Vaccination status (PCV13) of children with pneumococcal meningitis

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Abstract

Pneumococcal meningitis in children is one of the reasons for the development of serious neurological complications. According to various authors, in developed countries, the incidence rate ranges from 8 to 34 cases per 100,000 population, in Kazakhstan there is no etiological interpretation of bacterial meningitis, and therefore there are no official statistics on the incidence. To date, in more than 120 countries, the pneumococcal conjugate vaccine has been added to the vaccination calendar, which is the most effective method for reducing the incidence of bacterial meningitis pneumococcal etiology. This article reflects the effectiveness of vaccination and the risk of bacterial meningitis in children with pneumococcal meningitis in terms of using the PCV13 vaccine.

Keywords: pneumococcal meningitis, vaccination, PVC13, children

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Introduction

According to the WHO estimates, 1.6 million people die every year from invasive pneumococcal diseases (IPD), of which 0.7-1 million are children under the age of 5 years [1,2]. Pneumococcal meningitis (PM) is one of the reasons for the development of serious neurological complications [3]. The incidence rate of pneumococcal infection among children in the Asia-Pacific region for 1999-2010 was 100-200 cases per 100,000 children under the age of two years [4], and in developed countries, the incidence rate ranges from 8 to 34 cases per 100,000 population [5]. In Kazakhstan, there is no etiological interpretation of bacterial meningitis (BM); therefore, there are no official statistics on the incidence of IPD.

Currently, pneumococcal conjugate vaccine (PCV7, PCV10 and PCV13), as recommended by the WHO, has been included in the national vaccination calendars for children in more than 120 countries [6]. The incidence of adult pneumococcal infections has decreased as a result of the population effect of PCV, which has become widely used among children [7]. In the national calendar of vaccinations of the Republic of Kazakhstan, vaccination against hemophilic infection (Hib) and pneumococcus (PCV13) is used for children from 2 to 15-18 months.

The aim of this study was to evaluate the effectiveness of vaccination and the risk of the incidence of BM in children with PM in terms of the use of PCV13 (full dose, incomplete dose, and those not receiving the vaccine).

Material and methods

This study was conducted as part of the scientific project “Development of early diagnosis and preventive measures of hearing impairment after bacterial meningitis in children” AR05135091, implemented by grant funding for 2018-2020 on the basis of the Department of Pediatric Infectious Diseases, Nonprofit Joint Stock Company "Astana Medical University".

Table 1

| Vaccine name             | Vaccine status PM (n = 23) | incomplete dose | lack of vaccination |
|--------------------------|---------------------------|-----------------|--------------------|
|                           | full dose according to schedule | at large intervals |                    |
| Anti-pneumococcal vaccine| 2 (8.7)                    | 2 (8.7)         | 12 (52.1)          |
|                          |                           |                 | 7 (30.5)           |

Figure 1 - Reasons for refusing vaccination with PCV 13 in patients with PM

In addition, there were such reasons as an incomplete dose - 52.1% (n=12), lack of vaccination - 30.5% (n=7), parental refusal to vaccinate - 30.5% (n=7) and medical allotment - 34.8% (n=8) (Figure 1).

The reasons for the incompleteness of the course and the non-receipt of the anti-pneumococcal vaccine in children with PM are: allergic manifestations, frequent acute respiratory infections and relocations, which is 57.8%; religious denial of vaccination is observed in 42.1% of patients, medical rejection of vaccinations in children under 1 year of age (prematurity, neurological complications, etc.) - 31.5%, distrust of the vaccine (negative information received on television) - 26.3%; refusal of vaccinations due to fear of post-vaccination complications was recorded in 5.2% of patients.

According to a meta-analysis by Kai Duan, Jin Guo and Ping Lei, premature babies have a high tolerance to PCV 7, PCV 10 or PCV 13. Despite the difference in the content of antigen
and carrier protein in PCV, vaccinations of PCV 7, PCV10 or PCV13 can cause optimal immune response after vaccination in preterm infants with low and very low birth weight [7,9]. In our case, 31.5% of children with PM were born prematurely, which initially determined an increased risk of developing the disease, although timely vaccination from 2 months of life could serve as a factor in reducing the risk of IPD.

To assess the relationship between clinical indicators and vaccine status (not receiving the vaccine and not receiving the full dose of the vaccine) in children with PM, a Spearman correlation analysis was performed. A strong positive relationship was noted between the following indicators: between the severity (severe course) and the absence of vaccination (r=0.9; p≤0.001), between the severity (severe course) and the incomplete dose of vaccination (r=0.7; p≤0.05), prolonged temperature and lack of vaccination (r=0.9; p≤0.001), neurological complications and lack of vaccination (r=0.8; p≤0.001), number of hospital days (from 30 to 61 days) and the lack of vaccination (r=0.9; p≤0.001), combined antibacterial therapy and the absence of vaccination (r=0.8; p≤0.001) (Table 2).

### Table 2
The relationship between the clinical course of PM and vaccine status

| Indicators                                      | The strength of the connection, and P * |
|------------------------------------------------|----------------------------------------|
| 1 clinical course                              | 2 vaccination status                   |
| Severity (severe course)                       | not receiving the vaccine              |
|                                                | incomplete dose                        |
| Long temperature                               | not receiving the vaccine              |
|                                                | incomplete dose                        |
| Neurological complications                     | not receiving the vaccine              |
|                                                | incomplete dose                        |
| The number of bed days (from 30 to 61 days)    | not receiving the vaccine              |
|                                                | incomplete dose                        |
| Combined antibiotic therapy                    | not receiving the vaccine              |
|                                                | incomplete dose                        |
| *p≤0.001; **p≤0.05                             |                                        |

An average positive relationship was found between the duration of the temperature and the non-receipt of the full dose of vaccination (r=0.6; p≤0.05), neurological complications and the receipt of an incomplete dose of the vaccine (r=0.5; p≤0.05), the number of patients-days (from 30 to 61 days) and receiving an incomplete dose of the vaccine (r=0.6; p≤0.05), combined antibacterial therapy and receiving an incomplete dose of the vaccine (r=0.5; p≤0.05).

Subsequently, the effect of vaccination on cerebrospinal fluid microbiome was determined. A change in the cerebrospinal fluid microbiome was revealed in the group receiving vaccination and without vaccination (Figure 2).

The cerebrospinal fluid microbiome differs between the vaccinated and unvaccinated groups. In the unvaccinated group, streptococci are the predominant flora, while in the vaccinated group Staphylococcus, Neisseria, Haemophilus (Figure 3). The biodiversity of the microbial flora in the unvaccinated group is significantly different.

The Shannon index shows a significant difference in the biodiversity of cerebrospinal fluid microorganisms selected from patients with bacterial meningitis of an unconfirmed etiology. Shows the difference between vaccinated and unvaccinated groups. In the vaccinated group, bacteria belonging to the genera prevail: Neisseria, Haemophilus, Staphylococcus, while in the vaccinated group Streptococcus, Rothia, Granulicatella, Gemella, but also Haemophilus, Neisseria.

![Figure 2](image2.png)

![Figure 3](image3.png)

A clear separation of vaccinated and non-vaccinated groups is also shown using the Bray-Curtis and UniFrac methods (Figure 4).

According to the distribution of microorganisms that make up the cerebrospinal fluid in patients with bacterial meningitis of unknown etiology, a clear distinction is made into two clusters.
Conclusion

According to the national vaccination calendar of the Republic of Kazakhstan, it is necessary to vaccinate against vaccine-preventable infections that cause bacterial meningitis - Hib, S. pneumoniae and N. meningitidis for all children from 2 months, including premature.

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