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Antibacterial Therapy Rationalization by Using Antibacterial Card in Children with Community-Acquired Pneumonia.

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ABSTRACT

In Kazakhstan, as in many other countries, the relevance of antibiotic resistance is increasing every year. We developed antibacterial card with the aim of creating methods to monitor antibacterial therapy. This paper provides the results of implementation of monitoring method in antibacterial therapy for community-acquired pneumonia in children in infectious hospital environment.

Keywords: Antibacterial card, community acquired pneumonia, children

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INTRODUCTION

The role of antibiotics in practical medicine can scarcely be overestimated as millions of human lives have been saved due to antibiotics. However, cases of antibiotic resistance were recorded two years after the first antibiotic appeared. Seventy years have passed since then, new generations of antibiotics appeared. However, new antibiotic-resistant infectious strains appeared. Accoring to the Abbas et. al. [1], Zou et. al. [2], Pavydė et. al. [3] it has been found out that excessive and wrong administration of antimicrobials frequently results in adaptation of microorganisms due to mutations, genetic recombination, and selection; as a result, drug-resistant strains become dominating at population level, in medical treatment facilities or in environment. The new report made by the World Health Organization (WHO) [4] stated that there was a four-time difference in consumption of antibiotics between the countries of European regions WHO.

The resistant bacteria rate can vary in different regions; healthcare facilities frequently have no data concerning antibiotic resistance in the region. Moreover, the WHO data [5] a lack of appropriate supervision systems in many countries in the world results in a lack of information concerning spread and scale of antibiotic resistance.

Seasonal differences in antibiotic consumption demonstrate that antibiotics are used frequently to treat seasonal viral infections. In ten European countries from 1997 to 2001 there was a tendency to the increase of antibiotics consumption almost two times in ambulatory care at the beginning and at the end of the year in the period of upper respiratory infections [6].

An epidemiological survey was conducted in Korea in the period from 2008 to 2012 in order to identify total volume and principles of administration of systemic antibiotics. ATC/DDD method was used in 1,000 people a day in accordance with chemical classification of antibiotics. This monitoring demonstrated that the annual consumption of antibiotics varied between 21.68 and 23.12 DDD per 1,000 people per day. Ambulatory consumption of antibiotics made 80.9% of total consumption. Method of regression analysis revealed main antibiotics used in clinical practice: third generation cephalosporins, carbapenems and glycopeptides. Moreover, Yoon et al. reported that there was an annual increase in the number of antibiotics used that related to appearance of multiple drug resistance [7].

The literature contained very little information concerning methods and technologies to control and account the use of antibacterial agents in pediatric practice. In this connection, we decided to use antibacterial cards to assess the quality and quantity of antibiotics used in City Children's Hospital of Infectious Diseases (CCIHD), Astana.

An antibacterial card records information on antibiotics administered to patient three months prior to hospital admission and information on the dose and therapy duration during his/her hospitalization. Inventor's Certificate No. 115 dated January 26, 2014 "Ways to Solve Antibiotics Resistance Problem in Infectious Hospital" (Scientific Work) was obtained for this invention.

Antibacterial cards were implemented in the clinical practice of the hospital in 2009. The use of this technology in hospital environment enabled us to provide quantitative and qualitative characteristics of antibiotics used in the hospital in general and in each department. Therefore, the purpose of the research is to assess the efficacy of antibacterial card in using antibiotics in children with community-acquired pneumonia.

MATERIALS AND METHODS

Research design is observational study and retrospective analysis. Retrospective analysis of patient records was conducted for the period from 2007 to 2008. Antibacterial cards of patients in a sample size of 335, 349, 404 and 395 was analyzed in 2009, 2010, 2013, 2015 respectively in Department of Respiratory Infections. Antibacterial card is a record sheet, which contains data about the use of antibiotics in an outpatient basis in the last 3 months and about antibiotic prescribed during hospitalization. At the time of admissions doctor fills out the information about the use of antibiotics before admission. By analyzing the data, doctor prescribes an antibiotic that is required for further treatment. At the end of treatment, doctor records antibiotics that were received in the course of treatment. At the end of the year, heads of departments analyze data according to the results of antibacterial cards for local monitoring of antimicrobial card.

