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FUNCTIONAL STATE OF ENDOTHELIUM IN PATIENTS WITH ANKYLOSING SPONDYLITIS AFTER COVID-19

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Abstract

Currently, there is no doubt about the importance of the role of impaired endothelial functional state in the development of vascular pathology in a number of diseases, including rheumatic. With the advent and large-scale spread of a new coronavirus infection (COVID-19), a high rate of patient's hospitalizations with ankylosing spondyloarthritis (AS) and the development of extrapulmonary complications, such as myocardial injuries, kidney damage and vascular thromboembolism, were noted. The development of this phenomenon confirms the connection with pronounced endothelial dysfunction and its damage. This article presents the results of evaluation of endothelial dysfunction in AS patients undergoing COVID-19.

Keywords

ankylosing spondylitis, COVID-19, endothelial dysfunction.

Introduction

The coronavirus infection (COVID-19) caused by acute respiratory distress syndrome (SARS-CoV-2) has become a major challenge for patients with autoimmune rheumatic diseases. [2,3,7]. The high risk of complications, an increase in the number of hospitalizations and early incapacity in patients with AS and a previous coronavirus infection remain among the important problems that need to be solved. According to the references, the key for the development of most pathological processes in the body leads to endothelial dysfunction, which involves damage to endothelial cells and a mismatch between vasoconstriction and vasodilation. [1,6]. In autoimmune rheumatic diseases, including AS, immune complex inflammation comes to the fore in vascular damage, which is characterized by the development of productive lymphocytic vasculitis and activation of pro-inflammatory mediators, monocytes and T- cells, which lead to damage to the endothelium [5]. In recent years, data have appeared on damage to the endothelium and the violation of its vasoregulatory function in rheumatic diseases occurring with classic vasculitis of various organs, including AS [4,9]. In

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this article, we evaluated the severity of endothelial dysfunction in patients with ankylosing spondylitis who underwent COVID-19 by determining endothelin-1, as the main biomarker of endothelial dysfunction. The study of the severity of endothelial dysfunction and the development of methods for its correction in the future have as scientific as practical importance.

Materials and methods. The study of patients was carried out at the rheumatology department of the Tashkent clinical hospital. The study included 80 patients with a diagnosis of ankylosing spondylitis according to the modified New York criteria and EULAR. All patients were divided into 2 groups: main group included 40 patients with ankylosing spondylitis without postcovid period, control group included 40 patients with ankylosing spondylitis and postcovid period. Patients with obesity, hypertension, diabetes mellitus, cardiovascular and renal diseases were excluded from the study. The healthy control group included 40 healthy people with no acute and chronic diseases in anamnesis.

Mobility of the spine and hip joints was calculated according to the BASMI index. Disease activity and functional status were established based on BASDAI and BASFI indices. The number of affected enthesis was calculated according to MASES index. The type of joint damage (central or peripheral) was taken into an account. ESR and C-reactive protein levels were also determined. All patients underwent a blood test for HLA-B27. A blood pressure cuff was put on the projection of brachial artery to evaluate the flow- mediated vasodilatation. An air was bumped in up to 30 mm Hg above the systolic blood pressure for 5 min. We measured the diameter of brachial artery every 5s for 2 min. To determine endothelial- independent vasodilatation nitroglycerin tablet was given in 0,0025 mg/min dosage for 3 min. The blood sera of all patients were taken and analyzed using ELISA kit for Endothelin-1 to investigate the level of endothelin-1. 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.

Statistical analyzes were calculated on Origin Pro 7 and Microsoft Excel programs. Spearman's correlation test was used to determine the association between endothelial vasodilatation and clinical parameters for AS.

Results and discussions.

Disease activity in the study groups was assessed by VAS, BASDAI, and ASDASRB. Thus, the high activity of the disease according to VAS was established in patients of main group who underwent COVID-19 (7.04 ± 1.08) and was 1.5 higher compared to the indicators of control group (4,0±0,81). BASDAI and ASDAS (CRP) showed very high disease activity in patients of main group (5,8±0,32 and

