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УДК: 616.13-004.6-06:616.72-002:616.517

FEATURES OF THE INTERCONNECTION OF TRADITIONAL RISK FACTORS WITH THE ACTIVITY OF THE INFLAMMATORY PROCESS AND ATHEROSCLEROSIS IN PATIENTS WITH PSORIATIC ARTHRITIS

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CECHY WZAJEMNEGO POŁĄCZENIA TRADYCYJNYCH CZYNNIKÓW RYZYKA Z AKTYWNOŚCIĄ PROCESU ZAPALNEGO I MIAŻDŻYCY TĘTNIC U PACJENTÓW Z ŁUSZCZYCOWYM ZAPALENIEM STAWÓW

Abstract. The study of the connection of psoriasis and cardiovascular diseases is paid much attention by domestic and foreign scientists. The article is devoted to the study of the relationship of traditional risk factors (RF) for cardiovascular diseases (CVD) with the activity of the inflammatory process and atherosclerosis in patients with psoriatic arthritis (PsA). The study included 42 patients with PsA who did not have atherosclerotic CVD, diabetes, chronic kidney disease and other serious diseases, did not take statins, the control group consisted of 20 patients with psoriasis (PS) and 20 practically healthy individuals who had no signs of rheumatic, infectious and other inflammatory diseases were screened. It was revealed that in patients with PsA, the severity of the atherosclerotic process is more compared with patients with PS (the RF profiles were the same). The highest levels of C-reactive protein, fibrinogen, uric acid, intima-media complex thickness, atherosclerotic plaque frequency were found in patients in the PsA group, which may indicate a pathogenetic association of additional RF with the development of a more common atherosclerotic process.

Streszczenie. Badanie związku łuszczycy i chorób sercowo-naczyniowych jest przedmiotem szczególnej uwagi naukowców krajowych i zagranicznych. Artykuł poświęcony jest badaniu związków tradycyjnych czynników ryzyka (CF) w chorobach układu krążenia (CUK) z aktywnością procesu zapalnego i miażdżycy tętnic u pacjentów z łuszczycowym zapaleniem stawów (LzS). W badaniu wzięło udział 42 pacjentów z ŁZS, którzy nie mieli miażdżycowej CUK, cukrzycy, przewlekłej choroby nerek i innych poważnych chorób, nie przyjmowali statyn, grupa kontrolna składała się z 20 pacjentów z łuszczycą (PZ) i 20 praktycznie zdrowych osób, które nie miały objawów przebadano reumatyczne, zakaźne i inne choroby zapalne. Okazało się, że u pacjentów z LzS nasilenie procesu miażdżycowego jest bardziej porównywalne z pacjentami z PZ (profile CF były takie same). Najwyższe poziomy białka C-reaktywnego, fibrynogenu, kwasu moczowego, grubości błony wewnętrznej i środkowej, częstość blaszek miażdżycowych stwierdzono u pacjentów z grupy LzS, co może wskazywać na patogenetyczne powiązanie dodatkowego CF z rozwojem bardziej powszechnego procesu miażdżycowego .

Key words: psoriatic arthritis, psoriasis, cardiovascular diseases, dyslipidemia, atherosclerosis, C-reactive protein, uric acid.

Słowa kluczowe: łuszczycowe zapalenie stawów, łuszczyca, choroby sercowo-naczyniowe, dyslipidemia, miażdżyca, białko C-reaktywne, kwas moczowy.

Introduction. Psoriatic arthritis (PsA) is an inflammatory disease of the joints, enthesis and spine, associated with psoriasis [1]. Data on the frequency of PsA vary widely and make up 0.04-3% [2, 3, 4]. Most often, the disease begins at the age of 20 to 50 years. The incidence in men and women is the same [1, 12, 5]. The prevalence of PsA among patients with psoriasis (PS) is 5.4-34% or more [12, 6, 7, 8]. In turn, the population prevalence of PS in the vast majority of studies is estimated at an average of 0,5-5% with significant fluctuations depending on the climatic-geographical region [9, 7, 10].

