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Evaluation of IL-1β and IL-33 Levels Results in Children with Congenital Heart Defects

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Abstract Congenital heart disease (CHD) is the leading cause of birth defect-related morbidity and mortality, with 48.5% of cardiovascular deaths in children caused by CHD. Although simple CHD (e.g. ventricular septal defect) can be treated completely, complex CHD requires surgical intervention in early infancy and has a high mortality rate. The first year of life is critical for postnatal heart development. During this period, the structure and function of the infant heart change rapidly, with the heart rate declining from 150 beats per minute to 80 beats per minute and the systolic blood pressure rising from 55 mmHg to 100 mmHg. Almost 55.3% of CHD deaths occur in the first year of life. Although cardiomyocyte cell cycle activity is critical for heart development and damage repair, information on this process is limited. For example, data supporting that the average percentage of M-phase cardiomyocytes is 0.012 ± 0.003% is obtained from two samples only.

Keywords Congenital heart defects, Cytokines, Interleukin-1β, Interleukin-33, Serum

1. Introduction

Interleukin-1β (IL-1β) is a key proinflammatory cytokine that plays a central role in the activation of the innate immune response, the development of systemic inflammation and tissue remodeling [2,7,9]. Its concentration in the blood serum often serves as an indicator of the presence and severity of the inflammatory process, including in cardiovascular diseases [1,4,10]. In children with congenital heart defects, the IL-1β level can act not only as an inflammation marker, but also as a prognostic indicator of the risk of complications in the perioperative period. Interleukin-33 (IL-33) is a member of the IL-1 cytokine family and functions as an alarmin, a signaling molecule released during cellular damage and playing a key role in triggering the immune and inflammatory response [3,6,10]. IL-33 is particularly active in the cardiovascular system, where it is expressed in endothelial cells and fibroblasts, participating in the formation of inflammation, myocardial remodeling and the development of heart failure [5,8].

The aim of the study: determine the concentration of proinflammatory cytokines interleukin-1β (IL-1β) and interleukin-33 (IL-33) in blood serum in children with congenital heart defects.

2. Material and Methods of the Study

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Clinical studies were conducted in the cardiac surgery departments of the Tashkent Pediatric Medical Institute and the Era Med Multidisciplinary Medical Center from 2021 to 2024. The study involved 232 children, including 202 patients with a confirmed diagnosis of congenital heart disease. These patients were divided into two groups.

The first group included 92 children (47.4%) with cyanotic forms of CHD, which were divided into 2 subgroups. Subgroup 1a consisted of 47 children who underwent CPB with classical ultrafiltration. Subgroup 1b consisted of 45 children who underwent CPB with modified ultrafiltration. The second group consisted of 110 children (39.7%) with acyanotic forms of CHD, which were also divided into 2 subgroups. Subgroup 2a consisted of 57 children who underwent CPB with classical ultrafiltration. Subgroup 2b consisted of 53 children who underwent CPB with modified ultrafiltration.

The control group consisted of 30 (12.9%) practically healthy children.

The criteria for exclusion from the study were: children with severe genetic diseases and stigmas of dysembryogenesis, the presence of infectious and inflammatory diseases.

The diagnosis of congenital heart disease and the type of defect were established based on echocardiography data.

Kits for quantitative determination of IL-1β and IL-33 by ELISA (Human IL-1β ELISA Kit, Human IL-33 ELISA Kit - manufactured by R&D Systems).

3. Research Results

The study revealed a clear dependence of the IL-1β level

on the presence and nature of congenital heart disease. In children in the control group who did not have cardiovascular pathology, the IL-1β level was 2.9±0.4 pg/ml, which corresponds to normal physiological values and reflects the absence of an active inflammatory process (Fig. 1).

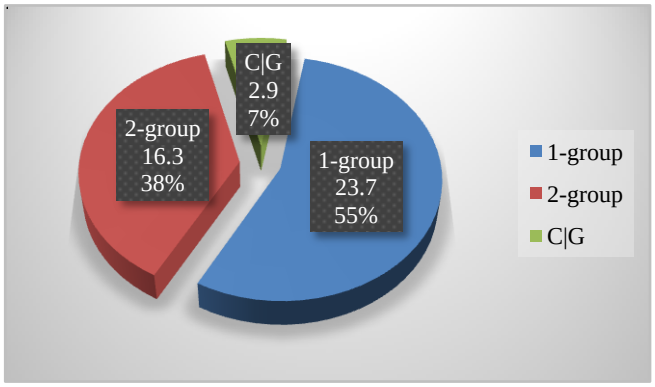

Figure 1. Average levels of proinflammatory cytokine IL-1 (pg/ml) in children with CHD

