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Clinical and Laboratory Peculiarities of Prolonged Current of Non-Social Pneumonia in Children

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Abstract: Respiratory diseases occupy one of the leading places in the structure of morbidity and mortality in children. Pneumonia plays an important role among them. This is due to both the high frequency of respiratory tract lesions in children and the severity of the prognosis of many late diagnosed and untreated pneumonia. The proportion of pneumonia, in which the clinical picture does not correspond to radiological data, has significantly increased, and the number of low-symptom forms of the disease has increased. There are also difficulties in the etiological diagnosis of pneumonia, since over time, the list of pathogens is expanded and modified. Community-acquired pneumonia has been associated primarily with Streptococcus pneumoniae. Currently, the etiology of the disease has expanded significantly, and in addition to bacteria, it can also be represented by atypical pathogens (Mycoplasma pneumoniae, Chlamydophila pneumoniae), fungi, as well as viruses (influenza, parainfluenza, metapneumoviruses, etc.), the role of the latter is especially great in children under 5 years old. In the last 10 years, pneumonia has taken the leading place among these diseases. Community-acquired pneumonia is an acute illness that arose in an out-of-hospital setting, accompanied by symptoms of lower respiratory tract infection and fresh focal infiltrative changes in the lungs. The aim of the study was to identify modern clinical and laboratory features of the protracted course of community-acquired pneumonia in children. We analyzed 853 case histories of children treated in Prospectively, 123 children were under our supervision, who were divided into group II. The 1st main group included 65 children (community-acquired pneumonia, prolonged course), the 2nd control group included 58 children (community-acquired pneumonia, acute course).

In the process of complex clinical and laboratory examination of children, biochemical, microbiological and immunological research methods were used. Enzyme immunoassay (determination of markers interleukin-4,6, tumor necrosis factor-alpha) was carried out in a private clinic INNOVA in the city of Samarkand, microbiological studies.

When studying the anamnesis of these children, a number of unfavorable factors were noted. Thus, 45.5% (56) of the mothers of the observed children had toxicosis in the first and second half of pregnancy, the threat of miscarriage in 42.3% (52), and grade I-II anemia in 84.6% (104). In the main group, 21.5% of children were born with asphyxiation, and in the comparison group, 2.5 times less (8.6%; $P < 0.05$). When analyzing the medical history, it was noted that the premature birth of children among patients with community-acquired pneumonia was 4.9%: 6.2% in the main group and 3.4% in the comparison group. 57.5% (88) of mothers had acute respiratory infections during pregnancy,

The majority of mothers of children - 69.6% - had foci of chronic infection.

Laboratory data: The data showed that the level of interleukin-4 in children with community-acquired pneumonia was 2.3 times higher than the control, increasing to 10.8 ± 0.9 pg / ml ($P < 0.01$), in relation to the control group.

interleukin-6 was 13.4 ± 0.3 pg / ml and was 2 times higher than in the control group ($p < 0.05$).

Tumor necrosis factor-alpha up to 63.5 ± 3.2 pg / ml compared with ($P < 0.01$) control group.

In order to correct the revealed changes, differentiated treatment regimens for children with community-acquired pneumonia have been developed and recommended. In the acute period of the disease, Bronchomunal P (3.5 mg) was prescribed 1 capsule / day until the symptoms of the disease disappeared, but not less than 10 days.

With a protracted course of the disease, 1 capsule / day for 1 month. In the next 2 months, the use of the drug, 1 capsule for 10 days with a 20-day interval between courses.

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Key words: *community-acquired pneumonia, cytokines, prolonged course, treatment, Bronchomunal P, children.*

Relevance: In the world, bronchopulmonary diseases remain one of the unsolved problems of modern pediatrics. In the last 10 years, pneumonia has taken the leading place among these diseases. According to the World Health Organization (WHO), pneumonia is the most frequent cause of death of children in the world, in particular, in the structure of mortality among children under 5 years of age, it is 17.5%, annually claiming the lives of about 1.1 million children in this age group. Thanks to the successes achieved in recent years in the diagnosis and treatment of community-acquired pneumonia (CAP) in children, the course of the disease has changed, the number of severe forms of the disease has significantly decreased, and mortality has decreased. There is a growing need to revise the traditional approaches to the diagnosis of the disease and improve the effectiveness of treatment.

