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Serum levels of soluble endoglin in patients with systemic lupus erythematosus: association with disease activity and neuropsychiatric manifestations

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Abstract. ***Background.*** Nervous system involvement in systemic lupus erythematosus (SLE) is frequent and diverse. The causes and mechanisms underlying these manifestations remain poorly understood. Recently, the biomolecule endoglin, which is associated with certain neurological and autoimmune diseases, has garnered the attention of researchers; however, its role in the pathogenesis of neuropsychiatric systemic lupus erythematosus (NPSLE) remains unclear. The ***purpose*** was to investigate the serum level of soluble endoglin in patients with SLE, to evaluate its association with demographic parameters and inflammatory activity, and to determine its diagnostic value as a potential marker of NPSLE. ***Materials and methods.*** A total of 96 patients with SLE aged between 19 and 55 years were examined. The level of soluble endoglin in the blood serum was determined using an enzyme-linked immunosorbent assay. ***Results.*** In patients with SLE, the level of endoglin was significantly higher by 90.4 % ($p < 0.001$) compared to the control group. The increase in soluble endoglin concentration was associated with longer disease duration and higher disease activity, as measured by the SLEDAI-1 index. It was not related to sex factors, patient age, or glucocorticoid use. As the level of soluble endoglin increased, the proportion of patients with nervous system involvement also rose. Analysis of mental health indices in patients with SLE, depending on the quartile distribution of endoglin levels, showed that nearly all assessed mental health parameters significantly worsened from the 1st to the 4th quartile. In the Q_4 group, the proportion of patients with confirmed anxiety disorders, depressive disorders, and cognitive dysfunction was statistically significantly higher by 2.4, 5.52, and 2.74 times, respectively ($p < 0.05$), compared to the Q_1 group. A high frequency of memory and sleep disturbances was observed in all quartile groups, without statistically significant intergroup differences. ***Conclusion.*** The serum level of soluble endoglin in patients with SLE was 90.4 % higher than in healthy individuals. Elevated serum levels of soluble endoglin were associated with worsening mental health indices, specifically a significant increase in the proportion of individuals with pronounced anxiety, depressive and cognitive disorders, and insomnia.

Keywords: systemic lupus erythematosus; neuropsychiatric disorders; depression; anxiety; cognitive disorders; endoglin

Introduction

Nervous system disorders in patients with systemic lupus erythematosus (SLE) are quite frequent and diverse. According to various authors, the prevalence of neuropsychiatric SLE (NPSLE) ranges from 12 to 95 %. It manifests itself from banal headaches and cognitive impairment to such rare manifestations of the disease as Guillain-Barre syndrome, a life-threatening autonomic dysfunction [1, 2]. The Association of NPSLE with higher morbidity and mortality has been described in numerous studies [3]. The causes and mechanisms of these lesions are diverse. They are most commonly attributed to the high activity of the disease, the index of damage to internal organs, consistently high titres of autoantibodies (antiphospholipid antibodies, anti-ribosomal, anti-Sm, etc.), and a history of neurological manifestations [4, 5]. However, despite numerous studies, the pathogenesis of NSSLE is still poorly understood [2, 4]. Recently, the endoglin biomolecule (ENG), which is associated with the pathogenesis of certain neurological [6, 7] and autoimmune diseases, has attracted the attention of scientists. Endoglin (ENG, also known as CD105) is a cell surface glycoprotein that is widely distributed in various cells and tissues throughout the human body. As reported, ENG induces activation and proliferation of endothelial

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cells, and its expression is correlated with the degree of adverse disease. Prior studies have revealed the significant upregulation of circulating soluble ENG in patients with various cancers, atherosclerosis, and SLE. In addition, ENG is expressed in tumour cells, endothelial cells, and immune cells in the kidney. The study published in 2025 investigated the role of endoglin in podocyte injury and apoptosis during the development of lupus nephritis, as well as the associated molecular mechanisms [8]. In adults, ENG is mainly expressed by active endothelial cells [9], especially in hypoxia [10], as well as syncytiotrophoblasts [11], macrophages [12], bone marrow stromal cells [13], vascular smooth muscle cells [14]. Today, we know about two isoforms of endoglin: L-endoglin is a predominantly expressed isoform [15] found in large quantities in the human liver [16], and sol-endoglin (a circulating form of endoglin) is induced in senescent endothelial cells [17]. Studies conducted on rodents have shown that sol-endoglin acts as an anti-angiogenic agent opposite to L-endoglin [18].

