Vaccinal Prevention of Controlled Infections in Children with Tuberculosis

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Abstract

Currently, the epidemiological tuberculosis situation in the Russian Federation remains unfavorable with the increased number of TB infected children. This group of children does not receive the necessary vaccination regularly, prior to dispensary deregistration of the phthisiopulmonology. The absence of on-time vaccination often leads to lack of individual protection of each child and the threat of epidemic well-being of the country due to the decrease in herd immunity. This article represents the experience of immunization of children with tuberculosis infection, by inactivated vaccines (ADS-M, Pneumo 23) and live vaccine (Russian bivalent measles-mumps vaccine). It also shows the clinical and immunological safety of vaccination in this group of children.

Keywords: children with various manifestations of tuberculosis infection, vaccinations, safety, efficiency

Introduction

In Russia, children receiving treatment for tuberculosis (TB) infection, in most cases, do not take root in accordance with the National vaccination calendar. This is because of cellular immunodeficiency, which occurs in patients as a result of exposure to the pathogen and in the result of tuberculosis treatment-FDI can lead to insufficient efficiency vaccination and/or the development of complicated current post-vaccination period, as it was indicated for patients with cancer diseases in anamnesis and for HIV-infected children [1, 2, 3, 4].

The incidence of tuberculosis in Russia remains high in child population (16.6 on 100,000 in 2012) [5]. The lack of timely revaccination leads to the deficiency of individual protection from preventable infections. In the implemented programs of preventable diseases TB infected children being at risk of high morbidity with these diseases by themselves also keep circulation of infectious agents in overall population.

Furthermore, it was a well-known fact about harmful impact of flu, chickenpox, Haemophilus influenza, and pneumococcal infections on the course of TB. This was another argument for vaccination children with tuberculosis infection [3, 6, 7]. In recent years, scientists studied different approaches in immunization of children infected with Mycobacterium tuberculosis [8, 9]. Purpose of the study was to evaluate the safety and effectiveness of immunization in children with TB infection.

Materials and Methods

In 2010-2012 at Saint-Petersburg Research Institute of children's infections and Saint-Petersburg Research Institute of Phthisiopulmonology 65 children aged 3 to 14 years with tuberculosis infection were examined. Based on complex examination (Diaskintest, Quantiferon-TBGold test, CT) in all 65 children tuberculosis of intrathoracic lymph nodes was diagnosed. In accordance with the National calendar of vaccination in Russia, all children participating in the study had to be vaccinated against measles, mumps and/or diphtheria based on their age; however vaccination was not done before their inclusion in the study due to their infection by tuberculosis. Before vaccination, the level of antibodies against measles, mumps and diphtheria were determined. Among 65 examined children: protective titers of antibodies to measles were identified in 40 children (61.5%); to mumps - in 44 children (67.7%); and to diphtheria - in 46 children (70.8%).

For children who have no protective antibody titers and undergone appropriate vaccinations: 11 children were vaccinated by ADS-M (diphtheria – second or third booster), 9 children were vaccinated against measles and mumps, and 10 children were vaccinated by Pneumo 23. The vaccination was carried out after 4 months of chemotherapy specific treatment (2 months (Isoniazid + Pyrazinamide+Rifampicin), after 2 months (Isoniazid, Pyrazinamide/Rifampicin) in age dosages). Immunologic examination included: leucocytes' subsets ($CD3^+$, $CD4^+$, $CD8^+$, $CD4^+/CD8^+$, $CD16^+$, $CD20^+$, $CD25^+$, $CD95^+$, HLAII), the level of cytokine-induced (IL1â,4,6, IFN-ã, TNF-á), specific Ig (A, M, G Å classes) were detected before the vaccination, on the 14th, and 30-45th days after the vaccination.

Results and Discussion

After Td boosted in 10 out of 11 vaccinated children, vaccination process was asymptomatic, and one 11 years old child on the third day after vaccination developed intercurrent acute viral respiratory infection. Local reactions (redness, induration at the injection is not more than 5 cm in diameter) were observed in one child who received a second booster Td. Observation of the child for three months after vaccination showed no negative flow dynamics of tuberculosis infection.

In nine patients vaccinated against measles and mumps, post-vaccination process was without complications, one child noted an increment in body temperature to 38 ° C, and short rash on the seventh day. After vaccination Pneumo 23 in one child fixed local reaction in the form of redness at the injection site no more 5 cm in diameter. Supervision over children during one-three months showed no adverse effect on tuberculosis. Thus, the introduction of living and nonliving vaccines proved safe in children with tuberculosis infection and incidence of reactions of vaccine does not exceed the specified in the instructions to vaccines.

