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FEATURES OF SKIN MICROCIRCULATION IN PATIENTS WITH PSORIASIS

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Abstract. ***Introduction.*** Psoriasis is a chronic inflammatory autoimmune skin disease involving the musculoskeletal system in the pathological process. This original study presents comparative results of studying the microcirculatory bed in the psoriatic papule and in a healthy area of the skin of patients with psoriasis. ***The aim*** was to study of the parameters of microcirculation in a pathological lesion of the skin in patients with psoriasis against the background of treatment under the influence of artificially created stress. ***Materials and methods***. 16 patients with psoriasis aged 18 to 25 years who were on inpatient treatment at the Regional Skin and Venereological Dispensary in Chita were examined. Microcirculation was evaluated by laser speckle interferometry. Statistical analysis and visualization are performed in the R language (http://cran.rproject.org), version 4.2.3. ***Results.*** The dynamics of interlayer blood flow obtained by laser speckle interferometry in a state of artificially modulated stress in a healthy area of the skin significantly differ compared with microcirculation in the affected area. ***Conclusion.*** The revealed changes in the microcirculation of the skin contribute to the understanding of the pathogenetic links of the formation of a pathological focus in patients with psoriasis.

Keywords: psoriasis, microcirculation, psoriatic papules, pathogenesis

ОСОБЕННОСТИ МИКРОЦИРКУЛЯЦИИ КОЖИ У БОЛЬНЫХ ПСОРИАЗОМ

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Резюме. ***Введение.*** Псориаз — хроническое воспалительное аутоиммунное заболевание кожи с вовлечением в патологический процесс опорно-двигательного аппарата. В данном оригинальном исследовании представлены сравнительные результаты изучения микроциркуляторного русла в псориатической папуле и в здоровом участке кожи пациентов с псориазом. ***Цель исследования*** — изучение параметров микроциркуляции в патологическом очаге кожи у пациентов с псориазом на фоне проводимого лечения при воздействии искусственно созданного стресса. ***Материалы и методы***. Обследовано 16 пациентов с псориазом в возрасте от 18 до 25 лет, находившихся на стационарном лечении в ГУЗ «Краевой кожно-венерологический

диспансер» в г. Чите. Оценку микроциркуляции проводили методом лазерной спекл-интерферометрии. Статистический анализ и визуализация выполнены на языке R (http://cran.rproject.org) версии 4.2.3. ***Результаты исследования.*** Показатели динамики межслоевого кровотока, полученные методом лазерной спекл-интерферометрии, в состоянии искусственно модулированного стресса в здоровом участке кожи достоверно отличаются по сравнению с микроциркуляцией в пораженном участке. ***Заключение.*** Выявленные изменения микроциркуляции кожи вносят вклад в понимание патогенетических звеньев формирования патологического очага у пациентов с псориазом.

Ключевые слова: псориаз, микроциркуляция, псориатические папулы, патогенез

INTRODUCTION

Psoriasis is a chronic immune-mediated inflammatory skin disease characterized by impaired keratinization and inflammatory reactions in the dermis. The pathogenesis of dermatosis includes the interplay between environmental triggers, hereditary component, inflammatory and autoimmune reactions, which directly affects the alteration of skin microcirculation in psoriasis patients [2, 12]. According to the literature, autoantibodies and immune complexes in dermatosis contribute to vascular wall damage, which correlates with the duration, severity of the pathologic process and clinical symptoms of the disease. The main factors contributing to angiopathies in psoriasis are local skin damage, changes in interstitial metabolism, formation of hypersensitivity and changes in vascular permeability [3, 5].

Microcirculatory disorders in patients with psoriasis are caused by imbalance of hemostasis and coagulation [6]. Thus, scientific studies show an increase in the concentration of C-peptide, plasminogen, fibrinopeptide A, homocysteine and a decrease in the level of antithrombin III. The correlation between hemodynamic disturbance and the frequency of disease exacerbations was determined. Changes in the rheological properties of blood in patients are fixed in case of a long history of the disease, presence of foci of chronic infection, long-term intake of systemic glucocorticosteroids and cytostatics, complicated course of psoriasis.