To date, the main direction of scientific research is to determine the characteristics of the occurrence of community-acquired pneumonia in children; determination of the frequency of occurrence, clinical and laboratory features of CAP; determination of the cytokine and interferon state of immunity, their relationship and the development of modern methods of therapeutic and prophylactic measures.

Today in our Republic, large-scale measures are being taken to implement a comprehensive program aimed at early diagnosis and reduction of complications of somatic diseases, including among the child population. Based on this, in order to solve urgent problems in this area, it is necessary to raise to a new level not only the quality of medical care to the population, but also to create conditions, a healthy environment for the prevention of CAP, especially among children, and to develop optimal methods for treating CAP.

Objective of the study: to identify modern clinical and laboratory features of the protracted course of community-acquired pneumonia in children.

Materials and research methods: To achieve the goal of the research, 853 case histories were retrospectively analyzed in the Samarkand Regional Children's Multidisciplinary Center for 2015-2018. Prospectively, 123 children were under our supervision, who were divided into group II. The 1st main group included 65 children (community-acquired pneumonia, prolonged course), the 2nd control group included 58 children (community-acquired pneumonia, acute course).

In the process of complex clinical and laboratory examination of children, biochemical, microbiological and immunological research methods were used. The enzyme immunoassay (determination of markers interleukin-4,6, tumor necrosis factor-alpha) was carried out in the private clinic INNOVA in the city of Samarkand.

Microbiological studies were carried out in accordance with the standards of modern clinical microbiology, were carried out by taking material from the depth of the throat and determined by the bacterioscopic method in smears stained according to Gram.

Among the surveyed children with community-acquired pneumonia, the largest proportion are children aged 6 months to 7 years, with a peak incidence from 2 to 4 years, which does not contradict the literature data. Moreover, boys were sick more often than girls.

Research results: Based on a retrospective and prospective analysis of 853 case histories of children with confirmed community-acquired pneumonia who underwent inpatient treatment in the period from 2015 to 2018 at the age of 6 months to 7 years, we found that community-acquired pneumonia of a protracted course is recorded in 10.8% of cases.

The main complaints during hospitalization of patients in the hospital were productive cough in 62.6% of cases, dry in 37.4%. Dry cough was significantly more common in the main group - 66.2%, while productive cough, on the contrary, was significantly more common in the comparison group - 94.8%. In the same group of children, cough was significantly more effective. An increase in body temperature at the beginning of the disease to febrile numbers was recorded in 51.2% and subfebrile -

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in 15.4% of cases. The febrile fever prevailed significantly more often in the children of the main group. Children complained of decreased appetite, weakness, and fatigue in 55.2% of cases, while in 30.1% of cases these complaints were mild (Table 1).

Table 1
Characteristics of presented complaints in children with community-acquired pneumonia, depending on the course

Complaints	**Внебольничная пневмония**					
	Main group (n = 65)		Comparison group (n = 58)		Total (n = 123)	
	Abs.	%	Abs.	%	Abs.	%
Dyspnea	5	7,7	6	10,3	11	
Cough						
Dry	43	66,2	3	5,2	46	37,4
Productive	22	33,8	55	94,8	77	62,6
Effective	20	30,8	50	86,1	70	56,9
Ineffective	45	69,2	8	13,8	53	43,1
Body temperature						
Norm	14	21,5	27	46,6	41	33,3
Subfebrile	10	15,4	9	15,5	19	15,4
Febrile	41	63,1	22	37,9	63	51,2
Intoxication symptoms						
Weakly expressed	25	43,1	12	20,7	37	30,1
Expressed	21	32,3	10	17,2	31	25,2
Wheezing	7	10,8	2	3,4	9	7,3

It was found that 65 children were re-hospitalized with a diagnosis of community-acquired pneumonia; when analyzing extracts from the case histories, we found that these children showed a regression of radiological changes, which is characterized by a decrease in the size of pneumonic infiltration by less than 50% by the end of the 2nd week and not complete resolution by the end of the 4th week from the onset of the disease with an improvement in the clinical picture. These children were admitted on average 8.2 ± 0.1 weeks after discharge from the hospital.

