JOURNAL OF ADVANCED SCIENTIFIC RESEARCH

ISSN: 0976-9595

Journal of Advanced Scientific Research (ISSN: 0976-9595)
Vol.5. Issue 9 page 2
Impact factor 9

Editorial Team

C/O Advanced Scientific Research,
8/21 Thamotharan Street,
Arisipalayam, Salem

Journal of Advanced Scientific Research (ISSN: 0976-9595)
Vol.5. Issue 9 page 3
Impact factor 9

INQUIRY OF THE CORRELATION OF THE FEATURES OF ATHEROSCLEROSIS AND PROINFLAMMATORY CYTOKINES IN SYSTEMIC SCLEROSIS

Agzamova G.S.[1], Abduazizova N.X.[2], Tashmukhamedova M.K.[3] Aripova N.N.[4]

[1]DSc, professor of the Department of faculty and hospital therapy №1 with course of professional pathology of Tashkent Medical Academy of Uzbekistan
[2]PhD, associate professor of the Department of faculty and hospital therapy №1 with course of professional pathology of Tashkent Medical Academy of Uzbekistan
[3]Assistant of the Department of faculty and hospital therapy №1 with course of professional pathology of Tashkent Medical Academy of Uzbekistan
[4] PhD, assistant of Department of internal disease №2 with endocrinology of Tashkent Medical Academy of Uzbekistan

Abstract In a number of studies, it has been confirmed that cardiovascular complications caused by atherosclerotic damage of blood vessels lead to a decrease in life expectancy in systemic diseases. This calls for a systematic approach to the diagnosis and treatment of systemic sclerosis (SS) and further research to address this issue. The aim of the study was to analyze the relationship between risk factors and inflammatory mediators of early atherosclerosis in patients with systemic scleroderma. Materials and methods 86 patients involved in the study were divided into three groups according to the type of treatment: patients in group 1 (n-34) received conventional treatment according to the recommendations of the standard of care for SS, group 2 (n-29) received treatment according to the standard of care for patients in the 2nd group (n-29) statin (atorvastatin drug in the amount of 20-40 mg for 6 months) in addition to traditional treatment, tocilizumab (8 mg/kg) according to the scheme (8 mg/kg) dose in the form of injection once every 4 weeks) was prescribed for 6 months. Before treatment and after treatment, general clinical (general blood analysis, general urine analysis), biochemical (AlT, AsT, bilirubin, urea, creatinine, total protein), lipid spectrum indicators (Chol, LDLP, HDLP, TG), cytokine (IL-6) was checked in blood serum based on immunological examinations (SRP, RF) and special laboratory analyses. An increase in the thickness of the intima media complex (IMC) (from 0.9 to 1.2 mm) and an atherosclerotic plaque (local enlargement of the IMC ≥ 1.2 mm) were used as criteria for atherosclerotic damage to the vessels. Through this examination, the thickness of IMC the right and left carotid arteries was checked and their average was calculated. In this way, atherosclerotic damage of vessels was evaluated. Results. Analyzing of cardiovascular risk factors in patients with SS according to the number of occurrences, it was found that among the patients included in our study, family anamnesis, arterial hypertension, the increase in the amount of total cholesterol and TG were

reliably higher than in the control group (p<0.05). SS is a disease characterized by a high rate of cardiovascular complications. Early atherosclerosis risk factors were found in 77 (89.5%) patients in the study group and 17 (56.7%) in the control group. 1-3 risk factors were found in 32.5% of patients, 3-5 risk factors in 18.6% and more than 5 risk factors in 38.4%, and no risk factors were observed in 10.5% of patients. In the control group, 1-3 risk factors were recorded in 26.7%, 3-5 risk factors in 13.3%, and more than 5 early atherosclerosis risk factors in 16.7%. Changes in IL-6 levels in relation to disease activity and progression, IL-6 levels increased as disease activity increased in SS patients, and IL-6 levels were observed to be higher in the acute course of the disease. IL-6 cytokine was found to be correlated with lipid spectrum indicators and SRP, and it was distinguished that there is a positive correlation between IL-6 and SRP, atherosclerosis risk factors Chol, TG, LDLP and negative correlation between HDLPs. Conclusions In patients with systemic scleroderma, there was a positive correlation between IL-6 and SRP, atherosclerosis risk factors, body weight index, Chol, TG, LDLP and negative correlation between HDLP. In patients with systemic scleroderma, a positive effect of monoclonal antibody drugs on the cardiovascular system was revealed, that is, it was manifested by an increase in the ejection fraction of the left ventricle by 6.1% and a decrease in the thickness of the IMC by 8.8%.

