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THE INFLUENCE OF OBESITY ON CLINICAL AND LABORATORY INDICATORS OF PSORIATIC DISEASE

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Psoriasis is a chronic, inflammatory, systemic immune-mediated disease of a multifactorial nature in which genetic factors play a dominant role in development. Psoriasis is characterized by an accelerated proliferation of epidermocytes and a violation of their differentiation, immune reactions in the dermis and synovial membranes, an imbalance between pro- and anti-inflammatory cytokines, chemokines, and frequent pathological changes in the musculoskeletal system. A close connection between psoriasis and obesity has recently been proven. It is known that in the pathogenesis of psoriasis and obesity, inflammatory processes play a decisive role, which form a vicious circle at the level of the immune system, which must be broken for the successful treatment of these diseases. The results of our study established that dietary obesity in patients with psoriasis leads to metabolic disorders, complicates the course of psoriasis, affects the deterioration of the dermatological index of the quality of life of patients, leads to the ineffectiveness of standard treatment and frequent relapses of psoriatic disease.

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

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ВПЛИВ АЛІМЕНТАРНОГО ОЖИРІННЯ НА КЛІНІКО-ЛАБОРАТОРНІ ПОКАЗНИКИ ПСОРІАТИЧНОЇ ХВОРОБИ

Псоріаз – хронічне, запальне, системне імуноопосередковане захворювання мультифакторіальної природи, за якого домінуюче значення в розвитку відіграють генетичні фактори. Псоріаз характеризується прискореною проліферацією епідермоцитів і порушенням їх диференціювання, імунними реакціями в дермі і синовіальних оболонках, дисбалансом між про- і протизапальними цитокінами, хемокінами, а також частими патологічними змінами опорно-рухового апарату. Нещодавно було доведено тісний зв'язок між псоріазом і ожирінням. Відомо, що в патогенезі псоріазу та ожиріння вирішальну роль відіграють запальні процеси, які утворюють порочне коло на рівні імунної системи, що необхідно розірвати для успішного лікування цих захворювань. Результати проведеного нами дослідження встановили, що аліментарне ожиріння у хворих на псоріаз призводить до метаболічних порушень, ускладнює перебіг псоріазу, впливає на погіршення дерматологічного індексу якості життя пацієнтів, призводить до неефективності стандартного лікування та частих рецидивів псоріатичної хвороби.

Ключові слова: псоріаз, 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. 0119U000272.

Psoriasis is a chronic, inflammatory, systemic immune-mediated disease of a multifactorial nature, in which genetic factors play a dominant role in its development. Psoriasis is characterised by accelerated proliferation of epidermocytes and impaired differentiation, immune reactions in the dermis and synovial membranes, imbalance between pro- and anti-inflammatory cytokines, chemokines, and frequent pathological changes in the musculoskeletal system [14].

Statistics show that psoriasis is one of the most common skin diseases, affecting 1–2 % of the world's population, and its prevalence in the United States is 3.2 %. In Ukraine, statistics on the incidence of psoriasis differ significantly from the European and global averages, as the prevalence of the disease has been steadily increasing over the past decades. It may be due to imperfect medical and statistical systems and under-diagnosis of psoriasis due to low patient referrals.

Hereditary factors, dysfunction of the immune, endocrine, and nervous systems, as well as the influence of environmental factors, play a crucial role in the development of psoriasis [2]. The disease often manifests itself in childhood and is often associated with the development of comorbid conditions. The course of psoriasis and related comorbidities have several specific features that make it essential to study the issues of diagnosis, care and treatment of psoriasis.

