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State of immunity in preschoolers with acute respiratory viral infections associated with adenoid vegetations

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Abstract

Introduction. Acute respiratory infections are the most common infectious diseases worldwide among children of different age groups.

Materials and methods. 59 children between the ages of 3 and 7 participated in the study. The first group included 22 patients with an acute respiratory viral infection, the second one consisted of 23 patients with acute respiratory viral infections associated with adenoid vegetation, and 14 apparently healthy children were included in the control group. Immunology research was conducted during the acute period of the disease. Statistical processing of received data was done with the standard statistical software EZR 1.41.

Results. After the research, most of the patients with acute respiratory viral infections were identified an actual increase in CD3+, CD4+, CD8+, CD22+- cells and IgA, IgM in the blood serum. Simultaneously, in patients with acute respiratory viral infections associated with adenoid vegetation during the acute period, the increase in total lymphocytes was identified due to CD4+, CD8+, CD22+ cells and IgG. A comparative analysis of the study results of both groups of patients showed that children from the second group had a significantly higher level of CD3+- cells, while the CD22+- lymphocytes, IgA, IgM and IgG were significantly lower from the similar indicators of the first group.

Conclusions. The acute period of the disease in children with acute respiratory viral infections, associated with adenoid vegetation, had an imbalance in both the cell and the immune system's humoral component.

Keywords: immunity, cellular, humoral, adenoid, children, infection.

Стан імунітету в дітей дошкільного віку, хворих на гострі респіраторні вірусні інфекції на фоні аденоїдних вегетацій

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Вступ. Гострі респіраторні інфекції найпоширеніші інфекційні захворювання у всьому світі серед дітей різних вікових груп.

Мета. Вивчення клітинної та гуморальної ланок імунітету в дітей дошкільного віку, хворих на гострі респіраторні вірусні інфекції на фоні аденоїдних вегетацій.

Методи дослідження. У дослідженні взяли участь 59 дітей віком від 3 до 7 років. До першої групи увійшли 22 пацієнти з гострою респіраторною вірусною інфекцією, до другої – 23 пацієнти з гострими респіраторними вірусними інфекціями, які пов'язані з аденоїдною вегетацією, а в контрольну групу – 14 практично здорових дітей. Імунологічне дослідження проводили в гострий період захворювання. Статистичну обробку отриманих даних проводили за допомогою стандартного статистичного програмного забезпечення EZR 1.41.

Результати. Після проведених досліджень у більшості хворих на гострі респіраторні вірусні інфекції виявлено фактичне збільшення CD3+, CD4+, CD8+, CD22+- клітин та IgA, IgM у сироватці крові. Водночас у хворих на гострі респіраторні вірусні інфекції, пов'язані з аденоїдною вегетацією в гострий період, було виявлено збільшення загальної кількості лімфоцитів за рахунок CD4+, CD8+, CD22+ клітин та IgG. Порівняльний аналіз результатів дослідження обох груп пацієнтів виявив, що у дітей другої групи був достовірно вищий рівень CD3+- клітин, тоді як CD22+- лімфоцити, IgA, IgM та IgG були значно нижчими від аналогічних показників першої групи.

Висновки. Гострий період захворювання у дітей з гострими респіраторними вірусними інфекціями, пов'язаними з аденоїдною вегетацією, мав дисбаланс клітинного та гуморального компонента імунної системи.

Ключові слова: імунітет, клітинний, гуморальний, аденоїди, діти, інфекція.

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Introduction

Acute respiratory infections (ARI) are the most common infectious diseases worldwide among children of different age groups. Almost 90% of the world's population is infected with this disease at least once a year. The absence of specific immunity contributes to the rapid spread of ARI and its complications, leading to economic losses [1]. According to WHO, they account for 80%-90% of infectious pathologies [2]. More than a hundred million ARI cases among children under five years are recorded worldwide each year, with a mortality rate of 104.8 children per 100,000 population [3]. Every year more than 6 million people are registered as suffering from ARI in Ukraine. Besides, the high incidence is determined among children (> 60,000 per 100,000 of the child population) [4, 5, 6]. The etiological structure of ARI is diverse, with more than 200 viruses. Influenza viruses, parainfluenza, rhinoviruses, respiratory syncytial virus, adenoviruses, reoviruses and enteroviruses play an essential role [7, 8]. Viruses directly affect the respiratory tract's mucous membranes and indirectly affect the immune system. They reduce mucous membranes' barrier function, contribute to the respiratory tract's obstruction, and decrement gas exchange [8, 9]. The highest incidence of ARI is determined in children aged three to 14 years because they attend the preschool establishments and schools [8]. In addition, besides, it is due to the development of their immune system. This child's development is characterized by a lack of the immune system's humoral component, a decrease in the complement system's activation, incomplete fusion of the cytokine, and T-cell immunosuppression [10].