Keywords: Systemic scleroderma, early atherosclerosis, risk factors, inflammatory mediators

In systemic sclerosis (SS) with varying degrees of severity and progression, complications resulting from internal organ damage are usually the cause of death in many patients [1-3,13]. Primary damage to the heart that develops directly as a result of SS is manifested by changes in the myocardium, pericardium and valvular apparatus [6,12]. Cardiac pathologies in patients can also appear as secondary lesions under the influence of acute sclerodermic kidney and pulmonary hypertension [2,14-16]. Vasculopathies in SS are characterized by remodeling of the microcirculatory network, which may contribute to the development of various changes in the cardiovascular system [4-5,8,11]. Endothelial dysfunction and hemorheological disorders characteristic of systemic sclerosis are also risk factors for the early development of atherosclerosis [7-10].

The aim of the study was to analyze the relationship between risk factors and inflammatory mediators of early atherosclerosis in patients with systemic scleroderma.

Materials and methods. Clinical research was conducted in 2020-2022 in the departments of rheumatology and arthrology, cardiorheumatology and arthrology specialized outpatient treatment course of the multidisciplinary clinic of the Tashkent Medical Academy. 86 patients with

a diffuse form of SS, aged 18 to 50 years (average age 37.6±10.3 years), with an average disease duration of 10.7±7.9 years, were involved in the study. 75 (87.2%) of them were women and 11 (12.8%) were men. As a control group, 30 healthy individuals, 26 (86.7%) women and 4 (13.3%) men, matched to patients with SS in terms of gender, age, risk factors, arterial blood pressure, lipid spectrum, were taken. All patients involved in the study were divided into three groups according to the type of treatment: patients in 1st group (n-34) received conventional treatment according to the recommendations of the standard of care for SS, 2nd group (n-29) received treatment according to the standard of care for patients in the 2nd group (n-29) statin (atorvastatin drug in the amount of 20-40 mg for 6 months) in addition to traditional treatment, tocilizumab (8 mg/kg) according to the scheme (8 mg/kg) dose in the form of injection once every 4 weeks) was prescribed for 6 months. Before treatment and after treatment, general clinical (general blood analysis, general urine analysis), biochemical (AlT, AsT, bilirubin, urea, creatinine, total protein), lipid spectrum indicators (Chol, LDLP, HDLP, TG), cytokine (IL-6) was checked in blood serum based on immunological examinations (SRP, RF) and special laboratory analyses. The amount of IL-6 was determined in the laboratory of the Republican Specialized Pediatric Scientific and Applied Medicine Center using immunoenzyme analysis Human IL-6 ELISA 1 x 96-Well Strip Microplate equipment. Accordingly, IL-6 levels of 0-10 pg/ml were taken as normal values.

Also, ECG, EchoCG, chest x-ray, USD of internal organs, EGDFS according to the instructions, dopplerography of the carotid artery were conducted. Blood lipid spectrum indicators were determined by HUMAN (Germany) equipment chol, LDLP, HDLP, TG. Doppler imaging of both carotid arteries was performed on Samsung Medison SonoAce X6 (CHINA) to detect signs of early atherosclerosis. An increase in the thickness of the intima media complex (IMC) (from 0.9 to 1.2 mm) and an atherosclerotic plaque (local enlargement of the IMC ≥ 1.2 mm) were used as criteria for atherosclerotic damage to the vessels. Through this examination, the IMK thickness of the right and left carotid arteries was checked and their average was calculated. In this way, atherosclerotic damage of vessels was evaluated.

