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COMPARATIVE EFFECTIVENESS OF PULSE THERAPY IN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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The study included 18 patients with SLE, of which 9 were in the control group. A group of patients with ineffective standard therapy and high activity of the process was selected, i.e. the study included patients with a polysyndromic picture of systemic lupus erythematosus, all with more than 5-8 ARA criteria.

To standardize the assessment of the dynamics of clinical and laboratory parameters, we used the results of clinical symptoms, clinical blood tests with the calculation of index parameters of white blood cells, and the results of acute phase activity of the inflammatory process.

In order to objectify the assessment of the effectiveness of combination therapy, we compared the results of treatment with prednisolone alone and in combination with cyclophosphamide (control group). The results of the dynamics of clinical manifestations of SLE in patients receiving pulse therapy (Group 1) and standard therapy (Group II) are presented in Table 1. Analysis of the obtained results showed that the use of combination therapy was effective in relation to most extrarenal manifestations of the disease already in the first days after the end of treatment. Almost complete disappearance of the joint syndrome, significant reduction in skin and mucous membrane lesions, disappearance

Table 1.

Dynamics of clinical manifestations of SLE in patients receiving pulse therapy and standard therapy

Clinical sign	Patient groups			
	I (n=9)		II (n=9)	
	Before treatment	On the 7th day of therapy	Before treatment	On the 7th day of therapy
Fever	8	-	7	6
Articular syndrome	9	1	6	8
Skin and mucous membrane lesions	6	-	4	6
Lupus nephritis	6	1	6	6
Nervous system lesions	6	1	8	8
Vasculitis	6	1	4	4
Serositis	7	2	7	7
Lymphadenopathy	8	2	7	6

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Thrombocytopenia	2	-	1	1
Anemia	9	9	9	9
Leukopenia	7	5	6	6
ESR>15 mm/hour	9	3	9	9

lymphadenopathy, a decrease in the manifestations of carditis and polyserositis were observed in all patients. In 5 of 6 patients, we observed either a complete disappearance or a significant decrease in Raynaud's syndrome. As for the manifestations of lupus nephritis, in 4 of 6 patients with nephrotic syndrome, a decrease in edema syndrome, a decrease and stabilization of blood pressure were observed already on the 3rd day. During the days of combined therapy, such patients showed a significant increase in diuresis. Hematuria and proteinuria decreased in more than half of the patients.

In patients of the second group, who received standard therapy with the inclusion of prednisolone orally at a dose of 1-3 mg / day, at the end of the first week of therapy, no clear positive changes in clinical indicators were noted. Thus, fever and articular syndrome continued to persist. Skin and mucous membrane lesions were noted in two more patients. Lupus nephritis, vasculitis, serositis, leukopenia did not have positive changes in any patient. Analysis of the results of the peripheral blood picture showed (Table 2) that in patients of the first group, who received pulse therapy, at the end of the 7th day there was

Table 2.

Dynamics of peripheral blood parameters in patients with SLE who received pulse therapy and standard therapy

Indicators	In healthy people	Group I (n=9)	II group (n=9)
Erythrocytes	3,78±0,03	3,17±0,46	3,06±0,54
		3,33±0,43	3,02±0,62
Hemoglobin, g/l	123,20±0,10	67,61±2,47	71,39±2,31
		82,41±3,19	68,88±3,12
Color index	0,95±0,01	0,77±0,01	0,79±0,86
		0,81±0,01	0,76±0,01
SHE, (in pg)	30,21±0,14	28,48±0,18	28,59±0,15
		30,40±0,19	29,04±0,17
SSHE, (in %)	31,90±0,18	27,92±0,26	28,90±0,19
		31,54±0,35	28,73±0,23

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ESR, (µm3)	94,59±0,27	101,49±0,82	102,69±0,59
		95,80±0,76	100,62±0,47
Leukocytes	6,72±0,17	4,95±0,87	4,88±0,76
		6,74±1,09	5,01±0,61
Band	3,02±0,20	4,93±0,26	4,78±0,20
		2,12±0,14	4,41±0,09
Segmented	54,35±1,18	63,51±0,90	62,93±0,73
		53,06±1,49	60,34±0,78
Lymphocytes	35,29±1,00	26,56±0,69	25,81±0,61
		37,96±1,30	30,49±0,65
Monocytes	5,03±0,30	3,16±0,17	4,40±0,19
		4,65±0,28	4,59±0,18
Eosinophils	2,31±0,20	1,84±0,09	2,15±0,08
		2,20±0,19	2,17±0,14
ESR mm/h	7.50±0,06	43,56±2,33	39,23±3,11
		24,91±3,12	40,51±4,08

Note: MCH - mean corpuscular hemoglobin; MCH - mean corpuscular hemoglobin concentration; ESR - mean corpuscular volume.

