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CLINICAL EFFECTS OF HUMAN IMMUNOGLOBULIN ADMINISTRATION IN WOMEN WITH RHESUS SENSITIZATION AT THE PRE-GRAVID STAGE

The aim of the study – to evaluate changes in cellular immunity in rhesus-sensitized women in response to IVIG administration and the prognostic effectiveness of a method for the prevention of isoimmunization in the next pregnancy.

Materials and Methods. The study was performed on the basis of City Maternity Hospital No. 7" (Odesa) in 2014–2019. 37 rhesus-sensitized women were randomly splited in two clinical groups: main clinical group (n=19) where patients received human immunoglobulin for intravenous administration, and control group (n=18) where patients did not receive IVIG.

Results and Discussion. The state of cellular immunity in rhesus-sensitized women is characterized by a moderate decrease in the absolute and relative indices of T-lymphocytes while increasing the number of B-lymphocytes. The NK cell population did not differ from the control group. When analyzing subpopulations of T-lymphocytes, it can be concluded that the number of T-helper cells is increased and the number of T-suppressors is proportionally reduced. These changes explain the increase in the number of B-lymphocytes as a result of increasing antigenic load on cell receptors. In the group of women who received IVIG therapy, the ratio of chances of normalization of cellular immunity was 18.41 (95 % CI 2.62–166.74), T-helper – 14.93 (95 % CI) 2.45–107.8), T-suppressors – 14.57 (95 % CI 2.13 –127.57) and B-lymphocytes – 31.87 (95 % CI 4.1–333.41). According to the ROC analysis, the quality of the statistical model of IVIG application corresponds to AUC = 0.843 (95 % CI 0.689–0.941) According to the ROC analysis, the level of β-lymphocytes in the compared AUC groups = 0.58 (95 % CI 0.405–0.742).

Key words: pregnancy; rhesus sensitization; human immunoglobulin for intravenous administration.

КЛІНІЧНІ ЕФЕКТИ ЗАСТОСУВАННЯ ІМУНОГЛОБУЛІНУ ЛЮДИНИ У ЖІНОК З РЕЗУС-СЕНСИБІЛІЗАЦІЄЮ НА ПРЕГРАВІДАРНОМУ ЕТАПІ

Мета дослідження – оцінити зміни клітинного імунітету у резус-сенсибілізованих жінок у відповідь на введення ВВІГ і прогностичну ефективність методу для профілактики ізоімунізації при наступній вагітності.

Матеріали та методи. Дослідження проводили на базі КІ «Міський пологовий будинок № 7» (Одеса) у 2014–2019 роках. 37 жінок, чутливих до резусу, було випадковим чином поділено на дві клінічні групи: основну клінічну групу (n=19), де вихованці отримували імуноглобулін людини для внутрішньовенного введення (ВВІГ), контрольну групу (n=18), де пацієнти не отримували ВВІГ.

Результати досліджень та їх обговорення. Стан клітинного імунітету у резус-сенсибілізованих жінок характеризується помірним зниженням абсолютних і відносних показників Т-лімфоцитів при одночасному збільшенні числа В-лімфоцитів. Популяція NK-клітин не відрізняється від показників контрольної групи. При аналізі субпопуляцій Т-лімфоцитів можна зробити висновок про збільшення числа Т-хелперів і пропорційне зниження числа Т-супресорів. Дані зміни пояснюють збільшення кількості В-лімфоцитів внаслідок зростаючого антигенного навантаження на рецептори клітин. У групі жінок, які отримали терапію ВВІГ, відношення шансів нормалізації показників клітинного імунітету склало: по рівню Т-лімфоцитів – 18,41 (95 %, ДІ 2,62–166,74), Т-хелперів – 14,93 (95 %, ДІ 2,45 – 107,8), Т-супресорів – 14,57 (95 %, ДІ 2,13 – 127,57) і В-лімфоцитів – 31,87 (95 %, ДІ 4,1 – 333,41). За даними ROC-аналізу, якість статистичної моделі застосування ВВІГ відповідає AUC=0,843 (95 %, ДІ 0,689 – 0,941). За даними ROC-аналізу рівня В-лімфоцитів у порівнюваних групах AUC=0,58 (95 %, ДІ 0,405 – 0,742).

