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Functioning of the Immune System in Children, After Surgical Correction of Congenital Heart Defects

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Abstract: It is reported that the overall prevalence of CHD at birth has increased significantly over the past century, reaching a stable estimate of 9 cases per 1,000 live births over the past 15 years.

The results of scientific works have shown that the problem of the consequences of induced thymectomy for improving surgical access to the heart during its surgical correction in children in the aspect of the formation of immunopathological conditions remains relevant. In children with CHD, it is important to conduct immunological studies to assess the severity of the pathological process, severity, course, and prognosis of outcomes.

The study aimed to study the functioning of the immune system in children who underwent surgical treatment of congenital heart defects

Materials and methods: 58 children with CHD were examined based on the Bukhara Regional Children's Multidisciplinary Medical Center (BRChMMC) in the cityof Bukhara, whose mothers were excluded from immunological diseases. They were divided into 2 groups:

- the first group-30 children with ventricular septal defect(VSD) after surgery in the ageaspect.
- the second group - 28 children with Fallot's Tetralogy(TF) after surgery in the age related groups.

Indicators of cellular and humoral immunity, cytokine (IL-10, TNF-α) status were studied.

Results and discussion: A 2.4-fold increase in the relative content of NK cells was found ($p<0,01$)in VSD and TF, there is a persistent continuation of T-lymphocyte deficiency and a compensatory increase in suppressor (CDCD8) and, especially, CD-killers (CD16) activity.

A dynamic study of the concentrations of immunoglobulins G, A, and M showed a decrease in the synthesis of Ig A in all types of CHD after the surgical period.

A 4-fold increase in the titer of IL-10 and TNF-α was found in VSD and TF after surgery. This means that CHD in the postoperative period is characterized by a multidirectional immunomodulatory effect of TNF-α.

Conclusions: Thus, surgical correction of CHD with sternotomy (partial or complete removal of the thymus) later leads to a decrease in innate and adaptive immunity.

Keywords: CHD(Congenital heart defects), immune, thymus, thymectomy, surgical, immune response, T-killers, TNF-α, CD cells, Tetralogy of Fallot (TF), ventricular septal defect(VSD)

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Congenital heart defects (CHD) - the most common congenital anomaly, which affects approximately 1% of births and increases survival in this population increases the ability to assess long-term diseases. There is a wide range of congenital heart defects, from those that do not require medical or surgical intervention, to complex structural abnormalities that require highly specialized medical and complex surgical treatment.[3,11,15]

It is reported that the overall prevalence of CHD at birth has increased significantly over the past century, reaching a stable estimate of 9 cases per 1,000 live births over the past 15 years. This corresponds to 1.35 million newborns with CHD each year, which is a major health burden worldwide.[1,4,15]

The recent prevalence of CHD in Russia for the first time in Asia, it was higher, than in the previous year. Europe and in America, where the establishment of the disease, is likely, to be almost complete. This indicates a higher genetic or environmental susceptibility to CHD among Asian people.[4.7,18]

Due to the progress of modern medicine, which was achieved by improving diagnostic and surgical techniques, there is a decrease in mortality rates in patients with CHD.

The thymus, as the primary site of formation of the corresponding adaptive immunity, is an important organ[8].The thymus gland is very sensitive to a wide range of stressors that cause acute structural changes. Hypoxia is one of the most common complications in patients with congenital heart defects, and it provokes stress-induced thymic involution[10, 12]. Thymic dysfunction in combination with congenital heart defects can negatively affect physiological immune mechanisms.[5,15,45]

Frequent acute respiratory infections in CHD lead to a decrease in immunity and the formation of foci of chronic infections, the exacerbation of which is one of the reasons for late surgical correction, resulting in a high risk of complications, mortality, and a decrease in the quality of life of patients with CHD.[7,19,21]

The results of scientific works have shown that the problem of the consequences of induced thymectomy for improving surgical access to the heart during its surgical correction in children in the aspect of the formation of immunopathological conditions remains relevant. Complete thymectomy in early infancy reduces the number of circulating T cells and T-cell-mediated immune responses for at least 3 years[2,9,19].Because of this, the thymus must be at least partially preserved during surgery in early infancy to maintain protective immunity. [2,6,16]

In children with CHD, it is important to conduct immunological studies to assess the severity of the pathological process, severity, nature of the course, and predict outcomes, including, first of all, determination of the levels of lymphocyte subpopulations, immunoglobulins, autoantibodies, and cytokine profile indicators.[10,20,28]

According to some authors, it is important to determine the clinical and immunological features of CHD in children, both before and after cardiac surgery correction of the defect. To optimize measures in the postoperative period in CHD, it is necessary to study the indicators of the immune status and subclasses of immunoglobulins G. [9,18,10,43]

In the postoperative period, pediatricians should take into account the immune status of children with CHD, especially those with complex forms of malformations, to prevent the frequent development of acute, recurrent, and complicated forms of infection, since the functional state of blood cells in such children reflects the failure of the immune system [3,13,26].

