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DYNAMICS OF CLINICAL AND LABORATORY INDICATORS IN THE TREATMENT OF PATIENTS WITH PSORIASIS AND CONCOMITANT ALIMENTARY OBESITY

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Psoriasis is the most common chronic, genetically determined autoimmune polyetiological inflammatory disease with impaired epidermal proliferation, which is provoked by exogenous and endogenous factors and is manifested by erythematous and scaly elements, papules and plaques. There is still no consensus on the pathogenesis of this dermatosis. To objectively understand the pathogenesis of psoriasis, it is necessary to take into account the insufficiently studied comorbidity of this pathology. Numerous studies have shown a clear link between psoriasis and obesity. Systemic inflammation is a common link in the pathogenesis of obesity and psoriasis. In this study, we determined the effectiveness of standard treatment for patients with psoriasis and concomitant grade I-II alimentary obesity, by clinical and immunological examination of systemic inflammation. Found that the treatment of patients was ineffective and further led to the deterioration of patient's condition due to increased systemic inflammation, the progression of obesity and a more severe course of psoriasis.

Key words: psoriasis, alimentary obesity, pathogenesis, clinical presentation.

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ДИНАМІКА КЛІНІКО-ЛАБОРАТОРНИХ ПОКАЗНИКІВ У ХВОРИХ НА ПСОРІАЗ ІЗ СУПУТНІМ АЛІМЕНТАРНИМ ОЖИРІННЯМ

Псоріаз-найпоширеніше хронічне, генетично обумовлене аутоімунне поліетіологічне запальне захворювання з порушенням проліферації епідерми, яке провокується екзогенними та ендогенними факторами і проявляється еритематозними та лускатими елементами, папулами та бляшками. Досі немає єдиної думки щодо патогенезу цього дерматозу. Для об'єктивного розуміння патогенезу псоріазу необхідно враховувати недостатньо вивчену супутню патологію цієї патології. Численні дослідження показали чіткий зв'язок між псоріазом та ожирінням. Системне запалення є загальною ланкою в патогенезі ожиріння та псоріазу. У цьому дослідженні ми визначили ефективність стандартного лікування хворих на псоріаз та супутнє аліментарне ожиріння I-II ступеня шляхом клінічного та імунологічного обстеження системного запалення. Встановлено, що лікування хворих було неефективним і в подальшому призвело до погіршення стану пацієнта через посилення системного запалення, прогресування ожиріння та більш важкий перебіг псоріазу.

Ключові слова: псоріаз, аліментарне ожиріння, патогенез, клінічна картина.

This study is a part of the research project "Study of the pathogenetic role of the circadian molecular clock in the pathogenesis of metabolic diseases and systemic inflammation and the development of treatment methods aimed at these processes" (state registration No. 0120U101166).

Psoriasis is one of the most common chronic recurrent systemic autoimmune multifactorial diseases, which is characterized by the involvement of the skin, joints and internal organs in the pathological process. According to the results of clinical and epidemiological studies, psoriasis affects about 4 % of the population of our planet, regardless of sex, age and ethnic group. The causes of psoriasis are immunological disorders and genetic defects. However, despite the significant prevalence of psoriasis and a large number of studies on this problem, there is still no single view on the pathogenesis of this dermatosis, which is associated with insufficiently studied comorbidity of the disease [2].

Recently, there has been a steady trend of increased comorbidity of psoriasis and obesity. Obesity develops due to disorders of metabolism and eating behavior. It is characterized by the accumulation of adipose tissue in the body. Obesity can be both an independent multifactorial disease – primary obesity (alimentary and constitutional), and a syndrome that accompanies the course of other diseases – secondary obesity (symptomatic). In the structure of morbidity, primary obesity occurs in 95 % of patients, secondary – only in 5 % [5]. The main etiological cause for the development of primary obesity is the alimentary factor. The population of developed countries today is a hostage to readily available food. At the same time, food switches from a category of vital necessity to a category of pleasure. Thus, a disorder of eating behavior is gradually formed, which is a predictor of obesity. Most often, obesity occurs due to the consumption of food with high energy value (calories) in combination with insufficient physical activity and genetic susceptibility, although in isolated cases the disease occurs against the background of genetic endocrine disorders, medications or psychiatric disturbances. A person is considered obese if his/her body mass index (BMI) exceeds 30 kg/m2. It is established that obesity leads to an increased risk of many diseases, including psoriasis, contributing to its severe course with long periods of relapse [2, 3].

The purpose of the study was to establish the effectiveness of standard methods of treatment for patients with extensive psoriasis vulgaris of moderate severity, progressive stage, and concomitant grade I-II alimentary obesity by clinical and immunological examination of systemic inflammation.

Materials and methods. Extensive psoriasis vulgaris, progressive stage, moderate severity, and concomitant grade I-II alimentary obesity were diagnosed in 20 examined patients; the study group included 12 (60 %) men and 8 (40 %) women aged from 35 to 65 years.

The study was approved by the decision of the Committee on Bioethics and Ethical Issues of Ukrainian Medical Stomatological Academy. All patients signed informed consent to participate in the study.