Ключові слова: вагітність; резус-сенсибілізація; імуноглобулін людини для внутрішньовенного введення.

КЛИНИЧЕСКИЕ ЭФФЕКТЫ ПРИМЕНЕНИЯ ИММУНОГЛОБУЛИНА ЧЕЛОВЕКА У ЖЕНЩИН С РЕЗУС-СЕНСИБИЛИЗАЦИЕЙ НА ПРЕГРАВИДАРНОМ ЭТАПЕ

Цель исследования – оценить изменения клеточного иммунитета у резус-сенсибилизированных женщин в ответ на введение ВВИГ и прогностическую эффективность метода для профилактики изоиммунизации при следующей беременности.

Материалы и методы. Исследование выполнено на базе КИ «Городской родильный дом № 7» (г. Одесса) в 2014–2019 гг. 37 женщин с резус-чувствительностью были случайным образом разделены на две клинические группы: основная клиническая группа (n=19), где пациенты получали человеческий иммуноглобулин для внутривенного введения (ВВИГ), контрольная группа (n=18), где пациенты не получали ВВИГ.

Результаты исследования и их обсуждение. Состояние клеточного иммунитета у резус-сенсибилизированных женщин характеризуется умеренным снижением абсолютных и относительных показателей Т-лимфоцитов при одновременном увеличении числа В-лимфоцитов. Популяция NK-клеток не отличается от показателей контрольной группы. При анализе субпопуляций Т-лимфоцитов можно сделать вывод об увеличении числа Т-хелперов и пропорциональном снижении числа Т-супрессоров. Данные изменения объясняют увеличение количества В-лимфоцитов в результате растущей антигенной нагрузки на рецепторы клеток. В группе женщин, которые получили терапию ВВИГ, отношение шансов нормализации показателей клеточного иммунитета составило: по уровню Т-лимфоцитов – 18,41 (95 %, ДИ 2,62–166,74), Т-хелперов – 14,93 (95 %, ДИ 2,45 – 107,8), Т-супрессоров – 14,57 (95 %, ДИ 2,13 – 127,57) и В-лимфоцитов – 31,87 (95 %, ДИ 4,1 – 333,41). По данным ROC-анализа качество статистической модели применения ВВИГ соответствует AUC=0,843 (95 %, ДИ 0,689– 0,941) По данным ROC-анализа уровня В-лимфоцитов в сравниваемых группах AUC = 0,58 (95 %, ДИ 0,405–0,742).

Ключевые слова: беременность; резус-сенсибилизация; иммуноглобулин человека для внутривенного введения.

One of the most effective and widely tested methods of immunotherapy of autoantibody hyperproduction diseases is the treatment with high doses of intravenous immunoglobulin (IVIG) [1, 4]. IVIG is a medicine of normal polyspecific immunoglobulin derived from the pool of several thousand donors, which determines the content of all IgG, including antibodies to exogenous antigens, natural antibodies and anti-idiotypic antibodies [1, 6]. It is known that anti-idiotypic antibodies bind and neutralize pathogenic antibodies and interfere with their interaction with the autoantigen. Fragments (F)ab(2) contained in IVIG reduce functional activity or block the binding of autoantibodies to the corresponding autoantigens, such as antibodies to D-antigen [6, 7]. The suppressive effects of IVIG may also be due to its effect on B-lymphocyte receptors, which leads to a decrease in immunoglobulin production [1, 4, 6].

However, the mechanisms underlying the inhibition of B-lymphocyte proliferation during IVIG administration have not yet been studied. It is known that the binding of anti-idiotypic antibodies to antigenic determinants and surface IgM or IgG on B lymphocytes causes a decrease in antibody production. In addition, IVIG can reduce the level of antibodies, because the medicines contain antibodies to CD5 receptors of B lymphocytes [4]. Moreover, a number of studies have shown that IVIG induces apoptosis of B- and some T-cell lines [1]. Given the changes in cellular immunity in rhesus-sensitized women, the use of IVIG is a pathogenetic treatment.