The use of capillaroscopy contributes to a better study of microcirculatory parameters [1, 7, 8, 13]. Modern studies present the characteristics of microcirculatory disorders: at the progressive stage in psoriatic papules capillaries are thin, at the resolution of clinical symptoms they are dilated with a tortuous pattern. However, a 20% decrease in the number of functionally active capillaries was recorded at the border with healthy skin. The perivascular space is characterized by lymphocytic infiltration, edema, but numerous cytoplasmic outgrowths were detected on the endothelium. It is known that clinically healthy blood relatives with psoriasis have similar changes in microcirculation.

AIM

Study of microcirculation parameters in pathologic skin focus in patients with psoriasis on the background of the conducted treatment under the influence of artificially created stress.

MATERIALS AND METHODS

The study included 16 people with the diagnosis of “Disseminated psoriasis vulgaris of smooth skin and scalp, progressive stage, exacerbation” who were treated in the hospital on the basis of the State Institution of Health Care “Regional Skin and Venereological Dispensary” of the Ministry of Health of the Transbaikal Territory (Chita). All patients included in the study were prescribed standard systemic and topical therapy according to the Federal Clinical Recommendations of the Russian Society of Dermatovenerology and Cosmetology (RSDVC). Voluntary informed consent was obtained from all persons included in the study.

The study was performed by laser speckle interferometry in two stages. The first stage was at the moment of admission to the hospital, and the second stage was before discharge from the hospital. The stages included three periods, each of which lasted for three minutes: T1 — resting state, T2 — modulated stress, T3 — restorative resting state. Each period was accompanied by measurements of hemodynamic parameters. Stress was created by a color test implementing the Stroop effect. This method is designed to assess the formation of associative connections between cortical zones responsible for the perception of color and lettering. The mismatch between color and semantic meaning of words leads to a conflict of perception and, as a result, to stress. An mDLS (miniaturized Dynamic Light Scattering, Elfi-Tech, Rehovot, Israel) sensor attached to the skin recorded photons that were reflected from red blood cells moving in adjacent layers of blood flow (shear rate, or transverse velocity gradient). The first sensor was placed over the affected area of the outer surface of the forearm. The second sensor was placed above the first sen-

sor on healthy skin near the pathologic focus. The signal was integrated as three Hemodynamic Indexes (HI). The technique of spectral decomposition of the signal by Fast Fourier Transform (FFT) into frequency components associated with hemodynamic sources of different layer shear rates was used. The low-frequency (1–300 Hz) index (HI1) was determined by slow interlayer interaction, the high-frequency region (HI3) (3000–24 000 Hz) characterized fast layer shift processes. HI2 (300–3000 Hz) occupied an intermediate position. To evaluate the tendencies of blood flow redistribution between fast and slow processes, the HI1/HI3 ratio index was introduced. The summed index HI = HI1 + HI2 + HI3 demonstrated the volume of flow covered by sensor irradiation. The normalized indices RHI1, RHI2, RHI3 denote the relative contribution of each component to the overall dynamic processes (RHI1 = HI1/HI,

Table 1

Microcirculatory hemodynamic parameter prior to and after the treatment in healthy and affected areas of the skin

Таблица 1

Показатели микроциркуляторной гемодинамики до и после лечения на здоровом и пораженном участках кожи

