FEATURES OF HEMOSTASIS IN RHEUMATOID ARTHRITIS PATIENTS WITH ISCHEMIC HEARTH DISEASE

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ABSTRACT

As in the developed countries of the world, a number of scientific studies in the field of RA and AS have been carried out in recent years. Rheumatoid arthritis (RA) remains the focus of researchers due to its multifactorial origin, complex and completely unclear pathogenesis. This article presents materials on the effect of rheumatoid arthritis (RA) on the parameters of the hemostasis system in patients with coronary heart disease. In order to study this work, 86 RA patients with associated CAD were examined, and hemostasis parameters were compared with the RA group without CAD, which consisted of 40 patients. The influence of age, gender, RA disease activity on hemostasis parameters in this category of patients was analyzed.

Key Words: rheumatoid arthritis, inflammation, hemostasis, cardiovascular diseases, cardiovascular risk

INTRODUCTION

Rheumatoid arthritis (RA) is a global health problem with an estimated prevalence of 0.24% worldwide [1,2]. The World Health Organization (WHO) classifies it as one of the diseases with the greatest impact on society, ranking 42nd in the world in terms of disability [2,3].

Rheumatoid arthritis is a disease that occurs with a frequency of about 1% in the general population, while the probability of infection in women is 2.5 times higher than in men [3,4]. Most often, RA begins at the age of 40 to 70 years, with age the disease progresses [5,6]. The peculiarity of RA is that it is characterized by the development of a pathological process involving new joints and extra-articular systems, leading to the formation of irreversible changes leading to rapid disability of patients, as well as a progressive course characterized by a decrease in sensitivity to therapy.

The problem of coronary heart disease (CHD) and its complications in patients with rheumatoid arthritis (RA) is widely discussed in the literature [3,7]. And this is no coincidence. In the structure of the causes of premature death in RA, the largest share falls on coronary artery disease and its complications [4,8]. Epidemiological studies [9,10] show a high incidence of myocardial infarction and sudden coronary death in patients with RA. The relative risk (RR) at the same time exceeded the general population indicators by more than 2 times.

Purpose of the study. To study the indicators of coagulation and cellular hemostasis in patients with RA, depending on the degree of activity of the inflammatory process of associated coronary heart disease.

MATERIAL AND RESEARCH METHODS

A prospective and retrospective comparative study was carried out. The study included 86 patients with cardiovascular pathology in combination with RA, receiving treatment at the Bukhara Regional Multidisciplinary Medical Center in the Department of Rheumatology in 2018-2020.

Characteristics of rheumatoid arthritis. Characteristics of patients in the study group are presented in Table 1.

CHARACTERISTICS OF RHEUMATOID ARTHRITIS

Characteristics of patients of the study group are presented in table number 1.

	Total	Gender		Average age Me	Average duration of diseases Me	Clinical types	
Groups		F	M			Seropositive RA	Seronegative RA
Patients RA + IHD	86	65	21	55 ±3.1 P<0.05	8,3±1.2 P<0.05	31 (36%)	55 (64%)
Patients RA without IHD	40	29	11	50±2.5 P <0.05	8.9±0.5 P <0.05	25 (62,5)	16 (40)
Control healthy	30	19	11	51,7±4.1	-	-	-

Note: p-differences

The majority was diagnosed with a late stage of the disease - 47 (53.2%) advanced - in 22 (24.3%) early - in 17 (19.1%) patients. The group was dominated by patients with high RA activity, the average value of DAS 28 was 5.75 (4.60 7.38). Extra-articular manifestations of the disease were in 32 (32.5%) patients: rheumatoid nodules in 42 (46.8%) vasculitis - 12 (22%) peripheral polyneuropathy - 11 (15.9%) pleurisy - 5 (5.4%) Sjögren's syndrome 3 (3.1%). Most of the subjects were seropositive for RF - 57 (61%). Most of the patients had 2 and 3 x-ray stages of joint damage - 35 (37.2%) and 37 (62.8%) 2 and 3 functional class 17 (18.1%) and 55 (58.5%), respectively.

The diagnosis of ischemic heart disease (IHD) was verified on the basis of clinical, laboratory, and instrumental data [5]. All patients underwent ECG in 12 standard leads using a Schiller AT-10 Plus device (Schiller, Switzerland) and daily monitoring of blood pressure and ECG according to the generally accepted method using bifunctional monitors Cardio Tens-01 and Meditech card(x)plore (Hungary). The level of lipids in blood serum was determined by the enzymatic method on an automatic analyzer V/M HITACHI 902 (RocheB/M, France).

The main goal of our work was to study the parameters of coagulation and vascular-platelet hemostasis in patients with IHD in combination with RA. The influence of age, gender, disease activity on hemostasis parameters in this category of patients was analyzed.

Statistical processing was carried out on a TOSHIBA personal computer using the Microsoft Office Excel - 2008 software package, including the use of built-in statistical processing functions. The methods of traditional variational parametric and nonparametric statistics were used with the calculation of the arithmetic mean of the studied indicator (M), the standard error of the mean (m), relative values (frequency, %), the statistical significance of the measurements obtained when comparing the average values was determined by Student's t test (t) with the calculation error probability (p). Significant level p<0.05 was taken as statistically significant changes.

