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Specifics of Immune Status in Pre-School Children with Relapsing Bronchopulmonary Disorders

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The research deals with immune changes in pre-school children with relapsing bronchopulmonary disorders. It was established that cellular immunity was most affected in such patients. Specifics of immune changes are largely determined primary disorder. Relapsing bronchitis is followed by a decrease in phagocytic activity and activation of humoral response (elevated Ig G, Ig M, reduced Ig A) and cytokine disbalance (increase in IL-6 , decrease in IL 4). Recurrent pneumonia is followed by decreased phagocyte index and normal phagocyte number, elevated IL-4 and IL-6, reduced Ig A.

Keyword: relapsing bronchopulmonary disorders, immune status, pre-school children.

1. Introduction

Respiratory diseases are widely spread among pre-school children. In the recent 10 years morbidity has increased by 3,6 times [1]. Relapsing bronchopulmonary disorders are still the leading cause of morbidity rates (75-250 cases per 1000 children a year). Immune system is one of the main factors in determining susceptibility to the diseases [2, 3]. Basically, immunocompetent cells serve as protectors. However, during a long-term disease there is a high risk of immune system disorder. Recently, low immunity has been characteristic of the population of Ukraine, which could facilitate inadequate response to antigen stimulation [4].

The issue of immune deficiency is relevant in pre-school children as this period is a milestone for immune system (second leucocyte crossmatch, Ig M &Ig G adult normal values and reduced serum and secretory Ig A) [5]. In overwhelming majority of cases immune changes lead to immune disorder resulting in relapsing bronchopulmonary diseases [6]. Frequent disorders can cause increased consumption of Ig G, complement system and other immunity factors, which can aggravate the immunity disbalance [6]. Immune response however, depends on the primary disorder.

2. Aim of research: investigate the specifics of immune changes in pre-school children with relapsing bronchopulmonary disorders.

3. Materials and methods

120 children, age range 3 to 6 years (of average (4,2±0,4) years), with relapsing bronchopulmonary disorders were examined and divided into 3 groups. I group – 60 patients with relapsing bronchitis (RB), II group – 60 patients with recurrent pneumonia (RP). Control group- 20 healthy children of the same age. Serum Ig G, M, A were detected by means of ELISA, based on sandwich principle. Cellular immunity values were studied according to M. Jondal *et al.* and M.P. Silveirse *et al.* (1972). Absorbing capacity of neutrophils was studied according to

phagocyte index and phagocyte number(after Petrova technique, 1984), metabolic neutrophile activity – NBT spontaneous/stimulates tests (according to B. Park modified by Wixman and Mayamsky, 1979). Cytokine concentration (IL-6 and IL-4) in blood serum was detected by ELISA"STAT-Fax 303 Plus" (USA) and test systems "Diaclone" (France) according to iNBTinstructions. Statistic data was obtained through the use of Statistica 5.5A (StatSoft, USA). Medium values (M±m), M – medium value, m – standard deviation. Student's criterion was used for comparison of data.
Statistical credibility p<0,05.

4. Results and Discussion

Studying neutrophil phagocytosis values showed a significant deviation from the norm and difference between study groups. Patients with RB showed increased phagocyte activity. Phagocyte Number (5,52±0,04), in RB group was higher than in control group (p_N<0,05) and RP group (p<0,05). Phagocyte activity in RP group was lower than in RB and control group.
Overall, phagocyte activity was reduced in both groups (p_N<0,05). Phagocyte Index was the lowest in RB group (59,81±0,79) % and quite different from Phagocyte Index in RP group (p<0,05) (Table 1).

Table 1: Neutrophil phagocytosis in children with relapsing bronchopulmonary disorders (M±m)

Values	RB[1] (n=60)	RP[2] (n=60)	Control[3] (n=20)	P_{1-2}	P_{1-3}	P_{2-3}
NBT spontaneous, y.o.	25,3±1,2	22,8±1,1	21,6±0,9	<0,05	<0,05	<0,05
NBT stimulated, %	31,9±0,7	50,6±2,1	53,8±1,6	<0,05	<0,05	<0,05
Phagocyte number, y.o.	5,52±0,04	5,12±0,03	5,21±0,06	<0,05	<0,05	>0,1
Phagocyte index, %	59,81±0,79	62,17±1,12	67,24±1,79	<0,05	<0,05	<0,05

Macrophage processing function was also affected. Spontaneous NBT-test in RP group was similar to control group, in RB group slightly elevated. Stimulated NBT –test in both groups was decreased. NBT-stimulated test in RB group (31,9±0,7) %, was lower than control and (p_N<0,05) and RP group(p<0,05). Humoral immunity analysis showed correlation with primary disorder. Most expressed changes were observed in Ig A levels. Reduced Ig A was typical of both groups in comparison with control group (p_N<0,05) with no significant correlation with primary disorder (Table 2).

