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КЛИНИКО-ЭПИДЕМИОЛОГИЧЕСКИЕ ОСОБЕННОСТИ МИКОПЛАЗМЕННОЙ ИНФЕКЦИИ У ДЕТЕЙ РЯЗАНСКОЙ ОБЛАСТИ

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Обоснование. Острые респираторные инфекции являются актуальной проблемой педиатрии из-за высокого уровня заболеваемости и высокой частоты осложнений. ***Цель:*** проанализировать статистические показатели заболеваемости внебольничной пневмонией (ВП) у детей Рязанской области, определить клинико-эпидемиологические особенности микоплазменной инфекции и оценить ее роль в формировании ВП у детей. ***Материалы и методы.*** Проведен анализ показателей заболеваемости ВП у детей Рязанской области (2014-2016) и медицинской документации 106 детей (55 мальчиков, 51 девочка), получавших стационарное лечение в ГБУ РО Городская клиническая больница №11 (возраст от 9 месяцев до 17 лет). Всем пациентам проводили пульсоксиметрию, клиническое и лабораторное обследование, рентгенографию органов грудной клетки, определение специфических IgM-антител к *M. Pneumoniae* методом ИФА. ***Результаты.*** В Рязанской области отмечается рост заболеваемости ВП при стабильном уровне по России. У детей до 14 лет показатель в 1,5 раза превышает уровень 2014г. и в 2,8 раз – 2015г., в возрасте 15-17 лет – в 2 раза выше уровня 2014 г. Среди пациентов с микоплазмозом преобладали дети до 6 лет (50,9%). Пик заболеваемости пришелся на октябрь-декабрь. Заболевание начиналось остро без выраженных симптомов интоксикации и локальных изменений. У 77,3% детей была диагностирована ВП, преимущественно правосторонняя (48,8%), у 33,1% пациентов имела место смешанная бактериальная инфекция. Гематологические показатели свидетельствовали о наличии железодефицитной анемии у 12,3% детей, у 28% отмечался умеренный лейкоцитоз. Антибиотикотерапия проводилась с применением макролидов, в случае смешанной бактериальной инфекции – в сочетании с цефалоспоринами 3 поколения. ***Выводы.*** Отмечается рост заболеваемости ВП у детей. Выявлена сезонность в госпитализации детей с микоплазменной инфекцией, высокая заболеваемость среди детей дошкольного возраста, посещающих организованные коллективы и имеющих хроническую патологию. Микоплазмоз протекал в виде ВП у 77,3% пациентов, что повлияло на рост заболеваемости внебольничной пневмонией у детей.

Ключевые слова: *микоплазменная инфекция, внебольничная пневмония, заболеваемость, дети.*

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CLINICAL AND EPIDEMIOLOGICAL FEATURES OF MYCOPLASMA INFECTION IN CHILDREN IN RYAZAN REGION

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Background. Acute respiratory infections are an urgent problem of pediatrics due to the high incidence rate and high risk of bacterial complications. ***Aim.*** The aim of the study was to analyze the statistical indicators of the incidence of community-acquired pneumonia (CAP) in children of the Ryazan region, to determine the clinical and epidemiological features of mycoplasmal infection, and to assess its role in CAP morbidity in children. ***Materials and Methods.*** The analysis of the incidence of CAP in children of the Ryazan region (2014-2016) and of medical documentation of 106 children (55 boys, 51 girls) (age from 9 months to 17 years) was conducted. All patients underwent oxigenometry, clinical and laboratory examination, radiography, detection of specific IgM antibodies to *M. pneumoniae*. ***Results.*** In the Ryazan region there is noted an increase in the incidence of CAP in children as compared to the stable level of the incidence of CAP in Russia: in children under 14 years of age the incidence is 1.5 times higher than in 2014 and 2.8 times higher than in 2015, and is 2 times higher than in 2014 in 15-17 year old children. Most commonly mycoplasmosis was recorded in preschool age children, with the peak incidence in October-December. The disease began acutely without significant symptoms of intoxication and local changes. 77.3% of children had pneumonia, mostly right-sided (48.8%), and 33.1% had a mixed bacterial infection. Hematological indices indicated the presence of iron deficiency anemia in 12.3%, and moderate leukocytosis in 28% of children. Antibiotic therapy was carried out with the use of macrolides, and in case of mixed bacterial infection a combination of antibiotics with cephalosporins of the 3^{d} generation was used. ***Conclusion.*** In recent years there has been an increase in the incidence of CAP in children. Seasonality of hospitalization of children with mycoplasmal infection was revealed, and a high incidence of the disease in preschool children with chronic pathology. In 77.3% of examined children mycoplasmosis took the form of CAP, which influenced the incidence rate of CAP in children.