Adenoid vegetations perform an essential function of the immune system because it protects the mucous membrane of the child's rhinopharynx from various microbes that come from the air during breathing. They gradually increase to their maximum size at preschool age. Adenoid hypertrophy can cause apnea in children and recurrent infection [11].

The presence of adenoid vegetation in children load the disease's course and contributes to an acute recurrent inflammatory state. The obstruction of the posterior naris, nasal breathing is disrupted, and congestive phenomena are formed, leading to a delay of the mucociliary clearance that contributes to the microbes' growth [2, 12].

The work aims to study the cellular and humoral components of the immune system in preschoolers with acute respiratory viral infections associated with adenoid vegetations.

Materials and methods

This study was described in accordance with basic bioethical norms of the Declaration of Helsinki made by the World Medical Association concerning ethical principles on scientific and medical research. The study was conducted in accordance with the permission of the Ethics Commission of Municipal non-profit enterprise «Children's Clinical Hospital of Saint Zinaida» Sumy City Council, protocol No 6 of 12.09.19. We have surveyed 59 children between the ages of 3 and 7. The research was conducted based on the Municipal Non-commercial Organization "Children's Clinical Hospital named after Saint Zinaida" of Sumy City Council. An otolaryngologist had consulted all children for confirmation of diagnosis. The first group consisted of 22 patients diagnosed with an acute respiratory viral infection (ARVI), the second one included 23 children with acute respiratory viral infections, associated with adenoid vegetation, and the control group had 14 apparently healthy children who were divided by age and gender and were under the supervision of a pediatrician.

The study of the immune system's cellular component was conducted according to an initial review of the quality of CD3+-, CD4+-, CD8+-, CD16+-, CD21+- lymphocytes by the immunofluorescence technique with homogeneous antibodies in the blood serum. The study of the humoral component of the immune system was undertaken by determining the level of indices of IgG, IgA, IgM by the radial immunodiffusion technique (Mancini method) [13].

Statistical processing of the results was done with the help of the EZR 1.41. The following indicators were defined: mean (M), the error of the mean (m), level of difference between two means (confidence figure – p) [14].

Results

The average age of children in the control group was 4.86 years old, in patients of group

Table 1

State of the cellular component of the immune system in children with acute respiratory viral infections, (M ± m)

Immunological index	Group I (n=22)	Group II (n=23)	Control group (n=14)
	1	2	3
Lymphocytes, %	50,2 ± 1,09 $p_{1-2} > 0,05$ $p_{1-3} > 0,05$	51,3 ± 1,62 $P_{2-3} < 0,05$	48,7 ± 0,5
CD3+, %	46,15 ± 0,63 $p_{1-2} < 0,01$ $p_{1-3} < 0,001$	50,09±1,05 $p_{2-3} > 0,05$	56,04 ± 1,67
CD4+, %	39,2 ± 1,49 $p_{1-2} > 0,05$ $p_{1-3} < 0,05$	40,18 ± 1,59 $P_{2-3} < 0,05$	35,2 ± 1,11
CD8+, %	27,6 ± 1,46 $p_{1-2} > 0,05$ $p_{1-3} < 0,001$	26,39 ± 1,55 $P_{2-3} < 0,01$	19,5 ± 0,83
CD16+, %	36,09 ± 1,76 $p_{1-2} > 0,05$ $p_{1-3} > 0,05$	37,6 ± 2,0 $P_{2-3} > 0,05$	34,2 ± 1,82
CD22+, %	28,9 ± 1,29 $p_{1-2} < 0,05$ $p_{1-3} < 0,001$	24,39 ± 1,31 $P_{2-3} < 0,05$	21,8 ± 0,88

Notes: p_{1-2} – the reliability of the difference between the indicators of the group I and the group II ,
p_{1-3} – the reliability of the difference between the indicators of the group I and the control group ,
p_{2-3} – the reliability of the difference between the indicators of the group II and the control group.