THE AIM OF THE STUDY – to evaluate changes in cellular immunity in rhesus-sensitized women in response to IVIG administration and the prognostic efficacy of the method for the prevention of isoimmunization in subsequent pregnancy.

MATERIALS AND METHODS. The study was performed on the basis of City Maternity Hospital No. 7 (Odesa) in 2014–2019. In accordance with the standards of medical care, 37 rhesus-sensitized women were conducted according to the orders of the Ministry of Health of Ukraine No. 676 issued on 31.12.2004 "About approval of clinical protocols on obstetric and gynecological care – pregnancy management in women with immune conflicts" and No. 417 issued on 15.07.2011 "On the organization of ambulatory obstetric and gynecological care in Ukraine" [2, 3].

To evaluate the effectiveness of the use of human immunoglobulin for intravenous administration in complex therapy of rhesus sensitization, all women observed by stratified randomization method were divided into two groups.

Group I – the main group, consisted of 19 women with rhesus-sensitization, who, with the aim of preventing the development of hemolytic disease of the fetus and newborn, was introduced IVIG. The selection of patients in the main group was performed according to the following criteria: medicine for the next pregnancy of women with rhesus antibodies and obstetric obstetric history (antenatal fetal death from hemolytic disease in history, etc.); initially high rhesus antibody titer level (1:32 and above), 6-12 months postpartum. Exclusion criteria were severe extragenital diseases in decompensation stage. Contraindications to this therapy were allergic reactions to the introduction of immunoglobulins.

Intravenous immunoglobulin was administered at a dose of 5.0 grams in the amount of 2 transfusions at intervals of 1-2 days. The initial rate of transfusion was 1.4 ml / kg body weight / hour, after 10 minutes with good tolerability of the drug speed gradually increased to a maximum of 1.9 ml/kg body weight/hour and kept it until the end of administration. Intravenous immunoglobulin was administered under the control of blood pressure and heart rate. There were no responses to immunoglobulin administration.

Group II – (comparison group) consisted of 18 rhesus-sensitized women who were under standard care at the same time interval after delivery.

The cellular level of immunity was determined by flow cytofluorimetry (BD FACS apparatus, BD Biosciences, USA) [5].

Statistical analysis of the obtained data was carried out using the packages STATISTICA 10.0, IBM SPSS Statistics 22.0, MedCalc 14.8.1 and Microsoft Excel 2010 with the application AtteStat 12.5, an online SISA calculator (Simple Interactive Statistical Analysis).

RESULTS. Absolute and relative indicators of cellular immunity in different groups of women with rhesus sensitization are presented in tables 1 and 2.

All absolute and relative indicators of cellular immunity in the standard-management group of women did not statistically differ significantly during the observation period (Table 3, 4).

In the group of sensitized women who received IVIG, indicators of absolute and relative cellular immunity were statistically significantly different by most indicators (Tables 5 and 6).

Table 1. **Indicators of cellular immunity in different groups of women with Rh-sensitization**

Indices	CD3+	CD3+ CD16/56+	CD3+HLA-DR+	CD3+ CD4+	CD3+CD4+ HLA-DR+	CD3+ CD8+
Before treatment	56.81±1.69	4.08±0.41	2.83±0.32	59.59±1.39	4.59±0.46	16.48±1.34
Control	60.11±2.14	4.5±0.55	2.65±0.46	58.5±2.3	3.05±0.42*	17.83±1.91
Main	72.68±1.98*	5.36±0.46	4.05±0.42*	52.47±1.94*	3.75±0.54*	24.47±1.7*

Indices	CD3+CD8+ HLA-DR+	CD3+CD4+/ CD3+CD8+	CD3+CD4+ CD8+	CD3+ CD4-CD8-	CD19+	CD3-CD16/56
Before treatment	4.91±0.64	2.57±0.11	1.35±0.09	3.09±0.3	18.29±0.8	9.74±1.1
Control	4.72±0.77	2.55±0.19	1.4±0.13	3.09±0.4	16.22±1.3	9.94±1.56
Main	6.89±0.88*	2.22±0.14	1.3±0.12	2.98±0.4	11.21±1.13*	10.1±1.39