The numerator shows the values before treatment. The denominator shows the normalization of erythrocyte balance values 7 days after the start of therapy: the erythrocyte content significantly increased, although it still remained lower than in healthy children. The hemoglobin concentration increased significantly (severe anemia became moderate), and the color index returned to normal. MCH, MCH, and ESR values did not differ from those in healthy children. In terms of leukocyte content and leukocyte formula values, patients in Group 1 did not differ from healthy children in the second period of the study. The erythrocyte sedimentation rate in patients in this group significantly decreased compared to the value upon admission. This indicates the onset of the stage of attenuation of the immune-inflammatory process and the favorability of pulse therapy. Unfavorable results were obtained in patients of group II in the second period of the study. Thus, none of their indicators returned to normal in the second period of the study. Moderate hypochromic anemia became severe, the indicators of SSGE, SGE and ESR were still abnormal, which indicates the onset of severe anemia. Leukopenia, neutrophilia with a shift to the left, relative and absolute lymphopenia, persistent acceleration of the erythrocyte sedimentation rate still persisted. These general clinical laboratory data indicate the continued activity of the inflammatory process and its unfavorable course.

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A comparative assessment of the treatment results showed that in patients of group II, the overall clinical effect was worse than in patients of group I, which is confirmed by persistent fever, articular syndrome, an increase in the frequency of lesions of the skin and mucous membranes, lupus nephritis, vasculitis, serositis, leukopenia and negative indicators of white blood. The results of the study of white blood index indicators are presented in Table 3.

Table 3.

Dynamics of white blood cell index values in patients with SLE who received pulse therapy and standard therapy

Indicators	In healthy people	In patients	
		Group I	Group II
Leukocyte intoxication index (LII)	0,57±0,02	1,16±0,08	0,94±0,07
		0,49±0,06	0,69±0,05
Left shift index (LSI)	5,67±0,08	7,76±0,19	7,59±0,17
		4,10±0,59	4,03±0,14
Granulocyte-agronulocyte index (GAI)	1,52±0,02	2,48±0,10	2,48±0,08
		1,38±0,09	1,91±0,04
General intoxication index (GII)	7,77±0,14	11,38±0,26	11,01±0,21
		5,98±0,14	6,64±0,14
Neutrophil-lymphocyte ratio index (NLR)	1,67±0,02	2,75±0,23	2,83±0,18
		1,49±0,10	2,14±0,10
Neutrophil-monocyte ratio index (NMR)	12,44±0,31	31,95±0,64	20,52±0,35
		14,67±0,42	18,76±0,84
Lymphocyte-monocyte ratio index (LMR)	7,53±0,27	12,60±0,38	7,94±0,24
		10,03±0,76	6,64±0,89
Lymphocyte-eosinophil ratio index (LER)	15,79±0,76	10,88±1,04	10,44±0,76
		23,35±1,00	18,26±0,68

Note: the numerator shows the values before treatment, the denominator shows the values on the 7th day of therapy.

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Among the index indicators in patients of the 1st group, complete normalization occurred for LII due to a significant decrease in band neutrophils, GAI due to a decrease in the absolute and relative number of neutrophils, and ISNL due to a decrease in the number of neutrophils in peripheral blood. Normalization has not yet been noted for the ISI, OII, ISLM and ISLE indicators. It should be noted that the ISLE indicator in patients of this group has significantly increased due to an increase in the relative number of lymphocytes compared to the data upon admission. In our opinion, this additionally indicates the onset of the stage of attenuation of the immune-inflammatory process.

It should be emphasized that in most cases, patients of the 1st group showed a clear correlation between the positive dynamics of index indicators and clinical manifestations of SLE. In patients of the second group who received standard therapy, none of the studied index parameters normalized, with the exception of ISLM, which was restored due to a slight decrease in the number of lymphocytes and an increase in the number of monocytes. Here, correlative connections were also noted between the index parameters of white blood cells and the clinical manifestations of SLE.