In children of group 1 suffering from cyanotic forms of congenital heart disease (such as tetralogy of Fallot, transposition of the great vessels, etc.), a sharp and statistically significant increase in the concentration of IL-1β to 23.7±4.8 pg/ml was observed. This indicates a pronounced activation of the inflammatory cascade, which is probably associated with chronic hypoxia, systemic overload and tissue ischemia typical for this category of patients. In such children, inflammation has both a local (cardiac) and systemic nature, which can contribute to the progression of heart failure, myocardial remodeling and an increased risk of postoperative complications.

In children of group 2 with acyanotic heart defects (septal defects, patent ductus arteriosus, etc.), the IL-1β level was also significantly elevated compared to the control group and was 16.3±2.6 pg/ml. Although the cytokine values in this group are lower than in cyanotic CHD, they still indicate the presence of a systemic inflammatory response caused by volume overload, chronic activation of the endothelium and myocardium, and subclinical hypoxic stress.

These results indicate that IL-1β may serve as an important biomarker of inflammatory activity in children with congenital heart defects. Its increased concentration correlates with the severity of the defect and the severity of systemic hypoxia, which makes this indicator potentially significant in risk stratification, surgical treatment planning and postoperative monitoring.

Thus, the inclusion of IL-1β in the panel of laboratory markers in children with CHD can significantly improve the accuracy of clinical assessment, promptly identify subacute inflammatory process and predict the risk of complicated course of the disease. Comprehensive assessment of IL-1β along with other biomarkers (such as NT-proBNP, sST2, CRP, etc.) allows for a more personalized and pathogenetically substantiated approach to diagnosis and treatment of this category of patients.

The conducted analysis of the IL-33 level in children with various forms of congenital heart disease showed a significant increase compared to the control group:

Control group (healthy children): the IL-33 level was 2.3± 0.3 pg/ml, which corresponds to the normal physiological range and the absence of inflammatory activation.

Group 1 (children with cyanotic forms of congenital heart disease): the IL-33 level reached 19.2±3.6 pg/ml, which indicates an active inflammatory reaction and hypoxic-ischemic tissue damage.

Group 2 (children with acyanotic forms of congenital heart defects): the IL-33 level was 14.5±2.2 pg/ml, which also exceeds the norm and confirms the presence of systemic inflammatory activation, although the severity of the reaction is lower than with cyanotic defects (Fig. 2).

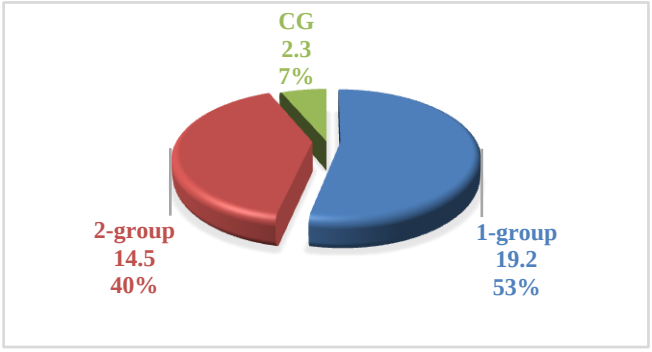

Figure 2. Average levels of proinflammatory cytokine IL-33 (pg/ml) in children with CHD

IL-33, in turn, signals the presence of an immune-inflammatory response and structural tissue damage.

IL-1β, a key proinflammatory cytokine, demonstrates a marked increase in patients with CHD, especially in cyanotic forms, indicating the presence of a systemic inflammatory background. Elevated IL-1β may contribute to worsening myocardial dysfunction, impaired cardiac tissue remodeling, and an increased risk of complications.

IL-33, in turn, is a signaling cytokine involved in both inflammatory and protective-regenerative responses. Elevated IL-33 levels in children with CHD, especially in cyanotic defects, reflect activation of stress-induced pathways and, possibly, a compensatory attempt to limit myocardial damage.

4. Conclusions

Thus, the integrated assessment of these cytokines allows for more accurate risk stratification, monitoring of the child's condition dynamics and predicting the outcomes of surgical treatment of congenital heart disease. Inclusion of these indicators in clinical practice can significantly improve the effectiveness of diagnostics, prognosis and individualization of therapy.

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