Life history was carefully analyzed in all observed patients. Most patients with community-acquired pneumonia were born from I - 36.6% (45) and II-III- 47.2% (58) pregnancies and, respectively, I and II-III deliveries, from IV and more pregnancies 16.3% (20) children. It should be noted that the majority of children with a protracted course of community-acquired pneumonia were born from repeated parity (76.9%; 50/65), which was reliable.

When studying the anamnesis of these children, a number of unfavorable factors were noted. Thus, 45.5% (56) of mothers of observed children with community-acquired pneumonia had complications of pregnancy and childbirth in the form of toxicosis in the first and second half of pregnancy, threats of miscarriage in 42.3% (52), grade I-II anemia in 84.6 % (104). The study revealed that the protracted course of community-acquired pneumonia was also influenced by the pathological course of this pregnancy, so significantly more often in mothers of children of the main group than in

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patients in the comparison group, toxicosis of the first and second half of pregnancy was encountered (63.1% versus 25.9 %) and the threat of miscarriage (56.9% versus 25.9%).

In general, in the group of patients with community-acquired pneumonia, in 55.3% (68) cases of mothers, a pathological course of labor was revealed in the anamnesis. The highest percentage of the occurrence of the pathological course of childbirth was noted in the group of children with a protracted course of community-acquired pneumonia compared with acute community-acquired pneumonia (64.6% versus 31.0%;).

In the main group, 21.5% of children were born with asphyxiation, and in the comparison group, 2.5 times less (8.6%; $P < 0.05$). When analyzing the medical history, it was noted that the premature birth of children among patients with community-acquired pneumonia was 4.9%: 6.2% in the main group and 3.4% in the comparison group.

57.5% (88) of the mothers of the observed by us contingent of children with community-acquired pneumonia had acute respiratory diseases during pregnancy, their highest frequency was recorded in children with a prolonged course of community-acquired pneumonia - 63.1% versus 48.3% in the comparison group. It has been established that the respiratory diseases suffered by the mother, especially in the last trimester of pregnancy, disrupt the clinical and immunological state of the newborn, which may be one of the reasons for the formation of a frequent morbidity in the child in the future, including one of the factors in the development of a protracted course of community-acquired pneumonia.

The majority of mothers of children - 69.6% had foci of chronic infection (diseases of the ENT organs, bronchopulmonary system, cardiovascular and genitourinary systems), in the main group this percentage was 1.8 times higher in relation to the comparison group (89.2% against 28%, respectively).

Therefore, such children should be included in the risk group for the development of a protracted course of community-acquired pneumonia due to pronounced changes in the functional activity of polymorphonuclear leukocytes - the main cellular effective link in antiviral defense.

As a result of the analysis, it was found that in 70% of cases, children were born from repeated pregnancy. In 35.7% of cases, there was a threat of termination of pregnancy; viral-bacterial infections and gestosis were noted in 30% of cases. More than half of the patients had a complicated obstetric history and intrauterine fetal hypoxia; in 20% of cases, mothers had somatic and gynecological pathologies. The pathology of the central nervous system (47.1%), frequent acute respiratory viral infections and pathology of the ENT organs (42.8% and 40%, respectively) were recorded with the highest frequency.

These data clearly indicate a significant frequency of adverse antenatal factors and perinatal pathological symptoms in children with protracted community-acquired pneumonia.

From which it follows that the development of a protracted course of community-acquired pneumonia in children is significantly influenced by an unfavorable premorbid background.

Analyzing the background conditions of children with community-acquired pneumonia, we found that 67.5% of children had grade I-II anemia, atopic dermatitis - in 32.5%, rickets - in 12.2% of patients and protein-energy malnutrition (PEM) - in 8.9%.

It should be noted that with a protracted course, these indicators were significantly higher than with an acute course of community-acquired pneumonia - almost 2 times. Background burdens are in fact already concomitant diseases that greatly aggravate the course of the underlying pathology and contribute to the development of a protracted course.

Thus, the presented data once again confirm that children with varying degrees of severity of background conditions and comorbidities are a risk group for the development of a protracted course of community-acquired pneumonia.

