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RESEARCH ON THE RELATIONSHIP BETWEEN THE SEVERITY OF THE COURSE OF PSORIASIS AND METABOLIC SYNDROME AND THE LEVEL OF INDICATORS OF SYSTEMIC INFLAMMATION

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In patients with moderate psoriasis with concomitant metabolic syndrome, the indicators of general clinical and biochemical blood tests and carbohydrate and lipid metabolism were determined, and indicators of systemic inflammation were assessed by the level of susceptible C-reactive protein, ceruloplasmin, interleukin-6 and tumor necrosis factor-α. A laboratory study found that in patients with moderate psoriasis with concomitant metabolic syndrome, an important role is played by the systemic inflammatory process, which is accompanied by the development of insulin resistance, impaired lipid and nitrogen metabolism, and regulation of vascular tone. Furthermore, an increase in the intensity of systemic inflammation is accompanied by an increase in skin lesions, an increase in systolic blood pressure, and a violation of lipid and carbohydrate metabolism.

Key words: psoriasis, metabolic syndrome, systemic inflammation, dyslipidemia, insulin resistance

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ДОСЛІДЖЕННЯ ЗАЛЕЖНОСТІ ТЯЖКОСТІ ПЕРЕБІГУ ПСОРІАЗУ ТА МЕТАБОЛІЧНОГО СИНДРОМУ ВІД РІВНЯ ПОКАЗНИКІВ СИСТЕМНОГО ЗАПАЛЕННЯ

У хворих на псоріаз середнього ступеня тяжкості з супутнім метаболічним синдромом визначали показники загальноклінічного та біохімічного аналізів крові та вуглеводно-ліпідного обміну, а також показники системного запалення – за рівнем чутливого С-реактивного білка, церулоплазміну, інтерлейкіну-6 та фактор некрозу пухлини-α. Лабораторним дослідженням встановлено, що у хворих на псоріаз середньої тяжкості з супутнім метаболічним синдромом важливу роль відіграє системний запальний процес, який супроводжується розвитком інсулінорезистентності, порушенням ліпідного та азотистого обміну, регуляції тонусу судин. Крім того, збільшення інтенсивності системного запалення супроводжується збільшенням ураження шкіри, підвищенням систолічного артеріального тиску, порушенням ліпідного та вуглеводного обміну.

Ключові слова: псоріаз, метаболічний синдром, системне запалення, дисліпідемія, інсулінорезистентність

The study is a fragment of the research project "Development of improved methods of diagnosis and complex treatment of chronic dermatoses and infections, which are mainly sexually transmitted, taking into account the determination of additional factors significant in the pathogenesis of these diseases", state registration No. 0117U000272.

Psoriasis is a common chronic dermatosis often combined with metabolic syndrome (MS). According to several authors, the prevalence of combined pathology in the population is from 30 % to 50 %, while the majority of psoriasis is from 2 % to 4 %, and MS is from 15 % to 24 % [10]. There is no doubt about common risk factors (RF), genetic, etiological, and pathogenetic mechanisms in developing these diseases [2, 8, 11]. In recent years, there has been an increase in the incidence of dermatosis combined with MS and the number of severe, atypical, disabling, resistant to therapy forms of the disease [10, 14]. The disease significantly worsens the quality of life. It reduces the work capacity and social activity of patients, which determines the medical and social significance of the problem.

Today, the question of the role of such pathogenetic factors as chronic systemic inflammation and insulin resistance (IR) in developing psoriasis in combination with MS remains open. Systemic inflammation is accompanied by a violation of lipid metabolism and oxidative stress, which leads to the production of pro-inflammatory cytokines and an increase in the course of dermatosis [2, 5]. Modern studies have shown that one of the critical factors that initiate the formation of systemic inflammation are cytokines (TNF-α, IL-6, IL-8, IL-12, IL-17), which, produced by cells of the skin and adipose tissue, can stimulate further triggering of reactions with the participation of susceptible C-reactive protein (c-CRP) [5]. Furthermore, the severity of the clinical course of psoriasis and the degree of metabolic disorders are directly related to the development of systemic immune inflammation [1, 5, 13]. However, various modifiable risk factors, such as MS, obesity, diabetes mellitus (DM), and cardiovascular disease, can influence the manifestation of psoriasis, increasing the risk of developing and worsening the course of the disease. Therefore, it stimulates the further in-depth study of the factors and mechanisms of the development of psoriasis in combination with MS.

