

SOME IMMUNOLOGICAL CHANGES IN INBRED CHILDREN WITH FREQUENT ILLNESS

The parameters of cellular immunity were studied in 17 children before and one month after treatment. The analysis of parameters of the cellular immunity (CD3+, CD20+, CD4+ and CD8+ regulatory subpopulations of T-lymphocytes) showed that they are within the limits of the standard norms both in the group of healthy children from inbreeding marriage and in group of relatively healthy ones from non-inbreeding marriage. However, in the sick children from inbreeding marriage the diseases induced more profound immune deficiency; and the consequence of that is less expressed effect from performed specific neurological treatment in these patients.

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Introduction

All living organisms are characterized by adaptability to the most various factors of the environment. Among them there are such that have been effecting on organisms during many geological epoch (force of gravitation, alternation of day and night etc.) and such, that work only for a short time and strictly locally (deficit of food, cooling etc.). In order to be adapted, the organism must have additionally to the stable attributes which are not varying during a life, the varying attributes depending on the environmental factors.

In the higher organisms, particularly in human, the high level of adaptation to the environment is achieved by that the genes define not only final attribute but also limits of attribute variations depending on the specific environmental factors. The variations of gene expression cannot be unlimited. They are limited by potentiality of the material substrate of hereditary structures, which are in the certain borders. Their property is called as the hereditary caused norm of the body response. It defines body homeostasis in the changeable environmental conditions. The long and regular effect of these factors on many generations can form positive or negative changes of their heredity. One of the factors forming negative changes in heredity of generations, are consanguine couples among their ancestors, when there is inbreeding depression of identical genes inherited from the general ancestors. The inbreeding among the nation results in decrease in number of heterozygous and increase in number of homozygous persons; from generation to generation the genes determining "negative" properties of the organism are even more often inherited. Hence, from generation to generation there is a restriction and attenuation of adaptive properties, including protective mechanisms of the system of immunity of the organism of the future generations. The present research is an attempt to show distinctions in the parameters of immunological status, which genetic determinacy has been proved between inbred children with frequent illness and identical group of children from not inbreeding marriage.

Materials and methods

Forty children at the age of from 1 till 6 years were studied who was noted somatic weakness and predisposition to catarrhal diseases. At all ill children there were evaluated parameters of cellular immunity before treatment and one month after the finish of the course of treatment. The control included characteristic findings of healthy children of the

same age. Immunological investigations were carried out in the laboratory of Scientific Research Institute of Epidemiology, Microbiology and Infectious.

All children were divided into 4 groups:

Group 1 - relatively healthy children from inbreeding (10);

Group 2 - healthy children from not inbreeding (13);

Group 3 - ill children from inbreeding (8);

Group 4 - ill children from not inbreeding (9).

The content of CD3+ T lymphocyte, CD20+ B lymphocyte populations, subpopulations of CD4+ T-lymphocytes and cytotoxic CD8+ lymphocytes were determined with use of monoclonal antibodies in the peripheral blood. The immunoregulatory index (IRI) was determined by calculation of the proportion CD4+/CD8+. Besides, the percentage of antigen-binding lymphocytes (ABL), specifically sensitized in relation to brain tissue antigens (TAG) were determined in all the studied children.

Determination of ABL to TAG of different organs were performed by method of Garib and Zalaliev (1989). According to this method the patient's lymphocytes were incubated with erythrocyte diagnosticum containing erythrocytes with TAG fixed of the membrane surface. The receptors are bound with TAG on the lymphocyte membranes and the "rosettes" from bounded lymphocytes and erythrocytes appeared on the erythrocyte membranes. The percentage of lymphocytes bounded with erythrocytes in relation to the total pool of the latter was calculated on the stained samples. The content of blood ABL related to TAG up to 2 % from total lymphocyte pool is considered as physiological, and more than 2 % - as a sign of organ pathology. Statistical processing of a digital material with calculation of average arithmetic value, average quadratic deviation, as well as reliability of differences were carried out with use of dispersion analysis and computer program XP - 2003. The differences between parameters were considered to be reliable in $p < 0.05$.

At the comparative analysis for obtaining of the objective information about the state of immunity system in studied groups we measured the following parameters of the changed cellular immunity: an orientation of changes, intensity of changes and character of immune response. Direction and degree of changes were measured by indexes of induction - II or index of suppression - SI. The mean of II reflects degree of increase, and SI - degree of reduction of the parameter in relation to the parameters in the compared groups. Introduction and use of II or SI increased considerably information value and efficacy of the assessment of the degree of parameter changes. The character of immune response was evaluated by the values of IRI: the increase (induction) of IRI is estimated as helper, and lowering (suppression) of IRI - as suppressing character of immune response of macroorganism.