I - 4.95 years old and in group II - 5.13 years old, (p > 0,05). The distribution of children by sex was as follows: the control group comprised 57% of boys and 43% of girls, group I - 55% of boys and 45% of girls, and II group - 56% of boys and 44% of girls, (p > 0,05). In the first group, the acute period of the disease in patients was characterized by an increase in the number of CD4+- lymphocytes ((39,20 ± 1,49) %) compared to the similar indicators of the control group ((35,2 ± 1,11) %), (p < 0,05), (table 1). In addition, patients from the first group have significantly higher levels of CD8+- ((27,6 ± 1,46) %) and CD22+- lymphocytes ((28,9 ± 1,29) %), compared to the similar indicators of apparently healthy children ((19,5 ± 0,83) %) and ((21,8 ± 0,88) %) and as a result (p < 0,001). Beyond that, at the onset of disease in patients with ARVI, a decreasing level of CD3+ cells ((46,15 ± 0,63) %) was determined compared to the control group ((56,04 ± 1,67)) %, (p < 0,001). However, increases of the lymphocyte count ((50,2 ± 1,09) %) and CD16+ cells ((36,09 ± 1,76) %) in patients from the first group compared to the similar indicators of the control group ((48,7 ± 0,5) %) and ((34,2 ± 1,82) %) as the result, (p > 0.05) were unreliable.

During the acute period of the disease in patients from the second group were defined significant increase in lymphocyte concentration ((51,3 ± 1,62) %), CD4+- ((40,18 ± 1,59) %) and CD22+- cells ((24,39 ± 1,31) %) compared to the similar indicators of the control group, (p < 0,05). Simultaneously, in the blood serum of patients with ARVI, associated with adenoid vegetations, the CD8+- lymphocyte count ((26,39 ± 1,55) %) was higher compared to the similar indicators of apparently healthy children (p < 0,01). In patients from the second group were determined an insignificant decrease of CD3+ cells ((50,09 ± 1,05) %) and the increase of CD16+ cells ((37,6 ± 2,0) %), (p > 0,05).

In patients with acute respiratory viral infections associated with adenoid vegetation, the level of CD3+- lymphocytes in the blood serum was higher than the similar indicator of patients with acute respiratory viral infections (p < 0,01).

The acute period of the disease in patients with ARVI was characterized by a significant increase of IgA ((0,95 ± 0,01) g/l) and IgM ((0,84 ± 0,02) g/l) compared to the similar indicators of virtually healthy children ((0,85 ±

0,02) g/l) and ((0,75 ± 0,02) g/l), as the result ($p < 0,01$), (table 2). Meanwhile, the level of IgG ((11,05 ± 0,19) g/l) in the blood serum in patients from the first group has increased slightly, compared to the level of the control group ((10,62 ± 0,02) g/l), ($p > 0,05$).

In patients from the second group, the concentration of IgG ((12,44 ± 0,27) g/l) significantly increased at the onset of disease, compared with the similar indicators of apparently healthy children, ($p < 0,001$). Furthermore, in patients with ARVI, associated with adenoid vegetation, the levels of IgA and IgM have tended to decrease ((0,82 ± 0,02) g/l) and increase ((0,79 ± 0,01) g/l), as the result ($p > 0,05$).

A comparative analysis of the indicators of the humoral component of the immune system in patients from the second group showed a significant decrease in blood serum, the concentration of IgA ($p < 0,01$) and IgM ($p < 0,05$), as well as the increase of IgG ($p < 0,001$), compared to the indicators of patients from the first group.

Discussion

A significant increase of CD4+-, CD8+-, CD22+- lymphocytes in the blood serum characterized the disease's acute period in both groups. Besides, patients in the first group showed a significant decrease of CD3+- lymphocytes and an increase of IgA and IgM, compared to patients' indicators from the control group. Simultaneously, the second group of patients had a significantly higher level of total lymphocytes and IgG in peripheral blood than children from the control group. When comparing indicators being studied in the second group, the level of CD3+- cell was significantly higher, and CD22+- lymphocyte counts, IgM, and IgG were substantially lower than the similar indicators of the first group.