A close link between psoriasis and obesity has recently been proven. Obesity is one of the most challenging medical and social problems of our time, resulting from an unhealthy lifestyle. It is a disease that manifests an excess of adipose tissue in the subcutaneous base and other body tissues [3]. In general, this disease occurs when the intake of energy in the body exceeds its expenditure, which leads to the accumulation of adipose tissue and weight gain. The causes of this imbalance are diverse and depend on the nature of food, nutrition, its qualitative and quantitative composition, and lifestyle, although nutrition plays a significant role. The factors that determine the development of obesity include genetic, demographic (age, gender, ethnicity), socio-economic (education, profession, marital status), psychological (nervous system overstrain), and behavioural (diet, physical activity, alcohol, smoking, stress). There are two types of obesity: primary and secondary. Primary (exogenous) obesity includes nutritional obesity, the main cause of which is overeating. Secondary (endogenous) obesity has the following forms: cerebral obesity caused by damage to the central nervous system, pituitary, adrenal, and ovarian, and obesity associated with thyroid dysfunction.

Overeating and excessive consumption of fatty foods combined with low physical activity are considered to be the essential factors of obesity, which in people with a hereditary predisposition leads to the development of this disease [14]. The composition and range of foods in the diet are essential in regulating body weight. Various marketing studies confirm that flour products, fatty meat, sausages and fast food are increasingly replacing vegetables and fruits in the diet of Ukrainians. Ukrainians often eat junk food, such as hamburgers, chips, chocolate bars, etc., which are very high in calories and develop food addiction. Although they seem full, hunger strikes again in an hour, and the weight from such food is constantly increasing [8]. Overeating is caused by irregular eating. Infrequent food intake contributes to weight gain, while more frequent food intake contributes to weight loss. It primarily concerns people who, due to working conditions, eat most of their food in the evening, after work. It causes excessive appetite and, inevitably, overeating. During sleep after a high-calorie meal, very little energy is expended, and food substances are stored as fat in adipose tissue, ultimately leading to obesity with all its consequences [2]. Depression, anxiety, and irritability also often lead to overeating. These conditions are primarily caused by low levels of serotonin in the brain. Low serotonin significantly affects cravings for sweets, flour and starchy foods. Thus, a depressed mood leads to overeating sweets, and saturation with them leads to satisfaction and a comfortable state [9]. Automation and mechanisation of modern labour processes and everyday life have led to a significant reduction in energy consumption for their implementation. Obese people often do not eat more than people of mean weight, but an inactive lifestyle, i.e. physical inactivity, leads to the development of nutritional obesity [5]. When comparing the lifestyle of an ordinary person of the past with that of today, it can be concluded that physical inactivity has entered all social and age groups. Private cars, developed public transport, computers as a workplace and a means of obtaining information, even remote controls for TVs reduce the movement necessary for our bodies metre by metre.

It is quite easy to determine obesity by calculating BMI, which is done by dividing weight (in kilograms) by the squared height (in metres). Obesity is diagnosed if the BMI exceeds 30 kg/m^2 ; BMI below 18.5 kg/m^2 is considered the standard of beauty, and this weight is achieved through diet and physical activity [2].

It is known that inflammatory processes play a crucial role in the pathogenesis of psoriasis and obesity, forming a vicious circle at the level of the immune system, which must be broken for the successful treatment of these diseases [3].

The purpose of the study was to investigate the features of the clinical course and laboratory parameters in obese patients with psoriasis.

Materials and methods. The study group comprised 140 patients with widespread uncomplicated vulgar psoriasis, progressive stage, moderate severity with concomitant nutritional obesity of the I-II degree, 90 (64.5 %) men and 50 (35.5 %) women aged 35 to 65.

To identify the features of the clinical course of existing psoriasis combined with alimentary obesity of the I-II degree, a group of patients consisting of 60 people of the appropriate age (25 women and 35 men) with widespread, vulgar psoriasis of moderate severity, progressive stage of the course with mean body weight was selected as a control for comparison of the studied indices.

All patients underwent a dermatological examination to determine the severity and prevalence of psoriasis – the PASI (Psoriatic Area and Severity Index) [6].

The effect of skin rashes on the quality of life of patients was studied using the DLQI (Dermatology Life QualityIndex) questionnaire, an index for assessing the quality of life of dermatological patients [7].

To study obesity, body mass index (BMI) was determined [9]. Individuals with a BMI of 30-40 kg/m² were included in the study.