Hypoxia is another well-known phenomenon that enhances endoglin expression in the endothelium, a mechanism that protects endothelial cells from apoptosis and supports angiogenesis [19]. The opposite effect was observed in the presence of tumor necrosis factor α (TNFα), which reduces endoglin expression in the endothelium [20]. An increase in blood sol-endoglin occurs during various pathophysiological processes, such as endothelial damage, migration, angiogenesis, and inflammation [21]. The level of sol-endoglin in the blood increases in pregnant women with preeclampsia [22], depressive disorders [6].

The clinical relevance of soluble endoglin levels in SLE has been explored in a limited number of studies. Findings from one such investigation demonstrated that endoglin levels in patients with SLE were comparable to those in healthy controls; however, a significant association was observed between elevated endoglin levels and the presence of antiphospholipid syndrome. These results point to a potential pathogenic role of soluble endoglin in the context of SLE [23]. The question of whether sol-endoglin levels can reflect the state of mental health in patients with SLE and serve as an early marker of neuropsychiatric damage remains unclear. The relationship of sol-endoglin with other comorbid conditions, as well as how the activity of this peptide changes under conditions of an active inflammatory process, has also not been studied.

Our study ***purposed*** to investigate the level of sol-endoglin in the blood serum of patients with SLE, to assess its relationship with demographic parameters, the activity of the inflammatory process, and to establish its diagnostic significance as a possible marker of NPSLE.

Materials and methods

Population

A total of 96 patients with SLE, aged 19 to 55 years, who were treated in the Rheumatology Department of the Research Institute for Rehabilitation of People with Disabilities at the Vinnytsia National Pirogov Memorial Medical University, were examined and informed about the purpose of the study.

The diagnosis of SLE was established based on the EULAR/ACR 2019 criteria [24]. SLE activity was evaluated using the SLEDAI index [25]. Organ damage was determined using the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SLICC/ACR DI) [26]. Antiphospholipid syndrome (APS) was diagnosed based on the 2006 International classification criteria [27]. Laboratory assessment of antiphospholipid antibodies (APL antibodies) included the determination of IgG class anticardiolipin antibodies (aCL) using an enzyme-linked immunosorbent assay (ELISA).

Among the examined patients with SLE, there were 7 (7.3 %) men and 89 (92.7 %) women; the average duration of the disease was 6.2 ± 0.4 years, the average age was 37.5 ± 0.9 years, and there was no difference between men and women. The control group consists of 20 practically healthy individuals, with a mean age of 39.00 ± 1.09 years, representative of the population by age and gender.

Methods

The following methods were used to assess the neurological condition of patients: the Zung Depression Self-Assessment Scale [28], the Spielberger Anxiety Scale [29], the Montreal Cognitive Assessment (MoCA) [30], and visual and auditory memory tests. Each patient was examined by a neurologist and psychiatrist.

The serum endoglin content was determined by the ELISA enzyme immunoassay using the Human ENG (Endoglin) ELISA Kit (Fine Biotech, Wuhan, China, Batch No. H0071G091) according to the manufacturer's instructions. Sensitivity of the method (minimum ENG concentration) was ≤ 0.094 ng/ml, and the coefficient of variation was < 10 %. Concentrations of standard solutions for constructing a calibration curve — 0.0, 0.156, 0.312, 0.625, 1.25, 2.5, 5.5, 10 ng/mL. Detection was performed on a Stat Fax 303+ analyzer (USA) at a wavelength of 450 nm (differential filter — 630 nm). The content of pro-inflammatory cytokines — TNFα, interleukin 1-beta (IL-1β) in blood plasma was determined by enzyme-linked immunosorbent assays using standard kits from Calbiotech (Germany) and Diaclone (France).