The purpose of the study was to identify risk factors and establish the dependence of clinical and laboratory parameters on the level of systemic inflammation in patients with psoriatic disease of moderate severity with concomitant metabolic syndrome.

Materials and methods. The clinical study included 40 people aged 40–65 with widespread psoriasis, stationary stage combined with MS. The study was conducted based on the inpatient department of Poltava's skin and venereological dispensary and the Research Institute of Genetic and Immunological Foundations of the Development of Pathology and Pharmacogenetics. Before the start of the study, all participants signed an informed consent, and the approval of the Bioethics Commission of Poltava Medical State University was obtained.

Psoriasis was diagnosed in patients according to the protocol (Order of the Ministry of Health of Ukraine dated 20.11.2015 No. 762), and MS-according to the criteria of the International Diabetes Association (IDF) and AHA/NHLBI (2005, modified in 2009).

PASI (Psoriasis Area Severity Index) and BSA (Body Surface Area) index were used to assess the severity of the clinical course of psoriasis and the area of skin damage [9].

The examination included a collection of anamnestic and dermatological data, identification of risk factors (RF) (obesity, type 2 diabetes, hereditary predisposition to psoriasis, obesity, type 2 diabetes, stress, infectious diseases, bad habits), the establishment of the seasonality of development. The anthropometric parameters of the patients were assessed-weight (kg), height (cm), waist circumference (WW) (cm), hip circumference (WW) (cm), and the index of abdominal-visceral obesity was calculated from the WW / WW ratio and body mass index (BMI) (kg/m2). In addition, blood pressure (BP)-systolic and diastolic blood pressure (SBP and DBP) were measured in patients.

The scope of laboratory tests carried out at the stage of inclusion in the study included the determination of general clinical and biochemical blood analysis (level of glucose, bilirubin, ALT, AST, total protein, urea, creatinine, triglycerides (TG), total cholesterol (OC) by generally accepted methods.

Carbohydrate metabolism studies were performed by determining the fasting glucose level using the glucose oxidase method (Deacon-DS, Russia) and fasting insulin according to the manufacturer's protocols (DRG, USA), calculating the index of insulin resistance (IR) (HOMA-IR) according to the formula: HOMA-IR = glucose fasting (mmol/l) × fasting insulin (μIU/ml) / 22.5.

Studies of lipid metabolism were carried out by assessing the level of OX and TG. The concentration of cholesterol in the composition of very low-density lipoproteins (VLDL-C) was determined by the ratio of TG/2.22.

The study of the inflammatory response was carried out by determining the concentration of the main biomarkers – high-CRP according to the manufacturer's protocols (JSC "Vector-Best", Russia), ceruloplasmin according to Ravin's method (Reagent, Ukraine), cytokines interleukin-6 (IL-6) and necrosis factor tumors-alpha (TNF-α) by immunoenzymatic method (CJSC "Vector-Best", Russia).

Statistical processing of the obtained data was performed using the program "STATISTICA 6.0" (StatSoft Inc., USA). Methods of descriptive statistics were used, and a comparison of indicators in groups was carried out by parametric (Student's t-test) and non-parametric (Pearson's $\chi 2$ test, Mann-Whitney test) statistics. Intergroup relationships in groups were assessed using Pearson and Spearman correlation analysis. For all types of analysis, differences at $p < 0.05$ were considered statistically significant.