Psoriatic lesions were of extensive nature in all patients. When determining the number of recurrences of psoriasis per year, we found that it was observed 2 times a year in 2 (10 %) patients, 3 times a year in 12 (60 %) patients and 4 times a year in 5 (25 %) patients. The PASI (Psoriatic Area and Severity Index) was used to assess the severity of psoriasis [12].

To assess the severity of alimentary obesity in the examined patients, we determined body mass index (BMI) [10]. Subjects with a BMI of 30-40 kg/m^2 were included in the study.

Determination of systemic inflammation was carried out at the Research Institute for Genetic and Immunological Foundations of Pathology and Pharmacogenetics of Ukrainian Medical Stomatological Academy. To assess the severity of systemic inflammation (SI) in the serum of patients, we determined the concentration of interleukin-33 (IL-33), interleukin-6 (IL-6) and high sensitive C-reactive protein (hs-CRP) by enzyme-linked immunosorbent assay on a multichannel photometer "STATFAX-303" (USA). For quantification of indicators, we used commercial test systems "interleukin-6-ELISA-BEST" (Russia), "CRP-ELISA-BEST" (Russia), "Human IL-33 ELISA Kit" "eBioscience™/Affymetrix" (USA) according to the recommended methods. The obtained indicators were compared with those of the reference values recommended by the manufacturers of diagnostic test systems.

In order to assess the treatment efficacy in patients with extensive psoriasis vulgaris, moderate severity, progressive stage of the course, and concomitant alimentary obesity, we evaluated clinical, laboratory and anthropometric parameters before and after treatment. All patients received treatment according to the protocol. The diet, sedatives (herbal tincture, which patients took before meals, 30-50 drops 3 times a day, 30 days), detoxifiers (solution of Reosorbilact Yuriia-Farm, Ukraine 200.0 i.v. by drop infusion once a day, 10 days), antihistamines (Desloratadine 5 mg once a day, 10 days), hepatoprotectors (essential phospholipids 5.0, diluted in the patient's blood in a ratio of 1:1, once a day, 10 days), vitamins (Aevit 1 capsule once a day for 30-40 days). Statistical processing of the obtained results was performed using the "Statistica 7.0" software, by the Wilcoxon-Mann-Whitney method. The difference was considered reliable with an error probability $p<0.05$.

Results of the study and their discussion. Alimentary obesity was observed in all patients of the study group. When calculating BMI and analyzing indicators in accordance with the classification of obesity by BMI, it was found that 7 (35 %) patients had grade I obesity, whereas 13 (65 %) patients had grade II obesity. The average group BMI was 36.7±1.8 kg/m².

Based on an objective examination of the clinical presentation, the average PASI index was calculated. It was (21.8±1.4), which corresponds to the average severity of psoriasis.

In the study of systemic inflammation, the mean group values of hs-CRP, IL-33 and IL-6 were calculated. In the analysis of the obtained results, it was found that all patients presented with an increased hs-CRP (13.99±2.98 IU/l), IL-33 (73.69±7.5 pg/ml), and IL-6 (13.01±1.54 pg/ml), which indicates the presence of a systemic inflammatory process in all examined subjects (table 1).

Table 1

Indicators of systemic inflammation in patients with extensive psoriasis of moderate severity and concomitant grade I-II alimentary obesity (M±m), n=20

Index	Value	Reference value
IL-33, pg/ml	73.63±6.5	0-54.8
IL-6, pg/ml	12.9±1.45	0-10
hs-CRP, IU/l	13.43±1.28	0.068-8.2

Analyzing the results, it should be taken into account that excess fat deposition is not only an accumulation of excessive fat cells overloaded with triglycerides, but also an important element of the endocrine system, which possesses endo-, auto- and paracrine functions that cause subclinical inflammation. Obesity causes a mild chronic systemic inflammatory response, which provokes increased insulin resistance through the augmented production of inflammatory mediators by excess fat cells. Moreover, tissues remote from the adipose tissue do not demonstrate a clear inflammatory reaction, but

they are exposed to elevated levels of adipokines, which are secreted by activated and hypertrophied adipocytes.

IL-33 is known to be expressed in adipose tissue by adipocytes and macrophages, and its production increases with weight gain, reflecting the close link between obesity and inflammation.

In turn, IL-33 activates mast cells, basophils, eosinophils and natural killer cells, contributing to inflammatory and autoimmune diseases. In obese patients, low-intensity chronic inflammation can be detected when plasma levels of hs-CRP and inflammatory cytokines such as interleukin-33 (IL-33) and interleukin-6 (IL-6) are elevated. The results of multicenter studies prove a threefold increase in the expression of IL-33 by subcutaneous adipose tissue in obese patients. In psoriasis, IL-33 is released during cell damage to warn the immune system and initiate the inflammatory processes by activating the NF-kB immune response [6, 9, 13].

