

Interconnection of traditional risk factors with the activity of the inflammatory process and atherosclerosis in patients with psoriatic arthritis

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Abstract

The article is devoted to the study of the relationship of traditional risk factors for cardiovascular diseases with the activity of the inflammatory process and atherosclerosis in patients with psoriatic arthritis. The study included 32 patients with PsA who did not have atherosclerotic cardiovascular disease, diabetes, chronic kidney disease and other serious diseases, did not take statins, the control group consisted of 19 patients with psoriasis. It was revealed that in patients with psoriatic arthritis, the severity of the atherosclerotic process is more compared with patients with psoriasis (the risk factors 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 psoriatic arthritis group, which may indicate a pathogenetic association of additional RF with the development of a more common atherosclerotic process.

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

ПСОРИАЗЛЫ АРТРИТПЕН АУЫРАТЫН НАУҚАСТАРДА ДӘСТҮРЛІ ТӘУЕКЕЛ ФАКТОРЛАРЫНЫҢ ҚАБЫНУ ПРОЦЕСІНІҢ БЕЛСЕНДІЛІГІ ЖӘНЕ АТЕРОСКЛЕРОЗБЕН ӨЗАРА БАЙЛАНЫСЫ

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Отбасылық медицина кафедрасы, П.Л. Шупык атындағы жоғары оқу орнынан кейінгі білім берудің ұлттық медициналық академиясы, Киев, Украина

ТҰЖЫРЫМДАМА

Мақала жүрек-қан тамырлары ауруларының дәстүрлі қауіп факторларының псориазды артритпен ауыратын науқастарда қабыну үдерісінің белсенділігі және атеросклерозбен өзара байланысын зерттеуге арналған. Зерттеуге атеросклеротикалық жүрек-қан тамырлары ауруы, қант диабеті, созылмалы бүйрек ауруы және басқа да күрделі аурулары болмаған, тежеуіштер қабылдамаған псориазды артрит бар 32 науқас қатысты, бақылау тобы псориазы бар 19 науқастан тұрды. Псориазды артрит бар науқастарда атеросклеротикалық процестің ауырлығы псориазы (қауіп факторларының профилдері бірдей болған) науқастарымен салыстырғанда көбірек болғаны анықталды. Псориазды артрит тобындағы пациенттерде С-реактивтік ақуыздың, фибриногеннің, несептік қышқылдың, интима-медиа кешені қалыңдығының, атеросклеротикалық түйіншек жиілігінің ең жоғары деңгейі анықталды, бұл қосымша қауіп факторларының кеңірек тараған атеросклеротикалық процестің дамуымен патогенетикалық байланысын көрсетуі мүмкін.

Негізгі сөздер: псориазды артрит, псориаз, жүрек-қан тамырлары аурулары, дислипидемия, атеросклероз, С-реактивті ақуыз, несеп қышқылы, эндотелиалық әрекетсіздік

ВЗАИМОСВЯЗЬ ТРАДИЦИОННЫХ ФАКТОРОВ РИСКА С АКТИВНОСТЬЮ ВОСПАЛИТЕЛЬНОГО ПРОЦЕССА И АТЕРОСКЛЕРОЗОМ У БОЛЬНЫХ ПСОРИАТИЧЕСКИМ АРТРИТОМ

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РЕЗЮМЕ

Статья посвящена изучению взаимосвязи традиционных факторов риска сердечно-сосудистых заболеваний с активностью воспалительного процесса и атеросклерозом у больных псориатическим артритом. В исследование было включено 32 пациента с псориатическим артритом, которые не имели атеросклеротических сердечно-сосудистых заболеваний, сахарного диабета, хронической болезни почек и других тяжелых заболеваний, не принимали статины, группа контроля состояла из 19 пациентов с псориазом. Выявлено, что у больных псориатическим артритом выраженность атеросклеротического процесса больше по сравнению с больными псориазом (профили факторов риска были одинаковы). Самые высокие уровни С-реактивного белка, фибриногена, мочевой кислоты, показатель толщины комплекса интима-медиа, частота атеросклеротической бляшки были обнаружены у пациентов в группе с псориатическим артритом, что может указывать на патогенетическую связь дополнительных факторов риска с развитием более распространенного атеросклеротического процесса.

