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Pharmacoeconomical Analysis of Rational Use of Antibiotics for Treatment of Childhood Pneumonia

Z.A. Ubaydullaeva*; Kh.S. Zaynutdinov, PhD; ScD

The Tashkent Pharmaceutical Institute, Tashkent, Uzbekistan

Abstract

The purpose of this study is to estimate the treatment costs of pneumonia in children in the clinic of the Republican Specialized Scientific Practical Medical Center of Pediatrics (RSSPMCP) of Uzbekistan. We performed a pharmacoeconomical analysis for treatment of childhood pneumonia by cost-effectiveness and cost-minimization methods. It was determined that monotherapy on the basis of ceftriaxone is the preferable scheme of antibacterial therapy for moderate community-acquired pneumonia (CAP) in children without respiratory comorbidities. This therapeutic scheme was associated with a small percentage of side effects and was the best option to cut the expense of treatment.

Keywords: *community-acquired pneumonia*; *antibiotic therapy*; *pharmaco-economical analysis.*

Introduction

An immaturity of the immune system in children and a broad range of pathogens, including bacteria, atypical agents, and viruses, promote a high frequency of pneumonia among the respiratory infectious diseases in children [1]. In the developed world, the annual incidence of pneumonia is ~3–4 cases per 100 children <5 years old [2, 3]. In 2006, the rate of hospitalization for CAP in children through age 18 years, using data from the Healthcare Cost Utilization Project's Kids' Inpatient Database, also based on ICD-9-CM discharge diagnosis codes, was 201.1 per 100 000 [4].

In the structure of common morbidities in Uzbekistan, respiratory diseases occupy the first place. The analysis of morbidity in children under the age of 14 showed that the prevalence of respiratory diseases is 32.86 per 1,000 in the population, and the highest morbidity is observed in the city of Tashkent. Among the respiratory diseases in children, pneumonia is one of the most widespread pathologies. Pneumonia kills an estimated 1.1 million children under the five years of age every year; this is more than AIDS, malaria and tuberculosis combined [5, 6]. Antibiotic therapy is the mainstay of treatment of bacterial pneumonia. The efficiency of antibacterial therapy depends on timely onset of treatment, rational selection of the drug, and dosing regimen. Most cases of pneumonia require oral antibiotics, which are often prescribed at a health center. These cases can also be diagnosed and treated with inexpensive oral antibiotics at the community level by trained community health workers. Hospitalization is recommended only for severe cases of pneumonia, and for all cases of pneumonia in infants younger than 2 months of age [7].

The cost of antibiotic treatment for all children with pneumonia in 66 countries, which determine the maternal, newborn and child survival in the framework Countdown to 2015, is estimated at around $109 million per year. The price includes the antibiotics and diagnostics for pneumonia management [7].

Antibacterial drugs are very costly; therefore, searching for effective strategies for treatment by using methods of pharmacoeconomical analysis becomes very important. Antibiotic resistance is a serious and growing phenomenon in contemporary medicine and has emerged as one of the pre-eminent public health concerns of the 21st century, in particular as it pertains to pathogenic organisms. A WHO report released in April 30, 2014, states, "This serious threat is no longer a prediction for the future, it is happening right now in every region of the world and has the potential to affect anyone, of any age, in any country" [7]. Irrational use of antibiotics leads to the growth of antibiotic resistance and

***Corresponding author:** Zebiniso A. Ubaydullaeva, The Tashkent Pharmaceutical Institute; Tashkent, Uzbekistan. E-mail: zenda.bella@mail.ru*

to an increase in costs of treatment. Currently, the problem is finding ways to decrease costs of respiratory disease treatment by using various indicators to adjust disease prognosis, choosing optimal strategies of treatment, and introducing new approaches to the organization of medical actions. Recently, there has been growing interest in the economic assessment of health and health care programs, as well as in performing a pharmacoeconomical analysis [8-10].

The purpose of this study is to estimate the treatment costs of pneumonia in children in the clinic of the RSSPMCP of Uzbekistan.

