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TREATMENT OF COMMUNITY-ACQUIRED PNEUMONIA IN CHILDREN: OPTIMIZATION OF ANTIBIOTIC THERAPY

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Summary. *Community-acquired pneumonia is one of the most common infections in children with an annual incidence of 34 to 40 cases per 1000 children in Europe and North America. Pneumonia is a common cause of death in children under five years of age worldwide. Thus, about 1,8 million children die from pneumonia annually. According to the statistics of the Ministry of Health of Ukraine, about 80,000 children every year suffer from community-acquired pneumonia in Ukraine.* ***Material and methods:*** *Retrospective analysis of 100 case histories of children aged 3-9 years old with outpatient segmental/polisegmental pneumonia who were in inpatient treatment in the pulmonology department of regional hospital from January 2017 to December 2018. The representativeness of the comparison groups is represented by age and sex. Methods of examination: clinical-anamnestic, laboratory and instrumental (pulse oximetry, chest X-ray).* ***Results:*** *Most of the children (58%) were admitted to the hospital on the first day of the illness. In 33% of children, comorbidity was noted. All children had fever, an unproductive cough, while symptoms of intoxication (76 ± 4.27%) and dyspnea (52 ± 4.49%) were more pronounced in children 3-6 years old. In the general analysis of blood in children of the first age group, in most cases, leukocytosis was more than 12 G / L (56 ± 4.96%), neutrophilic shift of the leukocyte formula to the left of 88 ± 3.25% and elevated ESR (84 ± 3.66%). X-ray in children of the first age group was dominated by polysegmental pneumonia at 54 ± 4.44%, while in children of the second age group segmental pneumonia was more common (64 ± 4.66%). Half of the children of both age groups prescribed antibiotics of the first line - a group of penicillins and cephalosporins. When starting antibiotic therapy with penicillins, the symptoms of pneumonia decreased already in the 2nd day in 16% ± 3.67% in the group of children 3-6 years old and in 18% ± 3.84% of children 7-9 years.* ***Conclusion.*** *Pneumonia is one of the most common diseases in children, and one of those that can cause many complications and even death. Accordingly, the treatment of this disease should be maximally effective and short-lived. The best choice for treating pneumonia is a group of oral aminopenicillins, which were administered in the first days of the disease and showed significantly better results than patients treated with cephalosporins.*

Keywords: *community-acquired pneumonia, children, antibiotic therapy.*

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Introduction. Community-acquired pneumonia is one of the most common infections in children with an annual incidence of 34 to 40 cases per 1000 children in Europe and North America [1]. Pneumonia is a common cause of death in children under five years of age worldwide. Thus, about 1,8 million children die from pneumonia annually [2].

According to the statistics of the Ministry of Health of Ukraine, about 80,000 children every year suffer from community-acquired pneumonia in Ukraine [3]. The highest incidence of pneumonia is in younger patients, with a gradual decrease in age-related morbidity. So, the frequency of pneumonia in preschool age is 4 per 100 children; in school (6-9 years old) - 2 per 100 children [4].

Despite the extensive study of etiology, mechanisms of pneumonia pathogenesis, the introduction of medical records of treatment of this ailment in the medical practice, and increased professional education of doctors, today it is not possible to take control of this disease. Such circumstances characterize pneumonia as a medical and social problem, in connection with which there is a need for its further study.

It is established that the cause of pneumonia is most often bacteria, with pneumococci isolated in about 50% of cases. Among other bacteria by frequency: the *Haemophilus influenzae* - 20%, Chlamydophila pneumoniae - 13%, and mycoplasma - 3%; Staphylococcus aureus; Moraxella catarrhalis; Legionella pneumophila and gram-negative bacteria.

In this case, in the age group of 6month - 5 years are dominated by S. pneumoniae (70-88%), H. influenzae type b (up to 10%), M. pneumoniae (15%), whereas in the older age group - Str. Pneumoniae (35-40%), M. pneumoniae (23-44%), C. pneumoniae (15-30%) [5].