Ключевые слова: псориатический артрит, псориаз, сердечно-сосудистые заболевания, дислипидемия, атеросклероз, С-реактивный белок, мочевая кислота, эндотелиальная дисфункция

Introduction

The accumulated results of scientific research suggest that chronic inflammatory diseases with autoimmune genesis are associated with the development of atherosclerosis and increased cardiovascular morbidity and mortality compared with similar indicators in the general population [2]. Increased cardiovascular risk is observed against many inflammatory diseases, including rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, and psoriatic arthritis (PsA) and psoriasis [1, 17].

Psoriasis (PS) is one of the most common skin diseases. According to static data, over 125 million people suffer from this pathology in the world (Kubanov AA, et al., 2010; Scarpa R. et al., 2010). One of the most severe disabling manifestations of this disease is joint damage - PsA that occurs in 6 - 42% of patients with psoriatic skin lesions (Myers W.A. et al., 2006; Landells I. et al., 2008). PsA is one of the main forms of inflammatory diseases of the joints and the spine and is a systemic progressive disease associated with PS, which leads to the development of erosive arthritis, bone resorption, multiple enthesiopathies and spondylarthritis (Badokin V.B. et al., 2010; Gladman DD, 2009). According to the collected data, the incidence of PS in the population is 2-3%, of which 13.8% to 47% of patients fall on the PsA [Louden B.A. et al., 2004]. Most often PsA manifests at the age from 20 to 50 years. Men and women are ill in about the same ratio.

In the absence of adequate treatment in patients with PsA, persistent inflammation, progressive joint damage, severe limitation of physical activity, and disability are observed (Melnichenko A. M. et al., 2010; Martynov AA et al., 2011). An important role in the development of the disease is the genetic predisposition in combination with adverse factors of the environment [Samtsev AV, Barbina VV, 2008; Kubanova AA and so on, 2010; Kubanov AA et al., 2013; Kubanov AA et al., 2014; Gudjonsson J.E., Elder J.T., 2012].

Deviation of fat metabolism in PS with high frequency of dyslipidemia is of great importance, and some researchers consider this disease as part of skin lipoidosis [3]. Especially often hypercholesterolemia occurs, which occurs 2.5 times more often than with other skin diseases (18 and 8%, respectively) [4]. Hyperlipidemia with PS is just as likely to be higher than that in the controls. For this disease, dyslipidemia occurs with an increase in the proatherogenic fractions of lipids and a decrease - antiatherogenic [5-7, 18].

Attention is drawn to the presence of association of cardiovascular catastrophes with an increase in the serum sickness rate of many mediators, which are traditionally used to assess the activity of the inflammatory process, primarily C-reactive protein (CRP) [8]. Even a small increase in CRP concentrations in a few months and years can reflect not only the severity of the inflammatory process, for example, in the tissues of the musculoskeletal system, but also subclinical inflammation in the vascular wall, which is 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 hs-CRP) allows assessing the risk of development, recurrence and progression of vascular complications of atherosclerosis [8, 18].

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 [9].

According to a study conducted by LURIC to evaluate the effect of smoking on blood coagulation rates, active smokers showed an elevated level of fibrinogen (FG), which proved to be an independent predictor of cardiovascular disease (CVD) mortality [10]. This is confirmed by the data of the FRISC study, where the increase in FG level was associated with an increased risk of death in short- and long-term follow-up and / or an increased risk of subsequent acute myocardial infarction (MI) [11].

Based on the results of the meta-analysis of Fibrinogen Studies Collaboration, individual data from participants in all of the prospective studies found in the MEDLINE and Embase databases that included information on baseline FG and subsequent CVD and / or death due to an established cause during, at least 1 year of follow-up (the analysis included 154 211 participants in 31 studies aged ≥ 40 all age groups noted a correlation between plasma levels of FG and the risk of coronary heart disease (CHD), stroke, vascular and non-vascular mortality. The data included 154 211 participants in 31 studies aged ≥ 40 years), during the observation period 8.9 ± 4.9 years, 4681 first cases of non-fatal MI, 2,263 non-fatal stroke and 13210 fatal cases were recorded, including 2437 - from CHD, 512 from stroke, 992 from other vascular causes and 8007 from non-vascular pathology (including 4856 - from cancer). However, no diagnostic threshold in the level of FG within its normal values was found [12].

Lindahl B. et al. It has also been shown that elevated levels of CRP and FG associated with an increased risk of CVD, both in patients with a history of MI or unstable angina, and in practically healthy individuals [13].