The study of the connection of PS and cardiovascular diseases (CVD) is paid much attention by domestic and foreign scientists. The results of clinical studies published in recent years, suggest a pathogenetic relationship between them, which is multifactorial [Ahlehoff O. et al, 2011]. In particular, it has been shown that PS and CVD are common risk factors (RF). Much attention is paid to the study of general mechanisms for the development of PS and diseases of the cardiovascular system [Balci DD et al 2009].

It has been established that up to 50% of deaths among patients with PSA are due to atherosclerosis-dependent CVD. Thus, according to the data of the meta-analysis of data [11], in 55% of patients with PsA there was an increased risk of developing CVD in this group of patients in relation to the population as a whole, whereas the overall CVD in patients with arthritis was 45% higher than the average population rate , in particular, the risk of developing myocardial infarction (MI) was higher by 68%, cerebrovascular disease - 22%, and heart failure - 31% [9-10]. Most authors believe that this is due to the presence of atherogenic dyslipidemia (DLP) and systemic inflammation in patients with PSA.

Attention is drawn to the presence of association of cardiovascular catastrophes with an increase in serum sickness of many mediators, which are

traditionally used to assess the activity of the inflammatory process, primarily C-reactive protein (CRP) [13]. Even a slight increase in CRP concentrations in a few months and years, reflecting the activity of the inflammatory process characteristic of the PS and PSA, may be a RF for subclinical inflammation in the vascular wall associated with the atherosclerotic process. In this regard, the determination of the level of CRP with the help of a highly sensitive method (the so-called luch-CRP) allows to specify the risk of development, recurrence and progression of vascular complications of atherosclerosis [13, 14].

In addition to CRP, the role of uric acid (UA) as an unconventional RF for CVD and its complications is studied at the present stage. It is stipulated that among patients with PS from 19 to 30% there is hyperuricemia, the level of which depends on the wounds of the area affected by the skin and. Titov V. N. and colleagues. (2013) have shown that in subjects with low and average risk on the SCORE scale, the concentration of uric acid (UA) in serum is associated with an average correlation with lipid profiles, regardless of the presence or absence of a metabolic syndrome, with the relationship of the UA content with triglycerides (TG) (positive) and with total cholesterol of high density lipoprotein (TCh HDL) (negative) was detected in all studied groups [11, 15].

In the general population, the frequency of asymptomatic elevation of the UA is 5-7%, according to other data - up to 12-25%. Important clinical associations of hyperuricemia are DLP, hypertension, obesity, diabetes mellitus, gallstone disease and nephrolithiasis. Asymptomatic hyperuricemia is detected in 25% of patients with hypertension, including 75% of patients with severe hypertension (SHEP, 2000) [16]. Taking into account the "traditional" RF of CVD, obesity and metabolic syndrome, the researchers found that the level of UA 6.8-11.1 mg / dl (more than 400 μmol / l) increased 3.29 times the probability of a high level of TCh and 1.52 times - an increased amount of CRP in serum [18]. The elevated UA stimulates the activation of RAAS, enhances endothelial dysfunction and provokes hypertension. In a large meta-analysis based on 18 studies, which included 55607 subjects with an average follow-up period of up to 6 years, it was found that the presence of asymptomatic hyperuricemia increases the risk of hypertension by 40% (RR 1.41; 95% CI: 1.23-1, 58) [17].

In modern literature, there is a rather large number of studies devoted to the search for additional RFs of CVD, the definitions of which may improve the assessment and prognosis in patients with PsA with different levels of cardiovascular risk. However, until now, there is no clear answer to many of the key issues that could significantly improve the effectiveness of prevention programs and significantly reduce the high mortality and morbidity rates of CVD in patients with PsA.

Aim. Determine the features of atherosclerotic process, cardiovascular risk in patients with PsA.