All patients underwent a general and biochemical analysis of blood taken in the morning on an empty stomach. Lipid metabolism was determined by assessing the level of total cholesterol (TC) and triglycerides (TG), and the concentration of cholesterol in very low-density lipoprotein (VLDL) was determined by the ratio of TG/22.5. Dyslipidaemia was diagnosed when the level of FPG exceeded 5.2 mmol/l, triglycerides – above 1.7 mmol/l, HDL-C less than 1.0 mmol/l. The evaluation of indicators was performed according to the criteria of the US National Cholesterol Education Program [10, 11].

Systemic inflammation (SI) in the blood serum was determined using interleukin-33 (IL-33), interleukin-6 (IL-6) and high-sensitivity C-reactive protein (hsCRP). The study was carried out by enzyme-linked immunosorbent assay using a multichannel photometer STATFAX-303 (USA). For quantitative determination of indicators, commercial test systems Interleukin-6 ELISA-BEST, CRP ELISA-BEST, and "Human IL-33 ELISA Kit" "eBioscience™/Affymetrix" (USA) were used according to the recommended methods. The obtained values were evaluated in comparison with the reference values of diagnostic test systems. The study was performed before treatment and on day 28 of treatment.

Statistical processing of the results was performed using Statistica 7.0. The difference was considered significant at an error probability of $p<0.05$.

Table 1

Data of general clinical blood test and biochemical blood test of the examined patients (M±m)

Index (reference value)	Meaning	
	Psoriasis patients with obesity I-II degree (n=140)	Patients with psoriasis without obesity (n=60)
Haemoglobin. (g/l) Men – 130–160 Women – 120–140	128.5±5.8	147.3±6.5
Red blood cells. (10^9/l) Men – 4.5–5.0 Women – 4.0–4.5	4.2±0.4 4.6±0.5	4.6±0.5
Colour index 0.85–1.1	0.93±0.09	1.2±0.1
White blood cell count, (10^9/l) 4.0–9.0	7.2±1.3	5.2±1.2
Neutrophils, rods, (%) 1.0–6.0	1.53±0.21	2.4±0.35
Segmented neutrophils, (%) 47.0–72.0	63.25±3.1	65.8±3.2
Eosinophils, (%) 0.5–5.0	3.8±1.2	2.5±0.7
Basophils, (%) 0–1.0	9.0±0.2	0.7±0.4
Lymphocytes, (%) 19.0–37.0	26.73±2.62	20.1±1.9
Monocytes, (%) 3.0–10.0	4.65±0.58	5.3±0.73
ESR, (mm/h) 2–15	11.5±1.1*	7.3±1.0
Total protein. g/l 64.0–83.0	61.7±2.4	68.3±2.8
Albumin. g/l (38–54)	45.3±2.6	46.5±2.5
Globulin. g/l (20–30)	26.8±2.3	24.7±2.5
Albumin–globulin ratio (1.2–2)	1.7±0.19	1.83±0.17
Total bilirubin, μmol/l 8.0–21.0	18.6±1.7	14.7±1.5
ALT, units/l men – 5.0–41.0 women – 5.0–31.0	38.9±2.9	36.5±2.3
AST, units/l: men – 5.0–41.0 women – 5.0–31.0	39.6±2.7	36.3±2.4
Thymol sample, OD (H–S) (0–4)	1.4±0.15	1.3±0.17
FPG, mmol/l 3.0–6.2	7.5±0.3	5.2±0.2
HDL (1.04–1.55 μmol/l)	0.98±0.1	1.3±0.2
LDL (0–2.59 μmol/l)	3.95±0.25*	2.9±0.15
TG, mmol/l (0–1.7)	2.4±0.05*	1.5±0.08
Glucose, 3–6 mmol/l	6.05±0.7	5.5±0.5
Urea, mmol/l 2.5–8.3	5.04±0.23	5.2±0.21
Creatinine, mmol/l 50.0–120.0	87.95±6.7	89.2±6.3

Note: * probability of difference error $p<0.05$

Results of the study and their discussion. The PASI index was calculated in all patients, which reflects the area, as well as the intensity of colouration, infiltration and peeling of psoriatic rashes. According to the results of the study, it was determined that in patients with psoriasis with concomitant alimentary obesity of the I-II degree, the PASI index was 21.7±1.54 and in patients with psoriasis without obesity – 15.2±1.2, which corresponds to the mean severity of psoriasis in both groups of patients. In turn, the PASI index in patients with concomitant alimentary obesity of the I-II degree was by 30.3 % higher.