RESULTS OF THE STUDY AND DISCUSSION

As you know, normally most platelets are in an inactive form in all vessels of the bloodstream. However, under pathological conditions, such as systemic inflammation, platelets can spontaneously activate without contact with the subendothelium [4]. The process of aggregation consists in the attachment of activated platelets in the

blood stream to each other and to previously fixed platelets in the area of damage, mediated by fibrin and von Willebrand factor [6,7].

We have evaluated the parameters of hemostasis depending on the activity of RA. The studied patients were divided into groups with moderate and high activity according to the RA classification. The group with moderate RA activity included 33 people whose DAS 28 was below 5.1, on average - 4.68 (4.51; 4.88). In the group with high activity (DAS28 more than 5.1) 43 people, in this group the average value of DAS 28 was 6.21 (5.56; 6.68).

The study of the level of PT, PTI, APTT, INR, fibrinogen in the study group was carried out. In our study, the activity of PT, APTT and INR in RA in association with CVD were lower than the values of the control group ($p1<0.05$). The superiority of such factors as APTT, higher values of PTI and fibrinogen in RA+CHD were more accurately observed in comparison with the group, which included patients with RA only ($p1<0.05$).

To assess the dependence of the dynamics of coagulation hemostasis parameters depending on the activity of RA, the values in patients with moderate and high RA activity were considered. The table shows that the levels of PT, APTT, INR in RA in association with CHD were lower (and higher values of fibrinogen and PTI) in RA + CHD with high RA activity compared with the group, which included patients with only moderate RA activity ($p <0.05$). GH-GAT values were lower, while other platelet values Ptc, MPV, PDW were higher than control values and in the group of patients with RA + CHD ($P <0.05$) with a high activity of the inflammatory process, in comparison with the group of RA with moderate activity ($P1<0.05$). When evaluating the relationship between indicators of coagulation and growth hormone and clinical manifestations of coronary artery disease and RA, it was found that the longer the duration of the disease and the higher the activity of the inflammatory process, the more pronounced hypercoagulability.

Since atherothrombosis is the leading pathogenetic mechanism for the development of cardiovascular accidents, it is of undoubted interest to assess the state of hemostasis in patients with RA and IHD depending on age.

To assess the effect of age on the parameters of the hemostasis system, all patients were divided into 2 age groups: group I consisted of 40 patients under 50 years of age (inclusive), group II consisted of 46 patients over the age of 50 years. According to the material, it can be seen that the levels of PT, APTT, INR in RA in association with coronary artery disease were lower (and higher values of PTI and fibrinogen) in patients with RA + IHD over 50 years of age in comparison with the RA+ IHD group under the age of 50 years ($p <0.05$). In this regard, we can assume an increased risk of thrombus formation in people of the older age group with RA.

In a comparative analysis of the timing of the development of concomitant diseases in RA patients who fell ill at a young and old age, it was found that concomitant diseases in the latter develop in a shorter time from the onset of RA. Thus, only the advanced age of RA onset is an independent risk factor for premature mortality [8,10].

The same picture was observed in the dynamics of the above indicators, analyzed depending on the duration of the disease. The table shows that the levels of PTI, fibrinogen in RA in association with IHD were higher (and lower values of PT, APTT, INR) in patients with RA + IHD with a disease duration of more than 5 years compared with the RA + IHD group with a disease duration less than 5 years ($p <0.05$).

Our data confirm that chronic inflammation leads to disorders of the blood coagulation system in the direction of hypercoagulability, and subsequently to thrombosis, and the more experience and age of patients with RA + IHD and the higher the activity of inflammatory joint disease, the more pronounced are the changes in coagulation hemostasis towards hypercoagulation. Consequently, the majority of patients with coronary artery disease in combination with RA have an increased risk of developing thrombotic complications due to severe hyperfibrinogenemia and thrombinemia. In this regard, it can be assumed that there is an increased risk of thrombus formation with the progression of the disease. CAT scores were lower, while Ptc, MPV, PDW scores were higher in RA+IHD patients over 50 years of age and with a disease duration of more than 5 years ($P<0.05$) compared to the RA+IHD group aged less than 50 years and with disease duration less than 5 years.

The study of the hemostasis system allows you to determine the group of patients with the highest risk of developing thrombotic complications requiring special therapy and laboratory control.

CONCLUSION

Our data confirm that chronic inflammation leads to a violation of the blood coagulation system in the direction of hypercoagulability with subsequent thrombosis, and that the age and age of patients with RA + IHD, the higher the activity of inflammatory diseases of the joints, the more accurate is the change in coagulation hemostasis in relation to hypercoagulability. Consequently, the majority of patients with coronary artery disease have an increased risk of developing thrombotic complications due to severe hyperfibrinogenemia and thrombinemia in combination with RA. The study of the hemostasis system makes it possible to identify a group of patients with a high risk of developing thrombotic complications requiring special therapy and laboratory control. There were determined three main conclusions:

1. There is a direct correlation between the change in coagulation hemostasis depending on the severity of the activity of the inflammatory process in rheumatoid arthritis in association with coronary heart disease.

2. Indicators of vascular - platelet hemostasis have a high degree of activity in a positive correlation with the severity of the inflammatory process in rheumatoid arthritis in association with coronary artery disease.

3. Indicators of coagulation and vascular-platelet hemostasis are highly dependent on the duration and age of patients with rheumatoid arthritis in association with coronary artery disease.

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