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Patients whose age was between 1 month and 5 years with a clinical diagnosis of Upper Respiratory Infection (URI) complicated with community-acquired pneumonia and admitted in the City Children Infectious Hospital of Astana were selected into this study. Recommendations for treatment were provided by the Expert Advisory Board of The Republican Center for Health Development of the Ministry of Healthcare and Social Development of the Republic of Kazakhstan dated December 12, 2013 Protocol No. 9 "Clinical Protocol of Pneumonia Diagnostics and Treatment in Children".

Severe and moderate URI was diagnosed in 140 (42%) and 195 (58%) patients in 2009; 191 (54.7%) and 158 (45.3%) patients in 2010; 183 (45.3%) and 221 (54.7%) patients in 2013; 161 (40.8%) and 234 (59.2%) patients in 2015, respectively, according to the reviewed patient's records. All cases were complicated with community-acquired focal pneumonia: left-sided focal pneumonia in 9 (2.7%), 14 (4%), 19 (4.7%), 27 (6.8%) patients, right-sided focal pneumonia in 77 (23%), 162 (46.4%), 130 (32.2%), 179 (45.3%) and bilateral focal pneumonia in 249 (74.3%), 173 (49%), 255 (63.1%), 189 (47.9%) patients in 2009, 2010, 2013 and 2015, respectively.

Descriptive and comparative statistical analysis were assessed using SPSS 21.0 software. Frequencies and cross-tabulations of pre-selected variables were calculated using Pearson's x 2. P-value is less than 0.05 which means to be statistically significant. The clarity index was used to describe the absolute values. In addition, time series indicators were applied for statistical analysis of the average annual rates of antibiotics use. Time series indicators (abs. growth, the rate of growth/decline, the average growth rate, the average 1% growth/decline) of antibiotics use were calculated by alignment with the method of least squares.

RESULTS

Figure 1. Quantitative characteristic of antibiotics used in hospital before and after implementation of antibacterial card