At the heart of lesions of the vascular wall in psoriasis is a chronic inflammation of the endothelium of the vessels, which occurs on the background of severe imbalance vasodilator and vasoconstrictor factors, a violation of endothelium dependent vasodilatation and platelet hyper aggregation [Shustov V.Ya. et al., 1996; Zaerco V.V. et al., 2000; Severina A.S., 2007; Bilovol O.M., 2010; Gaziyevev A.R. et al., 2013]. Endothelial dysfunction is proven to be the stage preceding the onset of early atherosclerotic changes in the vascular wall [Celermajer D.S., Raitakari O.T., 2000].

It is known that an increase in the thickness of the Intima-Media complex (TIMC) of carotid arteries (CA) is considered a surrogate marker for atherosclerosis. The significance of this increase for CA is reported by O. Kimhi et al. [15] and C. Gonzalez-Juanatey et al. [10].

According to a prospective cohort study published on August 25 in *Arthritis & Rheumatology*, 90 patients with PsA who had been breathing for at least 24 months were included. Sonographic Arterial Ultrasound Studies and arterial rigidity markers were evaluated annually. In general, 57 patients (63%) achieved the minimum activity of the disease - defined as satisfying five or more compartments for seven areas of disease activity - for 1 year of follow-up, 69% achieved in 2 years and 46% from 1 year observation to 2 years of observation. Long-term control of inflammation is important for preventing the progression of subclinical atherosclerosis and arterial rigidity, regardless of the traditional CVD Risk Factors (RF). The data

from this study confirm the EULAR recommendation that disease activity should be optimally monitored to reduce the risk of cardiovascular disease in patients with PsA [19].

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

Aim

Establish the relationship between traditional risk factors (dyslipidemia, arterial hypertension) and the activity of the inflammatory process and atherosclerosis in patients with PsA.

Material and methods

The study included 32 patients with PsA who did not have atherosclerotic CVD, diabetes, chronic kidney disease, and other severe illness, did not take statins. As a comparison group, 19 people with PS were compared, compared by age and sex. 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. For the detection of CVD FR: anthropometry. In order to assess the presence of depression and / or anxiety disorders in patients, the Hospital Alert and Depression Scale (HADS) was used for the initial detection of anxiety and depression in patients (screening) in general medical practice. The burden of heredity was determined by the presence of atherosclerotic disease or the main RF (high blood pressure, diabetes, and adolescents) 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 index of activity of arthritis (Disease Activity Score - DAS28). The Alcohol Use Disorders Identification Test (AUDIT) questionnaire, developed on the basis of the WHO Cooperative Project (1989), has been used since the determination of the risk group and those who use alcohol-harmful alcohol. The use of tobacco was assessed during an interview with a patient in accordance with the Order of the Ministry of Health of Ukraine dated 03.08.2012 No. 601 "On Approval and Implementation of Medical-Technological Documents on Standardization of Medical Aid in the Termination of the Use of Tobacco Products".

A general clinical examination included: a complete physical examination of all patients in the primary and control groups once, determining the severity of psoriasis, articular examination, and blood pressure measurements. Laboratory testing 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 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. 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 (15 (46.87%) women and 17 (53.12%) men), patients with PS (comparison group) 32.3 ± 5.63 years (6 (35.3%) women and 11 (64.7%) men) respectively. The duration of the PsA varied from 3 to 20 years (Table 1).

The main clinical and demographic characteristics of patients in both groups are presented in Table 1.

According to the results of the initial survey, the frequency of the identification of the traditional and behavioral RF of CVD (smoking, alcohol abuse, sedentary lifestyle) in the group of patients with PsA did not significantly differ from the comparison group. The frequency of combination of RF 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 values of TCh the group of patients with PsA (Table 2) compared with the control group. The mean levels of TCh, TG, (low density lipoprotein) LDL cholesterol, very low density lipoprotein (VLDL) cholesterol were significantly higher in patients with PsA, and HDL cholesterol levels were significantly lower in comparison to those in the PS group ($p < 0.05$).

Increased levels of high-sensitivity CRP and UA in the group of patients with PsA were noted in 78.82% (18 persons) and 21.73% (5 persons) respectively (Table 2).

As can be seen from the data presented in Table 2 in the group of patients with PsA determined elevated levels of CRP, SC, TCh, LDL cholesterol, compared to patients with abnormal joints, in the absence of a significant difference in the combination of RF.

The obtained results indicate that the average value of TIMC CA in the group of patients with PsA is significantly higher than the mean value of this index in patients with PS ($p < 0.05$), indicating the presence of changes in the vascular wall, its thickening, which can be regarded as subclinical manifestations of atherosclerosis in patients with PsA (Table 2).