Results: the frequency of risk factors of early atherosclerosis in patients with SS is estimated based on a number of subjective, anamnestic and objective clinical-biochemical laboratory analyses. According to him, when analyzing cardiovascular risk factors in patients with SS according to the number of occurrences, it was found that among the patients included in our study, family anamnesis, arterial hypertension, the increase in the amount of total cholesterol and TG were reliably higher than in the control group ($p<0.05$) (Table 1).

Table 1.

The number of cardiovascular risk factors in patients with systemic scleroderma

Cardiovascular risk factors	Patients with SS,n=86		Control group,n=30	
	п	%	п	%
Smoking	10	11,6	3	10
Family anamnesis (AH, IHD)	49	56,9	9	30
Menopause	26	30,2	7	23,3
Body mass index > 25 kg/m2	26	30,2	13	43,3
Abdominal circumference >88 cm	31	25,6	11	36,7
Arterial hypertension	59	68,6	8	26,7
Chol > 5 mmol/l	75	87,2	12	40
LDLP > 3 mmol/l	81	94,1	13	43,3
HDLP < 0.9 mmol/l	63	73,3	0	0
TG > 1.8 mmol/l	83	96,5	9	35,3
AC E: 4.0 A: up to 3.4 mmol/l	85	98,8	2	6,7

Note: Chol - cholesterol, LDLP - low-density lipoprotein, HDLP - high-density lipoprotein, TG - triglyceride, AC - atherogenic coefficient for this and other tables.

SS is a disease characterized by a high rate of cardiovascular complications. As shown in Figure 1, when analyzing risk factors for early atherosclerosis in patients with SS, early atherosclerosis risk factors were identified in 77 (89.5%) patients in the study group and 17 (56.7%) in the control group.

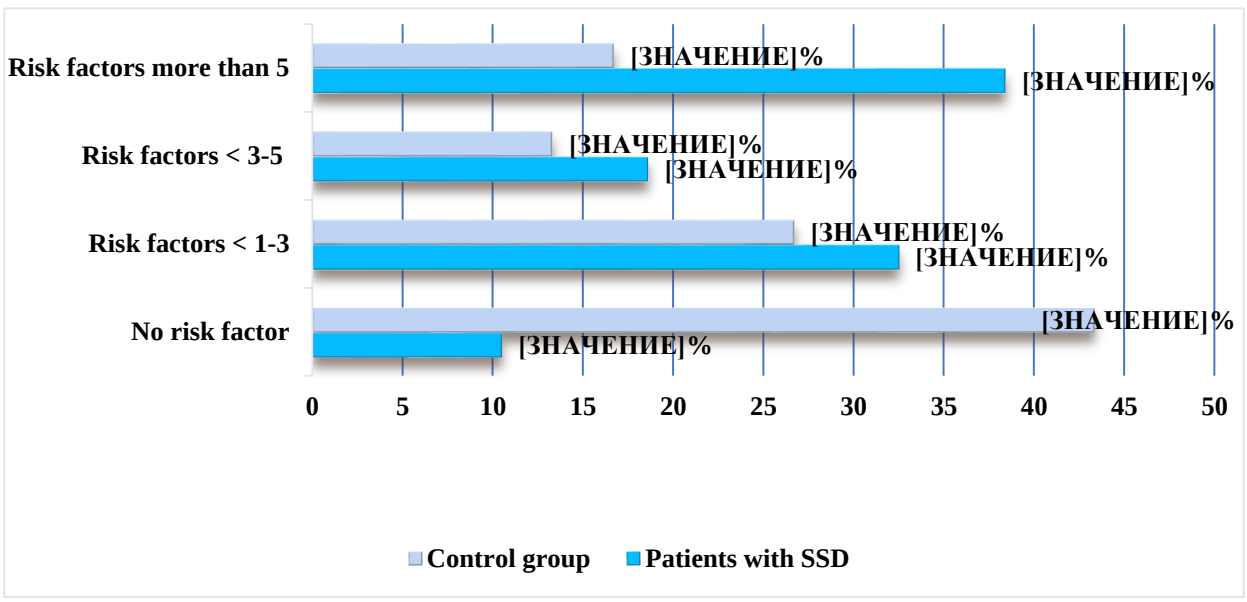

Figure 1. Analysis of cardiovascular risk factors in patients and control group (%)