Results of the study and their discussion. At the time of inclusion in the study, there were 25 men (62.5 %) and 15 women (37.5 %) among the patients. The age of patients varied from 40 to 65 years, and the average was 50.05±1.12 years. When included in the study, the average body weight of the patients was 100.57±1.74 kg (from 90 to 136 kg), and height was 167.42±0.91 cm (from 154 to 186 cm).

On average, the body mass index indices in patients with psoriasis on the background of MS were 35.24±0.85 kg/m^2. In contrast, in most patients, the VL and PRO exceeded the norm, corresponding to the sex, and were, on average, 117.05± 1.06 cm and 114.57±1.26 cm, respectively. Furthermore, it was found that in patients with psoriasis on the background of MS, the ratio of OT/OS indices was, on average, 1.02±0.006. In women, the average proportion of OT/OS was 1.0±0.009 with a norm of <0.85, and in men – 1.04±0.007 with a norm of <1.0. It indicates the prevalence of abdominal-visceral obesity among patients.

At the time of inclusion in the study, a pronounced increase in blood pressure indices, especially SBP, was noted in the patients, significantly exceeding the average indicators. Thus, SAD in some patients ranged from 150 to 180 mm Hg. Art. and the average value reached 165.37±1.08 mm Hg. Art., and the range of DAT was 80–120 mm Hg., with an average value of 93.04±1.45 mm Hg. Art.

All examined patients were diagnosed with vulgar psoriasis of medium severity. In patients with psoriasis on the background of MS, the mean PASI index was 14.23±0.184 points, and the BSA index was 17.52±0.88 %.

The duration of psoriatic disease ranged from 1 year to 44 years, with an average of 19.25±1.96 years. The onset of psoriasis occurred between the ages of 5 and 59. The course of independent diseases, particularly obesity, was 8.5±3.25 years (from 2 years to 23 years), and type 2 diabetes was 6.67±1.85 years (from 3 years to 9 years).

Among the patients included in the study, average body weight was found in 1 person (2.5 %), excess body weight – in 1 person (2.5 %), obesity of the 1st degree – in 21 people (52.5 %), obesity of the 2nd degree – in 12 people (30.0 %) and obesity of the 3rd degree – in 5 people (12.5 %). Only three patients (7.5 %) were diagnosed with type 2 diabetes.

Most of the included patients had RF: heredity for psoriasis, obesity, type 2 diabetes in the family history, emotional and psychological stress, physical stress (hypothermia, injuries, sunstroke), infectious diseases, and bad habits (smoking, alcohol). A detailed analysis of the anamnesis revealed that a more significant number of patients in the anamnesis had hereditary psoriasis – 11 people (27.5 %), while heredity on the maternal line was noted in 5 people (12.5 %), and on the paternal line – in 6 a person (15.0 %). Seven people (17.5 %) were diagnosed with hereditary obesity. At the same time, a much smaller number of patients had genetic type 2 DM – 2 people (5.0 %).

Among the causative factors that cause the development of psoriasis against the background of MS, emotional and psychological stress takes the leading position – noted in 35 people (87.5 %). Less frequently detected RFs were: physical stress – in 4 people (10.0 %), in particular, hypothermia – in 2 people (5.0 %), trauma-fracture – in 2 people (5.0 %), and infectious diseases – in 2 people (5.0 %), in particular, caused by angina – in 1 person (2.5 %), by blood transfusion – 1 person (2.5 %). In addition, harmful habits, aggravating during the combined pathology, such as smoking, were found in 21 patients (52.5 %), and alcohol was present in 1 patient (2.5 %).

The seasonality of the disease was registered mainly in the period of minimal solar activity, namely in the autumn-winter season in 6 people (15.0 %). In contrast, in the spring-summer season – in only one person (2.5 %), the undifferentiated type was found in 33 people (82.5 %). Among the examined patients, residents of the city made up the majority – 31 people (77.5 %), while residents of rural areas were a minority – 9 people (22.5 %).