The dynamics of biochemical parameters in the observed patients with SLE are presented in Table 4.

The data in the table indicate that complex therapy led to a significant normalization of biochemical parameters in the observed patients, but the degree of their normalization was different in the studied groups (Table 4). Thus, the concentration of sialic acids was completely normalized only in patients of group I, while in patients of group II, despite their significant decrease in comparison with the results upon admission ($P < 0.001$), complete normalization did not occur ($P < 0.001$). According to the concentration of diphenylamino acid, significant normalization occurred in patients of the first group. However, this indicator remained reliably high in patients of both groups. The latter indicator, in our opinion, is the most reliable among the indicators of acute-phase inflammation activity.

Malen's test, detected in all patients, by the end of the observation was the most positive in patients of group II ($P<0.001$) and the least positive in patients of group I ($P<0.001$). Interesting results were obtained when setting up the Veltman test. Thus, in patients of group II at the last stage of observation, a shift of the test to the right was noted ($P<0.01$), indicating the chronicity of the inflammatory process, and in patients of group I, statistical differences were not found compared with the control group.

Table 4.

Dynamics of biochemical blood parameters in patients with SLE who received pulse therapy and standard therapy

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Indicators	In healthy people	In patients	
		Group I	Group II
Sialic acids, units of optical density	187,73±1,64	326,1±6,87	311,7±3,01
		189,8±4,26*	264,1±2,24*
Diphenylamine acid, units of optical density	0,160±0,01	0,343±0,04	0,335±0,02
		0,204±0,03*	0,257±0,02*
Malena test	Отр	Положительная у 100% больных	
		22,2%*	77,7%*
Veltman test	0,36±0,01	0,20±0,01	0,20±0,01
		0,34±0,01*	0,40±0,01*
C-reactive protein, mm.:	Отр	3,30±0,06	3,24±0,05
		0,59±0,14*	1,91±0,07*
Blood protein, g/l	70,76±0,50	68,32±0,80	68,60±0,81
		69,21±0,28	65,53±0,23*
Albumins, in %:	59,19±0,41	48,10±0,41	48,01±0,43
		54,37±0,56*	52,18±0,23*
α-globulins	13,31±0,66	21,37±0,40	20,69±0,45
		15,02±0,33*	17,13±0,14*
β-globulins	11,97±0,35	14,21±0,31	14,56±0,29
		12,28±0,33	8,93±0,20*
-globulins	15,53±0,37	16,32±0,36	16,74±0,32
		18,33±0,46*	21,76±0,32*

Despite the therapy, CRP was detected in all the studied groups, with its highest content noted in patients of group II, and the lowest - in patients of group I ($P < 0.01$-0.001). This indicator most fully determines the degree of activity of the inflammatory process. In patients of group I, pulse therapy did not have a significant effect on total blood protein, and in patients of group II, hypoproteinemia occurred against the background of treatment ($P < 0.001$). Blood albumins still remained low in all compared groups ($P < 0.001$). Serum α-globulins, characterizing the severity of the inflammatory process, still remained high in all patients, with the highest in patients of group II ($P < 0.001$), and relatively low in patients of group I ($P < 0.01$). β-globulins were elevated in all groups of patients, and by the end of the observation - in patients of group II ($P < 0.05$) they significantly decreased, while in patients of group I at this time of the study no reliable differences were found. Serum γ-globulins in

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all patients at the last observation period significantly increased ($P < 0.001$), which indicated the chronicity of the inflammatory process, or indirectly one can assume the suppression of antibody formation or hyperimmunoglobulinemia. At the same time, the highest concentration of gamma globulins was recorded in patients of group II, rather than in patients of group I ($P < 0.05$). In general, in patients in this study, pulse therapy with methylprednisolone was effective in 77.7% of patients with SLE, persistent remission was noted in 66.6% of patients. In 22.2% of patients, despite the therapy, no noticeable clinical and laboratory effect was observed. As for standard therapy, for patients with high activity of the inflammatory process, with persistent vasculitis, visceritis, this method is ineffective and requires further improvement in relation to the use of pulse therapy.

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