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Table2.
The incidence of background diseases in children with community-acquired pneumonia

Analyzed indicators	Main group, n = 65		Comparison group, n = 58		Total, n = 123	
	Абс.	%	Абс.	%	Абс.	%
Anemia I, II degree	56	86,2	27	46,6*	83	67,5
Atopic dermatitis	29	44,6	11	19,0*	40	32,5
Rickets	10	15,4	5	8,6*	15	12,2
Protein energy deficiency	8	12,3	3	5,2*	11	8,9

Note: * - reliability of data between groups

When analyzing hematological parameters in most children with community-acquired pneumonia, no abnormalities were found.

Of all examined children, only 31% of cases had leukocytosis, 5% - leukopenia, in other cases, leukocyte counts did not go beyond the standard values (64%). Pronounced markers of bacterial inflammation in the form of leukocytosis, accelerated erythrocyte sedimentation rate and shift of the leukocyte formula to the left (stab shift) were observed in one child. In 4 children, only a stab shift of the formula to the left was recorded, in 2 children a slight acceleration of the erythrocyte sedimentation rate. Of all examined children with community-acquired pneumonia, 27% of children were diagnosed with an acceleration of the erythrocyte sedimentation rate without changes in other hemogram parameters.

Thus, in the hemogram in children with community-acquired pneumonia, inflammatory changes in the form of leukocytosis were recorded only in 31% of cases, in 26% - an isolated acceleration of the erythrocyte sedimentation rate. Considering that when assessing the clinical picture of community-acquired pneumonia in a third of children, minimal clinical manifestations of the disease were revealed, in 30% of cases they were worried about a prolonged cough or prolonged subfebrile condition in the absence of local physical changes in the lungs, all examined children were divided into 2 groups depending on the presence of clinical pictures of pneumonia and inflammatory bacterial changes in the hemogram.

Changes in the cardiovascular system were characterized by the following manifestations. The pulse was weak in 14.6% of children, tachycardia was observed in 86.0%, and in 65.0% of children the heart sounds were muffled.

ECG data were characterized, as a rule, by a change in the amplitude and configuration of the T wave (26; 21.1%), in some - by a shift in the S-T interval (34; 27.6%), which indicated a violation of metabolic processes in the myocardium. However, in each individual observation, the ECG analysis was of great practical importance, since it helped to identify and clarify the nature of the violations.

The diagnosis of pneumonia was confirmed not only by clinical observations, but also by X-ray and laboratory studies. According to the data of X-ray studies of the respiratory organs, 45.1% (69) of patients were diagnosed with bilateral focal pneumonia, 11.1% (17) - right-sided, and the focus of inflammation was localized mainly in the basal segments of the right lung. In 2.0% (3) - left-sided, and in 18.3% (28) - polysegmental.

X-ray examination, carried out in the first week of the disease, revealed many small infiltrative shadows in the pulmonary fields in 80 children (65.0%), an increase in the root and pulmonary pattern in 40 (32.5%), an increase in the transparency of the lung fields in 30 (24 ,4%).

On the basis of X-ray examination, in most cases, we diagnosed focal-confluent pneumonia, which was recorded in general in 87.8% of patients (Table 3.).

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Table3.
Distribution of the examined children depending on the form of pneumonia

Analyzed indicators	Main group, n = 65		Comparison group, n = 58		Total, n = 123	
	Абс.	%	Абс.	%	Абс.	%
Focal pneumonia	5	7,7	2	3,4*	7	5,7
Focal confluent pneumonia	54	83,1	54	93,1	108	87,8
Segmental pneumonia	6	9,2	2	3,4*	8	6,5

Note: * - reliability of data between groups (P <0.05)

A significantly significant incidence of focal pneumonia (7.7% versus 3.4%; P <0.05) and segmental pneumonia (9.2% versus 3.4%; P <0.05) in children with a protracted course of community-acquired pneumonia was established in comparison with community-acquired pneumonia of acute course.

Thus, the development of a protracted course depends on the form of pneumonia, as proven by the correlation analysis (Focal pneumonia - r = 0.896 and Segmental pneumonia - r = 0.715).

When analyzing the data obtained, we found that the clinical picture was of an individual nature, so with segmental pneumonia, in most cases, signs of severe respiratory failure and intoxication were detected, while with focal-confluent pneumonia, the leading symptom was bronchial damage and the tendency of patients to a prolonged course of bronchopulmonary process.