1-3 risk factors were found in 32.5% of patients, 3-5 risk factors in 18.6% and more than 5 risk factors in 38.4%, and no risk factors were observed in 10.5% of patients. In the control group, 1-3 risk factors were recorded in 26.7%, 3-5 risk factors in 13.3%, and more than 5 early atherosclerosis risk factors in 16.7% (Figure 1).

At the same time, the disorder of blood lipid metabolism is also important in the development of early atherosclerosis in patients with SS. According to it, in patients of 1st group, compared to the control group, all indicators of the lipid spectrum before and after treatment were reliably changed, and after 6 months of treatment, the indicators were unreliable compared to the beginning of treatment (Table 2).

Table 2

Lipid spectrum of indicators of patients of 1st group

Indicators	Control group (n-30)	Group 1 (n-34)	
		Before treatment	**After treatment**
Chol, mmol/l	4,8±0,09	6,08±0,19***	6,03±0,14**
TG, mmol/l	1,45±0,05	3,26±0,052**	3,15±0,06**
LDLP, mmol/l	2,16±0,06	3,35±0,062**	3,27±0,065**
HDLP, mmol/l	1,38±0,022	1,04±0,01**	1,05±0,023**
AC, mmol/l	2,48±0,14	4,86±0,13**	4,74±0,11**

Note: * - differences are significant compared to the indicators of the control group (*- p<0.05, ** - p<0.01, * - p<0.001);**

In 2nd group, the values changed reliably compared to the control group, but less reliable (p<0.05) decreases in chol, LDLP, AC and unreliable changes in TG, HDLP were observed after treatment (Table 3).

Table 3

Lipid spectrum of indicators of patients of 2nd group

Indicators	Control group (n-30)	Group 1 (n-29)	
		Before treatment	**After treatment**
Chol, mmol/l	4,8±0,09	6,07±0,18***	5,62±0,21**^
TG, mmol/l	1,45±0,05	3,17±0,07**	2,99±0,083**

LDLP, mmol/l	2,16±0,06	3,29±0,071**	3,04±0,064**^
HDLP, mmol/l	1,38±0,022	1,02±0,027***	1,06±0,021**
AC, mmol/l	2,48±0,14	4,95±0,19**	4,31±0,17**^

Note: * - differences are significant compared to the indicators of the control group (*- p<0.05, ** - p<0.01, * - p<0.001); ^ - differences are significant compared to pre-treatment indicators (^ - p<0.05).**

After 6 months of treatment of patients of 3rd group, chol, TG, LDLP and AC decreased reliably (p<0.01) compared to the beginning of treatment, and HDLP increased reliably (p<0.01) and showed normative indicators (4 -table).

Table 4

Lipid spectrum of indicators of patients of 3rd group

Indicators	Control group (n-30)	Group 1 (n-23)	
		Before treatment	**Before treatment**
Chol, mmol/l	4,8±0,09	6,11±0,24***	4,98±0,12^^
TG, mmol/l	1,45±0,05	3,22±0,065**	1,48±0,071^^
LDLP, mmol/l	2,16±0,06	3,21±0,057**	2,19±0,054^^
HDLP, mmol/l	1,38±0,022	1,03±0,026**	1,32±0,01^^
AC, mmol/l	2,48±0,14	4,93±0,16***	2,77±0,11^^

Note: * - differences are significant compared to the indicators of the control group (*- p<0.05, ** - p<0.01, *** - p<0.001); ^ - differences are significant compared to pre-treatment indicators (^ - p<0.05, ^^ - p<0.01).