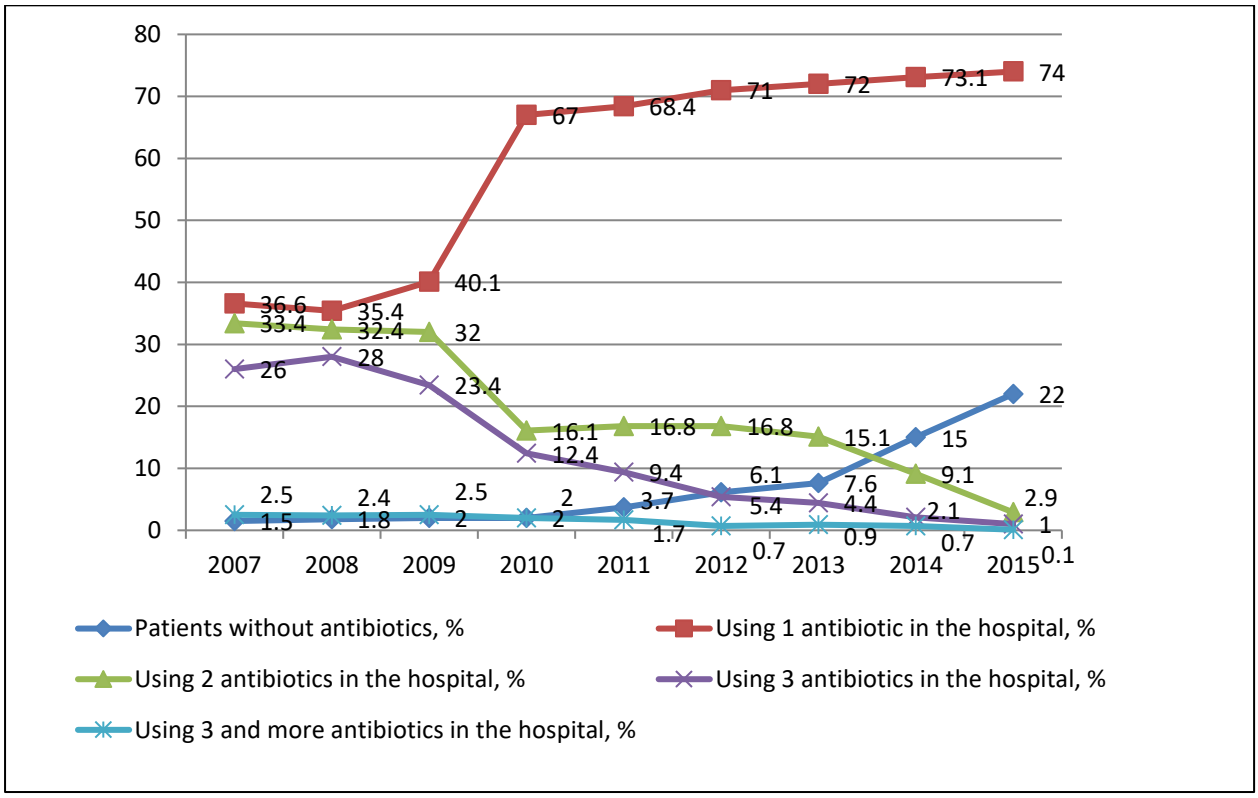

Figure 1 demonstrates the quantitative characteristic of antibiotics used for URI complicated with community-acquired pneumonia in CCIH for 2007 - 2015. As we can see from the figure, two courses of antibacterial therapy were administered to every third patient, three courses of antibacterial therapy were

prescribed to every fourth patient before 2009. Antibacterial card was implemented in 2009 in the hospital to monitor the quantitative and qualitative characteristics of antibiotics used.

According to the Table 1 presented above the results of implementation of antibacterial cards are characterized by drastic changes in the number of antibiotics used. Antibacterial monotherapy rate in the hospital increased by 1.8 times from 2010 compared to 2007 and remained at the similar level for the entire monitoring period. In addition, we can observe a clear reducing trend of antibiotics re-administration; e.g. the number of two courses of antibiotics reduced twice in 2010 vs. 2007; the number of three courses antibiotics treatment reduced by 2.1 times in 2010 and by 9 times in 2015 vs. 2007. The use of antibiotics for more than three courses of treatment reduced by 1.3 times in 2010 vs. 2007 and 25 times in 2015 vs. 2007. The most important aspect is that the number of patients with no antibiotics administered in the hospital increases every year since 2010; as is well-known, viral infections prevail in pediatric patients admitted to the hospital; every third patient discharged from the hospital in 2015 did not receive antibacterial therapy.

Table 1. Visibility indicator of absolute values of antibiotics used before and after the introduction of antibacterial cards in the hospital.

Years	2007	2008	2009	2010	2011	2012	2013	2014	2015
Visibility indicator without introduction of antibiotics, %	100	120	133	167	247	407	507	1000	1467
Visibility indicator after 1 course of antibiotics, %	100	97	110	184	187	194	197	200	202
Visibility indicator after 2 courses of antibiotics, %	100	97	96	48	50	50	45	27	8.6
Visibility indicator after 3 courses of antibiotics, %	100	108	90	48	36	21	17	8	3.8
Visibility indicator after 3 and more courses of antibiotics, %	100	96	100	80	68	28	36	28	4

Monthly analysis of antibacterial cards enabled revealed mistakes in etiotropic (causal) treatment, particular nosology, e.g. the use of gentamicin combined with the first generation cephalosporins or inadequate antibacterial anamnesis in outpatient environment resulting in re-administration of the 1st generation of cephalosporins for community-acquired pneumonia. The prescription was accompanied with extended infectious process requiring administration of another course of antibacterial therapy.

Synthetic penicillin and combinations with gentamicin were identified as the most commonly used antibiotics for community-acquired pneumonia in children for 2007-2009. Such combination was not used after monitoring by using antibacterial cards that resulted in reduced quantity characteristic of antibiotics used further for community-acquired pneumonia.

Analysis of work in departments is important based on the quantitative characteristics of antibiotics used in general in the hospital. In this connection, we analyzed prescriptions of antibiotics in Respiratory Infection Department. Figure 2 demonstrates quantitative characteristics of antibacterial therapy for URI complicated with community-acquired pneumonia before and after implementation of antibacterial card.