Methods

The case histories of 450 pediatric patients with CAP who were hospitalized in the clinic of the RSSPMCP during 2011-2013 were retrospectively reviewed. The age of patients was from 1 week of life up to18 years. The diagnosis was confirmed by clinical examinations, chest radiography, serologic methods, sputum examination, blood cultures, determination of microorganisms' sensitivity to antibiotics and antibiotic resistance. We chose the priority treatment schemes, which were most often used in the hospital. Antibacterial therapy was prescribed to all patients. The pharmacoeconomical cost of each treatment scheme was determined. The pharmacoeconomical analysis was carried out by the cost-effectiveness method.

The cost-effectiveness analysis (CEA) allows assessment of the economical expediency for application of the medical intervention by comparing the relative costs and outcomes (effects) of two or more courses of action [11]. In the context of pharmacoeconomics, the cost-effectiveness of a therapeutic or preventive intervention is the ratio of the cost of the intervention to a relevant measure of its effect.

We calculated a cost-effectiveness ratio (CER) by the standard formula:

CER = (DC+IC)/Ef, where DC - direct cost, IC — indirect costs, Ef — efficiency of treatment (number of the cured patients).

It should be noted that the achievement of the favorable outcomes (without developing any complications) at a level not less than 90% was considered a prerequisite of effective treatment. Intervention with the least value of CER was evaluated as the most preferable. Treatment of CAP was carried out on the basis of the approved treatment standards of the Republic of Uzbekistan. On completion of research, the most pharmacoeconomically rational scheme for treatment of CAP in children was determined.

Resuıts

According to our study, pneumonia accounts for 50–70% of all cases of bronchopulmonary pathology (BPP) (Fig.1). Statistically, illness rates among boys are significantly higher than girls. The sex differences in children in the immune responses to infectious diseases were demonstrated in a number of studies. In our study, there were 10% more boys than girls with BPP among the hospitalized children. Infants (from two weeks to 1 year) and toddlers (1-3 years) suffer from pneumonia more than other age categories. The prevalence of pneumonia in children of this age is promoted by immunological, functional and anatomic features of the child organism, and also by a wide range of infectious agents.

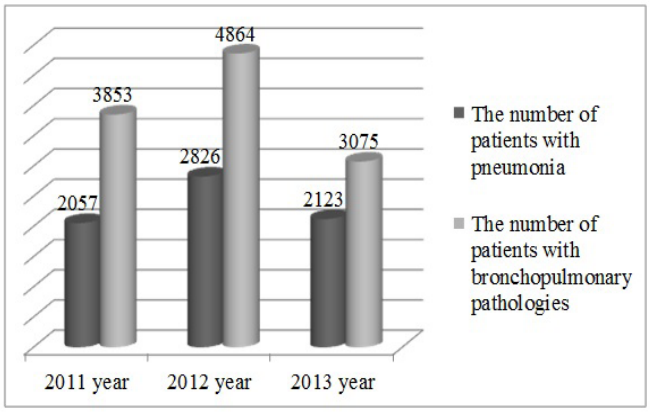

Figure 1.
Cases of bronchopulmonary pathology during 3 year period (2011-2013).

Many pathogens are responsible for CAP in children, most prominently bacteria such as *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Escherichia coli, Haemolytic streptococcus, Pseudomonas aeruginosa, Proteus spp., Klebsiyell spp*.etc.; viruses, fungi, protozoa are more rare causes of the disease. In infants, *Staphylococcus aureus* and *Escherichia coli* are more often pathogens of pneumonia; at a more advanced age, it is *Streptococcus pneumonia* (*Pneumococcus*). The Center's scientists revealed the following main pathogens: *Staphylococcus* in 30.6% of cases, *Streptococcus pneumonia* in 25% of cases, *Enterococcus* in 5.50% of cases, and negative response in 38.9% of cases. There was no difference among patients of each treatment scheme according to the pathogens and age.

Children suffered from pneumonia during the whole year, but more often in winter months, because over cooling and flu epidemics are provocative factors for CAP. This pattern was confirmed by results of our research; in 2011-2013, the greatest number of reported cases of CAP was in winter and autumn months. The incidence of disease considerably decreased in the summer months. In hospitalized children, moderate CAP was predominant.