Statistical analysis of the obtained results was carried out using the generally accepted methods of variational statistics, as implemented in the statistical software package Microsoft Office Excel 2007, to determine the arithmetic mean, quadratic deviation, and the average error of the arithmetic mean. The reliability of the results was estimated using the Student's t-test (discrepancies at $p < 0.05$ were considered statistically significant) and the Fisher criterion.

Ethic approval

The study complied with the basic bioethical norms of the Helsinki Declaration (1989), the Council of Europe Convention on Human Rights and Biomedicine (1977), the International Code of Medical Ethics (1983), the relevant provisions of the World Health Organisation and the laws of Ukraine. This study involves human participants and was approved by the Ethics Committee at the Research Institute for the Rehabilitation of People with Disabilities in Vinny-

tsia, Ukraine, on May 11, 2021. Participants gave informed consent to participate in the study before taking part.

Results

When studying the clinical and diagnostic value of sol-endoglin in patients with SLE, it was found that in the control group, endoglin levels ranged from 1.14–2.56 ng/ml (95% CI) with a median of 1.86 ng/ml and IQR [1.44; 2.15] ng/ml. At the same time, in patients with SLE, endoglin levels ranged from 1.58–6.53 (95% CI) with a median of 3.28 ng/ml and IQR [2.55; 4.24] ng/ml, respectively. On average, the level of endoglin in patients with SLE was 90.4 % higher ($P < 0.001$) compared to the control group.

Analysis of endoglin levels in SLE patients did not reveal statistically significant intragroup differences in gender or age. However, compared to the control group, the increase in endoglin levels was greater in men with SLE (123 %, $p < 0.001$), and lower in women with SLE (85 %, $p < 0.001$), respectively. Additionally, patients over 45 years of age had slightly higher endoglin levels than those under 45 years of age, as indicated by increases of 116 and 82.8 % ($p < 0.001$) relative to the control, respectively.

At the next stage, serum endoglin levels were ranked, according to which the general group of SLE patients was divided into four subgroups: 1st quartile (Q_1) included 24 individuals with endoglin levels of < 2.55 ng/ml; 2nd quartile (Q_2) — 25 subjects with endoglin levels of 2.55–3.28 ng/ml; 3rd quartile (Q_3) — 23 people with an index of 3.29–4.24 ng/ml; 4th quartile (Q_4) — 24 patients with an index > 4.24 ng/ml. Table 1 presents the clinical and demographic parameters of patient groups categorized by the quartile distribution of serum endoglin levels.

Analysis of the gender distribution revealed no statistically significant differences in the proportion of male and female patients between the Q_1, Q_2, Q_3 and Q_4 groups ($p > 0.05$). The quartile distribution showed a weak upward trend in the average age of patients and the proportion of people over 45 years of age from the 1st to the 4th quartile, but intergroup differences did not reach the probability limit.

It was found that from the 1st to the 4th quartile there was a tendency to increase the average duration of the disease: in the Q_4 group (with endoglin levels above 4.24 ng/ml), this index was statistically significantly higher (by 59.6 %, $p < 0.05$) than in the Q_1 group (with endoglin levels below 2.55 ng/ml). Additionally, in the Q_3 and Q_4 groups, the average duration of DMARD (disease-modifying anti-rheumatic drugs) therapy was statistically significantly higher than in the Q_1 (by 44.2 and 43.5 %, $p < 0.05$) and Q_2 groups (by 39.6 and 38.9 %, $p < 0.05$), respectively. Analysis of the frequency of glucocorticoids and the average daily dose (prednisolone) in patients with SLE did not reveal statistically significant intergroup differences depending on endoglin levels.