Detection of the etiological factor of pneumonia is extremely difficult, especially at the first contact with the patient. Therefore, the empirical appointment of the antibiotic, depending on the child's age and the contributing factors, takes place. In connection with hyperdiagnosis of pneumonia in outpatient settings, the frequency of antibiotic prescribing increases, which in turn leads to an increase in antibiotic resistance in the world.

Therefore, the study of the efficacy of pneumonia is very important for understanding the rational use of antimicrobials and preventing antibiotic resistance. From the standpoint of evidence-based medicine - antibiotic therapy is a rational method of treatment of mild pneumonia [8].

The aim of the work was to improving the treatment of commune acquired pneumonia in children by assessing the effectiveness of first-line antibiotic pharmacotherapy.

Material and methods. Retrospective analysis of 100 case histories of children aged 3-9 years old with outpatient segmental/polisegmental pneumonia who were in inpatient treatment in the pulmonology department of regional hospital from January 2017 to December 2018. The representativeness of the comparison groups is represented by age and sex. Methods of examination: clinical-anamnestic, laboratory and instrumental (pulse oximetry, chest X-ray). Statistical processing was performed using IBM SPSS Statistics, version 12. The verification of the diagnosis and severity criteria for pneumonia was in accordance with the guidelines for the

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management of the community acquired pneumonia in children: update 2017 British Thoracic Society Acquired Pneumoniain Children Guideline Group.

All parents signed an informed consent for the processing of personal data, so the study was conducted in compliance with the provisions of the UN Convention on the Rights of the Child.Common symptoms of community-acquired pneumonia include fever, cough, sputum production, dyspnea, and pleuritic chest pain, saturation less than 92%.

Criteria for inclusion in the study: children with acute course of unilateral pneumonia aged 3-9 years who were prescribed antibiotics from the group β-lactams, namely penicillins and cephalosporins.

Criteria for exclusion from the study: age below 3 and over 9 years, recurrent and bilateral pneumonia, complicated pneumonia.

Results. All patients were divided into 2 subgroups, depending on the type of starting antibiotic therapy - 50 patients who received penicillins and 50 - cephalosporins. Retrospective processing was made of 100 histories of diseases, children of patients with outpatient one-sided segmental / polysegmental pneumonia. The age of the surveyed was from 3 to 9 years. The average age was 6.6 ± 1.8 years. The distribution of the examined children in the age groups was as follows: from 3 to 6 years, 50 (50% ± 5.1%) and 7 to 9 years old - 50 (50% ± 5.1%). All age groups included children of both sexes: in the group of 3 to 6 years old, 22 girls (22% ± 4.14%) and 28 boys (28% ± 4.49%), from the age of 7.9 years - 24 girls (24% ± 4.27%) and 26 boys (26% ± 4.38%) (Table I).

Table I

Distribution of children by age and sex

Age, years	Children with community-acquired pneumonia, n=100			
	Boys		Girls	
	N	%	N	%
3-6	28	28±4,49	22	22±4,14
7-9	26	26±4,38	24	24±4,27
Total	54	54±4,98	46	46±4,98

Representation of the comparison groups represented by age and gender. Among all examined children, 67 ± 4.7% had no comorbidity, the rest - the following co-morbidities.

The examined children were divided into two age groups: the first - 3-6 years, the second 7-9 years, respectively. All children were prescribed β-lactam antibiotics of the penicillin group and cephalosporins. In the first group, 25 children received penicillins and 25 - cephalosporins, in the second group it was similar. Among the examined children of the first group, 48 ± 4.27% had a temperature of 39 °C or more and the rest 52 ± 4.39% of children - 38-39 °C. The situation in the second group is somewhat different from the previous one: 28 ± 3.47% of children complained about a temperature higher than 39 °C and 72 ± 4.8% at a temperature of 38-39 °C. Intoxication in the first age group was noted in 76 ± 4.27% cases and in 44 ± 4.96% - in the second group. Also, in the first age group, symptoms of shortness of breath (52 ± 4.49%) were more common in comparison with the second group (48 ± 4.38%).