Materials and methods. The study included 42 patients with PsA who did not have atherosclerotic CVD, diabetes mellitus, chronic kidney disease, and others. severe illness, did not take statins. As a comparison group, 20 people from PS were compared, compared by age and sex. As a control group, 20 practically healthy individuals who had no signs of rheumatic, infectious and other inflammatory diseases were screened. The selection of the control group was done according to the gender and age of the examined patients. The selected patients, at the time of inclusion in the study, had no hypertension and did not take anti-hypertensive medications. All patients were provided with a complex of clinical and instrumental and laboratory examinations, a survey. Anthropometry, blood pressure measurements, questionnaires for the detection of bad habits (smoking, alcohol abuse), anthropometry were used to detect FR, and in order to assess the presence of depression and / or anxiety disorders, patients used the Hospital Alert and Depression Scale (HADS), which was designed to initially detect anxiety and depression in patients (screening) in general medical practice. The burden of heredity was determined by the presence of an atherosclerotic disease or a major RF (high blood pressure, diabetes, and DLP) in relatives of the first-line patient (mother or father) who manifested before the age of 55 in men and women up to the age of 65 years. The PASI (Psoriasis Area Severity Index) calculator was used to assess the degree of skin lesions. All patients with PsA determined the Disease Activity Score (DAS28) index for CRP, and was assessed at an average level of two years. The Alcohol Use Disorder (AUDIT) questionnaire was used for determining the risk group and the number of people who use the health-hazardous amount of alcohol. Identification Test, developed on the basis of the WHO Cooperative Project (1989). Tobacco use was assessed during an interview with the patient in accordance with the Order of the Ministry of Health of Ukraine dated 03.08.2012 № 601 "On Approval and Implementation of Medical-Technological Documents on Standardization of Medical Aid in the Termination of the Use of Tobacco Products".

All patients and controls were provided with a complex of clinical and laboratory and instrumental research. A general clinical examination included: a complete physical examination, a determination of the severity of psoriasis, an articular examination. Laboratory research included determination of lipid, purine and high-sensitivity CRP indices.

In order to determine the state of the vascular wall, a duplex ultrasonic scan of carotid arteries (CA) was performed for all patients. According to the recommendations of the European Society of Cardiology, scanning of the CA was carried out in three planes - two longitudinal (front and rear) and one transverse. the thickness of the intima-media complex (TIMC) was evaluated in the zone of maximal thickening in the orientation of the scanning plane of the longitudinal axis of the vessel. It was calculated the average value of the TIMC of the right and left general CA as the mean of 9 measurements in 3 positions; the

diagnostic criterion for thickening TIMC was considered to be ≥0.9 mm, the presence of an atherosclerotic plaque, with a local thickening of TIMC of> 1.5 mm and more, or a thickening of more than 50% or 0.5 mm relative to other areas of TIMC.

The mathematical processing of the results was carried out in the IBM SPSS 20 and Statistica 6.0 programs, according to the GCP prior to the data processing. The results base and data preparation for mathematical processing were performed in MS Excel 2007.

Results. The average age of patients with PsA was 39.62 ± 5.8 years (20 (46,61%) women and 22 (52,38%) men), patients with PS (comparison group) 32.3 ± 5.63 years (8 (40%) women and 12 (60%) men respectively), the control group included 11 women (55%) and 9 men (45%), mean age 32.3 ± 5.63, respectively. Duration of PSA varied from 3 to 20 years. (Table 1).

The main clinical and demographic characteristics of the examined patients are presented in Table 1.

Table 1

CLINICO-DEMOGRAPHIC CHARACTERISTICS OF PATIENTS INCLUDED IN THE STUDY

Indicator	PsA n=42	PS without PsA n=20	Control group n=20
Age, years	39,62±4,8	32,3±5,63	30,75±2,13
Women,(n/%)	20 (46,61%)	8 (40%)	11 (55%)
Men,(n/%)	22 (52,38%)	12 (60%)	9 (45%)
Average duration of the disease	10,42±0,34*	4,1±0,57	-
DAS 28, points		-	-
Remission <2,6	4 (8,5%)	-	-
Low activity level 2,6-3,2	9 (21,42%)	-	-
Average degree of activity 3,2-5,1	22 (52,38%)	-	-
High degree of activity >5,1	7 (16,66%)	-	-
PASI, points	14,36±1,12*	7,2±1,05	-
Low activity level < 10 points n, %	8 (19,04%)	3	-
Average degree of activity ≥10>20 points n, %	27 (64,28%)	13	-
High degree of activity >20 points n, %	7 (16,66%)	3	-

Note: * the difference between the groups is significant p <0.05.