The study aimed to study the functioning of the immune system in children who underwent surgical treatment of congenital heart defects

Materials and methods: 58 children with CHD were examined based on the Bukhara Regional Children's Multidisciplinary Medical Center(BRChMMC) in the city of Bukhara, 58 children whose mothers were excluded from immunological diseases. They were divided into 2 groups:

- the first group-30 children with ventricular septal defect(VSD) after surgery in the childhood age periods.
- the second group - 28 children withFallot'sTetralogy(TF) after surgery in the childhood age periods.

Surgical correction of CHD was performed at the cardiac surgery centerTashkent Pediatric Medical Institute and the Republican Center for Thoracic Surgery named afterVakhidov, as well as abroad: in the Russian Federation, Ukraine, and India.

The control group consisted of 30 healthy peers.

The analysis of the general condition of the body was carried out with the help of a thorough collection of anamnesis of the disease and data from consultations with related specialists.

CHD was verified according to the requirements of the World Health Organization (WHO) and classified according to the International Classification of Diseases (ICD-10).

During the examination, clinical-immunological, biochemical, laboratory, and functional tests were performed (DOECHOCG, ECG, radiography) studies. The examination included Doppler echocardiography. The state of the immune response in children during and the first 6 months after CHD surgery was studied.

Immunological blood tests of sick children were performed in the immunomorphological laboratory of Institute of Human Immunology and Genomics. Indicators of cellular and humoral immunity, cytokine (IL-10, TNF-α) status were studied.

Results and discussion:

Indicators of immunity depending on the type of CHD illustrate their characteristics.A 2.4-fold increase in the relative content of NK cells was found (p<0,01)in VCD and TF, there is a persistent continuation of T-lymphocyte deficiency and a compensatory increase in suppressor (CDCD8) and, especially, CD-killer (CD16) activity.

Table 1.

Display-Tel'	Control group n=30	DMJP n=30	TF n=28
Leukocytes, andBS.	7800±54,6	7500±21*	7200±11,0*
Lymphocytes, %	36,77±Of 2.77	24,3±1,8*	19,0±1,7*
Lymphocytes,andBS.	3354 ± 34,0	1900±11*	2180±18*
$CD4^+$, %	45,2 ± 1,5	22,2±1,8*	33,0±4,0*
$CD4^+$,abs	1320 ± 23,7	1545±9,0*	1221±7,7*
$CD8^+$, %	20,8 ±of 1.8	to 21.2±1,2	31±1,9*
$CD8^+$,abs	366 ± 14,0	333±12,0	444±3,5
CD4/ CD8	2.2 ± 0.4	1.04±0.8	1.06±0.8

Parameters of cellular immunity in the examined children, (M ±m)

A dynamic study of the concentrations of immunoglobulins G, A, and M showed a decrease in the synthesis of Ig A in all types of CHD after the surgical period. Therefore, based on the above data, it should be concluded that surgical correction of CHD with sternotomy (partial or complete

removal of the thymus) in the future leads to a decrease in innate and adaptive immunity. The state of immune regulation in children with CHD is characterized by activation of the B-cell pathway. link against the background of an imbalance in the T-lymphocyte population.