All children complained about a dry, unproductive cough. However, after appointing antibiotics of the penicillin group, he became more productive on day 2 in the first group in 16% ± 3.67% of children, and in the second - at 18% ± 3.84%. In

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the rest of the children (in 9% ± 2.86% of the first group and 7% ± 2.55% of the second respectively) the cough changed to more productive on the third day. While in children receiving cephalosporins only 5% ± 2.18% of patients in the second group experienced improvement on the 2nd day. Cough became more productive at the 3rd day in 19 ± 3.92% of children in the first group and in 15% ± 3.57% of the second. In the other 11 children (6% ± 2.37% of the first and 5% ± 2.18% of the second group, respectively), the cough became damp for the 4th day. Reduction and disappearance of cough coincides in time with the date of discharge from the hospital (Table II).

Table II

Wet cough against the background of the use of β-lactam antibiotics

Increase of wet caught	3-6 years		7-9 years	
	Penicillin	Cephalosporins	Penicillin	Cephalosporins
On the 2-d day	16±3,67%	-	18±3,84%*	5±2,18%
On the 3-d day	9±2,86%**	19±3,92%	7±2,55%*	15±3,57%
On the 4-th day	-	6±2,37%	-	5±2,18%

*Note: * - p ≤0.05 - the difference is significant relative to the group of children 7-9 years receiving cephalosporins; ** - p ≤0.05 - the difference is significant relative to the group of children 3-6 years receiving cephalosporins.*

When all children were examined, pulse oximetry was performed. The oxygen saturation index was less than 95% in 7 ± 2,55% of children in the first and second groups, with 2 (2 ± 1,4%) children in the first group receiving penicillins it was 92% (the lowest figure) In the remaining children, the saturation index was 95-98%.

When auscultation of the lungs in all children was weakened breathing over the affected area of the lungs. While whitish rales were found in 88 ± 4.96% of patients in the first group and 80 ± 4.9% of children in the second group.

To verify the diagnosis, children were given a general blood test to determine inflammatory changes. In 90 ± 4.97% of children in the first group leukocytosis was observed, in 28 ± 3.5% of them it was twice the norm, whereas in children of the second group leukocytosis was 80 ± 4.9% and only 17 ± 2 , 71% exceeded the norm. One of the indicators of inflammation is the displacement of the leukocyte form to the left, which was observed in 88 ± 4.96% of children in the first group. At the same time, in children aged 7-9 years shifting the leukocyte formula to the left took place in 78 ± 4.88% of children. In 76 ± 4.85% of all examined children there was an increase in ESR in the general blood test. This indicator increased in 84 ± 3.67% of children in the first group and in 80 ± 4.9% of children in the second age group. To confirm the diagnosis of the examined children, an X-ray of the chest organs was performed. As a result, the following data were obtained: in the first group of children, segmental pneumonia was observed in 46 ± 4.27% of cases, while polysegmental - in 54 ± 4.44% of children. In the second group, on the contrary, segmental pneumonia was prevalent, which was 64 ± 4.66% of all cases and only 36 ± 3.37%.

Among the examined children, 47% ± 4.9% were admitted to the hospital on the first day, of which the children of the first group who were prescribed penicillins were 15 ± 3.57%, and cephalosporins - 12 ± 3.25%, while children of the second groups treated with penicillins - 12 ± 3,25%, and cephalosporins - 8 ± 2,71%. On the second day, 30% ± 4.5% were received, among which the children of the first group, who were prescribed penicillins - 10 ± 3.1%, and cephalosporins - 4 ± 1.95%, while the children of the second group treated with penicillins amounted to 11 ± 3,13%

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and cephalosporins - 5 ± 2,18%. On the third day, 23% ± 4.2% of the patients, including the children of the first group treated with penicillins 4 ± 1.95%, cephalosporins - 5 ± 2.18%, and the children of the second group who were prescribed penicillins - 7 ± 2.55 % and cephalosporins - 7 ± 2.55%. (Table III).