On chest x-ray, the configuration of the cardiac shadow was unremarkable in most cases. Nevertheless, in a number of cases there was a flattening of the waist of the heart, expansion of the borders to the left.

Thus, community-acquired pneumonia develops against the background of an unfavorable peri - and intrapartum periods, hereditarily burdened with a premorbid background, which can lead to a functional failure of the immune system, which contributes to an unfavorable course of the disease in children. On the part of the bronchopulmonary system, all the classic signs of community-acquired pneumonia were detected.

It is known that when prescribing antibacterial drugs for community-acquired pneumonia, a specialist must take into account the probable etiology of the disease. Practice shows that even a novice clinician should be able to determine the probable etiology of pneumonia according to clinical and radiological data, that is, think about "typical" or "atypical" pathogens. This will allow you to prescribe a drug of the appropriate spectrum.

The subjective error in prescribing the starting antibiotic is the wrong choice of the drug in 22.2% of cases. All patients underwent empirical choice of starting antibiotic therapy: treatment was started without taking into account the sensitivity of pathogens to antibiotics. It is known that inadequate use of 1st generation cephalosporins leads to a further increase in antibiotic resistance, and this aggravates the problem of treating pneumonia in children.

Laboratory tests: Consequently, the concentration of C-reactive protein in the blood serum was determined (norm 8 mg / l). In the course of a prospective study of 35 examined patients with community-acquired pneumonia in the initial period of the disease, in 28.6% (10) the content of C-reactive protein in the blood serum was increased, in 71.4% (25) children - C-reactive protein was within norms.

Among the markers of inflammation that have been actively studied in recent years, cytokines have attracted special attention. Cytokines are regulatory peptides produced by virtually all nucleated cells in the body.

Our data showed that the level of interleukin-4 in children with community-acquired pneumonia was 2.3 times higher than the control, increasing to 10.8 ± 0.9 pg / ml (P <0.01), in relation to the control group (Table 4).

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Table4.
The level of cytokines in the examined children with community-acquired pneumonia in a comparative aspect (M±m)

Indicators	Practically healthy children, n = 20	Patients with community-acquired pneumonia, n = 123
Interleukin-4	4,6±0,6	10,8±0,9**
Interleukin-6	6,7±0,2	13,4±0,3
Tumor necrosis factor-alpha	42,3±2,1	63,5±3,2*

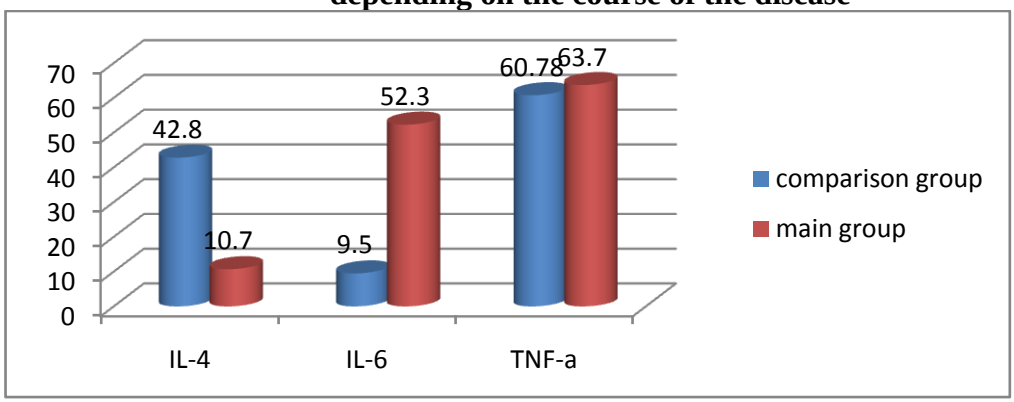
Admonition: * - the difference relative to the data of the control group is significant (** - P <0.01), (* - P <0.05).

Noteworthy is the fact that the level of interleukin-6, one of the most informative markers of inflammation in children with community-acquired pneumonia, was 13.4 ± 0.3 pg / ml and was 2 times higher than in the control group (p < 0.05). Perhaps this fact is due to a decrease in the level of lymphocytes, in particular of T-helper-1, producing interleukin-2, in the initial period of the inflammatory process, or a short period of secretion of this cytokine (1-2 days).