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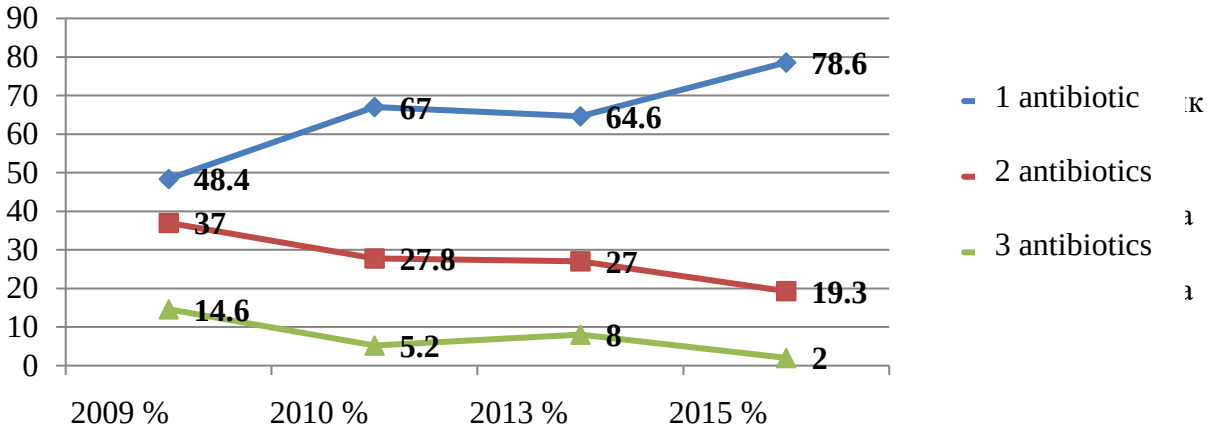
Figure 2. Antibacterial therapy for URI complicated with community-acquired pneumonia in Respiratory Infection Department before and after implementation of antibacterial card



After the analyses of antibacterial cards, we observed a clear increasing trend in antibiotic therapy effectiveness along with reduced number of drugs administered. The statistical significance between two groups is different, so until the introduction of antibacterial card monotherapy in children with community-acquired pneumonia was used in 48.4% of cases, while, after the introduction of antibacterial card monotherapy increased to 71.3% (1.5 times). (X_2 (1) = 60,681, df = 1, p = 0.001, p <0.05). There is average positive relationship (φ = 0,203, p = 0.0001, p <0.05) between the introduction of antibiotic cards and the rise of monotherapy.

The use of two antibiotics in combination is reduced to 37.0% and after the introduction of antibacterial cards (24.0%) reduced by 1.5 times. (X_2 (1) = 22,158, df = 1, p = 0.001, p <0.05). Also, the use of three antibiotics in combination decreased by 3 times after the introduction of antibacterial card from 14.6% to 4.8%, which also indicates the statistical significance of the difference (X_2 (1) = 38,473, df = 1, p = 0.001, p <0.05).

The results of our research demonstrated that reduced frequency of antibiotic treatment was characterized by appearance of parameters we interpreted as qualitative characteristic of antibacterial therapy.

The dynamics the annual average rate of antibiotics use in hospital before and after the introduction of antimicrobial card showed a different trend (Table 2). Trends of aligned indicators of the use of antibiotics tended to increase in the following groups: the use of one antibiotic before the introduction of antibiotic cards - Rgr (growth rate) =+0,14%; and after the introduction of antibiotic cards Rgr (growth rate) = +0.04%. Also treatment without antibiotics before implementation - Rgr (growth rate) = +0.42%; and after the introduction of antibiotic cards Rgr (growth rate) =+0,93%.

Table 2. Average annual indicators of antibiotics usage before (2007-2009) and after (2010-2015) the introduction of antibacterial card in the hospital.

Amount of antibiotics	Use of antibiotics, %				Rate of growth/decline, % (1)	Rate of growth/decline, % (2)
	M±m (1)	M±m (2)	95% CI (1)	95% CI(2)		
Without antibiotics	1,8 ± 0,1	9,5 ± 3,0	1,5-2,0	3,4–15,5	+0,42	+0,93
Use of 1 antibiotics	37,4 ± 1,4	70,9 ± 1,1	34,6–40,1	68,7–70,1	+0,14	+0,04