During the laboratory examination (table 1) in patients with psoriasis in combination with MS, a moderate and/or, in some cases, a marked increase in the level of ALT indices was found in 13 people (33.5 %) and AST in 7 people (17.5 %) (Table 1).

When studying lipid metabolism, hypercholesterolemia was detected in 40 people (100.0 %) and hypertriglyceridemia in 39 people (97.5 %), while an increase in the level of VLDL was observed in 9 people (33.5 %). The average value of CH was 9.01±0.2 mmol/l, TG – 3.42±0.05 mmol/l, LDPE 1.55±0.02 mmol/l.

Monitoring of the state of carbohydrate metabolism revealed an increase in the fasting blood glucose level in 10 people (25.0 %). The range of fluctuations of the index was 3.63 – 17.63 mmol/l in patients with coronary artery disease. The insulin level in fasting blood increased in 3 people (7.55 %). The average value of this result was 15.45±1.25 μU/ml. An increase in the HOMA-IR indicator was noted in 32 patients (77.5 %); the range of fluctuations of the index was 0.08–12.8, which indicates the prevalence of insulin resistance in patients.

The level of systemic inflammation in these patients was markedly increased. Thus, a high concentration of high-CRP in blood serum was observed in 39 patients (97.5 %). The concentration of high-CRP in the blood serum ranged from 7.5 to 17.5 mg/l, and the average value was 13.98±0.25 mg/l. In addition, a pronounced increase in pro-inflammatory cytokines, especially TNF-α, was noted. Thus, a high

level of IL-6 was found in 5 patients (12.5 %) and TNF-α in 37 patients (92.5 %). The concentration of IL-6 was 5.49±0.84 pg/ml, and TNF-α was 20.68±9.71 pg/ml. When examining the ceruloplasmin level in patients, no significant changes were found; the mean index was 215.94±10.08 mg/l.

Table 1

Data of laboratory examination of patients with psoriatic disease in combination with metabolic syndrome

Index	Meaning	
	Reference, M±m	Patients, M±m
Erythrocytes, $\times 10^{12}$/l	4.75±0.75 (4.0–5.5)	4.39±0. 08 (3.1–5.0)
Hemoglobin, g/l	140±20 (120–160)	148.3±2.55 (119.0–167.0)
Color indicator	0.97±0.125 (0.85–1.1)	1.0±0.01 (0.9–1.2)
Leukocytes, x 10^9/l	6.5±2.5 (4.0–9.0)	6.46±0.33 (3.6–12.6)
ESR, mm/h	8.5±6.5 (2–15)	10.7±1.0 (3.0–26.0)
Eosinophils, %	2.75±2.25 (0.5 –5.0)	3.65±0.7 (0–1.0)
Basophils, %	0.5±0.5 (0–1.0)	0.12±0.05 (0–1.0)
Stab, %	3.0±2.0 (1.0–5.0)	1.72±0.17 (1.0–5.0)
Segmented, %	59.5±12.5 (47.0–72)	62.45±1.17 (50.0–80.0)
Lymphocytes, %	28.0±9.0 (19.0 –37)	27.85±1.1 (15.0–42.0)
Monocytes, %	6.0±4 (2.0–10)	4.87±0.31 (2.0–10.0)
Total bilirubin, μmol/l	14.5±6.5 (8–21)	14.22±0.9 (5.1–30.6)
ALT, u/l	20±15 (5–35)	**33.01±3.52 (8.0–110.0)***
AST, u/l	22.5±17.5 (5–40)	**32.45±3.54 (16.0–154.0)***
Total protein, g/l	73.5±9.5 (64–83)	73.82±1.01 (61.0–87.0)
Creatinine, μmol/l	85±35 (50–120)	87.95±2.74 (30.0–124.0)
Urea, mmol/l	5.4±2.9 (2.5–8.3)	5.05±0.23(2.5 –7.5)
Cholesterol, mmol/l	4.4±1.1 (3.3–5.5)	**9.01±0.2 (6.8–14.3)***
Triglycerides, mmol/l	1.645±0.645 (1.0–2.29)	**3.42±0.05 (2.5–4.65)***
VLDL mmol/l	0.88±0.75 (0.13–1.63).	**1.55±0.02 (1.14–2.11)***
Blood glucose, mmol/l	5.15±1.25 (3.9–6.4)	**6.32±0.43 (3.63–17.63)***
Insulin, mcU/ml	13.5± 11.5 (2–25)	15.45±1.25 (4.72 –25.04)
Insulin resistance index, HOMA–IR	<2.5	4.13±0.34 (0.08–12.8)
Ceruloplasmin, mg/l	315.0±135.0 (180–450)	215.94±10.08 (74.9–381.5)
C–reactive protein, mg/l	0.068–8.2	**13.98±0.25 (7.5–17.2)***
Interleukin–6, pg/ml	5.0±5.0 (0–10.0)	5.49±0.84 (0.9–24.0)
Tumor necrosis factor–α, pg/ml	3.0± 3.0 (0–6.0)	**21.41±2.09 (5.0–76.6)***