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 serum FG level > 4 g/l was observed in 7 (21.87%) patients, with an average serum FG level of 4.2 ± 0.2 g / L. It was also found that serum FH 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 order to identify the factors that caused the greatest influence on the degree of severity of atherosclerosis in patients with PsA, a correlation analysis of all the studied parameters was performed and an analysis of patient outpatient card data for the previous 2 years on the level of CRP, it was found that the greatest influence on TIMC CA was found to be DAS 28, TCh,

LDL cholesterol, CRP, FG, PASI ($r = 0.54, 0.68, 0.67, 0.53, 0.52, 0.43$, respectively). In the group of patients with DAS 28 of medium and high activity ($> 3,2$), a strong correlation between the amount of TIMC CA and uric acid ($r = 0.61$) was found. The level of HDL cholesterol was associated with the median power of the CRP and the level of uric acid. A direct correlation was found between the level of FG and CRP and SC, ($r = 0.54, 0.48$, respectively). This analysis in the group of patients with PS revealed: direct correlation between mean strength between TIMC and CA, LDL cholesterol, CRP ($r = 0.37, 0.39, 0.38$, respectively).

Conclusion

According to the results of our study, it was found that in patients with PsA, the severity of the atherosclerotic process was greater in comparison with patients with PS (profiles RF were identical).

According to the results of the correlation analysis in the group of patients with PSA, the greatest influence on the severity of the atherosclerotic process in the CA had CRP (average level for 2 years), DAS 28, TCh, LDL cholesterol, FG, PASI, and in patients with PS- TCh, LDL cholesterol, CRP .

The highest levels of CRP, FG, UA, TIMC score, and atherosclerotic plaque frequency were detected in patients with PsA, which may indicate a pathogenetic linkage of the immune-inflammatory process with the development of a more common atherosclerotic process.

Individuals with PsA require an additional examination (determination of levels of CRP, FG in serum, and ultrasound of CA) for a more accurate assessment of the risk of CVD.

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Table 1 Clinical and demographic characteristics of patients with CVD FR

Indicator	PS n=19	PsA n=32
Age, years	32,3±5,63	39,62±4,8
Women,(n/%)	7 (35,3%)	15 (46,87%)
Men,(n/%)	12 (64,7%)	17 (53,12%)
Average duration of the disease	4,1±0,57	10,42±0,34
DAS 28		
Remission <2,6	2 (8,69%)	0
Low activity level 2,6-3,2	5 (21,73%)	0
Average degree of activity 3,2-5,1	12 (52,17%)	0
High degree of activity >5,1	4 (17,39%)	0
PASI	14,36±1,12*	7,2±1,05

Table 2 Risk factors for CVD and the state of the vascular wall in the examined groups of patients

Indicator	PsA n=32	PS n=19
Smoking (at any time in the last 10 years), n,% of people	68,75% (22 of people)	52,63% (10 of people)
Abuse of alcohol, n,% of people	12,5% (4 of people)	10,5% (2 особи)
Hypodynamia, n,% of people	46,87% (15 of people)	47,3% (9 of people)
Adiposity, n,% of people	15,62% (5 of people)	15,78% (3 of people)
Stress,n,% of people	93,75% (21 of people)	84,2% (16 of people)
The heredity of cardiovascular disease is encumbered, n,% of people	68,75% (22 of people)	42,1% (8 of people)
TCh, mmol / l	5,37±0,2*	
	4,17±0,44	
TG, mmol / l	2,45±0,4*	1,52±0,3
HDL cholesterol, mmol / l	1,19±0,1*	0,76±0,1
LDL cholesterol, mmol / l	3,45±0,8*	2,43±0,3
VLDL cholesterol, mmol / l	0,81±0,4*	0,5±0,1
Index of atherogenicity, c.u.	3,69±0,9*	2,47±0,2
CRP, (mg/l)	8,5±1,79*	4,45±0,53
UA (mkmmol / l)	402,85±15,24*	326,68±15,59
Fibrinogen	2,94±1,02	1,97±0,77
SCORE	3,11±0,33*	1,43±0,11
<2 CVD RF	13.05%*	15,1%
3-5 CVD RF	69.56%*	68,1%
>5 CVD RF	17.39%*	16,8%
Average value TIM CA, мм	0,93±0,2*	0,7±0,1
TIMC >0.9	45,83%*	22, 58%
Number of atherosclerotic plaques CA	2*	0

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

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