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Evaluation of Endothelial Disorders in Patients with Ankylosing Spondylitis and Post Covid Period

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Abstract

Purpose of the study. To study the state of endothelial function in patients with ankylosing spondylitis who have undergone COVID-19 by assessing the flow-dependent vasodilation of the brachial artery and endothelin-1 in serum. The study involved 80 patients, of which 40 patients (average age 42,3±2,8 years) diagnosed with ankylosing spondyloarthritis who underwent COVID-19 (group I); 40 patients diagnosed with ankylosing spondyloarthritis (average age 46,3±5,7 years, who did not tolerate COVID-19, 32 healthy volunteers (average age 30,3±6,8 years) made up the control group. Endothelin-1 in serum was determined by enzyme-linked immunosorbent assay; flow-dependent vasodilation of the brachial artery was determined using Philips Affinity 70 (Release 3,0.3, Philips Healthcare, USA).

Results. Analysis of endothelin-1 levels showed statistically significant differences in this indicator between healthy children and patients with groups I and II (0.213 [0.012; 0.368] and 0.227 [0.15; 0.315] pmol/L, respectively; p=0,027). Flow-dependent vasodilation of the brachial artery in healthy individuals was 9.82 [7.8; 11.2]%, in patients of groups I and II this indicator tended to decrease - 9.46 [6.5; 10.8]% and 9, 11 (p = 0, 026).

Conclusion. A study of endothelial function in patients with ankylosing spondyloarthritis revealed an increase in nitric oxide concentration compared to that in healthy, probably compensatory, subjects. The flow-dependent vasodilation of the brachial artery and the endothelin-1 level did not significantly differ from similar parameters of the control group.

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INTRODUCTION

Ankylosing spondylitis (AS) is an autoimmune inflammatory disease with varying degrees of damage to joints, entheses, spine, skin and internal organs. The leading symptoms of the disease are chronic pain in the back and joints, morning stiffness. Since the end of 2019, the coronavirus infection (COVID-19) outbreak has caused serious concern around the world [4]. In the early stage of the pandemic, there was a sharp increase in the incidence of rheumatic autoimmune diseases, in particular the ankylosing spondylitis in patients with COVID-19. Penetrating into various organs and tissues, coronavirus infection leads to endothelial dysfunction, which is the trigger for the development of vascular disorders, including thrombosis [3]. Along with endothelial dysfunction, coronavirus infection triggers autoimmune mechanisms which underlie the development of hemolytic anemias, immune thrombocytopenias, and systemic diseases.

In recent years, numerous studies have been carried out in the field of studying the influence of a

new coronavirus infection on the clinical course of ankylosing spondylitis. In turn, coronavirus infection provokes the development of new clinical manifestations of AS. Given the comorbidity and susceptibility to frequent hospitalizations of patients with AS and postponed coronavirus infection, it is necessary to closely monitor the dynamics of their clinical condition and prevent the development of adverse complications.

MATERIALS AND RESEARCH METHODS

We studied 70 patients with ankylosing spondyloarthritis, which were divided into 2 groups. The main group included 80 patients with AS who underwent COVID-19 at the age of 20-46 years, of which 28 women (16%) and 52 men (84%). The average age of the patients was 38.4±1.2 years. The average duration of the disease was 9.3±2.1 years. The control group included 30 healthy volunteers. The average age of them was 34±2.7 years.

All patients were diagnosed with AS in accordance with the AS criteria. The exclusion criteria were clinical manifestations of coronary artery disease, stroke, high hypertension. Confirmation of the transferred coronavirus infection was the results of a quantitative analysis of IgG to SARS CoV-2 carried out by ELISA, as well as a study of a nasopharyngeal smear by PCR.