* Statistical significance of differences with indicators before treatment $p<0.05$

Table 2. **Absolute indices of cellular immunity in different groups of women with rhesus sensitization**

Indices	CD3+	CD3+CD4+	CD3+CD8+	CD19+	CD3-CD16/56+
Before treatment	1.12±0.07	1.55±0.08	0.38±0.04	0.68±0.05	0.27±0.06
Control	1.31±0.11	1.51±0.13	0.38±0.06	0.6±0.07	0.38±0.1
Main	1.5±0.09*	1.22±0.09*	0.49±0.06	0.36±0.05*	0.29±0.09

* Statistical significance of differences with indicators before treatment p<0.05

Table 3. **Result of variance analysis (One-way ANOVA) of relative indicators of cellular immunity in the study groups of women who received standard treatment**

One-way ANOVA						
Indices		Square Sum	Degree of freedom	SD	F	P
CD3+	Between groups	131.892	1	131.892	1.338	0.253
	Within groups	5225.453	53	98.593		
	Total	5357.345	54			
CD3+ CD16/56+	Between groups	2.071	1	2.071	0.341	0.562
	Within groups	322.243	53	6.080		
	Total	324.314	54			
CD3+ CD4+	Between groups	14.508	1	14.508	0.182	0.671
	Within groups	4215.419	53	79.536		
	Total	4229.927	54			
CD3+CD4+ HLA-DR	Between groups	28.682	1	28.682	4.370	0.041
	Within groups	347.863	53	6.563		
	Total	376.545	54			
CD3+ CD8+	Between groups	21.966	1	21.966	0.330	0.568
	Within groups	3531.743	53	66.637		
	Total	3553.709	54			
CD3+CD8+ HLA-DR	Between groups	0.431	1	0.431	0.031	0.862
	Within groups	743.767	53	14.033		
	Total	744.197	54			
CD3+CD4/ CD3+CD8+	Between groups	0.005	1	0.005	0.009	0.924
	Within groups	29.042	53	0.548		
	Total	29.047	54			
CD3+CD4+ CD8+	Between groups	0.032	1	0.032	0.099	0.755
	Within groups	17.261	53	0.326		
	Total	17.293	54			
CD3+CD4-CD8+	Between groups	0.000	1	0.000	0.000	0.991
	Within groups	146.785	53	2.770		
	Total	146.785	54			
CD19+	Between groups	52.141	1	52.141	1.929	0.171
	Within groups	1432.841	53	27.035		
	Total	1484.982	54			
NK	Between groups	0.490	1	0.490	0.011	0.917
	Within groups	2365.755	53	44.637		
	Total	2366.245	54			

Table 4. **Result of variance analysis (One-way ANOVA) of absolute indicators of cellular immunity in the studied groups of women, where standard treatment was conducted**

One-way ANOVA						
Indices		Square Sum	Degree of freedom	SD	F	P
CD3+	Between groups	0.432	1	0.432	1.913	0.172
	Within groups	11.964	53	0.226		
	Total	12.396	54			
CD3+ CD4+	Between groups	0.015	1	0.015	0.049	0.825
	Within groups	16.445	53	0.310		
	Total	16.461	54			
CD3+ CD8+	Between groups	0.000	1	0.000	0.000	0.995
	Within groups	4.111	53	0.078		
	Total	4.111	54			
CD19+	Between groups	0.080	1	0.080	0.711	0.403
	Within groups	5.937	53	0.112		
	Total	6.016	54			
NK	Between groups	0.145	1	0.145	0.918	0.342
	Within groups	8.392	53	0.158		
	Total	8.537	54			

Table 5. **Result of variance analysis (One-way ANOVA) of relative indicators of cellular immunity in the study groups of women treated with IVIG**