Table 1. Clinical and demographic parameters depending on the quartile distribution of serum endoglin levels in patients with SLE

Indices/Groups		Distribution of patients by endoglin level (ng/ml)			
		< 2.55	2.55–3.28	3.29–4.24	> 4.24
		Q_1	Q_2	Q_3	Q_4
Women	n (%)	24 (100)	23 (92)	20 (87)	22 (92)
Men		0 (0.0)	2 (8)	3 (13)	2 (8)
Age, years	M ± σ	36.30 ± 8.63	35.70 ± 8.87	39.10 ± 8.27	38.8 ± 10.2
Proportion of patients aged ≥ 45 years	n (%)	4 (16.7)	4 (16)	6 (26.1)	7 (29.2)
Duration of the disease, years	M ± σ	3.42 ± 1.95	4.00 ± 3.64	4.96 ± 2.79	5.46 ± 3.60*
Duration of DMARD therapy, years		2.71 ± 1.30	2.80 ± 1.32	3.91 ± 2.02*#	3.89 ± 1.70*#
Application of glucocorticoids	n (%)	17 (70.8)	20 (80)	20 (87)	19 (79.2)
Daily dose of glucocorticoids (prednisolone), mg	M ± σ	9.17 ± 4.29	12.40 ± 8.38	10.80 ± 4.67	12.50 ± 7.50

Notes (here and in Tables 2, 4): * — $p < 0.05$, compared to Q_1; # — $p < 0.05$, compared to Q_2.

Table 2. Indices of disease activity depending on the quartile distribution of endoglin levels in the blood serum of patients with SLE

Indices/Groups		Distribution of patients by endoglin level (ng/ml)			
		< 2.55	2.55–3.28	3.29–4.24	> 4.24
		Q_1	Q_2	Q_3	Q_4
ESR, mm/h	M ± σ	21.8 ± 11.1	24.6 ± 14.9	23.4 ± 10.0	23.1 ± 13.5
CRP, mg/l		10.00 ± 5.78	11.50 ± 9.15	9.13 ± 4.38	10.00 ± 4.57
TNFα, pg/ml		96.2 ± 41.2	146.9 ± 96.3*	123.6 ± 45.5*	131.30 ± 7.11*
IL-1β, pg/ml		18.80 ± 6.08	23.70 ± 8.63*	22.40 ± 5.93*	24.3 ± 10.8*
DI-1, points		5.75 ± 0.90	5.92 ± 1.26	6.35 ± 1.07*	6.59 ± 1.37*
SLAM-1, points		6.50 ± 1.82	6.32 ± 2.06	7.26 ± 2.65	8.24 ± 2.88*#
SLEDAI-1, points		13.90 ± 6.24	16.80 ± 7.43	17.20 ± 7.45	18.70 ± 8.17*
SLEDAI-1 > 10 points	n (%)	16 (66.7)	19 (76)	19 (82.6)	20 (83.3)

Analysis of disease activity indices concerning the level of endoglin in the blood serum of patients with SLE (Table 2) revealed no significant differences in ESR and C-reactive protein (CRP) levels. At the same time, there was a statistically significant increase in pro-inflammatory cytokine levels from the 1st to the 4th quartile: in Q_2, Q_3 and Q_4 groups, TNFα levels were higher by 52.7, 28.4 and 36.4 % ($p < 0.05$), and IL-1 β by 26.0, 19.1 and 29.3 % ($p < 0.05$) compared to Q_1 group.

Analysis of integral clinical and laboratory parameters of SLE activity revealed that an increase in disease severity was associated with a rise in the level of endoglin in the blood serum. So, in Q_4 group the DI-1, SLAM-1, and SLEDAI-1 indices were significantly higher (by 14.6, 26.8, and 34.5 %, $p < 0.05$) than in the Q_1 group. In addition, in the Q4 group, the largest proportion of patients with high disease activity and an SLEDAI-1 index > 10 points were found. Consequently, in microwave, an increase in serum endoglin levels was associated with an increase in the activity of the inflammatory process.

Correlation analysis confirmed the above patterns: in patients with SLE, statistically significant direct relationships were found between serum endoglin levels and pro-inflammatory cytokine levels, SLAM-1 and SLEDAI-1 indices.