Tumor necrosis factor-alpha is one of the main representatives of pro-inflammatory cytokines. When analyzing the content of tumor necrosis factor-alpha in patients with community-acquired pneumonia, we noted its increase to 63.5 ± 3.2 pg / ml compared with (P <0.01) the control group. The level of tumor necrosis factor-alpha in children diagnosed with community-acquired pneumonia was 1.5 times higher than in practically healthy children (43.2□2.11 pg / ml).

The study of the cytokine status of children with community-acquired pneumonia, depending on its course, showed the multidirectional nature of the imbalance of interleukin-4, interleukin-6 and tumor necrosis factor-alpha, the data obtained are presented in Fig. one

Figure: 1 Indicators of cytokine status in children with community-acquired pneumonia, depending on the course of the disease



As can be seen from the diagram, the children of the comparison group showed a significant 4-fold increase in interleukin-4 indices in relation to those of the main group (42.8 ± 6.8 versus 10.7 ± 2.6 pg / ml; P <0.01), while interleukin-6 indices had the opposite picture in the main group, they increased 5.5 times (52.3 ± 8.6 versus 9.5 pg / ml; p <0.01), and in the comparison group they decreased ... Indicators of tumor necrosis factor-alpha were increased in both groups in relation to the reference values (60.78 ± 12.5 and 63.7 ± 10.8 pg / ml, respectively, versus 42.3 ± 2.1 pg / ml).

Calculation of the correlation coefficient for interleukin -4 showed the presence of feedback with the level of leukocytes in the general blood test (r = –0.23). In addition, a weak direct relationship was found between interleukin-4 and the number of lymphocytes (r = 0.19) and monocytes in the CBC (r = -0.17). There was a weak feedback of interleukin-4 with the nature of the temperature reaction, stab and segmented neutrophils; the relationship with the age of patients and the erythrocyte sedimentation rate has not been established.

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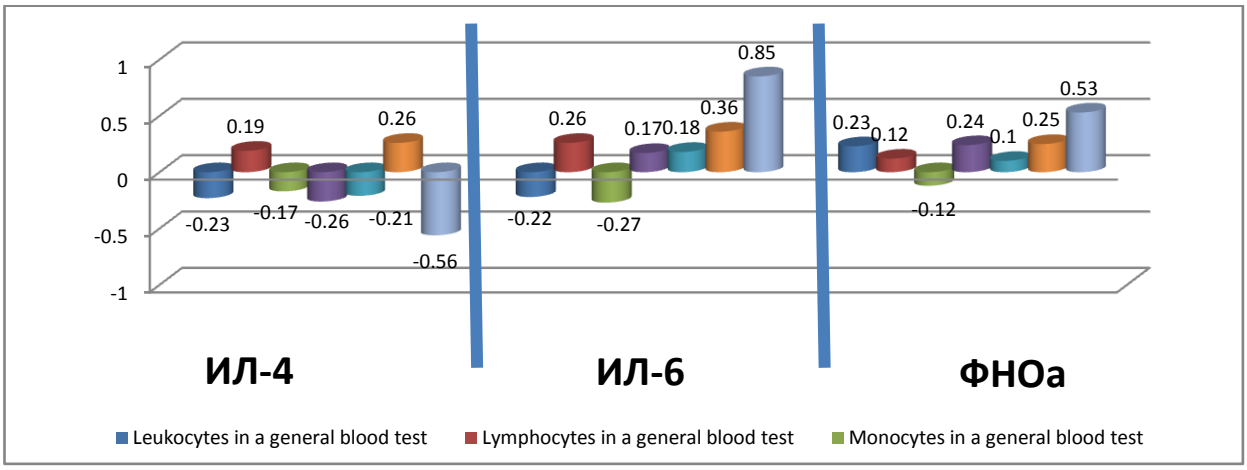
A strong direct relationship between interleukin-6 and the intensity of the febrile reaction (r = 0.85; P <0.05) was revealed, confirming the pyrogenic effect of this cytokine. We also checked the presence of a correlation between the level of interleukin-6 and the level of leukocytes (r = -0.22), stab (r = 0.17) and erythrocyte sedimentation rate (r = 0.16) in the general blood test.