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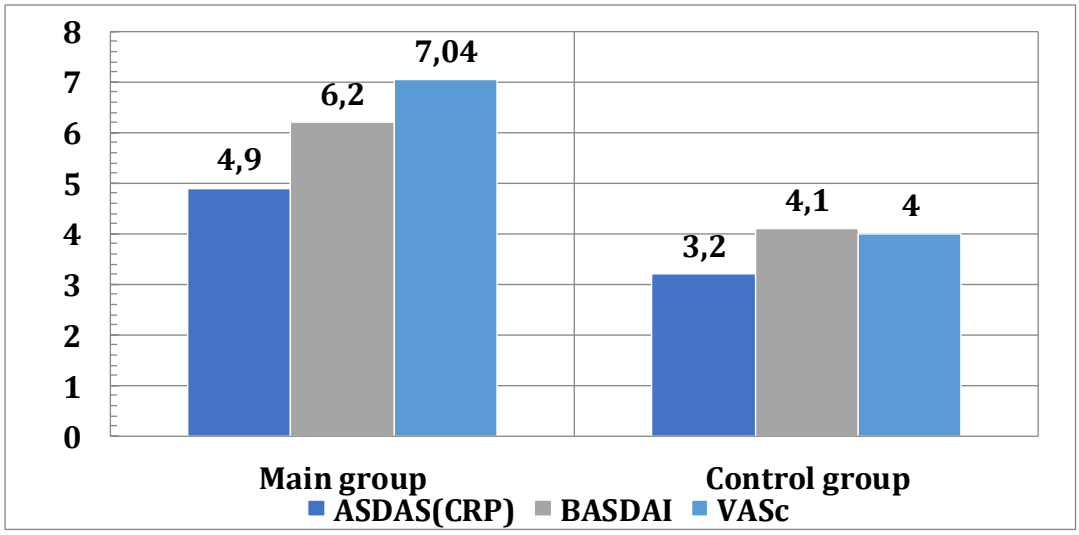
4,9± 0.45) and high activity in control group (4,1±0,621 and 3,2±0,61) (Fig.1). A comparative analysis of BASDAI indices in main group and control group showed that the highest scores were in main group patients when assessing the severity of neck, back, and joint pain (6,7±0,43), the level of joint pain during the week (7,1±0,47), and the duration of morning stiffness (6,2±0,66) compared to group II (4,2±0,44, 4.1 ±0,71, and 4.5 ±0,32, respectively).



* - validity of differences between the two groups $p < 0.05$

Figure 1. ASDAS(CRP), BASDAI, and VASc indices in main and control group patients

The endothelin-1 level was significantly higher in main group compared to control group (309.6 ±47,11 pg/mL versus 252,7±37,09 pg/mL, respectively, $p < 0.05$), while in control group the endothelin level was 5 times higher than the control group ($p < 0.01$). The data obtained by us indicate a pronounced endothelial dysfunction in patients in the post-covid period.

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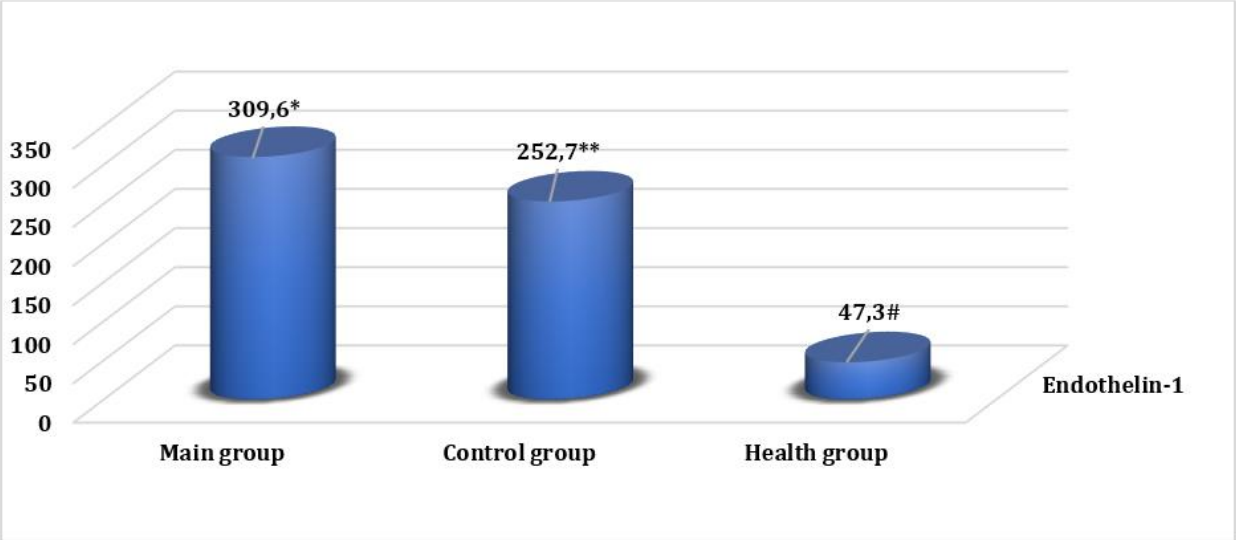

Note: reliable differences of indicators * - between the main and control groups; ** - between the control group and healthy controls; # - between the main group and healthy controls

Figure 2. Endothelin-1 level in the study groups

As described above, the functional state of the endothelium has been studied in various chronic diseases: diabetes mellitus, nephropathy, hypertension and others. However, data in relation to ankylosing spondyloarthritis are scarce and inconsistent. Taking this into account, we examined the degree of flow-dependent vasodilation in the brachial artery in order to assess endothelial function in the study groups (Table 1.).