Keywords: *mycoplasmal infection, community-acquired pneumonia, morbidity, children.*

Acute respiratory pathology remains an important problem of pediatrics due to a high level of morbidity, annual rise in autumn-winter season and high occurrence of complications in the form of bacterial pneumonia [1,2]. The most vulnerable population group with high morbidity level is children under 14 years of age because of a high risk of development of pneumonia. According to the data of Federal Service for Consumer Rights Protection and Human Welfare of Russia, the CAP morbidity index in Russian Federation in 2016 was 16.0% higher than that in 2015 (776.6 per 100 000 of population against 669.7 in 2015) [3,4].

According to WHO data, pneumonia continues to remain one of five main causes of mortality in children under 5 years of age (in 2015 920 136 children under 5 years of age died from pneumonia, that accounted for 15% of deaths of children of this age) [5].

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Of special importance is understanding of the contribution of atypical pathogens into the structure of acute respiratory infections (ARIs). This group includes *Mycoplasma pneumoniae, Legionella pneumophila, Chlamydophila, Coxiella burnetti*. The most important pathogen of this group in children with ARI is *M. Pneumoniae* which may cause inflammation of both upper and lower airways. In a human population respiratory mycoplasmosis accounts for 10-16% of all cases of ARI, and in the period of endemic outbreaks its occurrence may reach 30-40%. According to literature data, *M. Pneumoniae* causes up to 40% of CAPs in children and about 18% of infections in patients requiring hospitalization. According to results of study of Jain S. [et al.] conducted in 2222 children, *M. pneumoniae* is most commonly identified in children above 5 years of age – 19% against 3% in children under 5 years [6].

Peculiarities of the structure and influence of *M. Pneumoniae* on a macroorganism determine the clinical presentation of the disease. Intracellular localization protects it from the immune response and permits long persistence in an organism worsening the course of a chronic bronchopulmonary pathology and inducing exacerbations of the disease. Due a small size, a microorganism can easily spread through the air in droplets. Due to absence of the cell wall *M. Pneumoniae* is resistant to antibacterial drugs that act on the membrane of a microbial cell (betalactams and others), but is highly sensitive to the environmental factors, therefore contagion takes place only in close contact (in families and organized groups) [7].

In an organism mycoplasma replicates in the cytoplasm of ciliary epithelium forming microcolonies which produce hydrogen peroxide and superoxide that damage epithelium and lead to inflammation. Here, the microorganism releases specific CARDS-toxin (community acquired respiratory distress syndrome toxin) with the structure similar to that of *Bordetella Pertussis* exotoxin, which causes vacuolization of cells of bronchial epithelium, reduces motor activity of cilia and induces extensive zones of peribronchial and perivascular inflammation and determines the severity of damage to the lung tissue [8].

