endocrine disorders play an important role in the development of this dermatosis, in particular an increase in

the level of thyroidism is observed, which is associated with the deterioration of environmental conditions, and gain in neurological symptoms in the population. Thyroid disorders associated with its oppressed and increased functional activity are characterized by the development of autoimmune reactions, the appearance of circulating thyroglobulin antibodies, microsomal and thyroid stimulating immunoglobulins, which in turn enhances the allergic component. In addition, it should be remembered that the metabolism of thyroid hormones occurs in the skin. Nevertheless, studies of autoantibodies to thyroperoxidase (TPO) and thyroglobulin (TG) in psoriasis patients with look promising [9].

It is known today that skin biocenosis condition may be a highly sensitive indicator of the sensitization fidelity. It is proved that a microorganism and its microbial flora while physiological conditions are in a state of dynamic equilibrium [10]. Therefore, in each part of the body surface microflora is characterized by a relative stability. Possible changes in a microorganism are reflected in disorders of the microbial landscape of all skin topographic areas. It should be noted that numerous studies of skin microbial flora in psoriasis patients are often very episodic and not always structured, so they require further and more detailed in-depth study [11].

Despite the large number of suggested methods and means of treatment of psoriasis patients their effectiveness often remains not too high [12]. At present, there are a number of questions concerning etiology, multifactorial development, polymorphism of clinical manifestations, etc., which, in turn, does not allow developing a unified therapeutic concept [13]. According to modern clinical guidelines for the treatment of psoriasis patients, the use of 311 nm narrowband UVB therapy is pathogenetically conditioned since it produces a selective effect on skin structures and demonstrates powerful antiinflammatory and immunomodulatory properties. It is proved that waves of this band are the most therapeutically reasonable as they allow providing a significant rate of remission and duration of positive treatment results preservation than the use of waves of other bands [14]. In addition, UVB (311nm) does not require the use of chemotherapy, in turn, it does not cause to their specific side effects and does not have a number of contraindications that occur when using PUVA-therapy [15].

Thus, the review of studies on immunopathogenesis of psoriasis disease, the state of skin microbiocenosis and therapeutic tactics illustrates an open nature of the problem. The available data are scattered and are often accumulated chaotically. The information content of certain indicators reflecting individual mechanisms of psoriasis development is not defined. Therefore, their further study undoubtedly expands the scope of understanding of dermatosis development mechanisms and is quite promising for subsequent devising of coordinated therapeutic intervention and control of the therapy efficacy in such patients.

## THE AIM

The aim of our research is to increase the efficacy of treatment through studying changes in the skin microbial landscape and some immunological and endocrine parameters in patients with different clinical course of psoriasis against the background of the use of narrowband UVB therapy.

## MATERIALS AND METHODS

We observed 89 psoriasis patients (51 men and 38 women) who were determined the level of IL-4, IL-8, IL-10, TNF $\alpha$  content in their blood serum by means of a test system ("Protein circuit") implemented in a "sandwich-method" of solid-phase immunoenzyme analysis using horseradish peroxidase as an enzyme indicator following the recommendations by the manufacturer. The results were registered per the activity of the bound peroxidase using STAT-FAX-303 PLUS device at 492 nm wave extension. The IL level is expressed in pg/ml.

All the observed by us patients were examined for skin microbial flora taken from focal lesions in three stages. At the first identification stage a cultural study was carried out. In order to identify and quantify the microorganismal exchange on the skin surface we prepared culture dishes with a nutrient medium consisting of 5% blood agar and

Sabouraud agar. At the next stage, bacterioscopic examination of bacterial colonies plated from the skin as well as isolation of pure microbial cultures was performed. Then, the identification of the isolated cultures by their enzymatic properties on classical differential-diagnostic media was carried out with the following recalculation of the number of colonies grown on each CFU per 1 cm<sup>2</sup>.

Autoantibody levels to TPO and TG were detected by a solid-phase sandwich enzyme immunoassay method using reagent kits AT-TPO-IFA and AT-TG-IFA in accordance with the established methodology and instructions. Data received were expressed in IU/ml.