One-way ANOVA						
Indices		Square Sum	Degree of freedom	SD	F	P
CD3+	Between groups	3163.058	1	3163.058	33.001	0.000
	Within groups	5175.781	54	95.848		
	Total	8338.839	55			
CD3+ CD16/56	Between groups	20.630	1	20.630	3.663	0.061
	Within groups	304.164	54	5.633		
	Total	324.794	55			
CD3+ HLA-DR	Between groups	18.608	1	18.608	4.883	0.031
	Within groups	205.792	54	3.811		
	Total	224.400	55			
CD3+ CD4+ HLA-DR	Between groups	8.788	1	8.788	1.201	0.278
	Within groups	395.045	54	7.316		
	Total	403.834	55			
CD3+ CD8+	Between groups	800.859	1	800.859	12.705	0.001
	Within groups	3403.980	54	63.037		
	Total	4204.839	55			
CD3+ CD8+ HLA-DR	Between groups	49.410	1	49.410	3.207	0.079
	Within groups	831.945	54	15.406		
	Total	881.356	55			
CD3+ CD4+/ CD3+ CD8+	Between groups	1.485	1	1.485	3.211	0.079
	Within groups	24.974	54	0.462		
	Total	26.459	55			

Continuing Table 5.

CD3+ CD4+ CD8+	Between groups	0.037	1	0.037	0.118	0.732
	Within groups	16.752	54	0.310		
	Total	16.789	55			
CD3+ CD4- CD8+	Between groups	0.125	1	0.125	0.043	0.836
	Within groups	155.494	54	2.880		
	Total	155.618	55			
CD19+	Between groups	630.470	1	630.470	24.583	0.000
	Within groups	1384.888	54	25.646		
	Total	2015.357	55			
NK	Between groups	1.645	1	1.645	0.039	0.844
	Within groups	2284.600	54	42.307		
	Total	2286.246	55			

Table 6. **Result of variance analysis (One-way ANOVA) of absolute indicators of cellular immunity in the studied groups of women receiving complex therapy**

One-way ANOVA						
Indices		Square Sum	Degree of freedom	SD	F	P
CD3+	Between groups	1.788	1	1.788	8.662	0,005
	Within groups	11.148	54	0.206		
	Total	12.937	55			
CD3+ CD4+	Between groups	1.376	1	1.376	5.381	0,024
	Within groups	13.812	54	,256		
	Total	15.188	55			
CD3+ CD8+	Between groups	0.149	1	0.149	1.910	0,173
	Within groups	4.216	54	0.078		
	Total	4.365	55			
CD19+	Between groups	1.227	1	1.227	12.054	0.001
	Within groups	5.498	54	0.102		
	Total	6.725	55			
NK	Between groups	0.004	1	0.004	0.028	0.867
	Within groups	8.099	54	0.150		
	Total	8.104	55			

As a result of comprehensive treatment of rhesus-sensitized women using IVIG, a statistically significant decrease in the absolute (F = 12.054, p = 0.001) and relative (F = 24.583, p = 0.0001) numbers of B lymphocytes was observed. The indicators were consistent with those of the control group of women. In the group of women with standard observation, the level of B-lymphocytes did not change significantly (F = 0.711, p = 0.403 and F = 1.929, p = 0.171).

Discussion. Given the important role of immunoglobulins as regulators of the level of the immune response in the form of stimulating and suppressive effects on the B-cell system, there is a point of interest to evaluate the degree of change by subpopulations of T-lymphocytes. The state of cellular immunity in rhesus-sensitized women is characterized by a moderate decrease in the absolute and relative rates of T-lymphocytes while increasing the number of B-lymphocytes. The NK cell population did not differ from that of the control group. In the analysis of subpopulations of T-lymphocytes, we can conclude that the number of T-helpers is increased and the number of T-suppressors is proportionally reduced. These changes explain the increase in the number of B lymphocytes due to increasing antigenic load on cell receptors.

As a result of the therapy of rhesus-sensitized women, we can note a statistically significant normalization of the

absolute and relative indices of T-helpers (F = 5.381, p = 0.024 and F = 27.169, p = 0.0001) – a decrease in the data in the group with standard observation (F = 0.049, p = 0.825 and F = 0.182, p=0.671).