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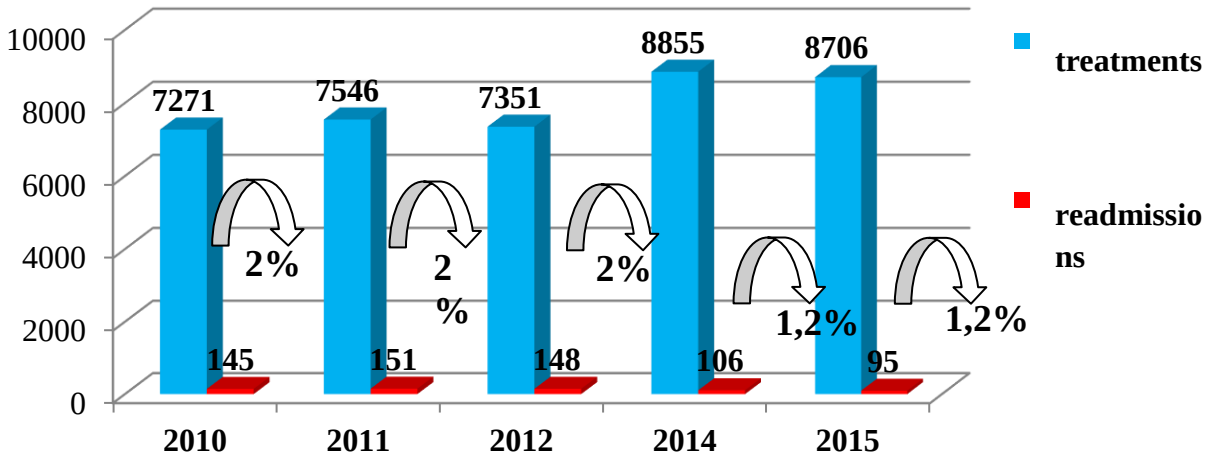
Use of 2 antibiotics	32,6 ± 0,4	12,8 ± 2,3	31,8-33,4	8,3-17,3	-0,06	-0,47
Use of 3 antibiotics	25,8 ± 1,3	5,8 ± 1,8	23,2-28,4	2,3-9,3	-0,15	-0,92
Use of 3 and more antibiotics	2,5 ± 0,03	1,0 ± 0,3	2,4-2,5	0,5-1,6	0	-0,79

1-indicators calculated before the introduction of antibacterial card
2-indicators calculated after the introduction of antibiotic card

In other groups trends of antibiotic use tended to decrease, and average annual rate declined of aligned figures during the use of 2 antibiotics in combination before the introduction of the card showed Rdec (decline rate) = -0.06%, and after the introduction of antibiotic cards Rdec (decline rate)= -0.47. The same trend was observed in the groups where three courses of antibiotics used before the introduction - Rdec (decline rate) (1) = -0.15%, and after the introduction of antibiotic cards Rdec (decline rate) (2) = -0.92. Finally, it worth mentioning that in the last group with the use of 3 or more courses of antibiotics prior the introduction of antibacterial card decreasing tendency was not observed, but after the introduction of antibiotic cards we have seen declines in the use of 3 and more courses of antibiotics with Rdec (decline rate) (1) = - 0 79%.

Statistical calculation of time series indicators demonstrate that the introduction of antibacterial card had a positive impact on the quantitative characteristics of antibiotic therapy in the hospital. This technology is a major step in the monitoring the antibiotic therapy in community-acquired pneumonia in children with the aim of preventing antimicrobial resistance.

Figure 3. Dynamics of hospital readmission rate.



Readmission rate proves qualitative characteristic of antibiotics. Figure 3 demonstrates the dynamics of readmission rate after implementation of antibacterial card in the City Children Hospital for Infectious Diseases for the period from 2010 to 2015. The readmission rates for the period from 2010 to 2012 were the same (145-148 readmissions), then reduced to 95 in 2014, i.e. 1.2% of total admissions. Meanwhile, we should note that the number of admissions significantly increased in 2014 and 2015 compared to 2010-2012. Thus, since 2008 the admission rate of children's population between 0 and 14 years old increased by 2.1 times in Astana, which was 109,990 and 234,900, respectively [8], [9].

We should also note that a certain parallel between the improved quality of antibacterial therapy and mortality rate could be observed. Thus, mortality rate reduced in 13 times in 2011 vs. 2007. Fatality rate remained low for 2011 - 2015.

