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STUDY OF THE IMMUNE STATUS OF FREQUENTLY ILL CHILDREN VACCINATED AGAINST HIB INFECTION

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XULOSA

Tadqiqot maqsadi. *Erta yoshdagi bolalarda Hib-infeksiyaga qarshi emlash bilan qamrov darajasini, AKT-XIB vaksinasining samaradorligini, Haemophilus influenzae b turi ga qarshi antitanalar darajasi va ularning saqlanishini, shuningdek emlash davrida kasallanish kamayishi bilan bog‘liqligini baholash.*

Materiallar va usullar. *Tashkil etilgan va tashkil etilmagan erta yoshdagi bolalar orasida kompleks klinik-epidemiologik va immunologik tadqiqot o‘tkazildi. Hib-infeksiya bilan kasallanish ko‘rsatkichlari, tashuvchanlik chastotasi hamda AKT-XIB vaksinasi bilan emlashdan keyingi spetsifik antitanalar darajasi baholandi. Immunologik va epidemiologik ko‘rsatkichlarni solishtirish uchun statistik tahlil usullari qo‘llanildi.*

Natijalar. *Hib-infeksiyaga qarshi emlash sog‘lom bolalar populyatsiyasida H. influenzae b turi tashuvchanligini 0,5–1,0% gacha sezilarli darajada kamaytirishi aniqlandi. Postvaksinal antitanalar darajasi bilan infeksiyaning generalizatsiyalashgan shakllari, jumladan yiringli meningit va pnevmoniya uchrash chastotasining kamayishi o‘rtasida bog‘liqlik qayd etildi. Olingan natijalar AKT-XIB vaksinasining erta yoshdagi bolalarda Hib-infeksiyani oldini olishdagi yuqori samaradorligini ko‘rsatdi.*

Xulosa. *Tadqiqot natijalari Hib-infeksiyaga qarshi emlashning yuqori profilaktik ahamiyatga ega ekanligini tasdiqlaydi. Olingan ma’lumotlar erta yoshdagi bolalar orasida profilaktik tadbirlarni optimallashtirish hamda ularning tibbiy- iqtisodiy samaradorligini asoslashda qo‘llanishi mumkin.*

Kalit so‘zlar: *infeksiya, tez-tez kasallanadigan bolalar, emlash, immunitet.*

РЕЗЮМЕ

Цель исследования. *Оценить охват вакцинацией против Hib-инфекции у детей раннего возраста, эффективность вакцины АКТ-ХИБ, уровень и сохранность антител к Haemophilus influenzae типа b, а также их связь со снижением заболеваемости в период вакцинации.*

Материал и методы. *Проведено комплексное клинико-эпидемиологическое и иммунологическое исследование среди организованных и неорганизованных детей раннего возраста. Оценивались показатели заболеваемости Hib-инфекцией, частота носительства, а также уровень специфических антител после вакцинации вакциной АКТ-ХИБ. Использованы методы статистического анализа для сопоставления иммунологических и эпидемиологических данных.*

Результаты. *Установлено, что вакцинация против Hib-инфекции сопровождается значительным снижением носительства H. influenzae типа b в популяции здоровых детей до 0,5–1,0%. Выявлена связь между уровнем поствакцинальных антител и уменьшением частоты генерализованных форм инфекции, включая гнойный менингит и пневмонию. Полученные данные свидетельствуют об эффективности вакцины АКТ-ХИБ в профилактике Hib-инфекции у детей раннего возраста.*

Заключение. *Результаты исследования подтверждают высокую профилактическую значимость вакцинации против Hib-инфекции. Полученные данные могут быть использованы для оптимизации профилактических мероприятий среди детей раннего возраста и обоснования их медико-экономической эффективности.*

Ключевые слова: *инфекция, часто болеющий ребенок, вакцинация, иммунитет.*

Haemophilus influenzae type b is one of the common causes of generalized infection (bacteremia) in children, half of them develop purulent meningitis, quite often (15-20%), pneumonia, and rarely other focal lesions.