At the same time, in the group of women treated with IVIG, normalization (in the form of an increase) of absolute and relative (statistically significant) T-suppressors (F = 1.910, p = 0.173 and F = 12.705, p = 0.001) was observed. In the group of women under standard care, these figures did not change significantly (F = 0.0001, p = 0.995 and F = 0.330, p = 0.568)

Considering the conducted researches of cellular immunity status in rhesus-sensitized women, the following indicators were chosen as the criteria of effectiveness of the conducted therapy: assessment of the population of lymphocytes – T-and B-lymphocytes, subpopulation of T-lymphocytes influencing the synthesis of antibodies – T-helpers and T-suppressors.

When evaluating the normalization of T-lymphocyte indices in the group of women with standard observation χ^2 was 0.59, the relative risk decreased by 50 %, NNT = 6 at the significance level p = 0.44. In the group of women treated with IVIG - χ^2 = 11.01, the relative risk decreased by 85 %, NNT = 2 at the significance level p = 0.001. The effectiveness of therapy for the normalization of B-lymphocytes in the standard therapy group did not differ from the indicators of change in T-lymphocytes. In the group of complex therapy with the inclusion of IVIG χ^2 was equal to 15.32, the relative risk decreased by 87 %, NNT=1, p = 0.0001.

In assessing the effectiveness of normalization of subpopulations of T lymphocytes, it is necessary to note the absence of statistically significant differences in the group of women with standard therapy. T-helpers – χ^2 = 2.37, relative risk decreased by 71 %, NNT = 4 at the significance level p = 0.12, T-suppressors - χ^2 = 0.71, relative risk decreased by 60 %, NNT = 4 at significance levels p = 0.40. In the group receiving IVIG therapy, T-helpers were χ^2 = 10.64, the relative risk decreased by 78 %, NNT = 2 at the significance level p = 0.001, T-suppressors – χ^2 = 9.16, the relative risk decreased by 83 %, NNT = 2, p = 0.02.

In the group of women with standard supervision, the ratio of chances of normalization of cellular immunity was: T-lymphocyte level – 2.5 (95 % CI 0.41–16.32), T-helpers – 5.09 (95 % CI 0.73 – 44.16), T-suppressors – 3.07 (95 % CI 0.41–27.85) and B-lymphocytes – 2.5 (95 % CI 0.41–16.32)

In the group of women who received therapy with IVIG, the ratio of chances of normalization of indicators of cellular immunity was: by the level of T-lymphocytes – 18.41 (95 % CI 2.62–166.74), T-helpers – 14.93 (95 % CI 2.45–107.8), T-suppressors – 14.57 (95 % CI 2.13–127.57) and B lymphocytes – 31.87 (95 % CI 4.1–333.41).

The statistical model with standard observation of rhesus-sensitized women on the level of normalization of T-lymphocytes proved to be less effective in comparison with the model of "IVIG treatment". The AUC in the standard observation group was 0.614 (95 % CI 0.438 –0.771), which, according to Juden's classification, indicates the quality of model as an “average” one. The AUC in the group of women receiving therapy for IVIG was 0.866 (95 % CI 0.716–0.954), this indicator corresponds to the "very good" quality of the statistical model of treatment.

In the ROC analysis of indicators of subpopulations of T-lymphocytes it should be noted that in the group of women with standard observation, the level of T-helper did not differ significantly from the indicators before treatment, AUC was 0.56 (95 % CI 0.385–0.725), indicating model quality as “unsatisfactory”. The AUC in the group of women treated with IVIG was 0.742 (95 % CI 0.575 - 0.870), it corresponds to a “good” quality of the statistical treatment model.

In the group with standard observation of the control panel of the level of T-suppressors recorded at the level of 0.566 (95 % CI 0.391–0.730) – “poor” quality of the model according to the Juden classification. In rhesus-sensitized women receiving complex therapy, the AUC for T-suppressors was 0.785 (95 % CI 0.622–0.902), which, in contrast to the previous group, corresponds to the “good” quality of the statistical model.