According to the results of the initial survey, the frequency of the detection of traditional and behavioral risk factors for CVD (smoking, alcohol abuse, sedentary lifestyle) in the PSA group was not significantly different from the group of patients with skin lesions and the control group. The frequency of combination of risk factors for CVD in patients with PsA is given in Table 2.

According to the results of the analysis of lipid metabolism, a significant difference was observed between the mean levels of HF in the group of patients with PSA (Table 2) compared with the control group. The median levels of CF, TG, LDL cholesterol, LDL cholesterol were significantly higher in patients with PsA, and HDL-C levels were significantly lower than those in the FP and control groups (p <0.05).

The increase in the levels of high-sensitivity CRP and SC in the group of patients with PsA was noted in 78.82% (18 persons) and 21.73% (5 persons) respectively (Table 2).

Table 2

CARDIOVASCULAR RISK FACTORS AND STATE OF THE VASCULAR WALL IN THE EXAMINED PATIENTS

Indicator	PsA n=42	PS without PsA n=20	Control group n=20
Smoking (at any time in the last 10 years), n,% of people	69,04% (29 of people)*	52,63% (10 of people) #	40% (8 of people)
Abuse of alcohol, n,% of people	11,9% (5 of people) r	10,5% (2 of people)	10% (2 of people)
Hypodynamia, n,% of people	45,23% (19 of people)	47,3% (9 of people) #	30% (6 of people)
Adiposity, n,% of people	16,66% (7 особи)	15,78% (3 of people)	5% (1 of people)
Stress,n,% of people	92,85% (39 of people)*	84,2% (16 of people) #	50% (10 of people)
The heredity of cardiovascular disease is encumbered, n,% of people	69,04% (29 of people)*	42,1% (8 of people)	40% (8 of people)
Incidence of DLP, %	83,3% (35 of people)*	62,5% (20 of people)	15% (3 of people)
TCh, mmol / l	5,37±0,2*	4,17±0,44	3,2±0,1
TG, mmol / l	2,45±0,2*	1,52±0,1#	1,32±0,2
HDL cholesterol, mmol / l	1,19±0,1	0,76±0,1#	1,32±0,1
LDL cholesterol, mmol / l	3,45±0,8*	2,43±0,3#	3,12±0,3
VLDL cholesterol, mmol / l	0,81±0,4*#	0,5±0,1#	0,62±0,1
Index of atherogenicity, c.u.	3,69±0,9*#	2,47±0,2#	2,7±0,2
CRP, (mg/l)	8,5±1,79*#	4,45±0,53#	0,77±0,2
UA (mkmmol / l)	402,85±15,24*#	326,68±15,59#	187,83±8,2
Fibrinogen	2,94±1,02	1,97±0,77#	1,9±0,2
SCORE	3,11±0,33*#	2,43±0,11#	1,71±0,11
<2 CVD RF, %	13,05%*	15,1%	14,9%
3-5 CVD RF, %	69,56%*	68,1%	67,9%
>5 CVD RF, %	17,39%*	16,8%	17,2%
Average value TIM CA, мм	0,93±0,02*#	0,7±0,01#	0,64±0,02
TIMC >0.9	45,83%*#	22, 58%	5%
Number of atherosclerotic plaques CA	6,25% (2 осіб)* #	0	0

Note: * the difference between the groups of patients is significant, p <0.05,
difference with rupture control is reliable, p <0.05.

As can be seen from the data presented in Table 2, the frequency of combining behavioral CVD risk factors was not different in the examined groups of patients (PsA and PS) compared with the control group. At the same time, in the group of patients with PsA and PS, dyslipidemia was found to be significantly more

frequent in 83.3% of Psa and 62.5% of PS and 15% of control group respectively (p <0.05).

According to the results of the survey, the risk of fatal cardiovascular events in the SCORE scale was determined (Table 2), the mean score of the study group was 3.11 ± 0.33.