In recent years, there has been an increase in the incidence of pneumonia, epiglottitis, otitis media, and bronchitis in infants caused by Haemophilus influenzae type b (Hib) [1-3,6]. Hib infection occurs only in humans, and children aged 2 months to 5 years are particularly susceptible. [6] According to literature data, the prevalence of Hib infection in children under 4 years of age is 40.3% [1,6]. Among children under 5 years of age, the incidence of Hib infection is 24% in children with otitis media, 10% in acute otitis media, and 7% in laryngitis [2]. According to data, the most severe form of otitis media of Hib etiology is associated with bronchopulmonary tissue necrosis, abscesses, and pleurisy (Gorbunov S.G. et al., 2012). Before the introduction of vaccination against IBD, the incidence of this etiological disease was high among children under 5 years of age, in other countries - in the USA - 60-130, in Australia - 53, and in Scotland - 25.5 per 100,000 children [8].

Unfortunately, official registration of hemophilia infection in Uzbekistan has not been established. First of all, due to the lack of domestic diagnostic test systems, it is impossible to etiologically confirm and register HIV

infection. Therefore, there is reason to believe that its prevalence in our country is high.

Given that the spread of IBD is often observed through airborne droplets, diagnosis and pathogen resistance are difficult, so antibacterial agents are used. Therefore, the most effective means of infection and protection of children is the use of special vaccines [4,5]. Today, in many countries, the problem of IBD infections has been solved by introducing vaccination from 2 months of age into the vaccination schedule of children. Due to vaccination, severe forms of this disease have disappeared [7].

In our country, the problem of infectious diseases and the study of immunity in children is a very important and urgent issue [6]. However, in the available literature, we have not yet identified the characteristics of the immune response andhemophilic infection eThere is no information on the nature of the development of antibodies in a group of sick children after vaccination. The aim of our work is to conduct a detailed study of immune parameters in a group of frequently ill children vaccinated against IBD.

MATERIAL AND METHODS

The study included 92 children aged 3 months to 6 years, of whom 53 were boys (59%) and 39 were girls (41%). The subjects were divided into 2 groups: group 1 consisted of 68 children (77%) with frequent illnesses, and group 2 consisted of 24 (23%) practically healthy children. Vaccination was carried out with the Pentovacina vaccine (Indonesia) during the period of remission of the main disease, when the child's condition was stable.

All children underwent a general clinical examination (body weight and height, general blood and urine analysis), ultrasound examination, nasal cavity radiography, allergist consultation, immunological examination, otolaryngologist consultation. In children with allergic diseases, an allergic (collection of allergic history data, skin prick test with allergen, total IgE content, FVD examination (children under 5 years old) immunologist (immunoglobulin A, M, G, cytokine status levels were determined) specialist consultation was performed. Children with nervous system diseases were consulted with a neurologist, and if necessary, infants underwent electromagnetic and neurosonography. Patients with kidney and urinary tract diseases, in addition to a physical examination, were consulted with a nephrologist, and additional kidney and bladder ultrasound, general urinalysis, Nechiporenko, Zimnitsky tests were performed when necessary.

The main immunoglobulin classes, cytokines, cortisol, determination of the level of antibodies to Haemophilus influenzae type B, clinical and immunological examinations were carried out at the Institute of Immunology of the Tashkent Medical Academy. Immunoglobulin (G, A, M) was determined by the turbidimetric method "Clima" (Spain). IgE in serum was determined by the ELISA method (reagent AOZT 'DIA - plus'), cytokine concentration by the ELISA method (ELISA). Antibodies to Hib infection (IgG - PRP) were determined by the ELISA method "ImmunozymHibIgG" (IBL, Hamburg).

RESULTS AND DISCUSSION

All children tolerated the vaccination satisfactorily, and no child had a major illness in the week following vaccination. Cortisol levels before and after vaccination were 175.8±14.8 and 220.5±23.2 nmol/l in group 1, and 177.5±23.4 and 189.4±27.3 nmol/l in group 2, respectively ($p>0.05$). The normal range for baseline cortisol is 123-626 nmol/l.