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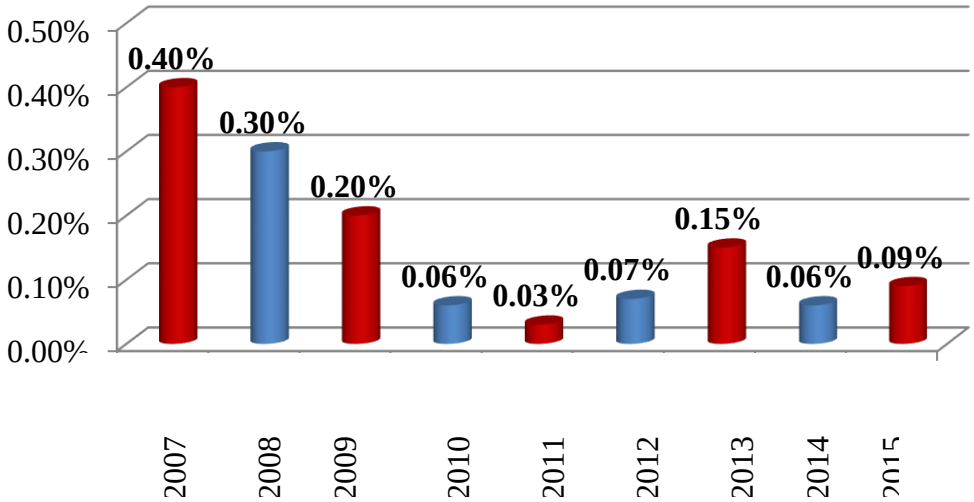
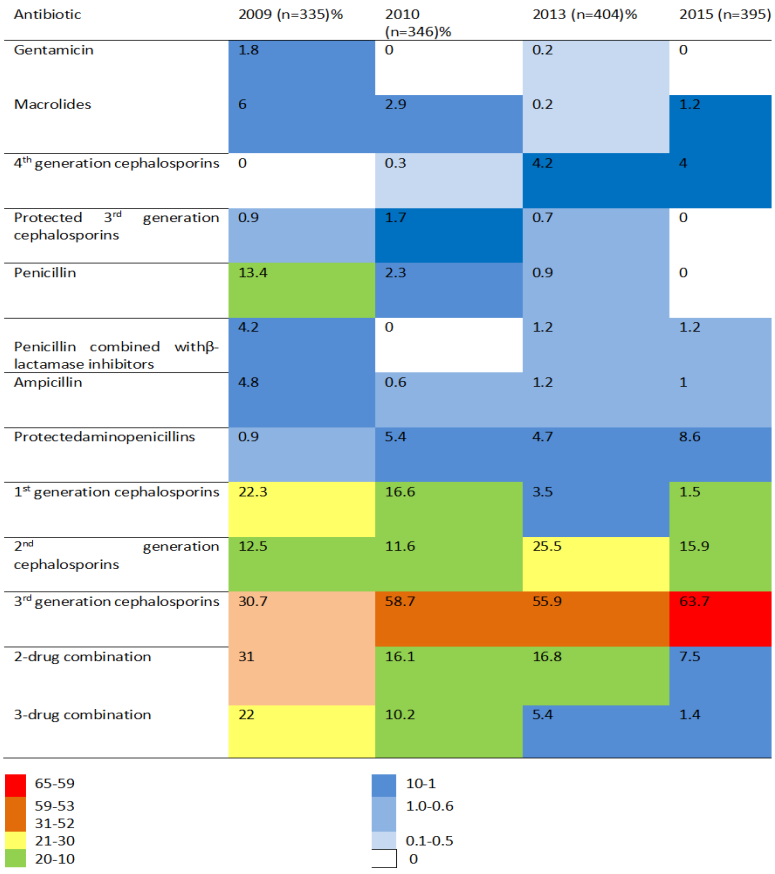
Figure 4. Dynamics of mortality rate before and after implementation of antibacterial card in the children infectious hospital



The quality of etiotropic treatment also improved due to the reduction in polypharmacy and the stages of the use of antibiotics adjusted at all stages of medical care in the hospital.