The reduction of CD3+- cells in the acute infectious inflammation occurs through a pathogen's action and may indicate immunoreactivity, which is first provided by subpopulations of T- lymphocytes. During the immunologic response and with increased production of cytotoxic cells at the disease heat, the number of CD8+- lymphocytes increase [15].

The adenoids play a central role in the development of upper respiratory tract infections and the spread of infection from the adenoids to other sites. In addition, insufficient immunity against infection can lead to the development of other diseases [16]. The increase of IgA and IgM levels in the blood serum in children with acute respiratory infections may indicate the immune system's activation in response to a viral infection. However, patients with adenoid vegetation and patients from the control group had substantially identical indicators of IgA and IgM, which may reveal immunological inertia during the infection process [17]. Other studies in children with adenoid vegetations have shown a decrease in serum IgA levels, which may increase the susceptibility to infections. The increase in the susceptibility of infection, according to the authors, is directly caused by a decrease in the IgA level. associated with a

Table 2

State of the humoral component of the immune system in children with acute respiratory viral infections, (M ± m)

Immunological index	Group I (n=22)	Group II (n=23)	Control group (n=14)
	1	2	3
IgA, g/l	0,95 ± 0,01 $p_{1-2} < 0,01$ $p_{1-3} < 0,001$	0,82 ± 0,02 $P_{2-3} > 0,05$	0,85 ± 0,02
IgM, g/l	0,84 ± 0,02 $p_{1-2} < 0,05$ $p_{1-3} < 0,01$	0,79 ± 0,01 $p_{2-3} > 0,05$	0,75 ± 0,02
IgG, g/l	11,05 ± 0,19 $p_{1-2} < 0,001$ $p_{1-3} > 0,05$	12,44 ± 0,27 $p_{2-3} < 0,001$	10,62 ± 0,02

Notes: p_{1-2} – the reliability of the difference between the indicators of the group I and the group II , p_{1-3} – the reliability of the difference between the indicators of the group I and the control group , p_{2-3} – the reliability of the difference between the indicators of the group II and the control group.

decrease in the number of cells secreting IgA. At the same time, immunity to viruses, bacteria and other antigens decreases and increases the likelihood of developing chronic sinusitis [18]. Ben-Yaakov A and colleagues (2011) have identified increased expression of CD14 cells in submucosal, lymphatic follicles and interfollicular layers of adenoids may be an important factor in the development and persistence of adenoids [19].

Thus, it can be concluded that the study of the immune system at the time of adenoid vegetation in children is essential, as research in recent decades has shown the broad benefits of trained immunity for protecting the host, but also permit potentially harmful effects in immune-mediated and chronic inflammatory diseases [20].

Considering that adenoids are constantly exposed to the impact of viruses, bacteria and allergens, they play an essential role in upper airway immunity as effectors of both the adaptive immunity of the mucosa and systemic type. Due to their immunological function and specific location, adenoids are considered reservoirs of viruses and bacteria. Therefore, repeated infections can contribute to hypertrophy [21].

This problem's further research we see in a more detailed analysis of immune biomarkers of protection and inflammatory activity in children of different age groups with acute respiratory viral infections, associated with adenoid vegetations. Consequently, it will give us new opportunities for optimizing patient treatment with this pathology. In conclusions: Preschool-aged patients with acute respiratory viral infections in the acute period of the disease have shown a significant decrease of the CD3+- lymphocyte level and an increase in CD4+-, CD8+-, CD22+- lymphocytes, IgA and IgM. In patients with acute respiratory viral infections associated with adenoid vegetation, at the disease's heat was defined a significant increase in total lymphocytes, CD4+-, CD8+-, CD22+- cells and IgG. In patients with acute respiratory viral infections, associated with adenoid vegetation, the level of CD3+- cells was significantly higher, and at the same time, the level of CD22+- lymphocytes, IgA, IgM, and IgG was considerably lower compared to the similar indicators of patients with acute respiratory viral infections.