Table III

Day of admission to the hospital of examined children with community-acquired pneumonia

Day of admission to the hospital	3-6 years		7-9 years	
	Penicillin	Cephalosporins	Penicillin	Cephalosporins
First	15±3,57%	16±3,67%	12±3,25%	15±3,57%
Second	6±2,37%	4±1,95%	11±3,13%	5±2,18%
Third-fourth	4±1,95%	5±2,18%	2±1,4%	5±2,18%

Almost half (44% ± 4.9%.) Of the examined children at the site was prescribed an antibiotic orally. Among them, children of the first group (3-6 years) penicillins were prescribed in 7 ± 2,55% of cases, and cephalosporins - at 15 ± 3,57%. Children of the second group (6-9 years old) penicillins were prescribed in 11 ± 3,13% of cases, cephalosporins - 8 ± 2,71% and macrolides - 2 ± 1,14%. On admission to the hospital, all children received an oral form of parenteral administration with the simultaneous replacement in some cases of a group of antibiotics. Thus, among the children of the first group, who were assigned penicillins in 2% ± 1.14%, there was a change in ceftaxime 100 mg/kg/day intravenously, and those treated with cephalosporins at 9 ± 2.86% were assigned ampysulbin at a rate of 100 mg / kg / day intravenously. While among children of the second group, who were assigned penicillins in 3 ± 1.70% were replaced by cefatoxime, those treated with cephalosporins in 5 ± 2,18% were replaced by ampysulbin and patients who received macrolides were also prescribed ampisulbin.

All children of both age groups prescribed penicillins and cephalosporins at an equal ratio of 50 ± 5.1%. In this case, in 76% of cases cephalosporin was prescribed by regular doctors in the department, 5% of mothers refused to use ampysulbine, and 19% of children in the history used antibiotics penicillin group for the last 3 months. In 36% ± 4.8% of the children of the first group there was stage therapy and in 38 ± 4.9% of the children of the second group. (Table IV). Drugs used in this case: amoxicillin in a dose of 75 mg/kg/day, cefpodoxime 10 mg/kg/day and amoxicillin protected by clavulanic acid -75 mg/kg/day.

Table IV

Staged antibacterial therapy in children aged 3-9 years with community-acquired pneumonia in treatment in a hospital

Group and dose of antibiotic	3-6 years		7-9 years	
	Penicillin	Cephalosporins	Penicillin	Cephalosporins
	Day of step therapy			
	3 day	4 day	4 day	5 day
Amoxicillin 75 mg/kg/day	12±3,24%	18±3,84%	16±3,66%	10±3,1%
Cephpodoxim 10 mg/kg/day	4±1,95%	2±1,14%	6±2,37%	4±1,95%
Amoxicillin with clavulanic acid, 75 mg/kg/day	-	-	2±1,14%	-

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The average duration of stay in the hospital of the first group of children receiving penicillin was 7 -9 days, namely 7 days - 11 ± 3,13%, 8 days -8 ± 2,71% and 9 days - 6 ± 2,37%, in while those receiving cephalosporins 8-12 days: 8 days - 6 ± 2,37%, 9 days - 5 ± 2,18%, 10 days - 8 ± 2,71%, 11 days - 4 ± 1, 95%, 12 days - 2 ± 1.14%. A similar situation was observed in the second group (Table V).

Table V

Duration of stay in the hospital of the examined children depending on starting antibiotic therapy

Discharge day	3-6 years		7-9 years	
	Penicillin	Cephalosporins	Penicillin	Cephalosporins
6	-	-	4±1,95%	-
7	11±3,13%	-	13±3,36%	-
8	8±2,71%	6±2,37%	4±1,95%	4±1,95%
9	6±2,37%	5±2,18%	4±1,95%	3±1,70%
10	-	8±2,71%	-	8±2,71%
11	-	4±1,95%	-	2±1,14%
12	-	2±1,14%	-	4±1,95%
14	-	-	-	4±1,95%
Average stay in the hospital	7.7±0.65*	9.74±0.76*	7.32±0.94**	10.6±1.33**

*Note: * - P = 0.049 - the difference is likely between the children of the first group who received the antibiotics of the penicillin and cephalosporins group; ** - P = 0,047 - the difference is likely between the children of the second group receiving antibiotics of the two groups: penicillins and cephalosporins.*

Discussion. Diseases of the respiratory system rank 3rd in the prevalence after birth defects of the heart and perinatal pathology among all diseases of childhood. Pneumonia takes the lead in the mortality rate among these diseases [5].