Показатель / Parameter	Участок воздействия / Area of impact	Состояние покоя (T1) / Resting state (T1)	Уровень значимости (p1) / Significance level (p1)	Состояние модулированного стресса (T2) / Modulated voltage state (T2)	Уровень значимости (p2) / Significance level (p2)	Восстановительное состояние покоя (T3) / Restorative state of rest (T3)	Уровень значимости (p3) / Significance level (p3)
Гемодинамический индекс (HI) / Hemodynamic Index (HI)	Здоровый участок / Healthy area	711±115	0,890	849±143	0,750	764±122	0,980
	Пораженный участок / Affected area	706±194		814±314		746±277	
Гемодинамический индекс 1 (HI1) / Hemodynamic Index 1 (HI1)	Здоровый участок / Healthy area	0,204±0,030	0,038	0,198±0,023	0,029	0,208±0,032	0,007
	Пораженный участок / Affected area	0,161±0,028		0,167±0,022		0,154±0,028	
Гемодинамический индекс 2 (HI2) / Hemodynamic Index 2 (HI2)	Здоровый участок / Healthy area	0,519±0,019	0,220	0,528±0,018	0,46	0,525±0,015	0,99
	Пораженный участок / Affected area	0,529±0,019		0,519±0,0257		0,525±0,0221	
Гемодинамический индекс 3 (HI3) / Hemodynamic Index 3 (HI3)	Здоровый участок / Healthy area	0,270±0,033	0,017	0,274±0,029	0,012	0,267±0,035	0,009
	Пораженный участок / Affected area	0,318±0,030		0,326±0,036		0,328±0,033	
Отношение HI1/HI3 / Ratio of HI1/HI3	Здоровый участок / Healthy area	0,710±0,141	0,064	0,673±0,105	0,018	0,715±0,145	0,020
	Пораженный участок / Affected area	0,514±0,119		0,5±0,115		0,479±0,113	

Note. Hemodynamic indices are dimensionless quantities. Statistical significance of comparing groups according to the paired Wilcoxon criterion: p1 – T1 (healthy area) and T1 (affected area), p2 – T2 (healthy area) and T2 (affected area), p3 – T3 (healthy area) and T3 (affected area).

Примечание. Гемодинамические индексы являются безразмерными величинами. Статистическая значимость сравнения групп по парному критерию Вилкоксона: p1 – T1 (здоровый участок) и T1 (пораженный участок), p2 – T2 (здоровый участок) и T2 (пораженный участок), p3 – T3 (здоровый участок) и T3 (пораженный участок).

Table 2

Microcirculatory hemodynamic parameter on response to stress stimulation in patients with psoriasis

Таблица 2

Показатели микроциркуляторной гемодинамики в ответ на стрессорную стимуляцию у больных псориазом

Показатель / Parameter	Участок воздействия / Area of impact	Состояние покоя (T1) / Resting state (T1)	Состояние покоя (T2) / Resting state (T2)	Состояние покоя (T3) / Resting state (T3)	Уровень значимости (p1) / Significance level (p1)	Уровень значимости (p2) / Significance level (p2)	Уровень значимости (p3) / Significance level (p3)
Гемодинамический индекс (HI) / Hemodynamic Index (HI)	Здоровый участок / Healthy area	711±115	849±143	764±122	0,003	0,018	0,004
	Пораженный участок / Affected area	709±296	814±314	746±277	0,48	0,64	0,93
Гемодинамический индекс 1 (HI1) / Hemodynamic Index 1 (HI1)	Здоровый участок / Healthy area	147±19,7	168±31,8	158±27,5	0,007	0,014	0,014
	Пораженный участок / Affected area	126±54,8	129±54,8	128±53,5	0,87	0,87	0,87
Гемодинамический индекс 2 (HI2) / Hemodynamic Index 2 (HI2)	Здоровый участок / Healthy area	370±64,1	448±73,4	401±65,6	0,004	0,033	0,005
	Пораженный участок / Affected area	416±212	421±176	433±204	0,85	0,85	0,85
Гемодинамический индекс 3 (HI3) / Hemodynamic Index 3 (HI3)	Здоровый участок / Healthy area	194±47,7	234±51,3	205±47,6	0,006	0,009	0,009
	Пораженный участок / Affected area	218±82	241±61,5	236±73,9	0,14	0,19	0,52
Отношение HI1/HI3 / Ratio of HI1/HI3	Здоровый участок / Healthy area	0,8±0,226	0,735±0,16	0,802±0,224	0,068	0,87	0,091
	Пораженный участок / Affected area	0,514±0,119	0,475±0,135	0,479±0,113	0,51	0,34	0,81