Immunization as living and non-living vaccines had no effect on TB infection. In order to evaluate the effectiveness of vaccinations the dynamics of specific antibodies was analyzed. All vaccinated children developed graft protective antibody titers to all antigens on the 14th day (Table 1).

It had been known that tuberculosis is characterized by disturbance of immunological parameters which correlate with severity and duration of tuberculosis infection. In this study, subsets of lymphocytes were analyzed before and after the 14th and 30^{th} days of vaccination). In the post-immunization period, no significant quantitative changes in T-cell subpopulations and their functional activity were identified (Table 2-4).

After vaccination with live vaccines, increased tendency in B-lymphocytes' quantitative (with 22.03 ± 5.31 to 27.02 ± 5.29) was observed. The increased of B-lymphocytes number is described in literature after immunization against measles and predominance of the immune response Th2 type of vaccine in the early stages of the process [10, 11, 12]. Thus, the study of immunological parameters indicated the safety of living and non-living vaccines' administration in these studied children.

Conclusions

When conducting small samples size research, the immunization by lifeless and live vaccines in children with tuberculosis infection is clinically safe and effective.

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Table 1: Quantity of specific antibodies before vaccination, the day 14 and day 30 after

the number of vaccinated	Geometric mean value of antibodies		
	before vaccina-tion	day 14	day 30
against measles (n=9)	0*	3.07±1.51*	4.83±1.49*
against mumps (n=9)	2.32±1.07	2,87±0.74	4.35±0.99
against diph-theria (n=11)	2.45±0.60 *	5,46 ±1.69*	7.23±1.64*

** Wilcoxon Matched Pairs Test, $p < 0.05$*

Table 2: Immunological parameters after immunization with Td (ADS-M) toxoid

	Leu-kocytes *10 ^{9}	**Lym-pho-cytes *10 ^{9}**	**CD3+ %**	**CD4+ %**	**CD8+ %**	**CD16 +%**	**CD20 + %**	**CD25 + %**	**CD95+ %**
before vaccina-tion	4.9± 2.06	1.81± 0.82	70.96 ±4.57	40.58 ±9.69	23.81 ±6.87	6.23± 4.86	17.17 ±6.57	14.94 ±6.86	20.7± 7.49
day 14	5.59± 2.54	1.74± 0.83	69.72 ±4.01	42.05 ±7.66	23.35 ±6.85	8,21± 3,68	18.66 ±3.24	13.15 ±4.92	18.73 ± 6.90
day 30	5.73± 1.42	1.99± 0.54	69,90 ±5.32	42.24 ± 8.43	24.63 ± 5.15	7,65± 3,11	17.54 ±5.75	12.68 ± 5.44	18.61 ± 5.44

Table 3: Immunological parameters after immunization PPV23

	Leuko-cytes *10 ^{9}	Lym-pho-cytes *10 ^{9}	CD3 + %	CD4+ %	CD8+ %	CD16 + %	CD20 + %	CD25 + %	CD95 + %
before vac-cination	5.23 ± 1.58	1.94± 0.84	65.69 ± 10.8	38.89 ± 13.27	23.60 ± 7.50	5.81 ± 5.31	17.94 ± 7.19	11.05 ± 3.64	19.5 ± 8.67
day 14	5.74 ±2.86	2.0± 0.61	63.44 ± 5.89	42.7 ± 10.12	21.3 ± 8.64	8.51 ± 3.54	18.83 ± 4.07	10.45 ± 2.07	17.68 ± 7.53
day 30	6.12 ±1.49	1.92± 0.24	68.82 ± 5.43	44.8 ± 9.14	21.89 ± 7.09	6.71 ± 5.92	20.55 ± 6.5	10.43 ± 4.2	19.5 ± 6.26

Table 4: Immunological parameters following immunization against measles, mumps

	Leuko-cytes *10 ^{9}	Lym-phocytes *10 ^{9}	CD3+ %	CD4+ %	CD8+ %	CD16 + %	CD20 + %	CD25 + %	CD95 + %
before vaccina-tion	6.34 ±1.85	3.17 ± 1.11	67.86 ±6.20	41.02 ±5.48	24.23 ±7.24	7.75 ±3.35	22.03 ±5.31	11.72 ±5.73	13.62 ±4.21
day 14	7.46 ±1.95	3.32 ± 1.82	67.35 ± 7.74	41.23 ±7.17	26.27 ±5.71	7.62 ±4.72	25.12 ±5.17	10.6 ±3.22	15.04 ±5.41
day 30	6.62 ±1.11	2.91 ±1.2	66.42 ± 7.98	39.7 ±6.13	23.65 ±4.39	7.82 ±4.89	27.02 ±5.29	11.16 ±3.73	14.26 ±6.65

** Wilcoxon Matched Pairs Test, $p < 0.05$*