Table 1

Ultrasound Doppler results of the brachial artery in the study groups

Indices	Main group	Control group	Healthy controls
Baseline blood flow velocity, m/s	0,56±0,09*	0,67±0,13	0,87±0,09
Initial BA diameter, mm	3,68±0,27	3,71±0,15	3,81±0,05
FMD on 60 sec, %	7,74±0,82*	9,87±1,47#	14,37±1,23
FMD on 120 sec, %	10,3±1,18*	13,6±0,87#	18,38±1,44
EIVD on 60 sec, %	14,21±1,47*	18,4±2,11	20,7±2,73

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EIVD on 120 sec, %	17,6±1,18*	20,3±2,71#	24,1±2,19
PI	3,19±0,7*	2,4±0,14	1,8±0,23
RI	0,96±0,4*	0,87±0,23	0,74±0,36

Note: * p <0.05 - reliable differences between the main group and healthy controls, **- reliable differences between the control group and healthy subjects

According to the results of the endothelial functional assessment, the examination of the initial diameter of the brachial artery showed no significant differences in the three study groups (p > 0.05). According to data from foreign studies, flow-mediated brachial artery dilation is directly proportional to the diameter of the artery, which means that in a vessel of 7 mm or less, the increase in the diameter of PA at each minute of dilation should be at least 10%. In the main group of patients, lower flow-dependent dilation (FMD) results were obtained compared to the controls and healthy control groups, namely, brachial artery dilation at 60 seconds in the main and control groups was below 10%, which confirms the presence of endothelial dysfunction in this category of patients (p < 0.05).

Comparing the FMD results at 60 seconds (1st minute dilation) between main and control groups, significant differences in parameters were obtained (p = 0.03), FMD of main group was lower than in control group on 120 seconds (2nd minute dilation),that is, at 120 seconds of dilation, the increase was below 10% (10,3±1,18 and 13,6±0,87, respectively). FMD results at 60 and 120 seconds in the control groups were 14,37±1,23 and 18,38±1,44%, respectively. It should be noted that in patients with AS who have undergone COVID-19, FMD on 60 seconds increases 61% less than in the control group, and on 120 seconds - by 56% less than in the control group. FMD at 60 and 120 seconds in the control group differed significantly from each other, indicating further vasodilation in subsequent minutes.

Thus, the results indicate a pronounced violation of the vasoregulatory function of the endothelium in patients in the postcovid period. This condition, according to literary sources, is justified by generalized endotheliopathy and the development of coagulopathy with perivascular inflammation.

The next step was the study of endothelium-independent peripheral vasodilation (EIVD) by testing with nitroglycerin (0.05 mg). 5 minutes after the

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administration of nitroglycerin, sublingual studies were conducted on the dynamics of the diameter of the brachial artery at 60 and 120 seconds after decompression. Thus, at 60 seconds, group I EIVD was reduced and significantly different from group II ($p < 0.05$). EIVD parameters of group II did not differ significantly from the control parameters, which showed an increase in the PA diameter of more than 10% at the 60th second of decompression. However, at the 120th second of decompression, a lower EIVD was observed in patients of group I, as opposed to the expected one, and amounted to 17,6±1,18%, while in group II the EIVD was 20,3±2,71%, which indicates PA dilatation less than 10%.

A pulse index (PI) study reflecting the vascular wall resistance index of the test vessel, which in group I showed high 3,19±0,7 values and was significantly increased in contrast to indicators II and control groups. The PI values in group II did not differ significantly from the control values and were close to the normal values.

The evaluation of the resistance index in the study groups, reflecting the difference between systolic and diastolic rates of vascular blood flow, showed significantly high values in group I compared to group II ($p = 0.03$). High RI (0,96±0,4) values in patients of group I indicate severe damage to the vascular wall of PsA due to risk factors, impaired systemic hemodynamics and association with cardiovascular events.