Note. Hemodynamic indices are dimensionless quantities. Statistical significance of comparing groups according to the paired Wilcoxon criterion: T1 and T2, p2 — T1 and T3, p3 — T2 and T3.
Примечание. Гемодинамические индексы являются безразмерными величинами. Статистическая значимость сравнения групп по парному критерию Вилкоксона: p1 — T1 и T2, p2 — T1 и T3, p3 — T2 и T3.

RHI2 = HI2/HI, RHI3 = HI3/HI). To evaluate the tendencies of blood flow redistribution between fast and slow processes, the HI1/HI3 ratio index was introduced.

Statistical analysis and visualization were performed in R language (http://cran.rproject.org) version 4.2.3. Assessment of the reliability of pairwise differences of all indicators between stages (T1, T2, T3) was performed using the Wilcoxon test. Decision on the statistical significance of hypotheses was made at the level of $p < 0.05$. Quantitative representation of indicators in the tables was performed in the format M±SD (mean value ± standard deviation).

RESULTS AND DISCUSSION

In the first phase of the study before treatment, a significant number of subjects showed a decrease in the relative normalized hemodynamic index RHI1 in all measurement periods: T1 (resting state) — healthy site = 0.00029, affected site = 0.00023 (p=0.038); T2 (modulated stress) — healthy site = 0.00023, affected site = 0.00021 (p=0.029); T3 (resting recovery state) — healthy site = 0.00027, affected site = 0,00021 (p=0,007). There was an increase in the normalized RHI3 index in the affected skin area compared to the healthy skin area: T1 (resting state) — 0.00038 and 0.00045 (p=0.017); T2 (modulated stress) — 0.00062 and 0.00064 (p=0.012); T3 (restorative resting state) — 0.00035 and 0.00044 (p=0.009) respectively (Table 1).

We have revealed changes in hemodynamic indices on the affected and healthy sites in response to stressor loading. Thus, on the healthy skin area in the period T2 (modulated stress) there was an increase in all normalized hemodynamic indices (RHI1 of the healthy site = 0.19788, affected site =

Table 3

Microcirculatory hemodynamic parameter on response to treatment in the T1 period

Таблица 3

Показатели микроциркуляторной гемодинамики в ответ на лечение в периоде Т1

Показатель / Parameter	До терапии / Before therapy	После терапии / After therapy	Уровень значимости (p) / Significance level (p)
Гемодинамический индекс (HI) / Hemodynamic Index (HI)	703±406	713±242	0,86
Гемодинамический индекс 1 (HI1) / Hemodynamic Index 1 (HI1)	123±70	131±44,1	0,73
Гемодинамический индекс 2 (HI2) / Hemodynamic Index 2 (HI2)	375±221	367±128	0,80
Гемодинамический индекс 3 (HI3) / Hemodynamic Index 3 (HI3)	215±115	215±75,5	0,81
Отношение HI1/HI3 / Ratio of HI1/HI3	0,463±0,105	0,612±0,099	0,004

Note. Hemodynamic indices are dimensionless quantities. Statistical significance of comparing groups according to the paired Wilcoxon criterion.
Примечание. Гемодинамические индексы являются безразмерными величинами. Статистическая значимость сравнения групп по парному критерию Вилкоксона.