Results and discussion

Comparison of the cellular immunity parameters of healthy children from consanguineous marriage (group 1) with identical group of children from the non consanguineous marriage (group 2) showed that all parameters of cellular immunity CD3 +, CD20 +, CD4 + - and CD8 + of T lymphocyte regulatory subpopulations were reliably higher 1.09, 1.20, 1.19 and 1.18 times, respectively, in children of group 2 ($P < 0.05$) (Table).

Study of antigen-binding lymphocytes (ABL), specifically sensibilized to tissue brain antigen were also reliably differed in comparative groups, that is ABL were reliably higher 1.67 times in the group of relatively healthy children from consanguinity marriage ($P < 0.05$) (Table 1).

It should be noted, however, that parameters of cellular immunity both in the group of healthy children from consanguineous marriage and in the group of children from the non consanguineous marriage are within the limits of the standard norms.

TABLE 1. DYNAMICS OF THE CELLULAR IMMUNITY PARAMETERS, ANTIGEN-BINDING LYMPHOCYTES IN HEALTHY AND ILL CHILDREN FROM CONSANGUINEOUS AND NON CONSANGUINEOUS MARRIAGES

Para- meters of cellular immunity	Healthy children of consanguineous marriage n -10	Healthy children of non consanguineous marriage n -13		The ill children of consanguineous marriage n-8		The ill children of non consanguineous marriage n-9	
	M±m	M±m	III↑ or SI ↓	M±m	OII or↑	M±m	OIII or TSI↓
CD3	50.70±0.65	55.08±0.54*	↑1.09	39.00±0.38*	↓1.30	41.11±0.82*	↓1.33
				43.88±0.72*●	↓1.16	48.89±0.48*●	↓1.13
CD4	27.30±0.42	32.62±0.51*	↑1.19	20.50±0.38*	↓1.33	23.22±0.40*	↓1.40
				23.25±0.53*●	↓1.17	25.11±0.26*●	↓1.30
CD8	20.40±0.62	24.00±0.28*	↑1.18	17.75±0.31*	↓1.15	18.67±0.41*	↓1.30
				18.13±0.48*	↓1.12	18.00±0.33*	↓1.33
IRI	1.34±0.03	1.42±0.02*	↑1.06	1.15±0.03*	↓1.16	1.24±0.02*	↓1.14
				1.29±0.03●	↓1.04	1.40±0.03●	↓1.01
CD20	16.60±0.56	19.85±0.27*	↑1.20	14.00±0.27*	↓1.19	16.00±0.24*	↑1.24
				16.00±0.27●	↓1.04	18.44±0.29●	↓1.08
ABL to TAG	2.70±0.30	1.62±0.14*	↓1.67	6.38±0.56*	↑2.22	5.56±0.24*	↑3.43
				5.88±1.03*	↑2.18	4.78±0.28*	↑2.95

Note: III↑ - induction index; SI↓ - suppression index; TIII↑ или TSI↓ - total induction index or suppression in comparison of parameters of healthy children.

* - p<0.05 - reliability of differences in relation to parameters of healthy children;

● - p<0.05 - reliability of differences in relation to period of disease progressing.

The study of the parameters of cellular immunity in group of patients from consanguinity marriage (group 3) and identical group of the patients from a non consanguineous marriage (group) allowed to establish that in the patients from groups 3 and 4 there was occurred reduction of the contents of CD4 + (T-helpers) and CD8 + (T-cytotoxic lymphocytes) T-lymphocyte regulatory subpopulations. Thus, the contents of CD4 + lymphocytes in the patients of groups 3 and 4 lowered in comparison of the parameters of the healthy persons 1.33 and 1.40 times, respectively, and the contents of CD8 + lymphocytes lowered by 1.15 and 1.30 times, respectively. The consequences of the differences in degree of lowering parameters CD4 + - and CD8 + - lymphocytes was the reliable decrease in IRI values (ratio CD4 + /CD8 +) 1.16 times in group 3 and 1.16 times in group 4 in comparison with those in the healthy persons (P < 0.05) (Table 1). The lowering change of parameters ИРИ indicated about functional domination in T-helper chain above the cytotoxic cells in the system of T-lymphocytes and seems to be indirect manifestation of the chronization of the process in these patients.

The results of study of the contents of antigen-binding lymphocytes (ABL), specifically sensitized to tissue antigens (TAG) of brain, showed that both in group 3, and in group 4 there is marked increase of these parameters in the peripheral blood of the patients. So, in the patients of group 4 the contents of ABL in relation to TAG of brain increased 3.43 times, and in the patients of group 3 exceeded 2.36 times the allowable high normal limit of the healthy persons (Table 1).