Note: * – compared to the reference value (p<0.05)

Correlation analysis of the studied parameters in patients with psoriasis on the background of MS revealed the following relationships between the PASI index and the BSA index (r=0.73; p<0.05), weight (r=0.37; p<0.05), BMI (r=0.34; p<0.05), insulin level (r=0.55; p<0.05), NOMA indicator (r=0.61; p<0.05), level HF CRP (r=0.71; p<0.05), IL-6 (r=0.69; p<0.05) and TNF-α (r=0.65; p<0.05). The level of SBP is correlated with the presence of a bad habit of alcohol (r=-0.36; p<0.05), the level of VLDL (r=0.32; p<0.05), urea (r=- 0.44; p<0.05). The level of OX correlates with the presence of hereditary obesity (r=0.47; p<0.05), the level of AST (r=0.68; p<0.05), ALT (r=0.32; p<0, 05) and total bilirubin (r=0.39; p<0.05). The blood glucose level is correlated with the onset of psoriasis (r=0.34; p< 0.05), the presence of a history of type 2 diabetes (r=0.69; p< 0.05) and the NOMA index (r=0, 37; p<0.05). The level of insulin correlates with weight (r=0.56; p< 0.05), BMI (r=0.39; p< 0.05), OT (r=0.34; p< 0.05), indices PASI (r=0.55; p< 0.05) and BSA (r=0.35; p< 0.05), the NOMA index (r=0.81; p< 0.05), the level of high-CRP (r=0.46; p<0.05), IL-6 (r=0.38; p<0.05) and TNF-α (r=0.38; p<0.05). The level of high-CRP is associated with PASI (r=0.71; p<0.05) and BSA (r=0.79; p<0.05) indices, ESR (r=0.4; p<0.05), the level of insulin (r=0.46; p<0.05), IL-6 (r=0.55; p<0.05) and TNF-α (r=0.38; p<0.05).

Thus, the obtained data indicate that dyslipidemia in the form of hypercholesterolemia and triglyceridemia, impaired carbohydrate metabolism, and activation of systemic inflammation, which may indicate a violation of metabolic processes, is an essential factor in the development and progression of psoriasis in patients with psoriasis on the background of MS and MS.

To evaluate the influence of chronic systemic inflammation on the course of psoriatic disease and MS, we divided all patients into four subgroups by quartiles depending on the level of high-SRP in blood serum (Table 2). The first group included patients with a moderate level of high-CRP (7.5-13.4 mg/l), the second – with an average level (13.4-13.9 mg/l), the third – with a high (14- 14.6 mg/l), in the fourth – with

a very high (15-17.2 mg/l). In the formed subgroups of patients, the averages of such indicators as anthropometry, the severity of the course of psoriasis, carbohydrate and lipid metabolism, and the inflammatory process were calculated (Table 2).

