Summary

CYTOKINE PROFILE RESPONSE IN PATIENTS WITH FRACTURES OF LONG BONES DURING COVID-19

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Key words: trauma, patients, coronavirus infection, immunological indicators, interleukins, diagnosis.

Introduction: The immune system swiftly responds to the onslaught of trauma and the infectious agents it triggers. However, the mechanisms of action of the COVID-19 virus remain unidentified to date. Distinctive alterations that occur in the immune system of trauma victims with COVID-19, setting them apart from changes observed in other diseases. This underscores the specificity of traumatic disease within this patient with COVID-19.

The study aims to assess the response of humoral immunity markers in patients with fractures of long bones and COVID-19 and to explore their role in early diagnosing infectious complications in this particular group of patients.

Materials and methods: To accomplish the study objectives, we assembled a retrospective dataset comprising 289 cases of skeletal bone fractures treated at the Kyiv City Clinical Hospital of Emergency Medical Care from March, 2020 to February, 2021, meeting the inclusion criteria for the study. The entire dataset consisted of 289 cases of skeletal bone fractures, categorized into two groups: the main group and the control group.

Results: On the first day of treatment, an increase in some pro-inflammatory cytokines (IL-6, IL-1β and IL-4) with a normal level of TNF-α, normal values of IFN-γ, IFN-α and a sharp decrease in the anti-inflammatory cytokine IL was observed among the patients of the main group -10. On the third day of the treatment, there was a significant increase in all pro-inflammatory cytokines (IL-6, IL-1β, IL-4 and TNF-α), both types of interferons, and an even sharper decrease in the anti-inflammatory cytokine IL-10. On the tenth day, the growth in the level of pro-inflammatory cytokines was noted, among which the level of TNF-α was the leader, a subnormal level of interferons and anti-inflammatory interleukin 10 was observed. Conclusions: The dynamics of pro-inflammatory cytokines in patients with long bone fractures against the background of COVID-19 tended to increase and had a maximum level on the third day of treatment. Anti-inflammatory cytokines demonstrate a tendency to depression and reach the reference value only on the 10th day of the study.

Keywords: cytokines, children, congenital heart defects, TNF-α.

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TUMOR NECROSIS FACTOR-A AND INTERLEUKIN-6 IN BLOOD SERUM OF INFANTS AND CHILDREN WITH CONGENITAL HEART DISEASES

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The aim of the study was to evaluate the levels of tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) in infants and children with congenital heart defects (CHD) in comparison with the levels in the control groups. Materials and methods. The volume study included 56 patients, including 35 cyanotic and 21 cyanotic with congenital heart disease, as well as 20 control subjects. We used a specific immunoassay to measure serum ghrelin, TNF-α and IL-6 levels. All patients’ cardiac diagnoses were based on clinical examination, laboratory tests, electrocardiography and echocardiography, and none of the patients had pulmonary hypertension. The body mass index (BMI) was calculated as the ratio of body weight (kg) and height squared (m). The study also included 20 healthy infants and children corresponding to age and gender as a control group. Informed consent was obtained from the parents. Results. The results of the analysis indicate a significant increase in IL-6 and TNF-α levels in cyanotic and acyanotic patients with congenital heart defects compared with the control group (P < 0.0001). The findings highlight the importance of cytokines in the pathophysiology of congenital heart defects and their effect on patient growth. It is suggested that elevated levels of IL-6 and TNF-α may stimulate the process of apoptosis, which may play a key role in growth retardation. These data indicate the presence of growth disorders in a significant proportion of patients with congenital heart defects. These results provide additional details about the nature of growth disorders in patients with congenital heart defects and highlight the importance of further research to better understand the molecular and immunological mechanisms associated with this condition. Conclusion. The findings of this study support the hypothesis of the effect of cytokines on growth in congenital heart defects. Elevated levels of IL-6 and TNF-α are likely associated with chronic congestive heart failure and hypoxia. Further research is needed to confirm these results and develop therapeutic strategies for managing growth retardation in children with congenital heart defects.

Keywords: cytokines, children, congenital heart defects, TNF-α, IL-6.