All psoriasis patients under our observation were evaluated per the Psoriasis Area and Severity Index (PASI) and the Dermatological Quality of Life Index (DLQI). The criteria for inclusion of patients in the study were such as psoriasis vulgaris (PV) and PV in combination with psoriatic arthritis (PsA), age of patients from 18 to 60 years, written consent of a patient to participate in the study. Criteria for excluding patients from the study were as follows: current erythrodermic and pustular forms of psoriasis, contraindications to the use of phototherapy, comorbidities that may significantly affect outcomes of the study, and participation in any other study.

In order to clarify the degree of corrective effect of narrow-band phototherapy on clinical manifestations of dermatosis, immunomicrobiological disorders and quality of life of patients we carried out a comparative analysis of its efficacy and efficacy of traditional therapeutic means.

All patients were divided into two groups. The first (main) group was formed by 46 patients with psoriasis vulgaris, which was verified in 35 (76.1%) patients, and PV in combination with psoriatic arthritis, which was diagnosed in 11 (23.9%) patients who had contraindications for the use of cytostatic therapy. The second group (comparative) consisted of 43 psoriasis patients comparable by age, sex and clinical course with those from the main group.

The main group of patients underwent UVB therapy on Daavlin 3 Series PC 311-24 unit using TL-01 lamps generating radiation in 310-315 nm and with a peak emission at a length of 311 nm in combination with conventional treatment means according to the modern clinical guidelines and in the light of available PsA. The initial dose was 0.1-0.2 J/cm<sup>2</sup> and depended on the skin phototype, which was determined by testing. With each subsequent procedure it increased by 0.05-0.1 J/cm<sup>2</sup>. If erythema was observed, the dose remained the same. Procedures were performed 3-4 times a week. The total number of procedures ranged from 12 to 18 and depended on the clinical course of psoriasis.

The comparative group was provided with traditional means and methods of therapy, i.e. hyposensitizing, antihistamine, non-steroidal anti-inflammatory medications, B vitamins, topical glucocorticosteroids, D3 vitamins, emollients, keratolytics under the modern clinical guidelines and in the light of available psoriatic arthritis. The treatment course lasted for 4 weeks.

The research results were statistically processed by using Microsoft Office Excel 2016 (Windows 10 Professional).

**Table I.** Changes in cytokine content within the comparison group psoriasis patients during their treatment course.

Indicators (M±m), pg/ml	Groups of examined patients			
	Patients with psoriasis vulgaris		Patients with psoriasis vulgaris and PsA	
	Before treatment	After treatment	Before treatment	After treatment
IL-4	67.31±3.02	65.12±4.82	74.38±2.65	71.37±3.90
IL-8	54.13±2.06	41.19±3.78	64.07±2.58	66.25±5.17
IL-10	36.51±1.85	33.87±2.94	37.13±1.52	25.94±1.82
TNFα	63.75±3.74	60.95±7.12	68.51±3.19	52.14±3.19

**Table II.** Changes in cytokine levels in the main group psoriasis patients during their treatment.

Indicators (M±m), pg/ml	Groups of examined patients			
	Patients with psoriasis vulgaris		Patients with psoriasis vulgaris and PsA	
	Before treatment	After treatment	Before treatment	After treatment
IL-4	67.31±3.02	48.19±3.24	74.38±2.65	56.49±4.01
IL-8	54.13±2.06	42.37±2.15	64.07±2.58	48.13±1.64
IL-10	34.51±1.85	15.98±3.39	37.13±1.52	23.08±1.43
TNFα	63.75±3.74	51.17±1.76	68.51±3.19	49.23±2.19

We determined the value of arithmetic mean value (M), the mean square deviation (G) and error in determining the arithmetic mean (m). The level of confidence of significance of differences (P) was determined using the Student's t-criterion. To determine the reliability of a relationship between two variation series, the correlation coefficient was calculated using such formula as  $r = \Sigma H / \Sigma M$ , where r is the correlation coefficient;  $\Sigma H$  is the sum of products of deviations from the arithmetic mean of the first and second series;  $\Sigma M$  is the maximum sum. A negative value indicated an inverse correlation, while a positive value indicated a direct correlation. The closer to the value 1 is value 2, the more likely a relationship between the indicators is.