Table 1

Indicators of INFγ before and after vaccination in healthy and pathological children, M±m (pg/ml)

Norm (pg/ml)	Cytokine	Children's group	Before vaccination (n)	After vaccination (n)	M±m (ng/ml)	p_1
1.01 ± 0.3	INFγ	1	n = 9	n = 4	0.77 ± 0.02*	>0.05
0.99 ± 0.35*	INFγ	2	n = 28	n = 25	1.09 ± 0.15*	>0.05

Table 2

Indicators of TNFα before and after vaccination in healthy and pathological children, M±m (ng/ml)

Norm (pg/ml)	Cytokine	Children's group	Before vaccination (n)	After vaccination (n)	M±m (pg/ml)	p_1
7.33 ± 0.6	TNFα	1	n = 9	n = 4	8.12 ± 1.35*	>0.05
6.65 ± 1.24*	TNFα	2	n = 28	n = 25	8.04 ± 0.67*	>0.05

Note: 1 – group of healthy children, 2 – group of children with various pathological changes, r1 – comparison of indicators before and after vaccination.

*r2>0.05 – comparing the indicators of children in groups 1 and 2

Thus, the cortisol index in both groups was not significantly different (r>0.05) in relation to age and vaccination.

In 2 groups of children, a tendency to increase in IgG concentration (p>0.05) was observed under vaccination conditions. As for IgA and IgM, the indicators before and after vaccination were average in both groups, and the dynamics practically did not change (p>0.05). The upper limit of the norm of IgE values before and after vaccination was observed in practically all healthy children (less than 60 IU/ml). In two infant boys, low IgA values were detected before and after vaccination (0.11 and 0.12 g/l before vaccination: 0.13 and 0.2 g/l and after). This may be due to the late response of children to the vaccine.

Table 3

In healthy and existing children with various changes in health, titer of antibodies against "HIB" before and after vaccination

Negative indicator (less than 0.15 μg/ml)		Estimated rate (0.15 to 1.0 μg/ml)	A positive indicator (1.0 μg/ml solution)
1 (before)	10 (16%))	40 (66%)	11 (18%)
(later)	0	2 (3%)	60 (97%)
2 (before)	4 (23.5%)	8 (47%)	5 (29.5%)
(later)	0	1 (5.5%)	17 (94.5%)

IgG and IgA concentrations were significantly lower than the norm before and after vaccination, but did not change significantly in dynamics (p>0.05). IgM levels were observed at the norm before and after vaccination.

Thus, no profound changes in the main classes of immunoglobulins were detected in healthy and sick children vaccinated against Hib infection.

To further investigate the effect of vaccination against Hib infection, we assessed the status of cytokines (TNFα and INFγ, IL5, IL13).

As can be seen from Table 1, the indicator INFɣand TNFα showed no significant differences in the dynamics of cytokine levels in both groups before and after vaccination (p>0.05). As for interleukins, IL5 and IL13 indicators in all children did not differ from the norm, the dynamics remained unchanged, but when the indicators were observed in individual patients, the differences between them were significant.

The main objective of the study was to develop and evaluate the effectiveness of antibodies (IgG) against Haemophilus influenzae type b.

Table 3 shows antibody levels before and after vaccination in healthy children and children with various health conditions.

Table 2 shows that negative antibodies were observed in 23% of practically healthy children before vaccination and in 16% of children with various health changes, while a doubtful antibody index was observed in 17% of healthy children and 66% of children with various health changes, and a positive index was observed in 29.5% of practically healthy children and 18% of children with various health changes.

After vaccination, positive antibodies were detected in all girls. In the group of practically healthy children, 3 boys, and in two children with various changes in their health, the presence of doubtful antibody titers indicates a negative immune response to vaccination. One child (an 8-month-old child from the group of practically healthy children) had a low IgA index (0.11 g / l and 0.13 g / l before and after vaccination, respectively). Two other boys (one - 2 years old, the other - 2 years and 5 months old) were included in the group of children with allergic diseases. The mothers of these children had a history of serious illnesses during pregnancy and took hormonal drugs.

CONCLUSIONS

1. Vaccination against Haemophilus influenzae B is generally safe in healthy children and in groups of children with health conditions. No serious adverse events have been observed during vaccination.

2.Vaccination against Haemophilus influenzae type B does not cause relapses or complications in the early post-vaccination period in children with chronic disease.

3. Vaccination against Hemophilus V infection does not significantly affect humoral and cytokine indicators of immunity in practically healthy and frequently sick children, including children with allergic diseases.

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