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Vaccination of premature infants and children with congenital heart disease in Irkutsk using conjugated pneumococcal vaccines

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Study aim*: analyzing the results of pneumococcal infection vaccination conducted to reduce infantile morbidity and mortality in 2011-2012 at the expenses of the Irkutsk municipal budget.* ***Patients and methods****. Vaccination using the 7- and 13-valent pneumococcal conjugated vaccine was conducted for more than 700 risk group children: premature infants, children with congenital heart diseases or bronchopulmonary dysplasia from 2 months to 2 years of age. 193 vaccinated children had been observed for 1.5 years. 30% of premature infants and 46% of children with congenital heart diseases were vaccinated using the PCV7/PCV13 vaccine at the age of 2-6 months, 52 and 40% - at the age of 7-11 months, accordingly. The PCV7/PCV13 vaccine was administered together with other vaccines of the national preventive vaccination calendar in 65% of cases.* ***Results****. Rate of general post-vaccinal reactions (body temperature increase from 37.6 to 38.0°C) – 4%; no local reactions were registered. No other unfavorable phenomena were noted in the post-vaccinal period. No cases of pneumonia, meningitis, acute otitis media and bronchoobstructive syndrome were registered within the observation period.* ***Conclusions****: pneumococcal infection vaccination of premature infants with congenital heart diseases and bronchopulmonary dysplasia conducted in Irkutsk proved high efficacy and safety of the used vaccine – PCV7/PCV13.*

Keywords*: children, pneumococcal vaccine, premature infants, congenital heart disease.*

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INTRODUCTION

Pneumococcal infections in younger children pose a formidable global problem of public health. It is well known that *Streptococcus pneumoniae* (pneumococcus) may cause both severe invasive infections (meningites, invasive pneumoniae (sometimes with empyemata), sepsis (including occult bacteremia, i.e. fever with hidden infection nidus)) and less severe, yet much more

frequent diseases, such as otites media, sinusites, pneumoniae and bronchites. The problem is the gravest in the group of 0-5-year-old children – it's estimated that the morbidity rate among them is 0.29 cases per child per year in the developing countries and 0.05 cases per child per year in the developed countries; 7-13% of cases of pneumococcal infection are severe and require hospitalization. The highest invasive pneumococcal infection morbidity risk is noted in risk groups, i.e. children, who are artificially fed from small age or insufficiently fed, with low birth weight (including premature infants) and those living in congested conditions [1]. Apart from the aforementioned, the World Health Organization also deems environmental pollution one of the risk factors increasing rate and severity of pneumococcal infections.

A big number of scientific works is dedicated to the anthropogenic pollution's influence on population health in our country. It has been revealed that ecological pressing considerably contributes to the morbidity rate (including infectious morbidity) [2, 3] due to the reduction in immune response in children living in polluted areas [4]. It is also known that the highest volumes of air pollutant emissions from stationary sources are in Ural, West and East Siberian economic regions (59% of all emissions in Russia). According to several authors, role of ecologic factor in children's health aggravation is indisputable. Industrial pollution of places of residence increases the chronic pathology level by 60%, including the level of respiratory diseases – by 67% [5].

It should also be taken into account that the highest level of severe disease forms and fatal outcomes is registered in the aforementioned risk groups [6]. Treatment of this category of patients is extremely expensive.

Thus, as long as there is no cohort pneumococcal infection immunization in Russia, protection of risk group children is the first-priority task, which is why various territories of the Russian Federation are conducting pneumococcal infection vaccination programs for children with background pathology [7, 8]. Urgency of pneumococcal infection prevention in smaller children, especially in the invasive infection risk group children, is undoubted. This problem is especially urgent in territories with high level of environment pollution, such as Irkutsk.

Study aim: to study efficacy of pneumococcal infection vaccination at the expense of the Irkutsk municipal budget aimed at reducing infantile morbidity and mortality rate in 2011-2012.

PATIENTS AND METHODS

Study participants

In order to study safety and efficacy of the pneumococcal infection vaccinal prevention of risk group children using the conjugated vaccine, we observed 193 children of the following age groups (age at the time of vaccination beginning):

- 2-6 months – 66 (34.2%) children;
- 7-11 months – 63 (32.6%);
- 12-23 months – 35 (18.1%);
- over 24 months – 29 (15%) children.

Study inclusion criteria were the following diseases (conditions): prematurity, congenital heart diseases (CHD), bronchopulmonary dysplasia, resuscitation measures in anamnesis.

Study methods

Vaccination efficacy and safety were appraised by analyzing outpatient cards of the vaccinated children throughout the observation period (18 months). Children were actively visited in the post-vaccinal period the following day after vaccination; later, children's condition was controlled by means of telephone survey of parents.

Initially, vaccination of 2-6-month-old children was conducted according to the Prevenar vaccine instructions using the scheme 3+1; in 7-11-month old children – 2+1; in 12-23-month-old children – 1+1. Children over 24 months of age received vaccine only once. However, due to the shortage of vaccine in 2012 children of 2-6 months of age were vaccinated using the scheme 2+1 [9].