## RESULTS

During the examination of 89 psoriasis patients it was noticed that among factors initiating the development of a pathological process the most frequent were nervous and psychic ones, bacterial and viral infections in 43.3% and 24.5% of patients respectively. It should be noted that 32.2% of patients could not indicate the probable cause of dermatosis manifestation. Hereditary predisposition to psoriasis development is traced in 43.9% of patients. Associated pathology was observed in 25.7% of patients. Psoriasis relapses occurred mainly during autumn-winter period in 68.2% of patients, the spring-summer type was identified in 11.5% of patients, absence of seasonal influence – in 20.3%. Progressive course of psoriasis was established in 66.5% of patients, and in-patient – in 33.5%. The PASI index ranged from 18 to 65 points.

The result of examination of patients from the comparison group upon the application of recommended therapy testify only a slight correction of cytokines content (Table 1). A statistically valid confirmation of the reduction of IL-8 level was obtained only in patients with PV, i.e. up to

41.19±3.78 pg/ml (before treatment – 54.13±2.06 pg/ml;  $p < 0.05$ ), IL-10 level in patients with psoriasis vulgaris in combination with PsA, i.e. up to 25.94±1.82 pg/ml (before treatment – 37.13±1.52 pg/ml;  $p < 0.05$ ) and TNFα level in the same category of patients, i.e. up to 52.14±3.19 pg/ml (before treatment – 68.51±3.19 pg/ml;  $p < 0.05$ ). However, the value of these parameters remained beyond the physiological oscillation line.

Probable suppression of autoantibodies to TG was registered in comparison group patients with psoriasis vulgaris and PsA (up to 130.16±9.83 IU/ml (before treatment – 156.48±7.12 IU/ml;  $p < 0.05$ ). It should be noted that this indicator also remained outside the amplitude of physiological fluctuations.

The degree of microbial skin contamination in psoriasis patients from the comparison group also decreased significantly. In patients with PV the number of *S. aureus* fell to 316.32±16.11 CFU/cm (before treatment – 415.81±14.25 CFU/cm,  $p < 0.05$ ). *S. epidermidis* – up to 57.29±4.08 CFU/cm (before treatment – 93.40±5.38 CFU/cm,  $p < 0.05$ ). *S. saprophyticus* – up to 20.17±1.96 CFU/cm (before treatment – 37.65±3.02 CFU/cm,  $p < 0.05$ ). *Micrococcus* spp. – up to 17.13±2.45 CFU/cm (before it was 25.19±2.16 CFU/cm,  $p < 0.05$ ) and *Bacillus* spp. – up to 61.42±2.17 CFU/cm (before treatment – 78.15±3.12 CFU/cm,  $p < 0.05$ ). However, as indicated by the data, the degree of microbial skin contamination in such patients remained outside the limits of physiological fluctuations. Only the number of other microorganisms did not exceed the control values of 8.04±0.34 CFU/cm (before treatment – 7.92±0.81 CFU/cm,  $p > 0.05$ ). Microbial contamination in patients with psoriasis vulgaris in combination with psoriatic arthritis has changed likewise.

The quality of life of such patients improved, but this process shows no signs of possible justification. In particular, in patients with PV DLQI was 17.1±3.0 points



(before treatment –  $18.2 \pm 2.4$  points;  $p > 0.05$ ). and within the presence of PsA –  $21.6 \pm 2.8$  points (before treatment –  $23.5 \pm 1.9$  points.  $p > 0.05$ ).

The analysis of clinical efficacy of treatment of patients from the comparison group allowed stating the absence of “clinical remission” in all cases of observation, “significant improvement” – in 11 (26.1%) people, “improvement” – in 17 (39.1%), “without changes” – in 13 (30.4%), “deterioration” – in 2 (4.3%). Dermatosis relapses within 12 months after the end of therapy were registered in 30 (69.6%) patients.