References

1. CHernysheva, OE. The use of recombinant a-2b-interferon in the treatment of acute respiratory viral diseases in children. Zdorov'e rebenka. 2016; 6 (74): 69-73. DOI: 10.22141/2224-0551.6.74.2016.82135.
2. Berezhnij, VV. Acute respiratory diseases in children: an early starting approach to therapy. Evidence database (review). Sovremennaya pediatriya. 2019; 1(97): 89-101. DOI: 10.15574/SP.2019.97.89
3. Troeger, C, Forouzanfar, M, Rao, PC, et al. Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory tract infections in 195 countries: a systematic analysis for the Global Burden of Disease Study 2015. The Lancet Infectious Diseases. 2017; 17(11): 1133-1161. DOI: 10.1016/S1473-3099(17)30396-1.
4. Kramaryov, SO, Yevtushenko, VV. Approaches to antibacterial therapy of acute respiratory infections in children. Topical infectology. 2015; 1: 7-12.
5. Kvashnina, LV, Matvienko, IN. Recurrent respiratory infections in children: is prevention possible? Pediatriya. Vostochnaya Evropa. 2016; 4(4): 3-14.
6. Barchan, GS, Shklyar, AS, Cherkashyna, LV, et al. Immune disorders in recurrent respiratory infections on the background of undifferentiated connective tissue dysplasia. Azerbaijan Medical Journal, 2020; 1: 10-16. DOI: 10.34921/amj.2020.27.15.002.
7. Desforges, M, Le Coupanec, A, Dubeau, P, et al. Human coronaviruses and other respiratory viruses: underestimated opportunistic pathogens of the central nervous system? Viruses. 2020; 12(1): 14. DOI: 10.3390/v12010014
8. Kosenko, IM. Recurrent respiratory infections in children: modern approaches to rational pharmacotherapy. Pediatriya. 2018; 1: 51–56. DOI: 10.26442/2413-8460_2018.1.51-56.
9. Bohmwald, K, Galvez, N, Ríos, M, et al. Neurologic alterations due to respiratory virus infections. Frontiers in cellular neuroscience. 2018; 12: 386. DOI: 10.3389/fncel.2018.00386.
10. Kushnareva, MV, Vinogradova, TV, Keshishyan, ES, et al. Features of the immune status and interferon system in young children. Rossijskij vestnik perinatologii i pediatrii. 2016; 61(3): 12-21.

11. Torun, MT. "Neutrophil-to-lymphocyte and basophil-to-lymphocyte ratios in children with adenoid vegetation: Can they be prognostic markers?." (2020) Ann Med Res 2020; 27(7): 1844-8. DOI: 10.5455/annalsmedres.2020.04.376
12. Popovich, VI, Koshel', IV. ARVI and acute rhinosinusitis: interrelated links of one process. Medical Nature. 2016; 17(390): 60-61.
13. Mancini, G, Carbonara, AO, Heremans, JF. Immunochemical quantitation of antigens by single radial diffusion Immunochemistry. 1965; 2(3): 235–239.
14. Smolyar, NI, Fedoriv, YaM, Zavojko, L. Metodichni rekomendaciï po statistichnij obrobci. L'viv. 1995: 17.
15. Melnikova, IY, Buryak, VN, Dudko, MV, Melnik, SI, Batrachenko NV. Clinical and immunological features in acute respiratory-viral infections in children with bronchial asthma. Pediatrics. Consilium Medicum. 2020; (1): 58-61.
16. Wang, H. Chronic adenoiditis. Journal of International Medical Research. 2020; 48(11): 0300060520971458.
17. Kruchko, TA, Tkachenko, OY, Harshman, VP, Ivanenko, OP. The problem of effective and safe treatment of acute respiratory infections in children. Childs health. 2017; 12(1): 18-23.
18. Eun, YG, Park, DC, Kim, SG, et al. Immunoglobulins and transcription factors in adenoids of children with otitis media with effusion and chronic rhinosinusitis. International journal of pediatric otorhinolaryngology. 2009; 73(10): 1412-1416.
19. Ben-Yaakov, A, Maly, B, Abu-Ita, R. et al. Identification and immunolocalization of the innate immune receptor CD14 in hypertrophic adenoids and tonsils. Immunological investigations. 2011; 40(2): 150-159.
20. Netea MG, Domínguez-Andrés J, Barreiro LB, et al. Defining trained immunity and its role in health and disease. Nat Rev Immunol. 2020; 20(6): 375-388. doi: 10.1038/s41577-020-0285-6.
21. Marseglia GL, Caimmi D, Pagella F, et al. Adenoids during childhood: the facts. Int J Immunopathol Pharmacol. 2011; 24(4): 1-5. doi: 10.1177/03946320110240S401.