Statistical data manipulation

Statistical manipulation of results was conducting using non-parametric criteria (small sample and lack of normal distribution). We used criterion z; the calculation was conducted using the program "Biostatistics".

STUDY RESULTS AND DISCUSSION

One of the main goals of the departmental task program "Improvement of the medical-demographical situation in Irkutsk" for 2009-2012, adopted in 2009, was to improve specific prevention of the most formidable infectious diseases [subprogram "Prevention of spread of tuberculosis, human immunodeficiency virus infection (HIV-infection) and other formidable infectious diseases in Irkutsk"]. In conformity with the stated goal, 4.2mn rubles were assigned to finance vaccinal prevention in 2011, 4.6mn rubles – in 2012. Given limited financing, the priority area was chosen – vaccination of premature infants, children with CHD or bronchopulmonary dysplasia and children who required antenatal resuscitation measures using a conjugated pneumococcal vaccine (PCV7, PCV13).

It should be noted that, according to the statistical data, share of premature infants at Irkutsk maternity hospitals every year is ca. 7% (in 2010 – 6.7%); 85% of children out of them have a concurrent respiratory pathology (distress-syndrome and/or pneumonia). 5% of premature

infants have indications to artificial pulmonary ventilation. Ca. 50-70 children are annually born with CHD.

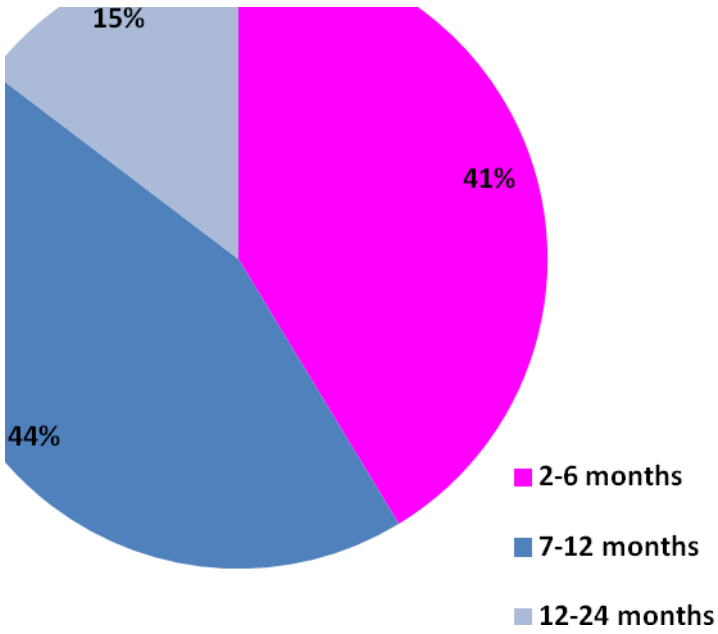
As the stated group of children is rather numerous, amount of budgetary funds directed to execute the priority preventive measure, i.e. pneumococcal infection vaccination, was 30% of the total amount of vaccine purchase financing.

It is evident that the stated funds did not allow conducting pneumococcal infection vaccinal prevention to risk group children to the required extent, which is why it was decided to start a co-financing program, i.e. it was planned to conduct the 2nd and the 3rd conjugated vaccine's administration at the expense of insurance companies or people's personal funds. Thus, a full-scale and effective pneumococcal infection immune prevention was ensured among the risk group children; the estimated vaccination coverage in the first stages of the program's fulfillment was to be not less than 75% of children of the aforementioned groups.

The total amount of purchased Prevenar vaccine (7- and 13-valent) doses in 2011 at the expense of the city budget and medical insurance companies was 507. 600 Prevenar 13 vaccine doses were purchased in 2012 at the expense of the municipal budget.

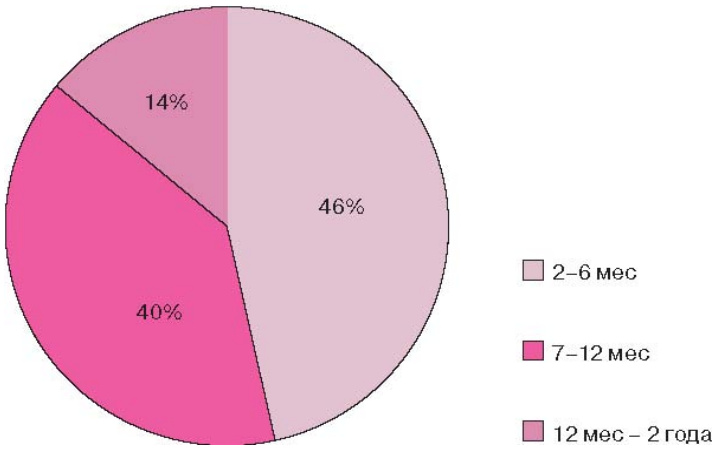
Diseases, which distinguished children into the risk group, are given in tb. 1 and 2.

Despite the opinion of several pediatricians that it is extremely difficult to vaccinate children with low and extremely low birth weight in the first half-year of life, 41% of premature infants in our study were vaccinated against pneumococcal infection before 6 months of age (pic. 1).