At the next stage, the frequency of comorbid conditions in patients with SLE was analysed depending on the level of endoglin (Table 3). It was found that among patients with endoglin levels above 2.55 ng/ml, individuals with probable (non-critical) APS are more common: the proportion of such patients in Q_2, Q_3 and Q_4 groups was 7.62, 6.21, and 8.93 times higher ($p < 0.05$) than in Q_1 group. Moreover, in almost all patients with verified APS, endoglin levels were higher than 4.24 ng/mL and their proportion in Q_4 group it reached 50 %. At the same time, in Q_1 and Q_2 groups there were no patients with APS at all. Among patients with endoglin levels > 4.24 ng/ml, the proportion of individuals with heart, vascular, lung, and kidney damage was slightly higher than among individuals with endoglin levels < 2.55 ng/ml, but these differences did not reach the limit of reliability. At the same time, from the 1st to the 4th quartile, there was a clear increase in the proportion of patients with nervous system damage. Among patients with endoglin levels above 3.29 ng/ml (Q_3 and Q_4) the proportion of individuals with peripheral nervous system damage exceeded 50 % and was 2.99–3.38 times higher ($p < 0.05$) than among patients with endoglin levels less than 2.55 ng/ml. Additionally, in Q_2, Q_3, and Q_4 groups, the proportions of patients with CNS damage were 2.32, 2.98, and 3.28 times higher compared to the Q_1 group ($p < 0.05$–0.001, respectively). Meanwhile, in Q_3 and Q_4 groups, patients with CVD (central venous disease) predominated.

Analysis of mental health indices of patients with SLE depending on the quartile distribution of endoglin levels revealed the following patterns (Table 4): almost all the studied indices of mental health of patients significantly worsened from the 1st to the 4th quartile. So, in Q_4 group the proportion of patients with verified anxiety (on the Spielberg-Hanin scale), depressive disorders (on the Zung scale), and cognitive dysfunction was statistically significantly higher by 2.4, 5.52, and 2.74 times ($p < 0.05$) than in Q_1 group.

It should be noted that all quartile groups had a high incidence of memory and sleep disorders (without statistically significant intergroup differences). At the same time, in patients in Q_3 and Q_4 groups there were significantly higher rates of insomnia (28.1 and 30.2 %, $p < 0.05$) than in the Q_1 group. Thus, an increase in serum endoglin levels was associated with a deterioration in the mental health indices of patients with SLE.

Analysis of endoglin levels in SLE patients, depending on the presence of APS, revealed more pronounced intergroup differences (Fig. 1). It was found that in patients with SLE without APS, the endoglin level was 2.94 ± 0.93 ng/ml, which was 57.2 % higher ($p < 0.001$) compared to the control. In patients with probable (non-critical) APS, endoglin levels were 3.58 ± 0.91 ng/ml, which was 91.4 % ($p < 0.001$) higher than in the control group and 21.8 % ($p < 0.05$) higher than in the "SLE without APS" group. In patients with SLE with confirmed APS, endoglin levels were 6.19 ± 1.24 ng/ml, which exceeded the values in the "SLE without APS" and "SLE with probable APS" groups by 110 % ($p < 0.001$) and

Table 3. Frequency of comorbid conditions depending on the quartile distribution of serum endoglin levels in patients with SLE, n (%)

Indices/Groups	Distribution of patients by endoglin level (ng/ml)			
	< 2.55	2.55–3.28	3.29–4.24	> 4.24
	Q_1	Q_2	Q_3	Q_4
APS (probable)	1 (4.2)	8 (32)*	6 (26.1)*	9 (37.5)**
APS	0 (0)	0 (0)	1 (4.3)	12 (50)**#§
Heart damage	3 (12.5)	6 (24)	8 (34.8)	7 (29.2)
Vascular damage	17 (70.8)	15 (60)	17 (73.9)	19 (79.2)
Lung damage	4 (16.7)	4 (16)	9 (39.1)	7 (29.2)
Kidney damage	2 (8.3)	6 (24)	3 (13)	2 (8.3)
Damage to the peripheral nervous system	4 (16.7)	6 (24)	13 (56.5)**#	12 (50.0)*#
Central nervous system damage	7 (29.2)	17 (68)*	20 (87)**	23 (95.8)***#
Including CVD	0 (0.0)	4 (16)*	12 (52.2)**	19 (79.2)***#

Notes: * — p < 0.05, ** — p < 0.01, *** — p < 0.001, compared to Q_1; # — p < 0.05, compared to Q_2; § — p < 0.05, compared to Q_3.

72.9 % ($p < 0.001$), respectively. Thus, SLE patients with clinically and laboratory-confirmed APS had the highest serum endoglin levels.