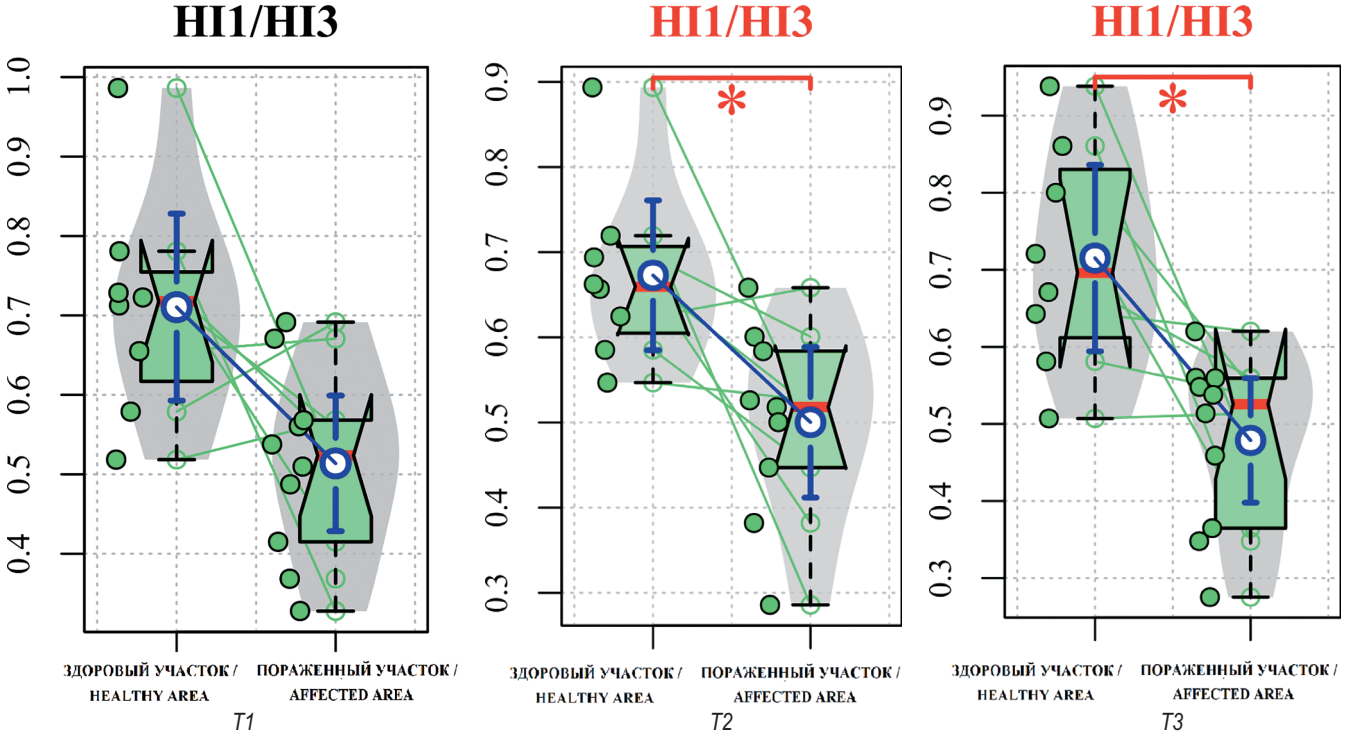

Fig. 1. Dynamics of the change in the ratio between slow and fast interlayer interactions in the HI1/HI3 ratio in healthy and affected areas by study period

Рис. 1. Динамика изменения соотношения между медленными и быстрыми межслоевыми взаимодействиями HI1/HI3 на здоровом и пораженном участках по периодам исследования

= 0.15848; RHI2 of the healthy site = 0.52768, affected site = 0.51720; RHI3 of healthy site = 0.29607, affected = 0.27562) with incomplete recovery of them at stage T3 (resting state recovery) (RHI1 of healthy site = 0.20681, affected site = = 0.17158; RHI2 of healthy site = 0.52487, affected = 0.58043; RHI3 of healthy site = 0.26832, affected site = 0.31635). However, no statistical changes between slow and fast interlayer interactions were detected in the psoriatic focus both at rest (T1) and under modulated stress (T2), which may indicate a lack of response in response to stress stimulation (Table 2).