Patients reported sleep disturbances, feelings of anxiety and anxiety, which led to a deterioration in quality of life. The study of the dermatological quality of life index (QOLI) found that in patients with psoriasis with concomitant alimentary obesity of the I-II degree, the index was 20.3±0.5 points, while in patients without obesity, it was 14.5±0.4 points. The obtained results prove a pronounced impact of the

disease on the quality of life of patients in both groups. The QOL in patients with concomitant alimentary obesity of the I-II degree is 28.6 % higher. Patients with psoriasis with concomitant nutritional obesity of the I-II degree noted dissatisfaction with the previous therapy due to the duration of treatment and short-term remission periods of up to 3 months with episodes of exacerbation 3-4 times a year, and sometimes the absence of complete regression of psoriasis. Patients with psoriasis without obesity noted the effectiveness of previous treatment with relapse of the disease 1-2 times a year, indicating a more severe course of psoriasis in combination with obesity.

When assessing BMI following the obesity classification, the patients in the study group were obese: 36.25 % of patients had grade I obesity and 63.75 % had grade II obesity. The BMI in the control group of patients with average body weight was 24.5 kg/m², which is 35.8 % lower than in the study group.

The results presented show in Table 1 that the level of general clinical blood counts in both groups is within the normal range.

At the same time, there were significant differences in the biochemical blood test parameters in patients of the study group compared to the control group. Patients with psoriasis with concomitant alimentary obesity of the I–II degree had higher glucose by 10 %, total cholesterol by 44.2 %, triglycerides by 60 % and LDL by 36 % and lower HDL by 4.6 %, total protein by 10.5 % compared to patients with psoriasis with mean body weight. The data obtained indicate a violation of the protein synthesising function of the liver due to a decrease in total protein and lipid metabolism with dyslipoproteidaemia.

To evaluate systemic inflammation, the level of hsCRP, IL-33, IL-6 in the study group of patients was investigated (Table 2).

Table 2

Indices of systemic inflammation in patients with widespread vulgaris moderate psoriasis with accompanying obesity I-II degree (M±m) n=20

Index	Meaning	Reference value
IL-33, pg/ml	73.63±6.5	0–54.8
IL-6, pg/ml	12.9±1.45	0–10
hc SRB, IU/l	13.43±1.28	0.068–8.2

The results of the study indicate that all patients with concomitant nutritional obesity had an increase in systemic inflammation in terms of hsCRP (13.99±2.98 IU/l), IL-33 (73.69±7.5 pg/mL) and IL-6 (13.01±1.54 pg/mL). It is known that obesity causes chronic low-intensity systemic inflammation, which provokes increased insulin resistance by increasing the production of inflammatory mediators by an excessive number of fat cells [3]. IL-33 is expressed in adipose tissue by adipocytes and macrophages, and its production depends on weight gain, reflecting the close association between obesity and inflammation. IL-33 activates mast cells, basophils, eosinophils and killer cells, contributing to inflammatory and autoimmune diseases. The expression of IL-33 in obese patients increases threefold. In psoriasis, IL-33 is released by damaged cells to initiate inflammation by activating the NF-kB immune response [7].

Adipocytes and macrophages secrete IL-6 in adipose tissue. The production of IL-6 by adipose tissue increases with increasing body weight. In turn, hs-CRP is the most essential acute-phase protein that attaches to the membrane of damaged cells and causes their death by activating complement cascade reactions and is a marker of IL-6 action. IL-6 regulates the production of hs-CRP in the liver, contributing to the chronic systemic inflammatory response [6].