Table 2

Dependence of clinical and laboratory parameters on the level of C-reactive protein (hs-CRP) in patients with psoriatic disease in combination with metabolic syndrome

Index	Subgroups depending on the level hs-CRP *mg/l*			
	first hs-CRP – 12.32±1.77 n=10	second hs-CRP – 13.65±0.18 n=10	third hs-CRP – 14.34±0.20 n=10	fourth hs-CRP – 15.61±0.86 n=10
PASI index, points	13.09±0.21	14.0±0.28 $p_1 < 0.05$	14.56±0.27 $p_1 < 0.05$ $p_2 > 0.05$	15.26±0.31 $p_{1.2} < 0.05$ $p_3 > 0.05$
BSA Index,	11.4±0.93	15.5±0.85 $p_1 < 0.05$	18.3±0.71 $p_{1.2} < 0.05$	24.9±0.72 $p_{1.2.3} < 0.05$
Waist circumference (WC), cm	117.4±6.1	116.7±4.22 $p_1 > 0.05$	117.8±10.13 $p_{1.2} > 0.05$	116.5±7.93 $p_{1.2.3} > 0.05$
Body mass index, kg/m2	34.93±0.57	33.2±0.57 $p_1 < 0.05$	37.33±2.13 $p_1 > 0.05$ $p_2 < 0.05$	35.5±2.52 $p_{1.2.3} 0.05$
Blood pressure, mm Hg st.: *systolic* *diastolic*	164.5±1.89 95.6±3.9	165.5±1.89 96.0±2.96 $p_1 > 0.05$	165.5±2.83 92.0±2.6 $p_{1.2} > 0.05$	166.0±2.21 90.0±1.67 $p_{1.2.3} > 0.05$
Blood glucose, mmol/l	6.51±1.1	5.93±0.47 $p_1 > 0.05$	5.87±0.44 $p_{1.2} > 0.05$	6.96±1.22 $p_{1.2.3} > 0.05$
Insulin, mcU/ml	11.18±1.89	14.84±1.56 $p_1 < 0.05$	16.59±2.18 $p_1 < 0.05$ $p_2 > 0.05$	19.19±3.55 $p_1 < 0.05$ $p_{2.3} > 0.05$
Index, HOMA-IR	3.22±0.64	3.91±0.5 $p_1 > 0.05$	4.08±0.45 $p_{1.2} > 0.05$	5.33±0.92 $p_{1.2.3} > 0.05$
Cholesterol, mmol/l	8.8±0.3	9.5±0.58 $p_1 > 0.05$	8.66±0.42 $p_{1.2} > 0.05$	9.07±0.27 $p_{1.2.3} > 0.05$
Triglycerides, mmol/l	3.55±0.13	3.34±0.1 $p_1 > 0.05$	3.26±0.09 $p_{1.2} > 0.05$	3.52±0.07 $p_{1.2.} > 0.05$ $p_3 < 0.05$
VLDL mmol/l	3.55±0.13	1.52±0.05 $p_1 < 0.05$	1.48±0.04 $p_1 < 0.05$ $p_2 > 0.05$	1.6±0.3 $p_{1.3} < 0.05$ $p_{2.} > 0.05$
Ceruloplasmin, mg/l	188.88±17.9	221.2±18.83 $p_1 > 0.05$	226.01±22.23 $p_{1.2} > 0.05$	227.68±21.96 $p_{1.2.3} > 0.05$
Interleukin-6, pg/ml	2.69±0.51	3.6±0.56 $p_1 > 0.05$	5.74±1.6 $p_{1.2} > 0.05$	9.93±2.37 $p_{1.2} < 0.05$ $p_3 > 0.05$
Tumor necrosis factor-α, pg/ml	13.91±1.94	14.68±2.17 $p_1 > 0.05$	26.57±5.75 $p_{1.2} < 0.05$	30.48±3.3 $p_{1.2} < 0.05$ $p_3 > 0.05$

Note: $p_1<0.05$ – significant difference between the indicators when compared with 1 subgroup; $p_2<0.05$ – significant difference between the indicators when compared with the 2nd subgroup; $p_3<0.05$ – significant difference between the indicators when compared with subgroup 3.