All patients underwent standard laboratory and instrumental methods for the diagnosis of AS. In an objective study tests were carried out by Otto-Schober, Thomayer, Kushelevsky 1, 2, 3. Clinical signs of disease activity were also assessed, such as the time of morning stiffness, the severity of the pain syndrome, the Lansbury index, the VAS score, and the BASDAI, ASDAS, BASFI questionnaire was also carried out. Patients underwent X-ray examination of peripheral joints, sacroiliac and vertebral joints (apparatus "Multix-Compact-Siemens", Germany), ECG, echocardiography ("Acuson-Aspen-Siemens", Germany, "Envisor-C-Philips", Netherlands). The blood sera of all patients was taken and analyzed using ELISA kit for Endothelin-1 to investigate the level of endothelin-1. Reactive hyperemia test and nitrotroglycerin (NTG) depended test were carried out to estimate the vasoregulatory function of brachial artery. The ACUSON 128 XP/10 ultrasound system was used to obtain an image of the right brachial artery, and to measure its diameter and blood flow rate.

RESULTS

In the study, the largest share of high and moderate disease activity occurred in the main observation group and amounted to 9 and 39%, respectively, while in the control group, patients with high disease activity were not found, and 15% of patients in this group were in remission. The data indicate the persistence of disease activity in the postcovid period.

Comparative characteristics of the assessment of the scales, as well as clinical and laboratory data of patients in both groups showed high indices of Lansbury, BASDAI, BASFI, ASDAS and VAS scales in the main group than in the control group: 39.2±1.4, 6.2±0.8 and 3.8±0.7, 5.8±0.7 and 17.3±1.1, 2.4±0.7, 3.2±0.9 and 1.8±0.4, respectively which indicates the severity of functional disorders. In 73.4% of the examined patients bilateral sacroiliitis was revealed, enthesopathies - in 96.1%, changes in the heart (disturbances of myocardial excitability, electrical conduction, valve damage, an increase in the size of the chambers) were detected in 68.4% of cases, 48, 3% of which account for the main group of patients.

ESR and C-reactive protein indices in the study and control groups were 47.3±2.1 and 22.5±1.6, 28.6±3.2 and 14.3±2.1, respectively. The values of the indices and laboratory parameters are shown in Table 1.

Table 1.

Clinical characteristics of indicators of the course of AS in patients of the main and control groups

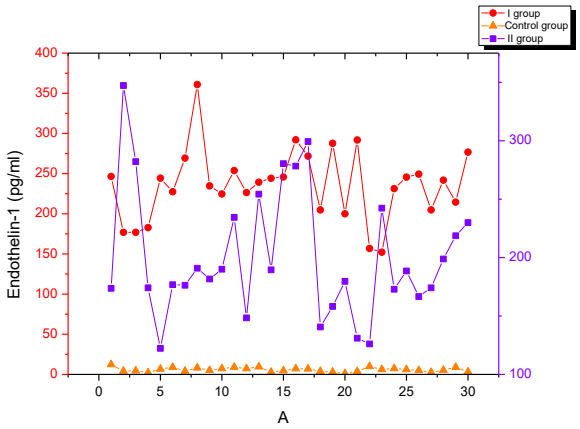
Criteria	Main group (n=50)	Control group (n=20)
Men	42 (84%)	16 (80%)
Female	8 (16%)	4 (20%)
Activity (by ESR)		
Minimum	4(8%)	9 (45%)
Middle	39 (78%)	8 (40%)
High	9(1,8%)	-
Remission	-	3 (15%)
C-reacive protein (mg/l)	28,6±3,2	14,3±2,1
ESR (mm/h)	47,3±2,1*	22,5±1,6
CIC (small, connected with IgG, units)	57,6±1,8*	28,2±1,3
VAS, sm	9,80±1,6	6,1±0,6
HAQ	1,8±0,6	0,8±0,3
BASDAI	6,2±0,8*	3,8±0,7
BASFI	5,8±0,7*	2,4±0,7
ASDAS (by ESR)	3,2±0,9	1,8±0,4
Cardiovascular disorders	48,3%*	20,1%
Enthesopathies	7,6%	2,5%

Note: * - significance of difference between indices of main and control grups, $p<0.05$.