Discussion

Thus, summarising the above results, it can be stated that in patients with SLE, the endoglin level is significantly higher by 90.4 % ($p < 0.001$) compared to the control group. Similar studies have not been conducted in patients with SLE, but high levels of sol-endoglin have been found in patients with juvenile dermatomyositis and severe vasculopathy [31]. Patients with rheumatoid arthritis have been shown to have higher levels of sol-endoglin than controls [32].

Our analysis of sol-endoglin levels in the serum of patients with SLE depending on the course of the disease showed that the increase in the concentration of the studied protein is associated with an increase in the duration of the disease ($p < 0.05$), and is not related to gender factors, patient age and the use of GC therapy. As for the literature data, it is known that in healthy young adults, endoglin levels are lower (by 30 %) than in healthy elderly people, and (by 71 %) lower than in patients with Alzheimer's disease [33].

The study found that an increase in serum endoglin levels accompanied the increase in disease severity. In particular, in the group with an endoglin level > 4.24 ng/ml, the DI-1, SLAM-1 and SLEDAI-1 indices were significantly higher (by 14.6, 26.8 and 34.5 %, $p < 0.05$) than in the group with an endoglin level < 2.55 ng/ml. In addition, the group with the highest level of this protein had the largest proportion of patients with high disease activity according to the SLEDAI-1 index > 10 points, and also had the highest concentration of TNFα and IL-1.

Another factor that obviously activates endoglin expression is phospholipid antibodies. In particular, in patients with SLE with antiphospholipid syndrome (APS), the level of endoglin was 2.1 times higher than in patients with SLE without APS, and 3.3 times higher than in the control group. As for the literature data, some studies have shown that in patients with SLE with secondary APS, higher levels of sol-endoglin in the blood serum are recorded, which are associated with the presence of anticardiolipin antibodies and antibodies to β-glycoprotein 1 [23].

Endoglin levels were not associated with damage to the heart, blood vessels, lungs and kidneys, but were associated with damage to the nervous system. Among patients with endoglin levels higher than 3.29 ng/ml (Q_3 and Q_4), the proportion of people with peripheral nervous system damage exceeded 50 % and was 2.99–3.38 times higher ($p < 0.05$) than among patients with endoglin levels lower than 2.55 ng/ml. Also, in groups Q_2, Q_3 and Q_4, the proportion of patients with CNS damage was 2.32, 2.98 and 3.28 times higher compared to group Q_1 ($p < 0.05$–0.001, respectively), with patients with CVD prevailing in groups Q_3 and Q_4. Similar patterns were found with mental health indices of patients with SLE. In the group with endoglin levels > 4.24 ng/ml, the proportion of patients with anxiety and depressive disorders, as well as cognitive dysfunction, was 2.4, 5.52 and 2.74 times ($p < 0.05$) higher than in the group with endoglin levels < 2.55 ng/ml.

As for the literature data, it has been reported that elevated endoglin levels have been reported are a marker of the increase in endothelial dysfunction in individuals with diabetic vasculopathy and nephropathy [34]. In men with diabetes mellitus, the development of erectile dysfunction was accompanied by an increase in serum endoglin levels

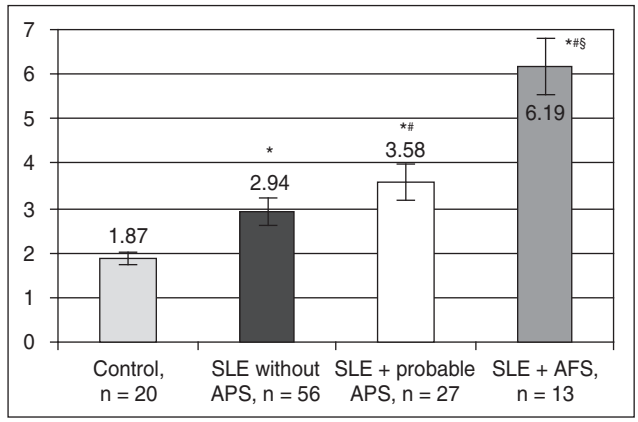

Figure 1. Serum endoglin levels (ng/ml) in patients with SLE depending on the presence of APS

Notes: * — $p < 0.001$, compared to the control; # — $p < 0.05$, compared to the "SLE without APS" group; § — $p < 0.05$, compared to the "SLE + probable APS" group.