As can be seen from the presented data (table 2), in the selected subgroups, there is a clear relationship between the parallel increase in the level of high-CRP and the increase in the level of the following indicators, PASI and BSA indices, BMI, insulin, triglycerides, LDL-C, IL-6, and TNF-α. Furthermore, the intragroup correlation analysis among subgroups of patients made it possible to establish the following reliable, positive, high-strength correlations between a low level of UV-CRP and BMI ($r=0.65$; $p<0.05$), as well as between a high level of UV-CRP and the index PASI ($r=0.82$; $p<0.05$), SBP ($r=0.77$; $p<0.05$) and IL-6 ($r=0.66$; $p<0.05$). These data indicate a relationship between the mutually determined increase in chronic systemic inflammation and the strengthening of the disturbance of metabolic processes, which determine the degree of damage and the course of psoriatic disease and MS.

Despite significant progress in developing therapeutic and preventive measures that improve the course of both psoriasis and MS, the incidence continues to grow steadily, the number of complications increases, and neither the etiology nor the pathogenetic mechanisms of these diseases are still poorly understood. Therefore, the study of FRs, which cause the development of psoriasis in combination with MS, becomes especially relevant.

The results of our work showed that the development of psoriasis in combination with MS is directly related to FR and factors characterizing the course of the disease and the severity of skin lesions. The data we obtained confirmed the statement that the development of psoriasis against the background of MS is associated with such risk factors as the hereditary nature of psoriasis (27 %), obesity (17.5 %), and type 2 diabetes (5.0 %), the presence of obesity in the anamnesis (95.0 %) and type 2 diabetes (7.5 %), psychoemotional and physical stress (87.5 % and 10 %, respectively), infectious diseases (5.0 %), smoking (52.5 %) and alcohol (2.5 %). In a similar study, it was shown that the multiple comorbidities of psoriatic disease are directly related to such critical factors as heredity, the presence in the anamnesis of a complex of conditions represented by MS, obesity, type 2 diabetes, cardiovascular diseases, non-alcoholic fatty liver disease, psychoemotional stress and bad habits [1, 5, 7, 12, 11].

It is important to note that among FR, psychoemotional stress is the most significant detection among the population and one of the critical factors that initiate the development of psoriasis. Furthermore, there is evidence in the literature that adaptive reactions to the action of psychoemotional trigger factors in psoriasis trigger a whole cascade of hormonal and metabolic changes that lead to the development of pathogenetic mechanisms [2, 5, 6]. The start, as a rule, begins with a violation of the sympathoadrenal system and an increase in catecholamines in the blood, which contributes to the mobilization of glycogen in the liver, and hyper production of norepinephrine from sympathetic nerve endings stimulates the intensification of lipolysis in adipose tissue.

In our study, we found evidence of increased metabolic activity and inflammation of the hepatobiliary system in patients with psoriasis against the background of MS, which was confirmed by increased activity of transaminases (AST, ALT) and lipids (OX, TG) in the blood of the examined patients. Mehta N.N. and co-author (2011) note that in patients with dermatosis on the background of MS, parallelism is observed between a violation of amino acid metabolism, inflammation in the affected skin, and the activity of transaminases (AST and ALT), inflammation in the liver [7, 8, 11]. The reliable positive correlation we found between the level of OX and the level of AST, ALT, and total bilirubin in patients confirms this position. It is reported that in the tissue of a psoriatic papule, an increase in the level of amino acids is also combined with hyperaminoacidemia and hyperaminoaciduria. One of the manifestations of changes in nitrogenous metabolism in psoriasis can also be hyperuricemia due to the hyperproduction of immune complexes due to the accelerated metabolism of purines in actively proliferating skin cells.

