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Modern Approaches To The Selection Of Protected Cephalosporins Iii For Therapy Of Community-Acquired Pneumonia In Children

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ABSTRACT

The aim of the study was to study the effectiveness of the use of protected cephalosporin III generation Extum in the treatment of community-acquired pneumonia in children. The study included 100 children with community-acquired pneumonia at the age from 1 to 15 years, who were observed and treated in the department of pulmonology. In the process of complex clinical and laboratory examination of children, biochemical, microbiological and immunological research methods were used. Microbiological studies have shown that in children with community-acquired pneumonia, S. Pneumonia occupies a significant place in the etiological structure and accounts for 42.0% of cases, a high sensitivity of pneumococcus to injectable cephalosporin of the third generation has been established. When included in complex treatment, protected cephalosporin of the third generation Extum leads to a decrease in the frequency of repeated acute respiratory infections and their complications by 2.2 times, the frequency of recurrent bronchitis and pneumonia by 1.7 times, which indicates a high therapeutic effectiveness of the proposed treatment.

KEY WORDS: pediatrics, pneumonia, cephalosporin, community-acquired pneumonia

1. INTRODUCTION

Currently, the general practitioner is of particular relevance to community-acquired pneumonia due to its high prevalence in the pediatric population [2,6]. The basis of the treatment of community-acquired pneumonia is antimicrobial therapy, the strategy of which is one of the complex and still unresolved issues of modern pulmonology [7]. The appointment of antibiotic therapy and the choice of a drug for treatment should be based on knowledge of the prevailing, etiologically significant bacterial pathogens, their virulence and sensitivity to antimicrobial agents. The lack of data on the etiology of the disease leads to the fact that pneumonia, as a rule, is encrypted under the code J18 ("Pneumonia without specifying the pathogen"), and antibiotic therapy, respectively, is carried out "blindly". In some cases, the initial choice of antibiotics may be incorrect, which leads to a lack of treatment effect [3].

An unprofessional approach to antibiotic therapy, irrational, uncontrolled administration of drugs often leads to resistance of microorganisms, chronicity of diseases [8]. In children aged 6 months. - For 5 years, the dominant role of bacterial pathogens in the etiology of community-acquired pneumonia, primarily pneumococcus, is generally noted (in 70–90% of cases). Haemophilus influenzae type B are detected less frequently (up to 10%).

In children older than 5 years, pneumococcal pneumonia accounts for 35–40% of cases, atypical pneumonia caused by M. pneumoniae and C. pneumoniae - 23–44 and 15–30%, respectively.

An important criterion for the use of antibiotics are clinical guidelines, modern diagnostic tests that allow timely detection and identification of bacterial infection. Much attention is paid to the study of biological markers - a relatively new direction in the diagnosis of pneumonia, as well as the assessment of the risk of an unfavorable clinical outcome and the effectiveness of the treatment [1]. Currently, modern biomarkers of inflammation include procalcitonin, C-reactive protein, and a number of pro-inflammatory cytokines (IL-6, IL-2, TNF-b).

The problem makes us think not only about the optimal choice of effective antibiotic therapy, but also about the possibilities of activating the protective-adaptive systems of the macroorganism in the fight against the pathogenic agent. Among the antibiotics currently used in clinical practice, one of the leading positions is occupied by cephalosporin. According to modern national and international clinical guidelines for the treatment of community-acquired pneumonia, all hospitalized children, regardless of age, are recommended to start empirical therapy with parenteral cephalosporin of the third generation [4]. Generation III cephalosporin are predominantly active against gram-negative microorganisms and streptococci / pneumococci [5,8]. Moreover, in recent years, protected cephalosporin of the 3rd generation Extum are increasingly used as the drug of choice. It is one of the basic third generation cephalosporin, which differs from other antibiotics of this class in its special pharmacokinetics, a combination of sodium sulbactam and sodium ceftriaxone. Studies have shown that Sulbactam is an irreversible inhibitor of most of the main β-lactamases, which are produced by microorganism resistant to β-lactam antibiotics and binds to some penicillin-binding proteins, therefore, the combination of ceftriaxone / sulbactam often has a more pronounced effect on sensitive strains.