In most cases, doctors in the district (53%) and regular doctors (76%) of the admissions department prescribed antibiotics of the cephalosporin group as starting antibiotic therapy, while in-patient physicians favored the penicillin group. According to the recommendations of the British Thoracic Society on the choice of an antibiotic for ovariectomized pneumonia: Oral antibiotics are effective and safe even in children with non-hospital pneumonia. Intravenous antibiotic is shown to children who:

1. Not able to assimilate, tolerate oral medicines (for example, due to vomiting).
2. Have symptoms of septicemia or complicated pneumonia.

With the empirical appointment of antibacterial agents for patients with pneumonia, preference is given to beta-lactam antibiotics, namely:

• Amoxicillin is a preparation of the first line (with an allergy a \ b penicillin number, use macrolides).

• Macrolides can be added at any age in the absence of the effect of first-line therapy.

• Macrolides should also be used in severe cases or in suspected pneumonia caused by mycoplasma or chlamydia.

• Co-amoxicillin recommended for patients with pneumonia associated with influenza.

• Intravenous administration of amoxicillin, co-amoxiclav, cefuroxime, cefotaxime or ceftriaxone is indicated for severe pneumonia [6].

According to the literature, in Ukraine there is a low level of resistance of bacteria to amoxicillin, so this antibiotic is a drug of choice in the treatment of pneumonia [7].

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With the initiation of antibiotic therapy with penicillins, the symptoms of pneumonia decreased by 2 nd day in 16 ± 3.67% in the group of children 3-6 years old and in 18 ± 3.84% of children 7-9 years old. While in the group where the starting therapy began with cephalosporins - in the 3rd day in 19 ± 3.92% (3-6 years) and 15 ± 3.57% (7-9 years), in 11 % of the rest of the children receiving cephalosporins (equally in both age groups) symptoms improved by 4 per day.

In the group of children receiving starting therapy in the form of antibiotics of the penicillin group, the transition to oral antibiotics was marked on the 3rd day, at the start of cephalosporins - at the 5th day. The average length of stay in the hospital was 7.7 ± 0.65 days for patients 3-6 years old and 7.32 ± 0.94 days for children 7-9 years old receiving penicillin.

In the group treated with cephalosporins, the average length of stay in the hospital was 9.74 ± 0.76 days in children 3-6 years old and 10.6 ± 1.33 days in patients aged 7-9 years.

That is, the optimization of pneumonia treatment is as follows:
- When prescribing antibiotics of the first line, prefer the penicillin group;
- In practice, doctors of pediatricians, general practitioners of family medicine and children's pulmonologists should give preference to the penicillin group as a starting antibiotic therapy in children with outpatient pneumonia, as in this group of antibiotics the condition is improved already on the 2-3rd day of the disease (in that time as on cephalosporins on day 4-5). In addition, the length of stay in the hospital of these children significantly decreased. Thus, the average number of bed-days spent in the hospital for children treated with antibiotics of the penicillin group was 7.32 ± 0.94 - 7.7 ± 0.65 depending on age, while in children receiving cephalosporins this rate was 9.74 ± 0.76 - 10.6 ± 1.33 (p = 0.047).

Conclusions. Pneumonia is one of the most common diseases in children, and one of those that can cause many complications and even death. Accordingly, the treatment of this disease should be maximally effective and short-lived. The best choice for treating pneumonia is a group of oral aminopenicillins, which were administered in the first days of the disease and showed significantly better results than patients treated with cephalosporins. Aminopenicillin or protected aminopenicillin is also preferred in the case of parenteral antibiotics.

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