We have established that dyslipidemia is registered in patients with psoriasis on the background of MS due to increased OX, TG, and VLDL levels in the blood. These data can be explained by the fact that the intensification of lipolysis in adipose tissue in patients contributes to hyperglycemia and significantly increases the content of free fatty acids in the blood, thus stimulating insulin secretion. We found a correlation relationship between the level of insulin and indicators characterizing the degree of obesity (weight, BMI), the degree of severity of the course and skin damage (PASI and BSA indices), the level of systemic inflammation (high-CRP, IL-6, and TNF-α). Similar results were reported by other authors who found that the increased level of free cholesterol in psoriatic plaques also correlates with the severity of the skin process. Yes, Baityakov V.V. (2011). [4, 7] believes that the cause of lipid disorders in psoriasis is a violation of lipoperoxidation processes and membrane-destructive processes in liver cells, blood vessels, and keratinocytes.

In our study, we obtained data indicating a violation of carbohydrate metabolism in psoriasis on the background of MS, the extent of which is evidenced by changes in the content of glucose, insulin, and the IR – NOMA index. These results are consistent with the data of other authors, who showed that glucose accumulation in affected and visually unchanged skin occurs at all stages of the disease. However, in several studies, hypoglycoderma or the absence of reliable changes was observed. It was established that in the stationary stage of psoriasis, the tendency to normalize the level of glucose and its metabolites is more characteristic [11, 12]. At the same time, it is essential to note the insulin resistance we discovered in patients with psoriasis on the background of MS, which may contribute to an increase in blood pressure due to the activation of the sympathoadrenal system, increased proliferation of vascular smooth muscle cells, and endothelial dysfunction.

According to recent studies, the pathogenetic relationship between psoriasis and MS is based on systemic immunological inflammation. The data we obtained showed that patients with psoriasis and MS have hyperproduction of several markers characterizing systemic immune inflammation, namely high-CRP and pro-inflammatory cytokines IL-6 and TNF-α. Today, it has been proven that Th1- and Th17-mediated cellular mechanisms and deregulation of pro-inflammatory cytokines IL-6 and TNF-α play an essential role in triggering immune inflammation, which in turn not only contribute to epidermal cell hyperplasia

but also suppress insulin signaling pathways and expression adipokines, thereby stimulating the synthesis of high-CRP, the development of IR and obesity [1, 6, 12, 13]. Furthermore, it has been shown that the excessive release of cytokines during the development of the inflammatory reaction during the exacerbation of psoriasis contributes to a change in the ratio of blood lipoprotein fractions. With a simultaneous increase in VLDL and LDL, the latter activates lipid peroxidation of keratinocyte membranes and the development of systemic inflammation [2, 9].

We have established and confirmed by correlation analysis that a consistent increase in the level of UV-CRP in subgroups of patients is associated with a constant rise in the severity of the course of psoriasis and damage to the skin of patients, which directly indicates pro-inflammatory shifts in immunoregulatory processes and activation of metabolic disorders. It is likely that as proliferation in the epidermis and inflammation in the dermis are stimulated in patients with psoriasis and MS, IL-6 and TNF-α are released into the bloodstream, and the content of high-CRP increases, the content of lipids (cholesterol, triglycerides, LDL) and the formation of IR occur, which increases pathophysiological processes. So, with psoriasis on the background of MS, a pathological closed circle is formed: insulin resistance – obesity – systemic inflammation – tissue remodeling – arterial hypertension – hyperinsulinemia – lipotoxicity, which not so long ago was called the "march of psoriasis" [5].

Conclusion

Thus, in patients with psoriasis and MS, a vital role is played by the systemic inflammatory process, which is accompanied by the development of insulin resistance (IR), disturbances in lipid and nitrogen metabolism, and regulation of vascular tone. An increase in the intensity of systemic inflammation is accompanied by an increase in skin damage, an increase in blood pressure, and a violation of lipid and carbohydrate metabolism. The processes of systemic inflammation and IR in patients with psoriasis and MS can be potential targets of complex therapy.

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