The challenge now is to simplify the treatment of community-acquired pneumonia, make it less traumatic, safer and cheaper. Skillful use of antibacterial agents just allows you to solve these problems, reducing all the main unpleasant moments for the patient and his environment - from the number of injections to the length of hospital stay. Obviously, for a balanced understanding of the role and place of protected third generation cephalosporin in the treatment of community-acquired pneumonia in children, additional clinical studies are needed.

In this regard, the purpose of our work was to study the effectiveness of the use of protected cephalosporin III generation Extum in the treatment of community-acquired pneumonia in children.

2. MATERIALS AND METHODS

The study included 100 children with community-acquired pneumonia at the age of 1 to 15 years, who were observed and treated in the pulmonology department of the center. As a control group, 20 practically healthy children of the same age were examined. The diagnosis was established on the basis of the classification of the main clinical forms of bronchopulmonary diseases in children, approved at a special meeting of the XVIII National Congress on Respiratory Diseases (2009).

Depending on the therapy, the following observation groups were formulated: Group I - 45 patients with community-acquired pneumonia who received basic therapy; Group II - 55 patients with community-acquired pneumonia on the background of basic therapy, receiving protected cephalosporin III generation Extum (at the rate of 75 mg / kg of body weight 2 times a day, every 12 hours).

In the process of complex clinical and laboratory examination of children, biochemical, microbiological and immunological research methods were used. Biochemical studies: the content of C-reactive protein in the blood serum was determined on an automatic immunochemiluminescent analyzer Immulite 2000; determination of the concentration of procalcitonin in the blood serum using an automatic immunochemiluminescent analyzer Advia Centaur. Biochemical studies were carried out in the center's biochemistry laboratory. Microbiological studies were carried out in accordance with the standards of modern clinical microbiology by sampling material from the depth of the throat, and smears were stained according to Gram and bacterioscopy was performed. The study of sensitivity to antimicrobial drugs was carried out by the disk-diffusion method.

Immunological studies: the concentration of cytokines – IL-1β, IL-4, IL-6, IL-8, TNF-α and IFNγ was determined by immunofement analysis using the Vector-Best test systems.

The data were processed by the Fischer - Student variation statistics method using personal computers and using a software package.

3. RESULTS AND DISCUSSION

Upon admission to the hospital, the main complaints of parents of sick children were cough 100%, shortness of breath - in 74.0%, fever - in 63.0% of children, loss of appetite - in 95.0%, lethargy - in 97.0% , pallor - in 95.0%, sleep disturbance - in 87.0%, runny nose - in 44.0%. Temperature reaction of varying degrees was observed in 63.0% of patients, in 37.0% of children, the temperature was normal. Febrile temperature was noted in 17.0% of children and lasted for 2-4 days, subfebrile - in 46.0% of children for 3-5 days. The main manifestation of community-acquired pneumonia was cough, mostly wet in 66.0% of patients, in 34.0% - dry. Signs of hypoxia in the form of cyanosis of the nasolabial triangle were observed in 77.0% of patients, in the remaining children, cyanosis occurred with crying and anxiety. Shortness of breath of a mixed nature with the participation of auxiliary muscles in the act of breathing was in 74.0% of patients. Percussion changes in the lungs in 64.0% had a local character in the form of a shortening of the pulmonary sound, 36.0% had a boxed tone of percussion sound. On auscultation, hard breathing was determined in 86.0% of cases, in 14.0% weakened breathing. Moist wheezing, sometimes in combination with crepitus, was heard in 84.0% of patients. Dry wheezing was heard in 64.0% of patients. The average duration of inpatient treatment for children with community-acquired pneumonia was 10.2 ± 0.3 days. According to the data of X-ray studies of the respiratory organs, bilateral focal pneumonia was diagnosed in 59.0% of patients, right-sided in 21.0%, and the focus of inflammation was localized mainly in the basal segments of the right lung. 2.0% - left-sided, 18.0% - polysegmental.

In the course of the study, in patients with community-acquired pneumonia in the initial period of the disease, the content of C-reactive protein in the blood serum was increased in 71.0%, and in 29.0% of children it was within the normal range. Studies have shown that the level of C-reactive protein in the blood serum of children with community-acquired pneumonia in the initial period of the disease was significantly higher (7 times), compared with the control group being 32.8 ± 5.6 mg / l.