It has been established that upon receiving their recommended treatment patients from the main group had a reliable decrease in cytokines activity (Table 2). In patients with psoriasis vulgaris of the disease IL-4 and IL-10 levels reached the limits of physiological fluctuations amounting to  $48.19 \pm 3.24$  pg/ml (before treatment –  $67.31 \pm 3.02$  pg/ml;  $p > 0.05$ ) and  $15.98 \pm 3.39$  pg/ml (before treatment –  $34.51 \pm 1.85$  pg/ml;  $p < 0.05$ ) respectively. Despite a significant decrease, the IL-8 and TNF $\alpha$  content remained outside the control values, amounting to  $42.37 \pm 2.15$  pg/ml (before treatment –  $54.13 \pm 2.06$  pg/ml;  $p < 0.05$ ) and  $51.17 \pm 1.76$  pg/ml (before treatment –  $63.75 \pm 3.74$  pg/ml;  $p < 0.05$ ), respectively. Against the presence of PsA, cytokine activity was also confidently suppressed though remained outside the physiological range. Thus, the IL-4 level reached  $56.49 \pm 4.01$  pg/ml (before treatment –  $74.38 \pm 2.65$  pg/ml;  $p < 0.05$ ) IL-8 –  $48.13 \pm 1.64$  pg/ml (before treatment –  $64.07 \pm 2.58$  pg/ml;  $p < 0.05$ ) IL-10 –  $23.08 \pm 1.43$  pg/ml (before treatment –  $37.13 \pm 1.52$  pg/ml;  $p < 0.05$ ) and TNF $\alpha$  –  $49.23 \pm 2.19$  pg/ml (before treatment –  $68.51 \pm 3.19$  pg/ml;  $p < 0.05$ ).

The study of autoantibody contents allowed stating the preservation of their physiological level to TPO in case of psoriasis vulgaris up to  $14.72 \pm 0.97$  IU/ml (before treatment –  $15.07 \pm 1.54$  IU/ml;  $p < 0.05$ ) and TG – up to  $81.25 \pm 4.12$  IU/ml (before treatment –  $86.75 \pm 5.80$  IU/ml,  $p > 0.05$ ). Against the presence of psoriatic arthritis, their levels are registered as decreased to physiological values. In particular, antibodies to TPO were up to  $15.02 \pm 0.89$  IU/ml (before treatment –  $25.73 \pm 0.95$  IU/ml;  $p > 0.05$ ), and to TG – up to  $85.62 \pm 6.24$  IU/ml (before treatment –  $156.48 \pm 7.12$  IU/ml,  $p > 0.05$ ).

After the treatment applied, the microbial contamination of focal skin eruptions was significantly suppressed in patients from the main group. The number of *Staphylococcus aureus* and *Staphylococcus epidermidis* in patients with PV decreased significantly, remaining however outside the physiological range and amounted up to  $235.83 \pm 24.39$  CFU/cm<sup>2</sup> (before treatment –  $415.81 \pm 14.25$  CFU/cm<sup>2</sup>,  $p < 0.05$ ) and  $42.38 \pm 1.95$  CFU/cm<sup>2</sup> (before treatment –  $93.40 \pm 5.38$  CFU/cm<sup>2</sup>,  $p < 0.05$ ) respectively. The levels of *Staphylococcus saprophyticus*, *Micrococcus spp.* and *Bacillus spp.* were reduced to the values of  $14.29 \pm 2.54$  CFU/cm<sup>2</sup> (before treatment –  $37.65 \pm 3.02$  CFU/cm<sup>2</sup>,  $p > 0.05$ );  $9.16 \pm 2.14$  CFU/cm<sup>2</sup> (before treatment –  $25.19 \pm 2.16$  CFU/cm<sup>2</sup>,  $p > 0.05$ ) and  $20.08 \pm 1.89$  CFU/cm<sup>2</sup> (before treatment –  $78.15 \pm 3.12$  CFU/cm<sup>2</sup>,  $p > 0.05$ ) respectively. The number of other microorganisms remained in the range of phys-