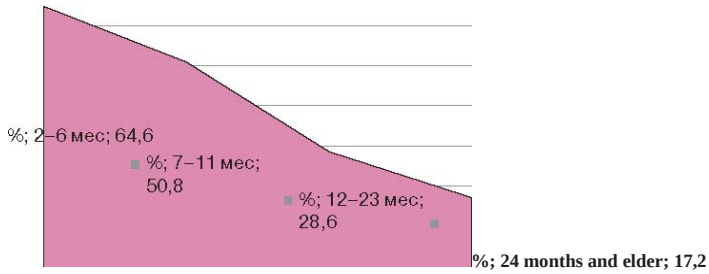
Pic. 1. PCV7 and PCV13 vaccination beginning in premature infants (%)

It was important to begin vaccination of children with CHD as soon as possible, as the operation and long-term hospital stay in the postoperative period increase the pneumococcal infection development risk several-fold. The observed children with CHD were vaccinated with PCV7/PCV13 in the first half-year of life in 46% of cases, in the second half-year of life – in 40% of cases (pic. 2).



Pic. 2. PCV7 and PCV13 vaccination beginning in children with congenital heart diseases

Among the vaccinated children 36 (18.7%) received 1, 130 (67.4%) – 2, 27 (14%) – 3 Prevenar vaccine administrations. PCV was concurrent with other vaccines in 59.1% of cases (114 children) among children who started to receive vaccination before 24 months of age; combination of vaccines in older children was registered only in 5 cases – 17.2% (pic. 3).



Pic. 3. Relation of combination rate of pneumococcal conjugated vaccine with other vaccines to the vaccination beginning age (%)

Pneumococcal infection vaccination was most frequently combined with the administration of Pentaxim vaccine and various viral hepatitis B vaccines, more rarely – with poliomyelitis vaccines (oral and inactivated) and hemophilic infection vaccines.

Observation of the vaccinated children displayed high PCV7/PCV13 vaccinal prevention efficacy level. No cases of pneumonia, meningitis, acute otitis media or bronchoobstructive syndrome were registered in the vaccinated children throughout the observation period. The developing acute respiratory infections did not require antibacterial therapy, including children who had earlier received antibiotics more than 8 times for a year.

Vaccination safety. Insignificant general reactions were revealed in 4% of the vaccinated children (body temperature increase from 37.6 to 38.0^{o}C), including 2 1-year-old children: one of them suffered from cerebral palsy, the other had a CHD (ventricular septal defect and circulatory deficiency (grade II)). Temperature reaction was also noted in 1 4-month-old premature infant (gestation duration – 32 weeks), who received a combination of PCV with Pentaxim vaccine.

It is commonly reckoned among pediatricians in Russia that it is difficult to combine Prevenar vaccine with other vaccines in children of the first half-year of life. Our analysis showed lack of significant differences in the number of unfavorable phenomena after PCV7 and PCV13 vaccination, whether they are administered to the risk group children separately or in combination with other vaccines ($p>0.05$). No statistically significant differences in the number of unfavorable reactions were revealed among premature infants, who were vaccinated in the first and the second half-year of life, as well. Given these facts, it may be recommended to vaccinate the risk group children with PCV (including premature infants) from 2 months of age, employing simultaneous administration with other vaccines according to the vaccination calendar if needed.

CONCLUSION

Specific prevention of pneumococcal infection with PCV7/PCV13 vaccine in children of the first half-year of life allows preventing severe diseases of bronchopulmonary and central nervous systems.

It is safe to vaccinate the risk group children with both 7- and 13-valent conjugated pneumococcal vaccine, including combination with other national calendar's vaccines.

In order to achieve epidemiologically significant reduction in the rate of diseases caused by *S. pneumoniae*, it is necessary to conduct cohort immunization of children of the first year of life (preferably, from 2 months of age).

Cohort vaccinal prevention is the most available, economical and effective means of fighting pneumococcal infection; there is an unconditional need in introducing vaccination against *S. pneumonia* into the national vaccination calendar in Russia as in 52 other countries.

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Table 1. Background pathology in 2-23-month-old children vaccinated with pneumococcal conjugated vaccine in Irkutsk

Background pathology, absolute	Vaccination beginning age			
	2-6 months	7-11 months	12-23 months	Total, absolute (%)
Total amount	66	63	35	164
Prematurity	31	33	11	75 (45.7%)
CHD	20	17	6	43 (26.2%)
Resuscitation measures (including artificial pulmonary ventilation) in anamnesis	9	11	11	31 (18.9%)
Perinatal contact with HIV and HIV-infection	6	9	10	25 (15.2%)

Table 2. Background pathology in children of 24 month of age and over vaccinated with pneumococcal conjugated vaccine in Irkutsk

Background pathology	Absolute	%
HIV-infection	5	17.2
Congenital heart diseases	10	34.5
Hydrocephaly	1	3.4
Congenital bronchopulmonary system's malformations	3	10.3
Cerebral palsy	1	3.4
Frequent and complicated respiratory infections in anamnesis (with antibacterial therapy 8-12 months for a year)	10	34.5
Pneumonia in anamnesis	3	10.3