Investigating the correlation of tumor necrosis factor-alpha with clinical and laboratory parameters, we established a direct relationship with the temperature response (r = 0.53; P <0.05), which proves the pyrogenic effect of this cytokine along with interleukin-6.

In addition, a direct relationship was established between the value of tumor necrosis factor-alpha in serum and the severity of leukocytosis in the general blood test (r = 0.23). Thus, tumor necrosis factor-alpha has a mainly central action and reflects the degree of intrathecal inflammation (Fig. 2).

Figure: 2. Indicators of correlation analysis of cytokines and clinical data in children with a protracted course of community-acquired pneumonia.



Thus, the studies carried out have shown that the patients examined by us show pronounced changes in the intercellular immune mechanisms, which are manifested by a violation of the production of pro-inflammatory and anti-inflammatory cytokines, which determines the nature of the course of the disease. The revealed direction of immune shifts and their severity indicate an important pathogenetic role of immune mechanisms in the development and progression of changes in the state of the immune system.

In order to prevent the protracted course of pneumonia, the drug Bronchomunal P (3.5 mg) was included in the treatment complex, 1 capsule per day for 10 days.

Children with a protracted course of community-acquired pneumonia Bronchomunal P 3.5 were prescribed 1 capsule / day for 1 month. In the next 2 months, the use of the drug 1 capsule for 10 days with a 20-day interval between courses - in order to prevent the chronicity of the process.

58 children with an acute course of community-acquired pneumonia were divided into 2 subgroups - group 1 A - 34 children, whose treatment complex included the drug Bronchomunal P 3.5; Group 1 B - 24 children who received traditional treatment.

65 children with a protracted course of community-acquired pneumonia were subdivided by a blind sample into 2 subgroups: Group 2 A - 35 children, whose treatment complex included Bronchomunal P 3.5; Group 2 B - 30 children who received traditional treatment.

In the course of dynamic observation, we found that the clinical symptoms of the dynamics of the bronchopulmonary process have statistically significant differences depending on the nature of the course of community-acquired pneumonia and the treatment. Against the background of the complex proposed treatment option in all children with both acute and protracted community-acquired pneumonia, the general condition first of all improved.

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Comparative analysis of the results showed the advantage of complex treatment, including Bronchomunal P 3.5, compared to traditional therapy.

In children with an acute course of community-acquired pneumonia who received Bronchomunal P 3.5 against the background of traditional therapy, in comparison with children receiving traditional treatment, the manifestations of respiratory failure decreased, the cough became softer, the amount of sputum decreased, the physical data also had a more pronounced positive dynamics.

By the 2-3rd day in the overwhelming majority of sick children with the inclusion of Bronchomunal P 3.5 (84.6%) symptoms of intoxication were not determined. Against the background of traditional therapy, these signs disappeared on average by 4.9 bed-days in the comparison group and 4.5 bed-days in the main group of patients.

Table 5.
The effectiveness of treatment for children with community-acquired pneumonia receiving various treatment regimens

Groups	The timing of the disappearance of the clinical symptoms of the disease				Bed days
	Temperature	Intoxication	Dyspnea	Cough	
1A	3,1±0,3	2,2±0,17	2,7±0,22	6,8±0,25	7,63±0,3
1B	5,2±0,4*	4,9±0,4*	3,2±0,4*	10,1±0,26	10,6±0,7
2A	5,3±0,41	2,1±0,32	4,3±0,27	5,9±0,61	7,86±0,3
2B	6,8±0,3*	4,5±0,2*	5,7±0,3	11,2±0,2*	11,7±0,5

* - Reliability of data compared with group A (* -P <0.05)

Positive X-ray dynamics by the 12th day of treatment was observed in 87.5% of patients who received complex treatment with the inclusion of Bronchomunal P 3.5 in both acute and prolonged community-acquired pneumonia, and only in 31.3% of patients on the background of traditional therapy.

During the analysis of the dynamics of the level of C-reactive protein during treatment in children with an acute course of community-acquired pneumonia, we found that the administration of Bronchomunal P against the background of traditional treatment contributed to a decrease in the inflammatory marker already on the 5th day of illness, and by the 10th day of treatment reaches in most cases the upper limits of the norm. With traditional treatment, this indicator also decreases on the 5th day of treatment, however, without significant differences with its level at admission, and by the 10th day, C-reactive protein is almost 2 times higher than the reference values.