To assess the activity of the disease, we determined the levels of small CICs, which showed the highest results in the main group and confirmed the high level of the inflammatory process in patients who have undergone coronavirus infection. Thus, in the main group, the levels of small CECs showed 57.5±1.8, while in the control group their level was 28.2±1.3. Thus, the data obtained indicate a high level of inflammation in AS patients who have undergone coronavirus infection.

The examination of vasoregulatory function of endothelium in patients with ankylosing spondylitis showed wider diameter of BA in patients of control

group (p<0.05) compared to the diameter inpatients of main group. The examined patients showed lower levels of flow-mediated dilation at the 60th second (p<0.01) in patients with AS, underwent COVID-19, compared to similar indicators in patients of control group. According to the literature, flow-induced dilation is inversely proportional to diameter of vessels, and in arteries with a diameter of 6 mm or less, the average dilatation of the vessel is 10% (Graph 1). The lesser value or vasoconstriction are considered pathological [9]. In patients of main group the flow-dependent dilation did not exceed 10%, which was significantly more common than in patients in control group (x^2=4.82, p<0.05). At the same time, the level of NTG-induced dilation in patients of main group was higher than in control (p<0.001). In patients of control group, the levels of endothelium-dependent and endothelium-independent dilation differed slightly from each other in contrast to patients with AS underwent COVID-19 (p<0.001).



Graph 1. Comparative analysis of endothelin-1 in patients of I, II and control groups

DISCUSSION

On the basis of the results obtained in our study, patients with ankylosing spondyloarthritis who underwent COVID-19 showed persistent activity of the underlying disease, as well as a significant decrease in functional activity. In addition, these patients also had a pathology of the cardiovascular system, which manifested itself in the form of arrhythmias, conduction disturbances, and metabolic disturbances. Thus, coronavirus infection has a direct negative impact on the course of autoimmune diseases, leading to the development of adverse complications.

The lack of connection between the indicators of the functional state of the endothelium and markers of the activity of systemic inflammation is, in our opinion, evidence that the main importance in the development of endothelial dysfunction is not so much the current activity of systemic inflammation as the duration of its existence. An indirect confirmation of this is the inverse relationship between ESRD and the duration of ankylosing spondylitis. The low correlation coefficient is explained by the fact that disease duration is not synonymous with the duration of active inflammation. Ankylosing spondylitis can occur with persistent inactive inflammation, as well as in waves, when periods of improvement are replaced by periods of exacerbation lasting from several weeks to several months and years.

CONCLUSIONS

Determination of the endothelin-1 level and flow-mediated vasodilatation in patients with AS confirmed the presence of endothelial dysfunction against the background of a high degree of disease activity and its severity in patients with AS undergoing COVID-19. Coronavirus infection has a direct effect on the triggering of autoimmune mechanisms, which, in turn, lead to an exacerbation of rheumatic diseases and the persistence of the activity of the process.

A direct negative effect of the postponed coronavirus infection on the course of ankylosing spondyloarthritis was established: a higher activity of the disease, which was confirmed by the BASDAI and ASDAS indices, as well as more pronounced impairments in functional activity, confirmed by the BASFI index. There was also a pathology of the cardiovascular system, which was manifested by impaired excitability, myocardial conduction, damage to the valve apparatus and rhythm disturbances. An increase in the levels of small CECs, ESR and C-reactive protein indices confirmed a higher degree of disease activity and inflammatory processes in AS patients who had undergone COVID-19.

It is necessary to further study the mechanisms of systemic inflammation in patients with ankylosing spondyloarthritis who have undergone COVID-19 and to develop an algorithm for treatment and prophylactic measures in order to prevent the development of adverse complications.

Conflict of interest - The author declares no conflict of interest.

Financing - The study was performed without external funding.

Compliance with patient rights & principles of bioethics - All patients gave written informed consent to participate in the study.

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