Original Article

EFFECTIVENESS AND HARMLESSNESS OF IMMUNIZATION AGAINST DIPHTHERIA AND TETANUS IN CHILDREN WITH ALLERGIC DISEASES

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Summary

The immunity status of 151 children without immunization and 68 vaccinated children with allergic diseases (bronchial asthma, atopic dermatitis, pollinosis), aged 1-15 years, inoculated with adsorbed diphtheria-pertussis-tetanus (DPT) vaccine and ADT-M toxoid was assessed. The control group included 61 clinically healthy children, matched by age and immunization history. Reimmunization with ADT-M toxoid of children with allergic diseases resulted in building up protective antitoxic immunity against diphtheria and tetanus, which was not different from that in the control group. Immunization with DTP- and ADT-M of children with history of allergic diseases did not lead to higher incidence of allergic and autoimmune reactions, as compared to hyposensibilization therapy.

Key words: allergic diseases, allergic reactions, children, immunity, diphtheria, tetanus

Introduction

Prophylactic immunization against childhood infections in children with allergic diseases is a major medical issue. [1, 2, 3]. On the one hand, this fact could be attributed to bad health of such children, who are unprotected against infections because they are not given vaccines, immunizations are not given, or immunization courses are not competed because of bad health. On the other hand, allergic diseases can lead to complications in infectious diseases, further increasing the importance of prophylactic measures in such children [3]. It is interesting that the reaction of the immune system depends on the vaccine itself, frequency of lack of reaction of children's immune system depends on the vaccine, frequency of injection and general health state of an inoculated child [2, 4]. It is known that immunization with Diphtheria-Tetanus-Pertussis (DTP) and associated Diphtheria-Tetanus-M-vaccine (ADT-M) can promote the IgE synthesis activation and initiate the histamine liberation from mast cells and basophiles

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[5]. Any vaccine for example Pertussis vaccine, have polyclonal action that can promote autoantibody formation during injection [6]. Therefore, immunization of children with allergy is necessary and requires individual approach to achieve protective immunity.

The aim of the study was to determine the state of immunity against Diphtheria and Tetanus, to assess the parameters of allergic and autoimmune reactions in children with allergic diseases which depend on the time of giving DTP and ADT-M vaccines.

Materials and Methods

The study group included children with allergic diseases (bronchial asthma, atopic dermatitis and pollinosis), of whom 151 had not been given vaccines, and 68 had had DTP and ADT-M vaccines. All children were examined at the consulting diagnostic center in Rostov-on-Don. The control group included 61 children without disease episodes during the last 3-6 months, who had been given a vaccine three times, revaccinated with DTP-vaccine and revaccinated once with ADT-M vaccine according to the National Immunization Schedule [6, 7]. The age of the children examined ranged from 1 to 15 years.

The level of antibodies to Diphtheria anatoxine (DA) and Tetanus anatoxine (TA) was measured by passive hemagglutination reaction (test-system "Microanalysis-Diphtheria, Tetanus", Scientific industrial company "Microanalysis", Moscow) 1.5-11 months after the last immunization. Defense antidiphtheria antibodies titer was 1:20, antitetanus antibodies titer was 1:10 (Sanitary rules and standards "Diphtheria prophylactics", Moscow, 2002). The level of antibodies formation was determined on mean geometric of antibodies titers calculation (MGT). Estimation of total IgE, specific IgE to DA and TA and antibodies to single-stranded DNA was made by enzyme-linked immunosorbent assay test-system ("Vector-Best" company, Novosibirsk). To estimate the specific IgE to DA and TA, the 15-20 mcg/mL of DA in 100 mcL was affixed to the plate "Dynatech", it was incubated at +4^{0}C for 18-20 hours. Then traditional ELISA on general principles was made. Serum samples were considered positive if their optical density was 0.1 OU higher than that in control samples.

Statistical programs "Statistica 6.0" for Windows XP with paired and unpaired statistic methods were used for statistical analyses of results. Mean values and standard error (m±SEM) were estimated for results analyses. Reliable data was assessed at the level of significance $p<0.05$.

Results and Discussion

Immunization of children with allergic diseases was performed according to National Immunization Schedule in compare and compared to hyposensibilization therapy with ketotifen, chloropyramine (Suprastin) and clemastine (Tavegil) medicines [8]. No clinical symptoms the process of immunization were registered in the children studied, only mild side effects such as tissue thickness, hyperemia less then 6 cm in diameter, slight illness on the site of immunization, temperature up to 37.5^{0}C, transitory intoxication symptoms as indisposition. All side effects seen in inoculated children were within the normal range.

Our results from assessment of antidiphtheria antitoxic protective immunity in children with allergic diseases (Table 1) have shown that the number of quantity of seropositive children was high enough after tree injections of DTP-vaccine and was (96.3±3.6%). Of the children studied, who received the complete course of DTP-vaccine inoculations and were revaccinated with ADT-M toxoid, all children (100%) became protected against Diphtheria. These results were the same as the ones for the healthy children (95.1±2.8% seropositive children). The level of antibodies formation (MGT) in healthy children was 1:467.7. Similar results (1:501.2) were found only in children who got a complete course of DTP-vaccine inoculations and reimmunization with ADT-M toxoid.