Table 4. Indices of mental health status depending on the quartile distribution of serum endoglin levels in patients with SLE

Indices/Groups		Distribution of patients by endoglin level (ng/ml)			
		< 2.55	2.55–3.28	3.29–4.24	> 4.24
		Q_1	Q_2	Q_3	Q_4
Memory disorders	n (%)	11 (45.8)	20 (80)	16 (69.6)	12 (50)
Spielberg-Hanin scale, points	M ± σ	38.6 ± 10.9	43.10 ± 9.26	43.70 ± 7.40*	43.50 ± 6.19*
Anxiety	n (%)	5 (20.8)	11 (44)	13 (56.5)*	12 (50)*
Zung Depression Scale, scores	M ± σ	46.30 ± 5.31	52.20 ± 9.53*	49.80 ± 6.41*	52.10 ± 9.59*
Frequency of depression	n (%)	2 (8.3)	9 (36)*	8 (34.8)*	11 (45.8)**
Cognitive function, scores	M ± σ	26.80 ± 2.28	24.60 ± 3.55*	24.80 ± 3.38*	24.20 ± 4.00*
Frequency of cognitive disorders	n (%)	4 (16.7)	15 (60)**	12 (52.2)**	11 (45.8)*
Insomnia	M ± σ	13.90 ± 6.10	17.80 ± 6.41*	17.80 ± 4.66*	18.10 ± 5.31*
Frequency of insomnia	n (%)	15 (62.5)	21 (84)	18 (78.3)	19 (79.2)

[35]. Endoglin expression is enhanced in renal interstitial fibrosis and plays a role in the progression of chronic kidney disease (CKD) [36]. A negative correlation was found between endoglin expression in cells and the development of lipid-mediated coronary sclerosis in patients with familial hypercholesterolemia [37]. Patients with arterial hypertension showed higher endoglin levels than normotensive patients [38].

It has been experimentally proven that endoglin plays an essential role in regulating neovascularization of the ischemic brain and ensuring the survival of neurons [39], and hypoxia is the primary stimulus for endoglin expression in brain endothelial cells [10]. According to A. Haarmann (2023) high sol-endoglin is a biomarker of severe ischemic-reperfusion brain damage after occlusion of large cerebral vessels in stroke patients [40]. According to other data, patients with cerebral vasospasm, cerebral infarction, and cerebral ischemia experienced a decrease in serum sol-endoglin levels after spontaneous subarachnoid haemorrhage [41].

The study found that increased serum endoglin levels were associated with poorer mental health indices in patients with SLE. Thus, in the group with endoglin levels > 4.24 ng/ml, the proportion of patients with verifiable anxiety (according to the Spielberger-Hanin scale), depressive disorders (according to the Zung scale) and cognitive dysfunction was statistically significantly higher by 2.4, 5.52 and 2.74 times ($p < 0.05$) than in the group with endoglin levels < 2.55 ng/ml. In the latter group, insomnia rates were significantly better by 28.1 and 30.2 %, $p < 0.05$, than in the group with high and very high serum endoglin levels.

Serum endoglin levels are one of the important biomarkers for the differential diagnosis of depressive and bipolar disorders [7]. According to a large longitudinal study of 332 patients with depression, endoglin levels were important and the most promising markers when evaluating antidepressant treatment [6].

Thus, the obtained data showed that excessive concentration of endoglin is a circulating marker of damage to the peripheral and central nervous system, since it is closely associated with cerebrovascular manifestations of the disease, damage to the psycho-emotional sphere (Spielberg-Hanin anxiety scale, depressive disorders on the Zung scale, cognitive dysfunction and insomnia). Endoglin levels are significantly elevated in patients with an active inflammatory process (characterized by high levels of TNFα and IL-1), in patients with APS, and are largely independent of age, gender, and GC use. In our opinion, the study of endoglin concentration should become a mandatory element of laboratory examination of such a contingent of patients, especially with psycho-emotional disorders.