An increase in the number of FG in blood serum> 4 g / l was observed in 11 (21.87%) patients, with an average serum FG level of 4.2 ± 0.2 g / L. It was also found that serum FG level is significantly higher in smokers than in non-smokers (p <0.01) and is directly related to the duration of smoking (r = 0.38, p <0 , 05).

In the comparative analysis of lipid metabolism indexes, it was found that the average levels of TCh, TG, and LDL cholesterol in patients with PsA significantly exceeded the corresponding indices in patients with PS and indicators of healthy individuals in the control group. In this correlation analysis, the greatest influence on TIMC CA was found on DAS 28, TCh, LDL cholesterol, CRP, FG, PASI (r = 0.54, 0.68, 0.67, 0.53, 0.52, 0.43 in accordance). In the group of patients with DAS 28 of medium and high activity (≥3.2), a strong correlation between the TIMC CA and the level of UA (r = 0.61) was found. The level of HDL cholesterol was associated with a strong feedback with CRP and a median power of reverse linkage with UA levels. There was a direct correlation between the level of FG and CRP and UA in the average strength (r = 0.54, 0.48, respectively). The given analysis in the group of patients with PS revealed: a direct connection of average strength between TIMC CA, TCh, LDL cholesterol, CRP (r = 0.37, 0.39, 0.38, respectively). The results of the correlation analysis confirm the relationship of inflammation with dyslipidemia, which plays a significant role in the progression of atherosclerotic vascular lesions and the subsequent formation of CVD.

According to the results of ultrasound examination of carotid arteries, it was found that patients with PsA and PS have a greater severity of atherosclerotic process than healthy peers, which is confirmed by the higher average values of TIMC in the group of patients with PsA (0.93 ± 0.02) p <0.05 compared with the group control (0,68 ± 0,02), with TIMC ≥ 0,9 detected in 45,83% of patients with PsA, which is proven complementary RF CDV and in 22, 58% of patients with PS, which is significantly higher than the control group indicator (5%). It should be noted that the presence of atherosclerotic plaques is diagnosed in 6.25% of patients with PsA.

Conclusions: 1.The prevalence of behavioral risk factors for CVD and their combinations is not different in the groups of patients with PsA, PS and control group.

2. DLD is more common in patients with PsA than in patients with psoriasis (p <0.05) and in the control group, which is manifested by increased levels of ZHC, LDL cholesterol and lowering of HDL cholesterol in patients with PsA compared to other subjects.

3. For patients with PsA, a greater severity of atherosclerotic vascular lesions is observed in comparison with patients with psoriatic skin and healthy peers, which is confirmed by the value of TCIM ≥ 0.9, found at 45.83%, whereas AB was found at 6.25%.

4. In the formation of atherosclerotic lesions in patients with PsA and PS there are significant additional FF associated with the course of the immune-inflammatory process characteristic of psoriatic disease.

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CHANGES OF ORAL MUCOSA CELLULAR REACTION IN RHEUMATOID ARTHRITIS MODELING

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ИЗМЕНЕНИЕ КЛЕТОЧНОЙ РЕАКЦИИ СЛИЗИСТОЙ РОТОВОЙ ПОЛОСТИ ПРИ МОДЕЛИРОВАНИИ РЕВМАТОИДНОГО АРТРИТА

Abstract. The work is devoted to investigation of the effect of the use of immunomodulators and drugs that improve microcirculation on the oral mucosa in modeling rheumatoid arthritis. We studied material from experimental animals with modeling rheumatoid arthritis and visual assessment of the severity of induced paw arthritis and the surrounding area. The comparison group was formed from animals with simulated rheumatoid arthritis but without receiving any treatment. 3 study groups were formed: group which received applications which improve microcirculation (Quertigial which includes quercetin and hyaluronic acid), group which received applications which immunomodulators (Imudon) and group which received applications of their combination (Quertigial and Imudon). A group of intact animals was also further investigated. Tissues of the oral cavity were obtained with performing histological research. Systemic changes had been detected in the oral cavity with