Table 2: Immunoglobulines in children with bronchopulmonary disorders (M±m)

Показники	RB[1] (n=60)	RP[2] (n=60)	Control[3] (n=20)	P_{1-2}	P_{1-3}	P_{2-3}
Ig A, g/L	0,43±0,02	0,49±0,01	0,71±0,02	>0,1	<0,05	<0,05
Ig M, g/L	1,21±0,04	1,39±0,05	1,14±0,04	<0,05	>0,1	<0,05
Ig G, g/L	11,4±0,2	13,6±0,4	10,2±0,4	<0,05	>0,1	<0,05

Ig M elevation was observed in patients with RB and RP. In patients with RP Ig M was mostly elevated (1,39±0,05) g/l in comparison with control group (p_N<0,05) and RB group (p<0,05).
Similar tendency was observed with Ig G. Its maximal levels were detected in patients with RP -(13,6±0,4) g/L- higher than control group(p_N<0,05) and RB group (p<0,05). In RB group Ig G level was higher than in control group, yet this adata was not credible. Cytokine status analysis in both groups showed changes in ro/anti-inflammatory pathways. All changes

correlated with primary disorder. IL 4 level in RB group was decreased-(0,73±0,01) pg/ml, which was credibly different from the same value in RP ($p<0,05$) and control groups ($p_N<0,05$). RP group showed maximal IL 4 level, yet it wasn't credibly different from control group (Table 3).

Table 3: IL 4 and IL 6 in children with relapsing bronchopulmonary disorders (M±m)

Values	RB[1] (n=60)	RP[2] (n=60)	Control[3] (n=20)	P_{1-2}	P_{1-3}	P_{2-3}
IL 4, pg/ml	0,73±0,01	1,27±0,03	1,13±0,04	<0,05	<0,05	>0,1
IL 6, pg/ml	5,23±0,78	5,95±0,57	0,18±0,04	>0,1	<0,05	<0,05

IL 6 in patients with relapsing bronchopulmonary disorders were higher than in control group ($p_N<0,05$). No significant difference in IL 6 values between RB and RP was detected. So, relapsing bronchopulmonary disorders in pre-school children is accompanied by changes in immune status partially determined by primary disorder. RB is characterized by cellular immunity disorder (decrease in phagocyte activity and normal phagocyte number) and moderate elevation of Ig G, Ig M and IL 6, reduced Ig A and IL 4.

RP was characterized by decreased phagocyte index and NBT-stimulates test, normal phagocyte number and NBT-spontaneous test, elevated Ig G and Ig M, elevated IL 4 та IL 6 and reduced Ig A.

The majority of researchers believe that RB and RP are characterized by decrease in immunocompetent cells quantity, changes in regulatory subpopulation ratio, receptors defects, proliferation inhibition in response to the antigens [5, 7]. Unfinished phagocytosis causes disorder of the reparation inflammatory phase with increased proliferation and sclerosis in tissues and further autoantigen formation [7].

Reduced level of Ig A is of particular importance, as normally it neutralizes toxins and viruses, inhibits bacterial adhesion, which improves mucocilliary clearance [5, 8]. Disorder of any of the abovementioned immune pathways can contribute to relapses of bronchopulmonary disease in pre-school children [9, 10].

4.1 Further clinical perspective: Establish a correlation between immune status changes and inflammatory process stage; follow-up of the patients on drug therapy.

5. Conclusions

(i) Pre-school children with relapsing bronchopulmonary disorders have expressed immune status changes, which depend on the primary disorder.

(ii) Relapsing bronchopulmonary disorders are followed by reduced phagocyte activity, expressed humoral activity (elevated Ig G, Ig M, reduced Ig A) cytokine disbalance (elevated IL 6 and reduced IL 4).

(iii) Cellular immunity deficiency (decreased phagocyte index and NBT-stimulated) and humoral immunity activation (elevated Ig G i Ig M, reduced Ig A) is observed in pre-school children with recurrent pneumonia.

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