However, the course of mycoplasmal infection depends not only on the biological properties of the causative agent, but also on the individual peculiarities of the immune response of a macroorganism to infectious agent. There is an increasing discussion of the role of *M. Pneumoniae* in the pathogenesis of a chronic bronchopulmonary pneumonia and bronchial asthma because of the ability of CARDS-toxin to induce intensive allergic inflammation in lungs, production of Th2-type cytokines and to provoke hyper-reactivity of the airways; 2-type cytokines including interleukins (IL)-4 and -5 released in the infection stimulate overproduction of IgE that play a key role in the pathogenesis of bronchial asthma [9-11].

The *aim* of study was to analyze statistical parameters of CAP morbidity in children of the Ryazan region, to determine clinic-epidemiological peculiarities of mycoplasmal infection and to evaluate its role in CAP morbidity in children of different age.

Materials and Methods

Parameters of CAP morbidity in children of the Ryazan region were analyzed according to the official medical statistics data for the period from 2014 to 2016, retrospective analysis was conducted of the medical documentation for 106 children (55 boys, 51 girls) with the age from 9 months to 17 years who were treated for mycoplasmal infection in children's infection department of the City Clinical Hospital №11.

All patients passed pulse oximetry on admission to hospital and in dynamics, clinical and laboratory examination, X-ray examination. Etiological verification of the causative agent was implemented by a method of immune enzyme assay (IEA) with determination of specific IgM-antibodies to *M. Pneumoniae* in the laboratory of the City Clinical Hospital №11.

Statistical processing of the obtained results was carried out using a standard program package Microsoft Excel 7.0.

Results and Discussion

According to the data of official medical statistics for the Ryazan region in the pe-

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riod from 2014 to 2016, an increase in CAP morbidity was noted in children of the age under 14 years with the relatively stable parameter for Russia: 1.5-fold increase in comparison with 2014 and 2.8-fold increase in comparison with 2015. In 2016 in total 2172 cases of CAP were recorded in the given age group (against 787 in 2015 and 1416 in 2014), thus, CAP morbidity in the Ryazan region was 1.76 times that in Russian Federation (Fig. 1) [1,3].

Among the teenagers of 15-17 years the CAP morbidity rate in the Ryazan region rose 2-fold in comparison with 2015 against the practically stable level in Russian Federation (Fig. 2) [1,3].

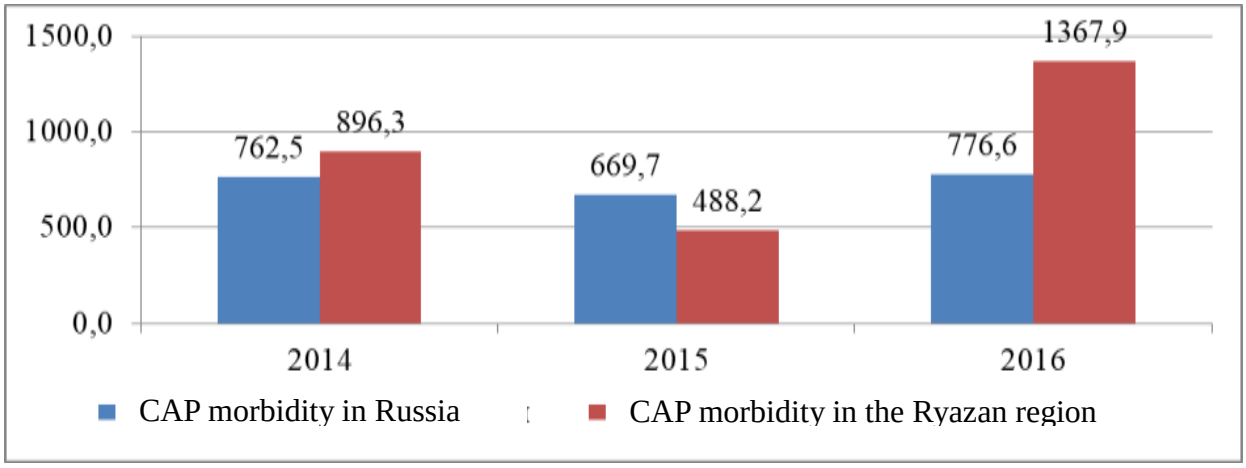

Fig. 1. Dynamics of CAP morbidity in children under 14 years of age (1/100 000) in the Ryazan region and RF (2014-2016)