During the assessment of antitetanus immunity it was established that 92.6±5.0% of the children with allergic disease who got tree doses of DTP-vaccine were seropositive, and 100% of the children who were revaccinated with DTP and ADT-M-medicines were seropositive. It was interesting that antibodies level to TA was higher than to DA, and it the level correlated with the number of injected doses of vaccines. The MGT in the children, who got tree doses of DTP-vaccine was 1:131.8, while MGT was 1:1000 in those inoculated and revaccinated with DTP- and ADT-M. Titer level of antitetanus antibodies in children with family history of allergy were not

had significantly different from titer level in healthy children inoculated with DTP-vaccine and revaccinated with ADT-M-anatoxine.

Table 1. Tense of immunity to Diphtheria and Tetanus at children with allergic diseases inoculated with DTP- and ADT-M

Immunization	Number of children	Antibodies to Diphtheria Anatoxin		Antibodies to Tetanus Anatoxine	
		Number of seropositive children (%±SEM)	MGT	Number of seropositive children (%±SEM)	MGT
V_1 DTP V_2 DTP V_3DTP	27	26 96.3±3.6	1:66.4 (45.7-95.5)	25 92.6±5.0	1:131.8 (81.3-213.8)
V_1 DTP V_2 DTP V_3DTP R_1DTP	20	16 80±8.9	1:133.5 (177.6-234.4)	20 100	1:316.2 (181.6-550.8)
V_1 DTP V_2 DTP V_3DTP R_1DTP R_2 ADT-M	21	21 100%	1:501.2 (288.4-870.9)	21 100%	1:1000 (616.6-1621.8)
Healthy children	61	58 95.1±2.8%	1:467.7 (331.1-660.7)	61 100%	1:1826.1 (1479.1-2344.2)

Increased concentrations of serum IgE are associated with reduced antibody response to immunization with DTP-vaccine [9], which is why we decided to study the level of IgE in children with allergic diseases after immunization.

To assess the safety of immunization in all the children studied, the parameters of allergic (total IgE and specific IgE to DA and TA) and autoimmune reactions were estimated. The results of from the investigation (Table 2) showed that the percentage of children with allergic diseases with increased level of total IgE had no correlations with the quantity of injected doses and the type of vaccine, and was 33.3-48.1% from all the children studied. These results did not show statistically significant difference in comparison with the healthy children (30%). However, the mean level of total IgE (33.3±4.9 IU/mL) in healthy children was lower that that in the children with allergic diseases, notwithstanding their immunization histories.

After immunization with DTP- and ADT-M, the total and middle IgE level in children with allergic diseases was the same, as compared with immunized children with the same pathology. These results have shown that increased level of total IgE in children with family history of allergy depended on factors other than immunization.

It is known [2, 3] that only in the early period after immunization with DTP- and ADT-M the short-term total IgE level increase is vaccine-related, and after two months it decreases to base level. That is why we decided to determine the specific IgE to DA and TA, which practically absent in the healthy children.

During assessment of specific sensibilization to the vaccines in children with allergic diseases it was established that frequency of specific IgE to DA were higher than to TA. The same results were found in healthy children. However, the level of specific sensibilization to diphtheria and tetanus vaccine components was higher in the children with history of allergic diseases, as compared to the healthy ones. In the children with allergic diseases, the specific IgE to DA and TA was established in 5 and 3 children, respectively.

During immunization, autoimmune reactions can be developed, depending on the presence of cross antigens structures between vaccines and proper body components [5]. Moreover, it is known that allergic and autoimmune processes have common pathogenic mechanisms [5]. That is why the marker of autoimmune process – level of antibodies to single-stranded DNA (denaturated) – was estimated in all the children studied. Increased levels of antibodies to DNA were established in the blood serum of 42.9-66.7% of the children with allergic diseases, irrespective of the time since last immunization, type of vaccine and times of injections. These

results were not significantly different from the results of uninoculated children with allergic pathology (54.0±7.0%). At the same time, the percentage of healthy children who were inoculated according to the National Immunization Schedule had a statistically lover level of antibodies to denaturated DNA (10.0±9.5% of the children studied).

In inoculated children with allergic diseases, the level of antibodies to denaturated DNA ranged from 33.6 to 45.5 U/mL, and had not statistically different from the level in uninoculated children with the same pathology (33.5±1.9 U/mL). There was no correlation with the time since last immunization and type of vaccine.

Table 2. Level of total and specific IgE in children with allergic diseases inoculated with antidiphtheria medicines

Immunization	Number of children	IgE		DA-IgE (%±SEM)	TA-IgE (%±SEM)
		M±SEM (IU/mL)	Number of children with higher normal level of IgE (%±SEM)		
V_1 DTP V_2 DTP V_3DTP	27	87,6±40,5	13 48,1±9,6	6 22,2±8,0	5 18,5±7,5
V_1 DTP V_2 DTP V_3DTP R_1DTP	20	84,4±36,7	7 35,0±10,7	1 5,0±4,9	- 0
V_1 DTP V_2 DTP V_3DTP R_1DTP R_2ADT-M	21	102,0±36,3	7 33,3±10,3	5 23,8±9,3	1 4,8±4,7
Uninoculated children	151	121,0±17,6	63 41,7±4,0	5 3,3±1,5	3 2,0±1,1
Healthy children	20	33,3±4,9	6 30,0±10,3	3 15,0±7,9	- 0

Conclusions

Immunization with DTP- and ADT-M in children with history of allergic disease leads to antidiphtheria and antitetanus protective immunity formation, which was the same as in the group of healthy children.

Immunization with DTP- and ADT-M in children with history of allergic disease, as compared with hyposensibilization therapy did not lead to formation of increased parameters of allergic and autoimmune reactions formation.

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