Introduction

Congenital heart defects (CHD) affect 1% of newborns every year, which is equivalent to up to 9 out of 1,000 newborns according to WHO. A recent study [1] revealed that CHD is often not detected...
during prenatal screening, which can affect morbidity and mortality. In their study, more than half of the diagnosed cases of CHD were not detected before birth. Sometimes signs of poor blood circulation appear during the examination of a newborn or later in the first months of life. These include blotchy skin, cyanosis around the mouth, and insufficient weight gain [2]. Children diagnosed with congenital heart disease could undergo several surgical procedures, numerous hospitalizations and many years of taking medications. On the other hand, some families may require a minimum of medical or nursing care. Many children with CHD live with complications related to their condition, including learning disabilities [3]. Unfortunately, the mortality rate among children with CHD is high and accounts for 12% of the total number of deaths of children [4]. CHD can be classified as defects with a violation affecting blood flow and violations of the integrity of the septa, such as "pale, right-to-left" blue" defects [5], can also be more simply divided into acyanotic and cyanotic [6]. Tumor Necrosis Factor-α (TNF-α) and Interleukin-6 (IL-6) in the Context of CHD: Tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) are cytokines with numerous immunological functions and are considered as potentially important catabolic factors [7, 8]. Special attention is paid to IL-6, which plays a key role in the network of regulation of immune and acute phase reactions [9]. Congenital heart disease is an anomaly in the development of the cardiovascular system, divided into cyanotic and acyanotic forms. Improved diagnostic and treatment methods are designed to reduce the impact of CHD, given its high prevalence and serious consequences. Special attention is paid to the stagnant effect, which is accompanied by a decrease in blood oxygen levels and activation of immunological processes involving cytokines [10].

This study is aimed at a more detailed understanding of the effects of TNF-α and IL-6 in the context of congenital heart defects. Special attention is paid to their importance in immunological processes and catabolic reactions associated with CHD. Measuring TNF-α and IL-6 levels in infants and children with CHD involves identifying links between the immune response and the nature of the defect. It is also interesting to conduct a comparative analysis of these levels with control groups to identify features in the cytokine profile. Such studies can significantly expand our understanding of the molecular basis of congenital heart defects and provide new perspectives for the diagnosis and treatment of patients with CHD.

The aim of the study was to evaluate the levels of tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) in infants and children with congenital heart defects (CHD) in comparison with the levels in the control groups.

Materials and methods

The study was conducted in the immunological laboratory of the Azerbaijan Medical University at levels TNF-α and IL-6 using ELISA in 56 patients with congenital heart defects, classified into groups: 26 girls, 30 boys; aged 0–16 years; 35 acyanotic and 21 cyanotic; and in 20 control subjects. The material was collected at the Educational and Therapeutic Clinic at the Azerbaijan Medical University, the Educational and Surgical Clinic at the Azerbaijan Medical University, as well as the M.A. Topchubashev Scientific and Surgical Center. The patients were subjected to a full physical examination, their weight and height were checked. They were considered abnormal if they were below the 5th centile compared to standard reference data for children by age [11]. All patients' cardiac diagnoses were based on clinical examination, laboratory tests, electrocardiography and echocardiography; and none of the patients had pulmonary hypertension. The body mass index (BMI) was calculated as the ratio of body weight (kg) and height squared (m). The study also included 20 healthy infants and children corresponding to age and gender as a control group. Informed consent was obtained from the parents.

The collection of samples was done using venipuncture. Three milliliters of blood were allowed to coagulate at room temperature for 60 minutes. The serum was separated by centrifugation at 5,000 vol. ft. for 10 minutes, and then stored at -20°C. Quantitative determination of TNF-α and IL-6 in blood serum was performed using ELISA kits.

Statistical methods

The data was analyzed using SPSS, version 26. The following statistical tests were used: Mean and standard deviation (SD) to describe quantitative data. The student t-test was used to compare between the two groups with respect to parametric data. The chi-squared test was used to compare between two groups with respect to nonparametric data. The Pearson correlation was used to correlate two quantitative variables. For all tests, probability (p) <0.05 was considered significant.

Results

Of the 56 patients with congenital heart defects (CHD), 33 (60%) had a weight below the 5th centile, and 21 (38.3%) had a height below the 5th centile (Table 1). There was no statistically significant difference between the groups (acyanotic and cyanotic) in terms of average age, gender, weight, height and body mass index (BMI) (all p > 0.05).
Table 1. Age and anthropometric data of patients and control group

<table>
<thead>
<tr>
<th></th>
<th>Cyanotic patients (n=21)</th>
<th>Acyanotic patients (n=35)</th>
<th>Control group (n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>30.5 ± 16.4</td>
<td>28.4 ± 15.6</td>
<td>31.1 ± 15.1</td>
</tr>
<tr>
<td>female/ male</td>
<td>10/11</td>
<td>30/17</td>
<td>15/10</td>
</tr>
<tr>
<td>weight</td>
<td>9.7 ± 7.4</td>
<td>10.9 ± 6.2</td>
<td>21.2 ± 9.9</td>
</tr>
<tr>
<td>height</td>
<td>76.8 ± 26.8</td>
<td>83.6 ± 21.9</td>
<td>98.4 ± 22.9</td>
</tr>
</tbody>
</table>

Serum TNF-α levels in patients with acyanosis were significantly higher than in patients with cyanosis (p = 0.000). While serum IL-6 levels did not show a statistically significant difference between acyanotic and cyanotic patients (p = 0.126) (Figure 1).