When analyzing the indicators of cytokine status, high levels of the cytokine IL-1β, 8 and TNF-α were characteristic, significantly higher than those in the control group. Analysis of the results showed that in community-acquired pneumonia, the level of IL-1β increases by 3.5 times compared with the data in the control group, which averaged 101.7 ± 6.7 pg / ml ($P < 0.01$). The level of IL-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 ($P < 0.05$). Our data showed that the level of IL-4 in children with community-acquired pneumonia was 2.3 times higher than the control. In community-

acquired pneumonia, the level of IL-4 increased to 10.8 ± 0.9 pg / ml (P <0.01), in relation to the control group. IL-8 is an important mediator of the inflammatory process in the lungs. Thus, in community-acquired pneumonia, the level of IL-8 averaged 44.5–4.3 pg / ml, which is 2.3 times higher than that in the control group (P <0.01). When analyzing the TNFα content in patients with community-acquired pneumonia, we noted its increase to 63.5 ± 3.2 pg / ml as compared with (P <0.01) the control group and increased 1.5 times (42.3□2, 1 pg / ml, P <0.05). Studies of the level of IFNγ in patients with community-acquired pneumonia showed a deep deficit in its content 1.3 times lower than in the control group (34.3 ± 2.7 pg / ml), P <0.01.

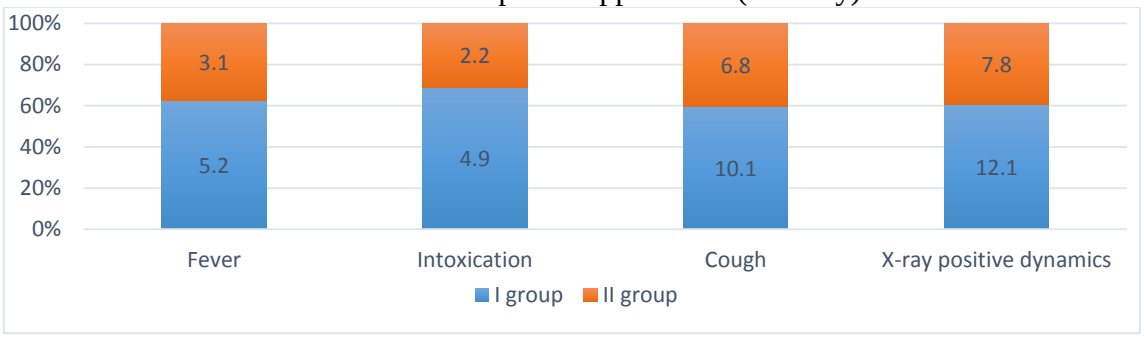
According to the results of bacteriological research among the examined children, it was revealed that the strain of Streptococcus pneumonia was found in 42.0% of cases and Staphylococcus aureus in 29.0% of cases. H. influenzae were less common in 18.0% of the examined and M. pneumonia in 11.0% of cases. Based on the results obtained, it can be argued that the main causative agents of community-acquired pneumonia are Streptococcus pneumoniae and Staphylococcus aureus. When studying the antibiotic sensitivity of the isolated microorganisms, it was found that Streptococcus pneumonia is most highly sensitive to ceftriaxone / sulbactam (protected cephalosporin of the 3rd generation Extum) (98.0%), cefoperazone (97.0%), cefotaxime (92.0%), cefepime (89.0%) and 60% to macrolides and 40% to amikacin. It should be noted that the high sensitivity of pneumococcus to injectable cephalosporins remains. The results of the study of the sensitivity of Streptococcus pneumoniae allowed the use of a protected III generation cephalosporin Extum (ceftriaxone / sulbactam) as the recommended means for empiric antibiotic therapy in community-acquired pneumonia.

A predictor of ineffective antibiotic therapy in patients with community-acquired pneumonia is a high level of C-reactive protein in the blood serum, which remains in the dynamics of the disease 28.2 ± 3.5 mg / l on the 10th day in children of group I. This made it possible to individualize the assessment of the course of community-acquired pneumonia, which became the basis for a differentiated approach to patients with the isolation of a group of children in need of antibiotic therapy. In the first group of patients, the following drugs were used as starting drugs: macrolides, cephalosporins of the second and third generations.