Increase in ABL related to TAG of any organ is a reflection of the development in its tissue of the processes of dystrophy cell destruction and intercellular structures. As a result specific for this organ tissue the structural and functional proteins or their fragments come into internal environment and appeared to be the cause of the endogenous intoxication of the body and acquired the status of antigen. One of manifestations of immunological response is differentiation and circulation of lymphocytes in the blood, specially sensitized and capable to bind tissue proteins on the surface of its membrane, that is, antigen-binding lymphocytes.

Hence, in the patients of these studied groups consequently, due to endogenous intoxication in the tissue of brain the processes of dystrophy and destruction develop. According to the data of investigations of ABL in patients of groups 3 and 4 the highest

degree of changes was found in the tissue of the brain in the patients of consanguineous marriage.

Thus, in the studied patients the secondary immune deficit has been developed characterized by disproportion of immune regulatory CD4 + - and CD8 + - T lymphocyte subpopulations and reduction of T-helper subpopulation activity and suppressor character of the immunity system before treatment and is accompanied by the expressed changes in the brain tissue.

All children were surveyed repeatedly after treatment. The preparations improving microcirculation and substance metabolism in brain, vitamins of group B were prescribed.

Effect of treatment on the dynamics of cellular immunity parameters in the patients from consanguineous marriage

During treatment of the children from consanguineous marriage (group 3) there are noted changes of cellular immunity parameters towards normalization. After treatment there was noted increase in the blood contents of CD4 + - and CD8 +- lymphocytes 1.13 and 1.02 times, respectively, in comparison with those before treatment. More intensive increase in the content of CD4 +- lymphocytes promoted increase in IRI more than 1.12 times in relation to parameters before treatment, that is a bit lower than parameters in the healthy persons (1.04) and indicated about functional prevalence of T-helper subpopulation and helper character of immunity after treatment (Table 1).

The study of dynamics of ABL related to brain tissue antigens showed that in the patients the effect of the treatment performed is reflected in unreliable reduction of their parameters. So, after treatment the contents of ABL related to TAG in the peripheral blood of the patients were lowered only 1.02 times in comparison with those before treatment (Table 1). The similar insignificant decrease in ABL related to TAG indicated that the treatment performed was ineffective and did not provide apparent extinction of processes of dystrophy and destruction in brain tissue. It is the important precondition for introduction of more effective agents into a complex of medical preparations for restoration of the broken structure and function of these bodies.

Thus, in group of the patients from consanguineous marriage after the course of treatment directed to stopping of the processes of inflammation in brain tissue and to restoration of damaged function in the patients, there were noted reliable changes in the parameters of cellular immunity towards the improvement, but slight decrease in intensity of the processes of dystrophy and destruction in brain tissue.

Effect of treatment on dynamics of the cellular immunity parameters in the children from non consanguineous marriage

In contrast to group 3 during and after the course of treatment in the patients the dynamics of parameters of cellular immunity is also characterized by increase in the contents of CD4 + - lymphocytes 1.08 times in comparison with parameters before treatment, whereas the parameters and CD8 + - lymphocytes tend to lowering (1.03 times) in the peripheral blood. Because of multidirectional changes of parameters CD4+ - and CD8 +- lymphocytes there was noted increase in values IRI to 1.40 vs. 1.24 before treatment (Table).

Dynamics of parameters ABL related to TAG of brain before and after treatment of the patients of group 4 indicated that the treatment provided decrease in blood ABL related to TAG of brain 1.16 times in comparison with parameters before treatment. However, after treatment the contents in blood ABL related to TAG of brain tissue of the patients remains 2.95 times higher than allowable ones in healthy persons. That is, the applied treatment has not supplied the complete stopping of the processes of destruction in the brain tissue.

The comparative analysis of the treatment efficacy in groups 3 and 4 shows, that the treatment performed has given more appreciable result in group of children from non consanguineous marriage, that is expressed in reliable differences in parameters CD3 + - and CD20 + - lymphocytes (43.88 ± 0.72 ; 48.89 ± 0.48 and 16.00 ± 0.27 ; 18.44 ± 0.29 , respectively, ($P < 0.05$).

Thus, the comparative analysis of immunological status of healthy and ill people in comparative aspect from consanguineous and non consanguineous marriage shows that in the ill children from consanguineous marriage the diseases induce more profound immune deficit state, the consequence of which is less favorable effect from specific neurological treatment of these patients.

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