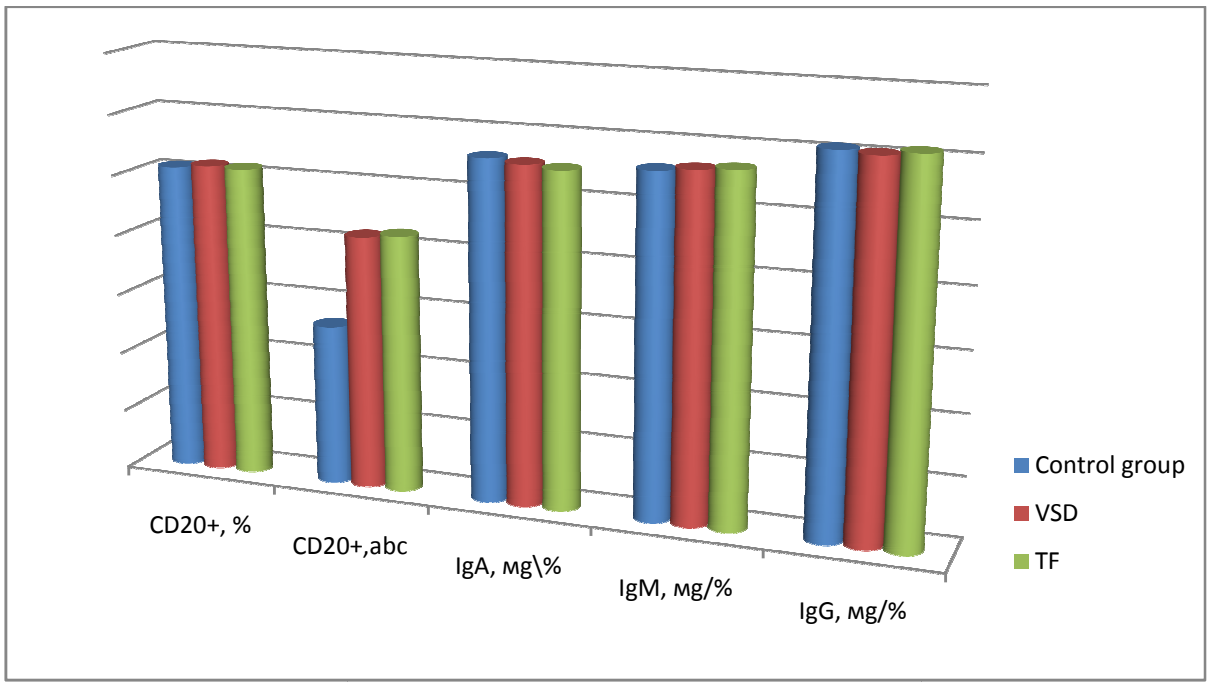

Figure 1. Indicators of the B-immune system in the examined children

Cytokine status in CHD after the surgical period determines the course and prognosis of the postoperative process. A 4-fold increase in the titer of IL-10 and TNF-α was found in VSD and TF after surgery. This means that, CHD in the postoperative period is characterized by a multidirectional immunomodulatory effect of TNF-α.

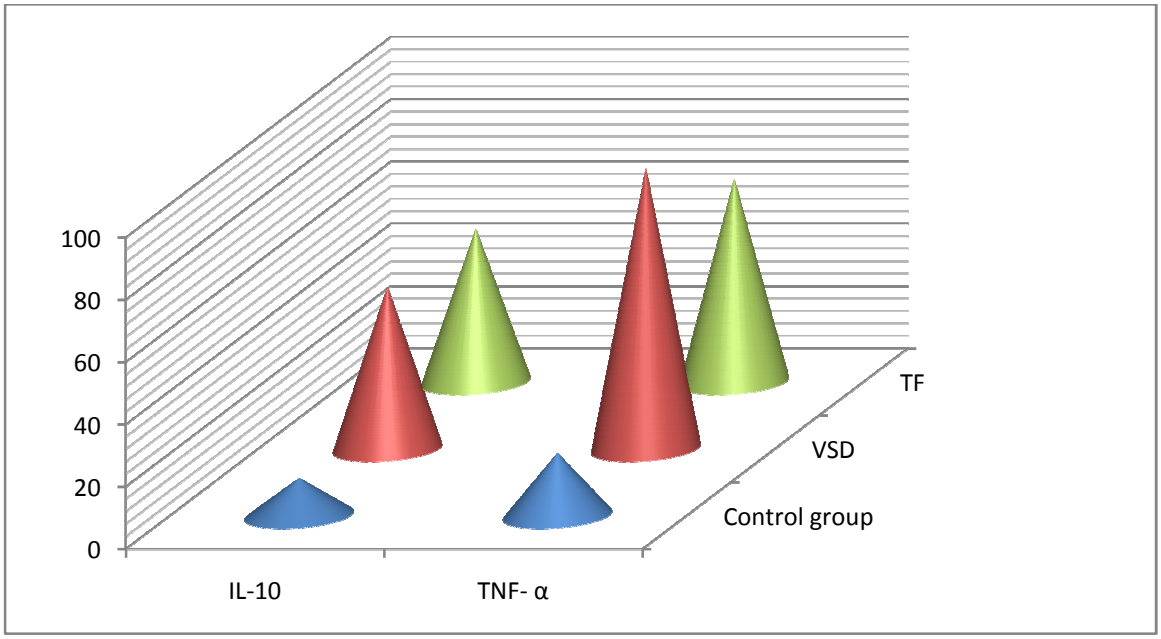

Figure 2. Cytokine status indicators in the examined children

At the stages of formation of adaptive immunity in CHD (in conditions of hypoxia, cardiac hemodynamics, and cardiac activity disorders), homeostasis and neuro-humoral regulation are

aimed at enhancing proliferative processes and compensatory hypercoagulation in the postoperative period.

Conclusions:

Thus, surgical correction of CHD with sternotomy (partial or complete removal of the thymus) later leads to a decrease in innate and adaptive immunity.The results of the study can be used in the development of differentiated approaches to immunomodulatory drugs in the treatment of patients with congenital heart defects in the postoperative period.

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