Our analysis revealed the most commonly used antibiotics for CAP treatment in children in the RSSPMCP (Table 1.). Clinical efficiency of the prescribed treatment schemes was different; it was noted that physicians preferred the cephalosporin antibiotics to ceftriaxone. The analysis of center expenses for purchases of antibiotics also confirmed that cephalosporin antibiotics were the first on the purchase lists. By the cost-effectiveness method, we analyzed the cost efficiency of cephalosporin antibiotics. Pharmacoeconomical indicators of each scheme were calculated separately according to prices for 12.31.2013 (Table 2). The length of stay in the

hospital was 7–10 days. The result showed that treatment with ceftriaxone was more clinically and economically effective than treatment with cephalosporin: 90% of children receiving ceftriaxone demonstrated clinical and laboratory signs of improvement within 48–72 hours. On the basis of CER, it was determined that ceftriaxone is the drug of choice for CAP treatment in children CER=0.035). In most cases, ceftriaxone was prescribed intramuscularly, 500 mg twice daily for 7–10 days. The cost of the treatment course with ceftriaxone for one pediatric patient is $7.15.

Table 1.

The most commonly used antibiotics for CAP treatment in children in the RSSPMCP

Type of antibiotics	The number of patients included in study
Ceftriaxone	202
Ceftazidime	112
Cefazolin	136

Table 2.

Calculation of CER for CAP treatment

The scheme of treatment	The course of treatment (days)	The price of daily dose (US$)	Direct cost (US$)	Ef	CER	Favorable treatment outcome
Ceftriaxone	7	1.02	7.15	202	0.035	90%
Cefazolin	8	0.77	6.15	136	0.045	75%
Ceftazidime	7.6	2.31	17.56	112	0.16	94%

The obtained results allow planning for purchase of antibacterial drugs and an approximate calculation of expenses for CAP treatment in children. Taking into account that annually an approximately identical number of patients take treatment in the analyzed hospital, it is possible to make certain calculations:

$$CT=N\times D\times S$$

CT - cost of treatment, N - number of patients, D - number of days, S - cost of daily dose of medicine.

Average number of CAP children treated in the RSSPMCP was 2,335.3; ceftriaxone was prescribed intramuscularly of 500 mg twice daily for 7-10 days. For ceftriaxone, CT = 2,335.3×7×1.02 ($) = $16,697.042

So, in the case of more the rational use of antibacterial therapy, ceftriaxone, the center would spend an average of $16,697.042 to purchase antibiotics. Whereas hospital received 15,153 units of antibacterial preparations of cephalosporin group to the sum of $24,632.42 from which 8,943 units arrived as humanitarian aid in 2013.

Discussion

The timely etiological diagnosis of pneumonia, identification of the pathogens and a determination of the disease's sensitivity to antibiotics are the basis for the right choice of antibacterial therapy. The analysis of case histories showed that cases of empirical prescription of antibiotics are observed. Empiric therapy with parenteral cephalosporin antibiotics should be prescribed for hospitalized infants and children who are not fully immunized, in regions where local epidemiology of invasive pneumococcal strains documents high-level penicillin resistance, or for infants and children with life-threatening infection, including empyema [12]. It is necessary to emphasize that the wrong prescription of antibiotics means that a further correction of antibacterial therapy is needed because of an inefficiency of initially prescribed medicine, an extension of treatment course and increase in the probability that undesirable side effects will emerge in patients, as well as formation of resistant strains of microorganisms. Finally, all this leads to an increase in the cost of antibacterial therapy [13].

The performed analysis showed that ceftriaxone is a drug of choice for the treatment of CAP. Therefore, ceftriaxone for treatment of CAP in children, as well as its purchase from domestic producers, allows a considerable decrease in hospital expenses. Our analysis gave us the opportunity to receive data about the existing real practice in the treatment of pneumonia in children and allowed us to define the ways to decrease economic loss connected with treatment of CAP in children.

Competing interests

The authors declare that they have no competing interests.

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