According to ROC analysis of the level of B lymphocytes in the compared groups, the AUC in women with rhesus sensitization and standard observation corresponded to the poor model quality – 0.58 (95 % CI 0.405–0.742). In the group of women receiving IVIG therapy, the quality of the statistical model corresponded to a “very good” level – 0.843 (95 % CI 0.689–0.941).

The ROS-analysis of the efficacy of therapy of rhesus-sensitized women IVIG on the normalization of cellular immunity showed (Fig. 1).

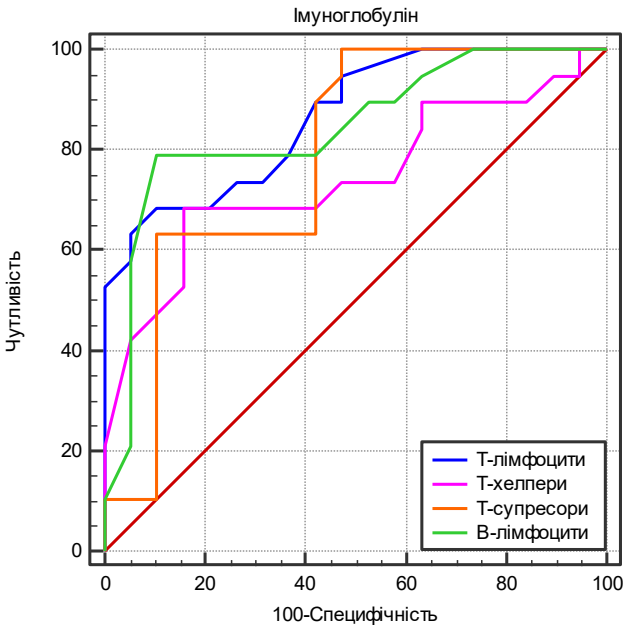

Figure 1. The result of ROC analysis of the main indicators of cellular immunity in women who received immunoglobulin for the treatment of rhesus isosensitization

In the group of women who received IVIG therapy, the odds ratio of normalization of cellular immunity indicators was: by the level of T-lymphocytes – 18.41 (95 % CI 2.62–166.74), T-helpers – 14.93 (95 % CI 2.45–107.8), T-suppressors – 14.57 (95 % CI 2.13– 127.57) and B lymphocytes – 31.87 (95 % CI 4. –333.41). According to the ROC analysis, the quality of the statistical model of the IVIG application corresponds to the “very good” level – 0.843 (95 % CI 0.689–0.941) According to the ROC analysis, the level of B lymphocytes in the compared AUC groups of women in

the comparison group corresponded to the poor quality of the model – 0.58 (95 % CI, 0.405–0.742).

The sensitivity of the use of IVIG was 0.82, specificity - 0.76, which corresponds to the high quality of the studied statistical model and allows to recommend for carrying out pre-gravidar preparation of women with Rh-isosensitization.

CONCLUSIONS. 1. The state of cellular immunity in rhesus-sensitized women, characterized by a moderate decrease in the absolute and relative indices of T-lymphocytes while increasing the number of B-lymphocytes.

2. The NK cell population does not differ from that of the control group.

3. In the analysis of subpopulations of T-lymphocytes, we can conclude that the number of T-helper is increased and the number of T-suppressors is proportionally reduced. These changes explain the increase in the number of B lymphocytes due to increasing antigenic load on cell receptors.

4. In the group of women who received therapy with IVIG, the ratio of the chances of normalization of indicators of cellular immunity was: by the level of T-lymphocytes – 18.41 (95 % CI 2.62–166.74), T-helpers – 14.93 (95 % CI 2.45–107.8), T-suppressors – 14.57 (95 % CI 2.13–127.57) and B lymphocytes – 31.87 (95 % CI 4.1–333.41.

5. According to ROC analysis, the quality of the statistical model for the use of IVG corresponds to a “very good” level – 0.843 (95 % CI 0.689–0.941) versus the control group corresponded to poor quality – 0.58 (95 % CI 0.405–0.742).

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