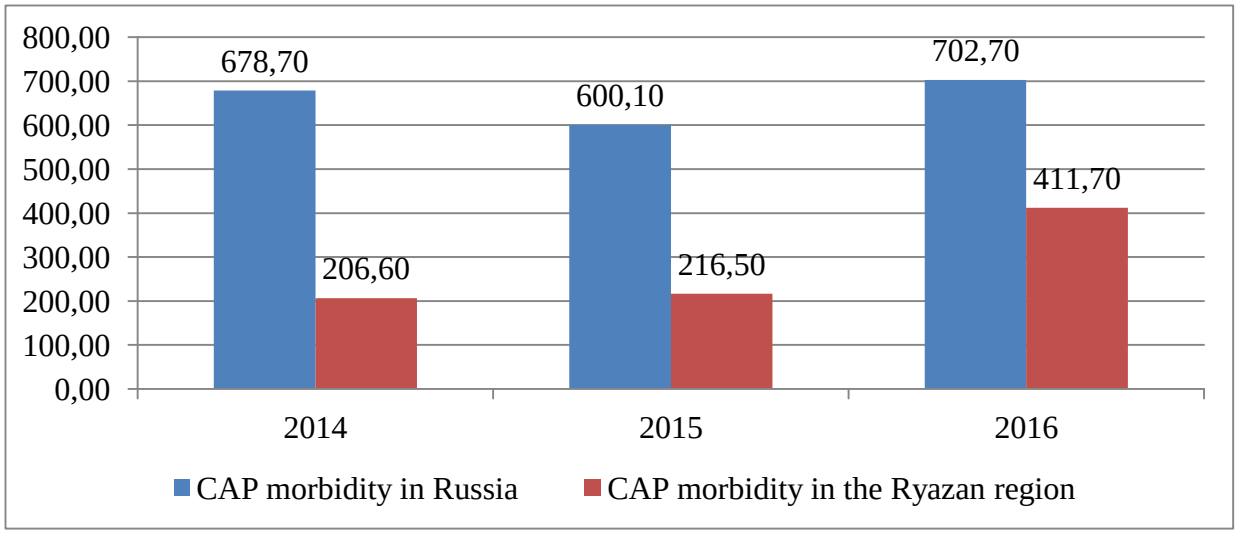

Fig. 2. Dynamics of CAP morbidity in children of 15-17 years of age (1/100 000) in the Ryazan region and RF (2014-2016)

There was noted a 3-fold increase in the incidence of pneumonia of pneumococcal etiology in children under 14 years of age (79.4/100 000 in 2016 against 26.1 in 2015), and 1.6-fold increase in children of 15-17 years of age (18.1 in 2016 against 11.2/100

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000 in 2015).

The number of patients with CAP in children's department of the City Clinical Hospital №11 in 2016 was 17% higher in comparison with 2015 (431 and 367, respectively) with the stable amount of children with infections of the lower airways (781 cases in 2016 and 794 – in 2016.).

Analysis of medical documentation of the treated patients showed that most children were hospitalized in the 4th quarter of 2016 (53.5%), with the peak admission to hospital in November with a gradual decline in December (Fig. 3) which agrees with the literature data about seasonal character of the disease [1,2,5].