The results of the study showed a more severe course of psoriasis in patients with concomitant alimentary obesity of the I-II degree compared to patients with psoriasis with average body weight, which is clearly seen in the PASI index, DYI and the frequency of psoriasis exacerbations.

Conclusion

Alimentary obesity in patients with psoriasis leads to metabolic disorders and systemic inflammation, which complicates the course of dermatosis and leads to a deterioration in the quality of life of patients, ineffectiveness of standard therapies and frequent exacerbations of psoriasis.

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RETROGRADE INTRARENAL SURGERY AS A METHOD OF IMPROVING THE ENDOSCOPIC MANAGEMENT OF OCCLUSIVE CONCREMENTS OF THE UPPER PARTS OF THE URETER

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The paper presents upper ureter stone treatment with use of retrograde intrarenal surgery. This is the latest method, which has advantages in treatment of complex cases of nephrolithiasis, stone translocations and residual cases. We analyzed treatment of patients with ureteral stones. Two representative groups were formed and underwent surgical interventions. Patients of first group underwent contact lithotripsy with semi-rigid ureteroscope, in patients of group 2 used flexible ureteroscope. We compare total operation time, average size and density of stones, presence of residual fragments, surgical and postoperative complications. Performing lithotripsy using a retrograde intrarenal surgery provides higher frequency of achieving "stone-free state", which is the ultimate goal of intervention. Also, this is a method that has fewer intraoperative complications, but has a slightly longer duration of surgical intervention. The use of combination of retrograde intrarenal surgery and semi-flexible ureteroscopy should facilitate operations, speed up patient recovery and minimize complications.

Key words: ureteral stones, retrograde intrarenal surgery, lithotripsy, flexible ureteroscopy.

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РЕТРОГРАДНА ІНТРАРЕНАЛЬНА ХІРУРГІЯ ЯК МЕТОД ПОЛІПШЕННЯ ЕНДОСКОПІЧНОГО МЕНЕДЖМЕНТУ ОКЛЮЗУЮЧИХ КОНКРЕМЕНТІВ ВЕРХНІХ ВІДДІЛІВ СЕЧОВОДУ

У роботі представлено аналіз результатів лікування конкрементів верхніх відділів сечоводу за допомогою ретроградної інтраренальної хірургії. Це новітній метод, який має переваги в лікуванні складних випадків нефролітіазу, особливо при транслокації конкрементів і резидуальних формах нефролітіазу. Проведено аналіз лікування пацієнтів із конкрементами сечоводу. Пацієнтам першої групи проводили контактну літотрипсію напівжорстким уретероскопом, у хворих другої групи використовували гнучкий уретероскоп. Визначали загальну тривалість операції, середній розмір і щільність конкрементів, наявність залишкових фрагментів, виникнення інтраопераційних і післяопераційних ускладнень. Проаналізувавши дані, виявили, що виконання літотрипсії методом ретроградної інтраренальної хірургії забезпечує більш високу частоту досягнення стану «stone-free», що є метою оперативного втручання. Також це метод, який має менше інтраопераційних ускладнень, але є технічно складнішим для освоєння та має трохи більшу тривалість оперативного втручання. Вірний напрямок на майбутнє – поєднання ретроградної інтраренальної хірургії та напівгнучкої уретероскопії, що має полегшити операції, прискорити одужання пацієнтів та мінімізувати ризики ускладнень.

Ключові слова: конкременти сечоводу, ретроградна інтраренальна хірургія, літотрипсія, гнучка уретероскопія.

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At this stage of development of medicine, the tactics for removing kidney stones and stones of the ureteropelvic segment are described in sufficient details in modern recommendations. Depending on the characteristics and location of the stones, the constitutional characteristics of the patient, and concomitant diseases, one or another treatment method is used – distant lithotripsy, laparoscopic operations, retrograde or percutaneous lithotripsy.