Adipocytes and macrophages secrete IL-6 in adipose tissue. Determination of arteriovenous cytokine difference showed an increase in its serum concentration, indicating the secretion of IL-6 by adipose tissue, which produces approximately 30 % of circulating IL-6 in the human body. Both leptin and IL-6 production by adipose tissue increase with weight gain. Circulating IL-6 is one of the most important factors determining the production of acute-phase proteins by the liver. It provides a rapid coordinated physiological response to tissue damage or infection, aimed at activating the body's defense mechanisms: the destruction of pathogenic microorganisms, removal of damaged cells and repair of damaged tissues [8]. It should be noted that hs-CRP is one of the most important proteins of the acute phase. It attaches to the membranes of damaged cells and causes their death by activating the reactions of the complement cascade. It is known that hs-CRP is a marker of the IL-6 action [7, 11]. The production of hs-CRP in the liver is regulated by circulating IL-6. Therefore, it can be argued that this cytokine, whose concentration increases in obesity, significantly contributes to the occurrence of a chronic systemic inflammatory reaction [9].

To determine the effectiveness of treatment for patients with extensive psoriasis vulgaris, moderate severity, progressive stage, and concomitant grade I-II obesity, we studied the clinical, laboratory and anthropometric parameters before and after treatment. (tables 2, 3).

Table 2

Dynamics of clinical and anthropometric parameters in the of patients with extensive psoriasis vulgaris of moderate severity and grade I-II alimentary obesity, who received treatment according to the protocol (M±m), n=20

Index/Value	Before treatment	14 days after treatment	1 month after treatment	6 months after treatment
PASI, points	21.8±1.4	19.2±1.5*	16.7±1.5*	25.4±1.75
BMI, kg/m²	36.7±1.8	36.9±1.7	37.2±1.5	38.5±1.6

Note: Hereinafter: *p<0.005 as compared to parameters before treatment

Table 3

Dynamics of laboratory indicators in the group of patients with extensive psoriasis vulgaris of moderate severity and grade I-II alimentary obesity, who received treatment according to the protocol (M±m), n=20

Index/Value	Before treatment	6 months after treatment
IL-33, pg/ml	73.63±6.5	76.34±9.76
IL-6, pg/ml	12.9±1.45	14.0±1.98
hs-CRP, IU/l	13.43±1.28	14.16±1.89

When studying the dynamics of the PASI index in study patients it was found that after 14 days of hospital treatment, there was a statistically significant decrease in the indicator by 11.9 % (PASI 11.9): from (21.8±1.4 points) to (19.2±1.5). 1 month after the treatment initiation by 23.4 % (PASI 23.4): from (21.8±1.4 points) to (16.7±1.5 points). The obtained results indicate the relative ineffectiveness of the therapy.

In the study of BMI, a slight increase in this indicator was observed throughout the treatment period. After 14 days of treatment, the rate increased by only 0.5 %, and after a month – by 1.4 % as compared to the corresponding parameter before treatment.

In the analysis of the long-term results of the study, 6 months after treatment, we revealed a slight increase in all examined indicators.

In the study of the clinical presentation and determination of the PASI index, there was an increase in the corresponding indicator by 3.6 points, which amounts to 16.5 % as compared to the corresponding indicator before treatment. This increase was due to the recurrence of psoriasis, which was observed in 100 % of patients.

Examining the indicators of SI, it was found that IL-33 increased by 2.71 pg/ml, which amounts to 3.7 %, IL-6 increased by 1.1 pg/ml, which is 8.5 %, and hs-CRP–by 0.72 IU/l, which is 5.4 % as compared to the corresponding indicators before treatment. In the study of obesity and determination of BMI, there was an increase in the corresponding indicator up to 1.8 kg/m2, which amounts to 4.9 % as compared to the corresponding indicator before treatment. Numerous studies have shown a clear link between psoriasis and obesity. It is established that obesity leads to an increased risk of many diseases, including psoriasis, contributing to its severe course with long periods of relapse, which are poorly amenable to standard therapy, and weight loss leads to a more favorable course of dermatosis [1]. The causes of psoriasis and abdominal obesity are immunological disorders and genetic defects. Recent studies have found that systemic inflammation is a common link in the pathogenesis of obesity and psoriasis. It manifests itself in increased numbers of macrophages that produce large amounts of proinflammatory cytokines. Hence, obesity and inflammation form a vicious circle of causation. Thus, obesity provokes inflammation, and inflammation, in turn, exacerbates obesity and prevents weight loss. The existing problem in treatment leads to a deterioration in the quality of life of patients, reduced efficiency, social activity, and sometimes disability of patients, which determines not only the medical but also the social significance of this issue [4].

The results of study indicate that the treatment of patients with extensive psoriasis vulgaris of moderate severity and concomitant grade I-II alimentary obesity according to the protocol was ineffective and subsequently even led to the deterioration of patients' condition due to the increased SI, the progression of obesity and a more severe course of psoriasis.

Conclusions

1. The standard method of treatment for patients with extensive psoriasis vulgaris of moderate severity and concomitant grade I-II alimentary obesity was ineffective and led to an increase in SI, BMI and PASI index in recurrence of the disease.

2. Treatment of patients with extensive psoriasis vulgaris of moderate severity and concomitant grade I-II alimentary obesity requires a personalized and comprehensive approach, taking into account the identified comorbidities.

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