Figure 5

Heat Map



DISCUSSION

As Stacevičienė et. al. stated despite the efficacy of PCV vaccination in different countries, WHO informs that mortality rate from pneumococcal infection in children aged under five remains high. Improved resistance of pneumococci to commonly used antibiotics, such as macrolides or cephalosporins and multiple drug resistance is another challenge in public healthcare. SPn antibacterial susceptibility varies widely between European countries, e.g. penicillin resistance of noninvasive SPn varies widely between 1.7% in Norway and 83% in Romania; erythromycin resistance varies between 1.2% in Czechia and 65.5% in Italy. Due to geographic variety, resistance of SPn strains depends on local antibacterial policies, therefore epidemiological studies and monitoring of antibacterial therapy is important for every geographic region [10].

The use of antibacterial cards contributed to the optimization of etiotropic treatment for patients admitted to the hospital with URI complicated with community-acquired pneumonia. Heat Map 1 illustrates this information: groups of antibiotics administered to patients with the above diagnosis in dynamics for the period between 2007 and 2015.

For example, gentamicin combined with β-lactamase antibiotics was administered to nearly every second patient in 2007; analysis of antibacterial cards demonstrated that 70% of patients with this antibiotic administered received the second course and sometimes several courses of antibacterial therapy. In this connection, administration of this antibiotic reduced to 1.8% in 2009 with further stabilization of this rate. Gentamicin administration reduced drastically from1.8% to 0, respectively in 2009 vs. 2015. Due to reduced use of gentamicin, the number of patients with re-prescribed antibacterial therapy decreased significantly.

Administration of macrolides is of utmost interest in therapy of community-acquired pneumonia in children; macrolides prescription rate reduced from 6% to 1.2 %, compared to 2009. Card analysis demonstrated failure of such drug in treating community-acquired pneumonia. In this connection, the use of this drug was limited.

The use of penicillin reduced significantly for the period from 2007 to 2015 from 13.4% to 0%, respectively; that correlates with the results of the study made by N.M. Bissenova and A.S. Yergaliyeva concerning the development of penicillin resistance for the same period from 28.0% to 37.0% [11].

With respect to antibacterial history, the need to administer inhibitor-protected aminopenicillin for admitted patients was identified due to inefficacy of cephalosporin antibiotics in therapy before hospitalization. As we can see from the figure, the rate of protected aminopenicillin administration increased from 0.9% to 8.6% for the period from 2007 to 2015 along with reduced rate of macrolides, aminoglycosides, penicillin prescription. According to domestic data, ceftriaxone showed the lowest rate of pneumococci resistance from 9.0% in 2010 to 15.0% in 2012, which is presented on the heat map. According to our data, the use of the 3rd generation cephalosporins increased to 55.9% in 2013 vs. 15% in 2007. This choice of antibacterial drugs demonstrates the antibacterial cards contribution to the rationalization of the use of antibiotics.

Correctness of actions was confirmed by data from N.M. Bissenova and A.S. Yergaliyeva concerning the fact that the rate of resistant strains in patients suffering from community-acquired pneumonia has been increased year by year [11]. Macrolides showed the highest rate of resistance: clarithromycin from 42.8% in 2010 to 60.0% in 2012; erythromycin from 40.0% to 51.8%; to azithromycin from 39.4% to 59.0%, respectively.

In summary, we should note that the optimization of antibacterial therapy by using antibacterial cards for patients with URI complicated with community-acquired pneumonia correlates with the data from bacteriological studies performed by national scientists [11]. The results of the study are consistent with the data from the heat map.

Series of long-administered antibiotics such as synthetic penicillin and penicillin combined with gentamycin were not used for five and more years due to the implementation of antibacterial cards.

As a result of antibacterial cards implementation, we could clearly see the increasing trend of non-antibiotic treatment and monotherapy and on other hand the reduction in antibiotic therapy with two and more antibiotics.

The reduced range of antibacterial drugs contributed to the rotation and cyclical use as well as to the reduction in the number of microorganisms' resistant strain.

Thus, the implementation of antibacterial cards in one of the largest children hospitals in Astana demonstrated positive results in reducing irrational use of antibiotics. Local monitoring of antibiotics prescriptions, in turn, may affect the reduction in antibiotics resistance. This is the reason for antibacterial cards implementation in common practice.

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