Clinical efficacy after the use of drugs was noted only in 17.8% of patients, in this regard, they underwent an antibiotic replacement. The duration of antibiotic therapy in patients with a moderate form of the disease was 8.4 ± 0.3 days, with a severe form - 11.2 ± 0.5 days. In 77.8% of children of group I, S. pneumonia continued to be secreted from the pharynx even after a 10-day course of antibiotic therapy. In the second observation group, the results of treatment, depending on the selected antibiotic with the established etiology of community-acquired pneumonia, were expressed by an improvement in the general condition and a decrease in symptoms of intoxication by 2-3 days, the cough became softer, the amount of sputum decreased, the physical data also had more pronounced positive dynamics.

Against the background of traditional therapy, these signs disappeared on average by 4.9 bed-days. In addition, the body temperature normalized 1.7 times faster (on average 3.1 ± 0.1 days, P <0.001) than in patients treated with traditional therapy (6.1 ± 0.3 days) (fig. 1).

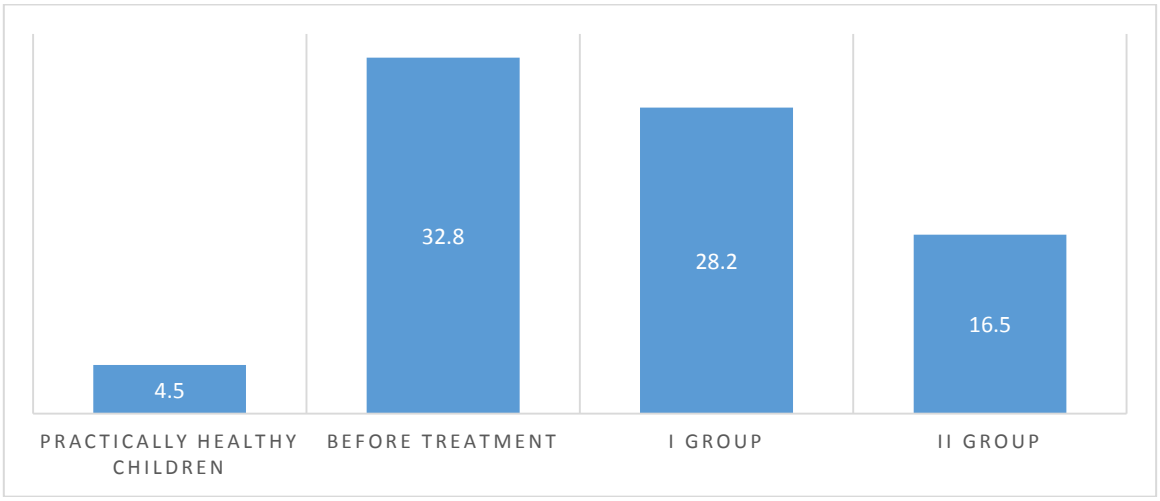
Figure 1. Duration of symptoms of community-acquired pneumonia against the background of different therapeutic approaches (bed-day)



Cough leveled off on average by 6.8 ± 0.2 bed-days, while in group I patients the cough disappeared on average by only 10.1 ± 0.3 bed-days. Positive X-ray dynamics by the 12th day of treatment was observed in 84.6% of patients with community-acquired pneumonia who received protected cephalosporin III of the Extum generation, and only in 32.1% of patients on the background of traditional therapy. Patients discharged from the hospital with improvement in their condition accounted for 96.4% in group II, while with traditional therapy - 66.7%. In general, the duration of antibiotic therapy for community-acquired pneumonia caused by typical bacteria is 10 days. The antibiotic should not be canceled in the early stages of the development of the disease (on the 3-4th day), since this does not achieve the eradication of pathogens, the development of antibiotic-resistant strains is potentiated.