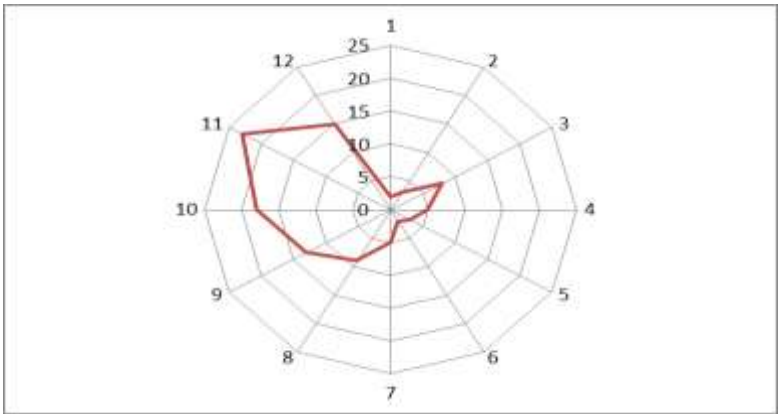

Fig. 3. The quantity of children hospitalized with mycoplasmosis in 2016 (n)

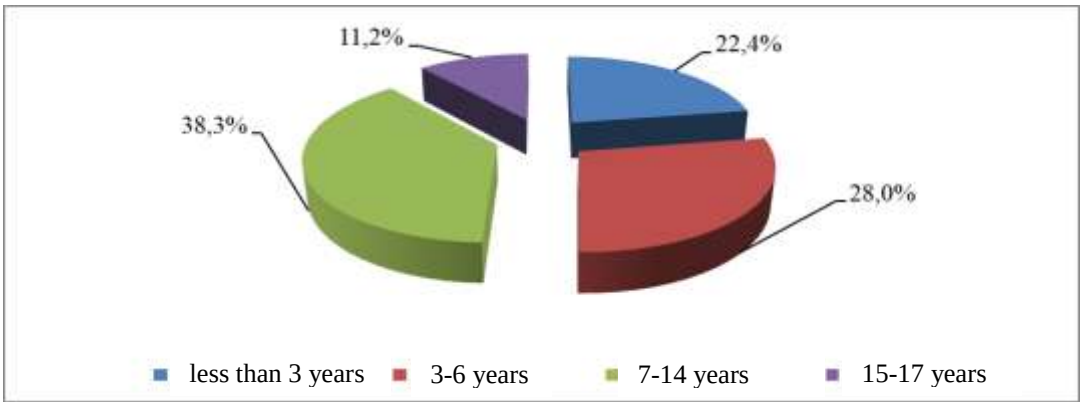

Fig. 4. Age structure of children with mycoplasma infection (n=106)

The disease started abruptly with elevation of temperature or with persistent low-productive cough with no evident symptoms of intoxication. In the first 3 days from the onset of disease 26.4% were hospitalized, 12.3% – on the 3th-5th day, but most children (63.2%) were admitted to hospital in 5 days after falling ill due to ineffectiveness of treatment in the outpatient clinic.

On admission each forth patient (24.5%) had I degree respiratory failure. On physical examination no local changes were found, in auscultation harsh breathing with a small amount of small-bubble and medium-bubble crackles was identified in 86 children (81,1%).

During examination 82 patients (77.3%) were diagnosed with community-acquired pneumonia, including a mixed bacterial infection in each fifth case (19.5%): besides *M. Pneumoniae*, there were also isolated *S. aureus, Str. Pneumoniae, Str. Pyogenes, K. Pneumoniae*.

The majority of patients with diagnosis of pneumonia (63.4%) were hospitalized after the 5th day of falling ill (52/82), with signs of

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I-II degree respiratory failure. Each fourth patient had some underlying disease, including anemia in 26.6% of children and organic damage to the CNS in 20% of patients.

Chest X-ray showed foci of non-homogenous infiltration that were denser near the roots, with uneven edges, often cord-like, «hairy», bilateral, non-symmetric, mostly located in lower parts of lungs. Reaction of pleura was seen in 16 patients (15.1%) and was confined to the interlobar pleura.