The detection of cytokine IL-6, which is considered the main marker of systemic immune inflammatory diseases, in the blood serum of patients with SS, evaluation of its changes and observation of its dynamics against the background of treatment is of particular importance in the prognosis of this disease. According to him, when the results were statistically processed, it was observed that the values at the beginning of the study increased reliably (p<0.001) in all groups compared to the control group. This indicates that this inflammatory marker is a reliable criterion in the diagnosis of SS.

When analyzing the changes in the amount of IL-6 in relation to the disease activity and course, it was found that the amount of IL-6 increased as the disease activity increased in patients with SS, and when it was evaluated according to the course of the disease, a higher level of IL-6 was observed in the acute course of the disease.

IL-6 cytokine was found to be correlated with lipid spectrum indicators and SRP, and it was distinguished that there is a positive correlation between IL-6 and SRP, atherosclerosis risk factors chol, TG, LDLP and a negative correlation between HDLP (Fig. 4).

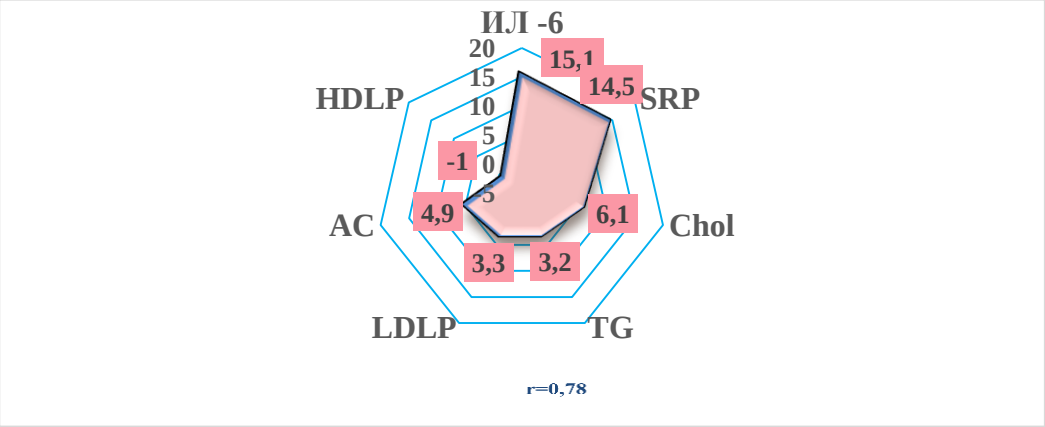

Figure 4. Correlation of interleukin-6 cytokine with lipid spectrum parameters and C-reactive protein

Thus, correct correlation of SRP and IL-6 markers to atherogenic lipoproteins and inverse correlation of antiatherogenic lipoproteins in patients with SS has been confirmed not only in the clinical practice of rheumatology, but also in other areas.

Conclusion Early atherosclerosis risk factors were identified in 89.5% of patients with systemic scleroderma, mainly the increase of atherogenic index, cholesterol and triglyceride levels. In 38.4% of patients, i.e., in almost 1/3, 5 or more risk factors were observed. Among traditional risk factors, family history, arterial hypertension, and hyperlipidemia prevailed (types IIb and IV according to the Fredrickson classification). In patients with systemic scleroderma, there was a positive correlation between IL-6 and SRP, atherosclerosis risk factors, body weight index, Chol, TG, LDLP and negative correlation between HDLP. In patients with systemic scleroderma, a positive effect of monoclonal antibody drugs on the cardiovascular system was revealed, that is, it was manifested by an increase in the ejection fraction of the left ventricle by 6.1% and a decrease in the thickness of the IMC by 8.8%. At the same time, due to the decrease in disease activity under the influence of treatment, a reliable change in dyslipidemia indicators was achieved (Chol 18.4%, TG 54%, LDLP 31.8%, AC 43.8% decrease and HDLP increase by 28.2%) and the exacerbation of atherosclerosis was prevented.