iological fluctuations, i.e.  $9.21 \pm 1.64$  CFU/cm<sup>2</sup> (before treatment –  $7.92 \pm 0.81$  CFU/cm<sup>2</sup>,  $p > 0.05$ ). Similarly, the concentration of microorganisms changed in the case of psoriasis vulgaris and PsA, making it  $250.13 \pm 15.19$  CFU/cm<sup>2</sup> (before treatment –  $525.12 \pm 31.78$  CFU/cm<sup>2</sup>)  $94.11 \pm 4.62$  CFU/cm<sup>2</sup> (before treatment –  $142.36 \pm 15.83$  CFU/cm<sup>2</sup>,  $p < 0.05$ );  $13.02 \pm 1.76$  CFU/cm<sup>2</sup> (before treatment –  $53.94 \pm 2.95$  CFU/cm<sup>2</sup>,  $p < 0.05$ );  $8.16 \pm 0.62$  CFU/cm<sup>2</sup> (before treatment –  $35.18 \pm 1.74$  CFU/cm<sup>2</sup>,  $p < 0.05$ );  $19.29 \pm 2.14$  CFU/cm<sup>2</sup> (before treatment –  $95.87 \pm 4.13$  CFU/cm<sup>2</sup>,  $p < 0.05$ ) and  $8.85 \pm 1.12$  CFU/cm<sup>2</sup> (before treatment –  $8.19 \pm 0.50$  CFU/cm<sup>2</sup>,  $p > 0.05$ ) respectively.

In patients with PV the DLQI was  $14.0 \pm 0.8$  points (before treatment –  $18.2 \pm 2.4$  points;  $p < 0.05$ ); in the presence of PsA –  $16.1 \pm 1.2$  (before treatment –  $23.5 \pm 1.9$  points;  $p < 0.05$ ).

The performed analysis of clinical expediency of the use of narrowband phototherapy allowed confirming the achievement of “clinical remission” in 32 (69.6%) of patients, “significant improvement” in 9 (19.6%), and “improvement” in 5 (10.8%). There were no cases of no positive changes or deterioration of the condition. In 12 (26.1%) of patients, psoriasis relapses occurred during 1 year after the end of treatment, but their severity was significantly lower than in patients from the comparison group.

## DISCUSSION

Analysing the obtained results, it can be stated that in patients from the main group there is a reliable suppression of cell activity in respect of cytokine production, the degree of which depends on the clinical course of dermatosis and significantly exceeds similar values in patients from the comparison group. It is proved that the recommended method of phototherapy, which was used to treat psoriasis patients from the main group produces a modulating effect on the levels of autoantibodies to TPO and TG, and significantly suppresses microbial contamination. Accordingly, the rate of DLQI and PASI indices decreases, and these were especially significant in patients from the main group as compared to the insignificant fluctuations in patients from the comparison group.

Thus, the presented data testify that an integrated use of narrowband UVB therapy in psoriasis patients is better in respect of the efficacy as compared to the monotherapy by traditional means of treatment due to its systemic anti-inflammatory, immunomodulatory and antimicrobial effect. Such a multidirectional effect, in turn, allows identifying this methodology as a limiting the pathological process through the clinical and pathogenetic influence.

## CONCLUSIONS

1. It is shown that traditional therapeutic means such as monotherapy produce insufficient corrective effect on immuno-microbiological disorders and clinical manifestations in psoriasis patients.
2. It has been established that narrowband phototherapy in combination with traditional means shows a more

accentuated corrective effect on the cytokines production, modulating effect on the content of autoantibodies to TPO and TG and the condition of automicroflora of focal skin eruptions in psoriasis patients.

3. It has been proved that the combination of UVB-therapy (311 nm) and traditional methods of treatment of patients with various clinical courses of psoriasis is effective, safe, convenient enough to use and allows obtaining in 70% of cases a complete clinical and predictable remission.
4. It is stated that the use of this combined method allows increasing the efficacy of treatment and limit clinical manifestations of psoriasis in the form of remission, significant improvement of patients' condition and quality of life in the absence of negative dynamic changes.

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## ORCID and contributionship:

Hennadiy Ye. Astsaturov - 0000-0002-9883-6038 <sup>A,B,C,D</sup>

Orysya O. Syzon – 0000-0002-7011-2521 <sup>A,B,D</sup>

Yuriy V. Andrashko <sup>A,E,F</sup>

## Conflict of interest:

The Author declare no conflict of interest.

## CORRESPONDING AUTHOR

**Hennadiy Ye. Astsaturov**

Department of Dermatology, Venereology,  
Danylo Halitsky Lviv National Medical University,  
69a, Pekarskaya str., Lviv, 79010, Ukraine  
tel: +380505497847  
e-mail: h.astsaturov@gmail.com

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