In the second phase of the study, incomplete recovery of the RHI index (RHI1 before treatment = 0.17496, after treatment = 0.18373; RHI2 before treatment = 0.53343, after treatment = 0.51473; RHI3 before treatment = 0.30583, after treatment = 0.30154) was observed after treatment in period T1 (resting state) (Table 3).

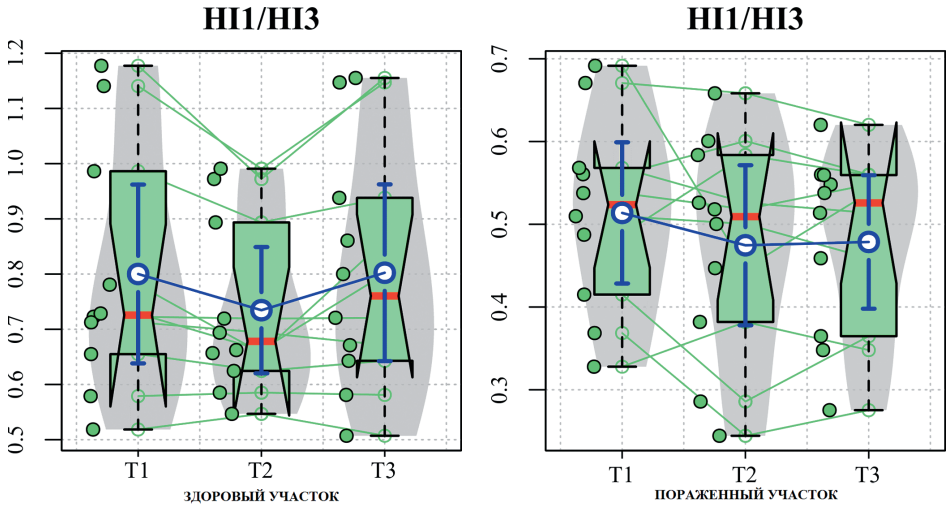

Fig. 2. **Dynamics of the change in the ratio between slow and fast interlayer interactions in the HI1/HI3 ratio in healthy and affected areas of the skin**

Рис. 2. **Динамика изменения соотношения между медленными и быстрыми межслоевыми взаимодействиями HI1/HI3 на здоровом и пораженном участках кожи**

How to explain the results obtained? It is known that the emerging local inflammation as well as the processes of neoangiogenesis change the character of blood flow in favor of turbulent flow [4], which affects hemodynamic functions: the hemodynamic index RHI1 decreases in all periods of measurement, while the RHI3 index increases on the affected skin area. This assumption is consistent with the results of studies [8, 10], the authors of which showed that the processes of inflammation and neoangiogenesis are caused by the appearance of cytokine-chemokine network. Based on this, we can conclude that a significant decrease in the HI1/HI3 ratio characterizes a change in the balance of interlayer velocity distribution (Fig. 1).

At the same time, the unequal response in the affected and healthy areas in response to the stressor load may be due to the processes of endotheliocyte maladaptation, the mechanoreceptors of which may have been blocked due to impaired wall blood flow, as well as specific proinflammatory cytokines, the action of which is caused by autoimmune inflammation [9–11] (Fig. 2).

CONCLUSION

1. Laser speckle interferometry-derived measures of interlayer blood flow dynamics demonstrated significant changes in the slow RHI1 and fast RHI3 components, unchanged by exposure to artificially induced stress.

2. At the healthy site, when the stress condition was induced, there was an increase in HI1 with incomplete recovery in the T3 period.

3. The observed change in microcirculation after the treatment is due to the reduction of systemic and local inflammation.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

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Consent for publication. Written consent was obtained from the patient for publication of relevant medical information within the manuscript.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Информированное согласие на публикацию. Авторы получили письменное согласие пациентов на публикацию медицинских данных.

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