These data indicate the presence of growth disorders in a significant proportion of patients with CHD. It is important to note that despite the similar average age, gender and BMI in both groups, differences in TNF-α levels highlight the possible effect of this cytokine on the development of cyanosis in the context of congenital heart defects. However, despite a significant increase in TNF-α levels in acyanotic patients, IL-6 levels did not show such a difference between the groups. This may indicate a variety of cytokines in the pathogenesis of CHD, where TNF-α may play a more significant role compared to IL-6.

These results provide additional details about the nature of growth disorders in patients with CHD and highlight the importance of further research to better understand the molecular and immunological mechanisms associated with this condition.

Discussion

Our results showed that patients with congenital heart defects, regardless of the presence or absence of cyanosis, had significantly higher levels of TNF-α and IL-6 than controls (p = 0.000).

We found that TNF-α in serum increased significantly in both acyanotic and cyanotic patients. Similarly, IL-6 serum was increased in both groups. TNF-α and IL-6 seem to be important mediators of the process, although this association is not fully established [12, 13]. Cardiac cachexia describes exhaustion mainly due to loss of lean body weight. Cachexia leads to a decrease in muscle strength and function and impaired immune function [14, 15]. This syndrome probably occurs in children with chronic congestive heart failure and chronic shunt hypoxemia [16]. In addition to insufficient intake of calories and protein, there is evidence that this syndrome may be caused by a circulating tumor necrosis factor that stimulates catabolism [17].

Conclusion

Serum levels of TNF-α and IL-6 are elevated in patients with CHD, whether acyanotic or cyanotic. In addition, the association of increased IL-6 levels with TNF-α can be explained by the possible effect of chronic congestive heart failure and chronic hypoxemia. Serum TNF-α and IL-6 levels are elevated in patients with congenital heart defects, whether acyanotic or cyanotic.

Prospects for further research

To study and understand the complex network of cytokines involved in heart remodeling in children with congenital heart defects in order to identify links between the immunological response and the nature of the defect, which will provide new prospects for diagnosis and treatment in patients with CHD.

References


Реферат

ФАКТОР НЕКРОЗУ ПУХЛИНИ-А ТА ІНТЕРЛЕЙКІН-6 У СИРОВАТЦІ КРОВІ У НЕМОВЛЯТ ТА ДІТЕЙ З ВРОДЖЕНИМИ ЗАХВОРЮВАНЯМИ СЕРЦЯ

Македова Лейла Вахід кизи

Ключові слова: цитокіни, діти, вроджені вади серця, фактор некрозу пухлини-а, інтерлейкін-6.

Мета дослідження. Оцінка рівнів фактора некрозу пухлини-а (TNF-α) та інтерлейкін-6 (IL-6) у немовлят та дітей з вродженими вадами серця порівняно з рівнями у контрольних групах.

Матеріали та методи. Дослідження проведені в Навчально-терапевтичній та Навчально-хірургічній клініках при Азербайджанському медичному університеті, а також в Науково-хірургічному центру імені М.О. Топчубашева (Баку, Азербайджан).

В дослідженні брали участь 59 пацієнтів з вродженою вадою серця, серед яких 35 мали аціанотичний симптом, а 21 - ціанотичний. Контрольну групу склали 20 здорових немовлят та дітей, що відповідають віку та статі. Загальноклінічні, лабораторні та інструментальні обстеження та лікування хворих проводили у відповідності до Європейських рекомендацій та за наявності інформованої згоди бацьків дітей. Кардіологічні діагнози пацієнтам були встановлені на основі клінічного обстеження, лабораторних досліджень, електрокардіографії та ехокардіографії. В жодного з пацієнтів не було виявлено легеневої гіпертензії.

Для вимірювання рівнів сироваткового грелюна, фактору некрозу пухлини-а та інтерлейкін-6 був використаний спеціфічний імуноаналіз.

Результати дослідження свідчать про значне підвищення рівнів інтерлейкіну-6 та фактору некрозу пухлини-а з ціанотичним та аціанотичним симптомами у пацієнтів з вродженими вадами серця порівняно з контрольною групою (P<0.0001). Зв’язок такого підвищення може бути пояснений можливим ефектом хронічної застійної серцевої недостатності та хронічної гіпооксії.

Отримані дані свідчать про важливість цитокінів у патофізіології вроджених вад серця та їх вплив на ріст і розвитоків пацієнтів. Передбачається, що підвищені рівні інтерлейкіну-6 та фактора некрозу пухлини-а можуть стимулювати процес апоптозу, що може відіграти ключову роль у затримці росту.

Висновки з цього дослідження підтверджують гіпотезу про вплив цитокінів на ріст при вроджених вадах серця. Підвищені рівні інтерлейкіну-6 та фактора некрозу пухлини-а, як правило, пов’язані з хронічною застійною серцевою недостатністю та гіпооксією. Подальші дослідження необхідні для підтвердження цих результатів та розробки терапевтичних стратегій з метою корегування затримки росту у дітей з вродженими вадами серця.

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