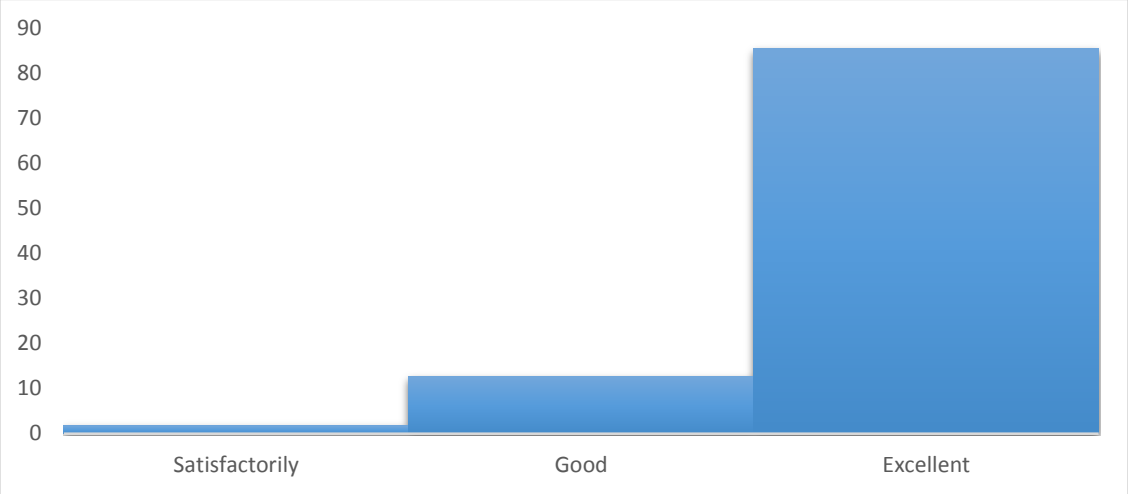
When assessing the effectiveness of antibiotic therapy in patients with community-acquired pneumonia, as well as when deciding whether to cancel it, it is necessary to take into account the dynamics of changes in the concentration of C-reactive protein (Figure 2). During the analysis of the level of C-reactive protein in the course of treatment in children of group II, there was a decrease in the inflammatory marker by the 10th day of therapy by 1.7 times compared with group I patients, compared to 2.0 times before treatment. With traditional treatment, this indicator also decreases on the 10th day, however, it does not have significant differences with the level at admission. The clinical efficacy of the protected 3rd generation cephalosporin Extum in children with community-acquired pneumonia was high, amounting to 96.4%.

Figure 2. Dynamics of changes in C-reactive protein in patients with community-acquired pneumonia



In 1.8% of children, the clinical response was assessed as “no effect”, in one - as “relapse”. The lack of effect could be due to the presence of chronic concomitant pathology. In patients of group II, while receiving Extum, the therapeutic effect was assessed as excellent in 85.5% of patients, as good in 12.7% and as satisfactory in only 1.8% compared with children in group I (Figure 3).

Figure 3. Evaluation of the results of using Extum, (%)



Analysis of the data obtained showed that after traditional therapy, children continued to experience repeated cases of acute respiratory diseases with their complications, recurrent bronchitis and pneumonia during the year. In children of the II group, the frequency of repeated acute respiratory diseases and their complications decreased 2.2 times, the frequency of recurrent bronchitis and pneumonia decreased 1.7 times compared with the I group of patients. Evaluation of the results of follow-up observations of children during the year showed a decrease in the frequency of recurrent diseases of the bronchopulmonary system, indicating the effectiveness of treatment.

Thus, the results obtained showed that in children with community-acquired pneumonia, it is advisable to use protected cephalosporins of the 3rd generation Extum in the therapy regimen. In the complex therapy of patients with community-acquired pneumonia, Extum showed clinical efficacy, good tolerance and a high safety profile. Rational use of an antibiotic prevents the development of resistance, helps to reduce the duration of the disease and prevents the development of complications, their introduction into everyday practice will contribute to adequate treatment and reduce the risk of complications and unfavorable outcomes in general.

4. CONCLUSION

1. Microbiological studies have shown that in children with community-acquired pneumonia, S. Pneumonia occupies a significant place in the etiological structure and accounts for 42.0% of cases, a high sensitivity of pneumococcus to injectable cephalosporins of the third generation and a tendency of increasing pneumococcal resistance to macrolides have been established.

2. Assessment of biomarkers of inflammation - C-reactive protein is an informative indicator in the diagnosis of community-acquired pneumonia in children, which can be used when choosing a differentiated therapy and evaluating its effectiveness.

3. When included in complex treatment, protected cephalosporin of the third generation Extum leads to a decrease in the frequency of repeated acute respiratory diseases

and their complications by 2.2 times, the frequency of recurrent bronchitis and pneumonia by 1.7 times, which indicates a high therapeutic efficiency of the proposed treatment.

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Consent

Written informed consent was obtained from all participants of the research for publication of this paper and any accompanying information related to this study.

Conflict Of Interest

The authors declare that they have no competing interests.

5. FINDING

No funding sources to declare.

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