Right-sided damage to the lungs was mostly noted (48.8%) in the form of polysegmental damage, in 34.1 % of cases – left-sided pneumonia, in 14 patients (17.1%) – bilateral pneumonia (Fig. 5). A destructive damage to the lobe of the right lung by a combined bacterial-fungal infection was noted in a patient with a severe damage to the CNS with the underlying moderate anemia (*M. Pneumoniae + S. aureus + C. albicans + K. Pneumoniae*).

Fig. 5. Chest X-ray of a child B., 13 years

In children of the early age the disease ran in the form of pneumonia in 62.5% (15 cases of 24 children of the given age group), in the rest of cases the disease took the form of obstructive bronchitis, in 2 cases it combined with sinusitis. In 16.7% of observations a combined bacterial infection was present (*M. Pneumoniae + S. aureus*). In 75.0% of cases (21/28) of the age group from 3 to 6 years inclusive, mycoplasmal infection ran with clinical and radiological signs of pneumonia, in the rest of cases – in the form of obstructive bronchitis. In 4 children β-hemolytic streptococcus was isolated, in 1 case – *E. Cloacae*, in 2 cases – *C. albicans*, in 1 case – a combined bacterial-fungal microflora (*M. Pneumoniae + C. Albicans + K. Pnevmoniae*).

In children of school age (7-14 years) there were noted radiological signs of pneumonia in 79.5% of cases (35/44), in the rest of patients the disease had the form of obstructive bronchitis. In 27.3% of patients bacterial or bacterial-fungal association was present. In most cases nonpathogenic (*Neisseria spp.*)

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and opportunistic pathogenic microflora (*Str. pyogenes; S. aureus; Str. Pneumoniae*) were isolated; *Candida* fungi.

In teenagers of 15-17 years mycoplasmal infection in all cases ran in the form of pneumonia, in 2 cases mixed bacterial flora was isolated (*M. Pneumoniae+Str. pyogenes*; *M. Pneumoniae +S. aureus*).

Bacteriological examination of pharyngeal swab identified opportunistic microflora in a part of patients – *S. aureus* in 9 patients (8.5%), *Candida* fungi in 11 patients (10.4%), *E. cloacae* in 3 patients (2.8%), group B and C hemolytic streptococcus in 13 patients (12.3%), and also bacterial and bacterial-fungal associations.

Clinical analysis of blood showed the normal amount of leukocytes in the majority of patients (71.1%), moderate leukocytosis in 28.3% with the total amount of leukocytes not more than $19x10^9$/L (Me=8.4). The majority of patients had accelerated ESR (up to 40-49 mm/min) with no leukocytosis.

Elevated level of C-reactive protein (> 30 mg/L) indicating a high probability of bacterial infection was determined only in 17 examined patients (16.0%), increased level of seromucoid (>0.2 Un) was found in 66 children (62.3%).

In patients with mycoplasmal pneumonia there was noted discrepancy between the extent on intoxication and spread of pathological process in lungs, existence of long-standing low-productive cough, absence of local physical symptoms.

In the examined children bronchitis ran with clinical symptoms of I-II degree respiratory failure. In each fifth patient the disease took a complicated course with bacterial associations with development of sinusitis (2 cases), acute otitis of the middle ear, infection of urinary tract (1 case).

In treatment antibiotics therapy was used with preparations of macrolide group, and in case of bacterial infection – in combination with 3^d generation cephalosporins [7,12].

Conclusions

1. Analysis of statistical parameters revealed increase in the CAP morbidity in children of the Ryazan region.

2. Hospitalization of children with respiratory mycoplasmosis into the infectious hospital of Ryazan shows a seasonal character; a high incidence of the disease is noted among pre-school children that attend organized groups and have a chronic somatic pathology.

3. In the examined children mycoplasmal infection predominantly ran in the form of pneumonia, which surely influenced the dynamics of the incidence of community-acquired pneumonia in children's population of the region.

4. The existence of combined bacterial infection contributed to a complicated course of the disease and required use of combined antibiotic therapy.

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Дополнительная информация [Additional Info]

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