With a protracted course of community-acquired pneumonia, the same picture of the dynamics of the level of C-reactive protein during treatment is observed. In the group of children who received Bronchomunal P, the C-reactive protein indicators on the 5th day of the disease decreased 1.6 times, while with traditional treatment only 1.2 times; on the 10th day of illness, C-reactive protein in children with a protracted course of community-acquired pneumonia who were on the proposed differentiated treatment decreased 4.8 times in relation to the indicators at admission, against the background of traditional treatment, these indicators by the 10th day reached on average 18.8 ± 2.3 mg / ml, which was 2 times higher than in the group of patients who received Broncho-Munal P (9.9 ± 1.3 mg / ml).

As can be seen from the table, interleukin-4 in the acute course of community-acquired pneumonia against the background of Bronchomunal P administration decreases from 17.8 ± 0.6 to 5.2 ± 0.2 pg / ml (p <0.01), while in the case of traditional its treatment has a significant decrease in indicators, which is especially pronounced when the drug Bronchomunal P. is prescribed to children with an acute course of community-acquired pneumonia.

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Table6.
Dynamics of the level of cytokines in children with community-acquired pneumonia depending on the methods of treatment and the nature of the course

Cytokines	Traditional treatment		Traditional treatment + Bronchomunal	
	Upon enrolment	After 3 months.	Upon enrolment	After 3 months.
Community-acquired pneumonia without protracted course				
Interleukin-4	17,1±0,9	9,7±0,7*	17,8±0,6	5,2±0,2*
Interleukin -6	10,5±0,4	8,9±0,4	11,7±0,4	7,6±0,3*
Tumor necrosis factor-alpha	60,7±3,7	58,3±3,7	64,8±2,4	42,1±0,8*
Community-acquired pneumonia with a protracted course				
Interleukin-4	11,5±0,4	10,2±0,1	10,7±1,2	5,3±0,2*
Interleukin -6	17,4±0,8	13,4±0,8	17,1±0,7	6,7±0,2*
Tumor necrosis factor-alpha	63,7±2,7	53,9±1,6	63,4±1,8	42,8±1,4*

Note: * - reliability of data before and after treatment ($p < 0.05$-0.01)

the average decrease reaches 9.7 ± 0.7 pg / ml. Interleukin-6 also

With a protracted course, Bronchomunal P contributes to a significant decrease in both interleukin-4 and interleukin-6 3 months after treatment. In the group of children with a protracted course of community-acquired pneumonia, who were on traditional treatment, there is a tendency to decrease, there is no significant difference in indicators before and after treatment.

Among patients discharged from the hospital with an improvement in their condition, 96.4% were children who received Bronchomunal P, and without changes in their condition - 3.6%, while with traditional therapy - 89.4% were discharged with an improvement in their condition and 10.6 % - no improvement.

CONCLUSIONS

1. A protracted course of pneumonia occurs among 10.8% of children aged 6 months to 7 years, significantly more often in boys (67.2%). The significance of the unfavorable course of the peri- and intranatal periods, aggravated by the premorbid background, influencing the protracted course of the underlying pathology, was determined.
2. Microbiological studies have shown that in children with community-acquired pneumonia, a significant place in the etiological structure is occupied by Staphilococcus aureus in 28.5% of cases, and Streptococcus pneumoniae in 23.1%.
3. Evaluation of biomarkers of inflammation of C-reactive protein and procalcitonin is an informative indicator in the diagnosis of community-acquired pneumonia in children, their increase confirms the bacterial nature of the pathological process, which can be used when choosing a differentiated therapy. An imbalance in the cytokine status in children with community-acquired pneumonia was revealed, expressed by an increase in the levels of interleukin-4, interleukin-6, and tumor necrosis factor-alpha, which contributes to a protracted course of the pathological process and serves as an additional criterion for assessing the severity of inflammation.
4. When Bronchomunal P was included in the complex treatment, the frequency of repeated acute respiratory infections and their complications decreased by 2 times. When using the proposed treatment regimen, the duration of the disease was reduced by 2.1 times compared with children receiving traditional therapy (1.4 times), which indicates the high therapeutic efficacy of prescribing the drug Bronchomunal P

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