References

1.Guseva N.G., Nevskaya T.A., Starovoitova M.N. Problem of activity in systemic scleroderma // Sovpemennaya rheumatologiya 2013 g. #2. 18-24.

2. Nasonov E.L., Eliseev M.S. The role of interleukin 1 in the development of human development. Scientific and practical rheumatology. 2016;54(1):60-77. doi: 10.14412/1995-4484-2016-60-77

3. Nasonov E.L., ed. Genno-ingenernye biologicheskie preparations vlechenii rheumatoidnogo arthrita. M.: IMA-PRESS, 2013.

4. Nasonov E.L., editor. Anti-V-cell therapy in rheumatology: focus on rituximab. M.: IMA-PRESS, 2012. S. 119-52.

5. Nasonov EL. Pharmacotherapy of rheumatoid arthritis: new strategy, new target. Scientific and practical rheumatology. 2017;55(4):409-419

6. Nasonov EL. Pharmacotherapy of rheumatoid arthritis: new strategy, new target. Scientific and practical rheumatology. 2017;55(4):409-19. doi: 10.14412/1995-4484-2017-409-419

7. Novikova D.S., Popkova T.V., Gerasimov A.N. Vzaimosvyaz cardiovascular factors of risk with arterial stiffness and ginseng with high activity of rheumatoid arthritis. Rational pharmacotherapy and cardiology. 2012; 8(6):756–765.

8. Novikova D.S., Popkova T.V., Kirillova I.G. Otsenka cardiovaskuyarnogo riska u bolnykh rannim rheumatoidnym arthritom v ramkax issledovaniya REMARKA (predvaritelnye danye). Scientific and practical rheumatology. 2015; 53 (1): 24–31.

9. Novikova D.S., Popkova T.V., Kirillova I.G. Otsenka cardiovaskuyarnogo riska u bolnyx rannim rheumatoidnym arthritom v ramkax issledovaniya REMARKA. Practical rheumatology. 2015; 53 (1): 24–31.

10. Oganov R.G., Gerasimenko N.F., Pogosova G.V., Koltunov I.E. Prophylaxis of cardiac and vascular diseases: puti razvitiya // Kardiovaskulyarnaya therapy i prophylactica. – 2011. No. 10(3). - S.5-7.

11. Oganov R.G., Denisov I.N., Simanenkov V.I. i dr. Comorbid pathology in clinical practice. Klinicheskie rekomendatsii.. Cardiovascular therapy and prevention. – 2017. No. 16(6). - S.5-56.

12. Osipova I.V., Starodubova Yu.N., Antropova O.N. Prognozirovanie multifakalnogo atherosclerosis u genshchin with rheumatoid arthritis -2018, No. 5. - S.124-131.

13. Palgueva A.Yu., Lityakov A.M. Rheumatoid arthritis kak factor riska rannego razvitiya atherosclerosis // Vetnik VGMU. -2010. #2 (9). - S. 1-9.

14. Petrov V.I., Shishimorov I.N., Magnitskaya O.B. i dr. Personalizirovannaya meditsina: evolutionary methodology and problems of practical surgery// Vestnik VolgGMU. – 2016, No. 1. - S. 3-13.

15. Pogosova N.V., Oganov R.G., Boytsov S.A. i dr. Effektivnost pervichnoy prophylactici zabolevaniy, obuslovlennyx atherosclerosisom, u patsentiov s vysokim serdechno¬-sudistym riskom v Rossii i drugikh stranax Evropy //Cardiology. – 2017, No. S1. - S. 334-335.

16. Popkova T.V., Novikova D.S. Po materialam novykh rekomendatsiy evropeyskoi antirheumaticheskoy ligi (EULAR) po snizheniyu cardiovascular riska and patients with vospalitelnymi artritami-2015/2016: Obshchaya charakteristicsika i discussionnye problems // Nauchno-prakticheskaya rheumatologiya. -2018, No. 3. - S. 272-279.