Study limitations. Despite the obtained results, this study has several limitations. The sample of patients with systemic lupus erythematosus (SLE) was relatively small and recruited from a single medical centre, which may limit the generalizability of the findings to the broader SLE population. The study design does not fully allow for the establishment of causal relationships between serum soluble endoglin levels and disease course or neuropsychiatric manifestations. The potential influence of immunosuppressive therapy on serum biomarker levels and neuropsychiatric symptoms should also be taken into account. Further studies involving larger cohorts, multifactorial analysis, and longitudinal observation could provide a deeper understanding of the pathophysiological role of soluble endoglin in the context of SLE.

Conclusion

The level of endoglin in the blood serum of patients with SLE is 90.4 % higher than in the control group. Endoglin levels are not associated with age and gender factors, GC use, but are associated with severe disease (DI), the presence of APS, and the activity of the inflammatory process (SLAM-1 and SLEDAI-1, TNFα, IL-1). With an increase in serum endoglin levels, the proportion of patients with damage to both the central and peripheral nervous systems significantly increases. Thus, at endoglin levels < 2.55 ng/ml, the proportion of individuals with central/peripheral NS lesions was 29.2 and 16.7 %, respectively, while at endoglin levels > 4.24 ng/ml, 95.8 and 50 %, respectively. High levels of the biomarker studied significantly correlated with poorer indices of mental health: an increase in the proportion of people with severe anxiety, depression, and cognitive disorders, as well as insomnia.

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Рівні розчинного ендогліну в сироватці крові хворих на системний червоний вовчак: зв'язок із перебігом захворювання та нейропсихічними проявами

Резюме. ***Актуальність.*** Ураження нервової системи при системному червоному вовчаку (СЧВ) є частими та різноманітними. Причини й механізми, що лежать в основі цих проявів, залишаються маловивченими. Останнім часом увагу дослідників привертає біомолекула ендоглін, яка асоціюється з окремими неврологічними й автоімунними захворюваннями, однак її роль у патогенезі нейропсихіатричного системного червоного вовчака (НПСЧВ) залишається невивченою. ***Мета:*** дослідити рівень розчинного ендогліну в сироватці крові пацієнтів із СЧВ, оцінити його зв'язок із демографічними показниками та запальною активністю та визначити діагностичну цінність як потенційного маркера НПСЧВ. ***Матеріали та методи.*** Обстежено 96 пацієнтів із СЧВ віком 19–55 років. Рівень розчинного ендогліну в сироватці крові досліджували за допомогою імуноферментного аналізу. ***Результати.*** В осіб із СЧВ уміст ендогліну був вірогідно вищим — на 90,4 % ($p < 0,001$) порівняно з контрольною групою. Зростання концентрації розчинного ендогліну асоціювалося з більш тривалим перебігом захворювання та вищою активністю за індексом SLEDAI-1, але не залежало від статі, віку пацієнтів чи застосування глюкокортикоїдів. Із підвищенням рівня розчинного ендогліну також зростала частка хворих з ураженням нервової системи. Аналіз показників психічного здоров'я в осіб із СЧВ залежно від квартильного розподілу рівнів ендогліну показав, що майже всі оцінювані параметри психічного стану вірогідно погіршувались від 1-го до 4-го квартиля. У групі Q_4 частка пацієнтів із підтвердженими тривожними розладами, депресією та когнітивними порушеннями була статистично значуще більшою — у 2,4; 5,52 і 2,72 раза відповідно ($p < 0,05$) порівняно з групою Q_1. Висока частота порушень пам'яті та сну спостерігалась в усіх квартильних групах без вірогідних міжгрупових відмінностей. ***Висновки.*** Рівень розчинного ендогліну в сироватці крові пацієнтів із СЧВ був на 90,4 % вищим, ніж у здорових осіб. Його збільшення асоціювалося з погіршенням показників психічного здоров'я — зі зростанням частоти виражених тривожних, депресивних і когнітивних розладів, безсоння.

Ключові слова: системний червоний вовчак; нейропсихіатричні розлади; депресія; тривожність; когнітивні порушення; ендоглін