Conclusion

Systemic inflammation and inflammatory mediators (CRP, TNF-α, IL-1,-6,-8,-17) can activate endothelial cells. As a result, the production of adhesion molecules, selectins, tissue factor, monocyte colony-stimulating factor increases with a simultaneous decrease in nitric oxide (NO) production. In turn, nitric oxide deficiency contributes to endothelial damage with subsequent violation of its functional state. Endothelial dysfunction is manifested by decreased vasodilation of the vessel, increased maximum systolic and decreased maximum diastolic blood flow velocities, as well as increased pulse index.
Thus, our results indicate a pronounced impairment of vasoregulatory function of endothelium in patients in the postvascular period. This condition, according to literature sources, is substantiated by generalized endotheliopathy and development of coagulopathy with perivascular inflammation.

REFERENCES:

1. Münzel, T., Sinning, C., Post, F., Warnholtz, A., Schulz, E., Mu¨nzel, T., & Mu¨nzel, M. (2009). *Pathophysiology, diagnosis and prognostic implications of endothelial dysfunction*. https://doi.org/10.1080/07853890701854702.

2. Sanchez-Piedra, C., Diaz-Torne, C., Manero, J., Pego-Reigosa, J. M., Rúa-Figueroa, Í., Gonzalez-Gay, M. A., Gomez-Reino, J., & Alvaro-Gracia, J. M. (2020). Clinical features and outcomes of COVID-19 in patients with rheumatic diseases treated with biological and synthetic targeted therapies. *Annals of the Rheumatic Diseases*, *79*(7), 988–990. https://doi.org/10.1136/annrheumdis-2020-217948.

3. D'Antiga, L. (2020). Coronaviruses and Immunosuppressed Patients: The Facts During the Third Epidemic. *Liver Transplantation*, *26*(6), 832–834. https://doi.org/10.1002/lt.25756

4. Uhrin, Z., Kuzis, S., & Ward, M. M. (n.d.). *Exercise and Changes in Health Status in Patients With Ankylosing Spondylitis*. Retrieved August 22, 2021, from https://jamanetwork.com/

5. Steyers, C. M., & Miller, F. J. (2014). Endothelial Dysfunction in Chronic Inflammatory Diseases. *Int. J. Mol. Sci*, *15*, 11324–11349. https://doi.org/10.3390/ijms150711324

6. Liew, J. W., Castillo, M., Zaccagnino, E., Katz, P., Haroon, N., & Gensler, L. S. (2020). *Patient-reported Disease Activity in an Axial Spondyloarthritis Cohort during the COVID-19 Pandemic*. *2*(9), 533–539. https://doi.org/10.1002/acr2.11174

7. Roux, C. H., Brocq, O., Gerald, F., Pradier, C., & Bailly, L. (2020). Clinical impact of COVID-19 on a French population of spondyloarthritis patients. In *Clinical Rheumatology* (Vol. 39, Issue 11, pp. 3185–3187). Springer Science and Business Media Deutschland GmbH. https://doi.org/10.1007/s10067-020-05413-9

8. Vasina, L. V., Petrishchev, N. N., & Vlasov, T. D. (2017). Markers of endothelial dysfunction. *Regional Blood Circulation and Microcirculation*, *16*(1), 4–15. https://doi.org/10.24884/1682-6655-2017-16-1-4-15

9. Ahmed, S., Zimba, O., & Gasparyan, A. Y. (2021). COVID-19 and the clinical course of rheumatic manifestations. *Clinical Rheumatology*, *40*(7), 2611–2619. https://doi.org/10.1007/s10067-021-05691-x

10. Sari, I., Okan, T., Akar, S., Cece, H., Altay, C., Secil, M., Birlik, M., Onen, F., & Akkoc, N. (2006). Impaired endothelial function in patients with ankylosing spondylitis. *Rheumatology*, *45*(3), 283–286.

https://doi.org/10.1093/RHEUMATOLOGY/KEI145

11. MB Rakhimova, KS Akhmedov THE IMPACT OF SEQUELAE OF COVID-19 ON THE COURSE OF ANKYLOSING SPONDYLITIS// Central Asian journal of medicine, 2021

12. Rakhimova M. B., Akhmedov K. S., Turaev Y. A. Endothelial dysfunction as a link in the pathogenesis of ankylosing spondylitis against the background of a new coronavirus infection //ACADEMICIA: An International Multidisciplinary Research Journal. – 2021. – Т. 11. – №. 3. – С. 2493-2498.

13. МБ Рахимова Нарушение Ритма И Проводимости У Больных Анкилозирующим И Псориатическим Спондилоартритом//Central Asian Journal of Medical and Natural Science, 2023