

Pertussis Seroimmunity Among Mother-Infant Pairs and Infant Immune Response to Pertussis Vaccination

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This study was designed to evaluate seroprevalence rates of antibodies to pertussis in mothers and their infants, and the immunogenicity of pertussis vaccine in the presence or absence of pertussis antibodies in infants. Blood samples were collected from 110 mother-infants pairs before the first dose of pertussis vaccination and from 69 infants 4-8 weeks after administration of the third dose of DTwP vaccine. Pertussis antibodies were >25 U/mL in 88(78.9%) mothers and 50(45.3%) infants with a mean titer of 67(SD 48.1) and 33.5 (34.7) U/mL, respectively. After administration of three doses of DTwP vaccine, 53(76.8%) infants were seroconverted (MCA titer 87.4 (51.3)U/mL. Immunologic response to vaccination was similar between the two groups of infants; 30/37 (81.1%) of seronegative infants and 23/32 (71.9%) of seropositive infants at pre-vaccination, showed seroconversion after the vaccination (P = 0.36). The results of this study demonstrated that most of the studied mothers were serologically immune to pertussis, and this immunity was transferred to their infants. Pre-vaccination antibody did not affect infants immune response to vaccination.

Key words: DTwP, Immunogenicity, Pertussis, Vaccine.

Maternal antipertussis antibodies can protect infant from infection and modify the severity of illness for varying period of time, depending on the levels of placental transmission and the rate of decay of passively acquired antibodies in infants(1,2). Some studies demonstrated that immune response to immunization with whole-cell pertussis (wP) vaccine was lower in infants with higher cord-blood antipertussis antibodies titers than in infants with a low levels of circulating maternal antibodies(3,4). This study was conducted to determine the pertussis antibody status among mothers and their 2 months old infants and also to detect the effects of infants prevaccination pertussis immunity status on their immunologic responses to DTwP vaccine currently being used in Sari-Iran.

Subjects and Methods

This study was conducted from February 2005 to July 2006, at the primary health centers affiliated to Sari Medical Faculty. Study subjects were apparently healthy mothers and their two months old infants who were consecutively brought for scheduled routine primary immunization of diphtheria-tetanus-whole-cell pertussis (DTwP)

vaccine at the ages of 2, 4 and 6 months. [DTwP vaccine: diphtheria toxoid 15 Lf, tetanus toxoid 10 Lf, pertussis 16 protective units; Razi institute, Iran]. Infants with a history of prematurity or birth weight <2500 g, neurological problems or undefined seizure disorders, acute febrile or nonfebrile illness, recipient of blood or blood products or immunoglobulin, and evidence of immunodeficiency in either mothers or infants were excluded. The study was approved by the Ethics Committee of the Mazandaran University of Medical Sciences and Iranian Ministry of Health Review Board. Objective of the study were explained to the parents before obtaining written consent from the participants and infant parents. Blood samples were withdrawn from each infant-mother pair just before the first dose; and only from infants 4-8 weeks after the administration of the third dose of DTwP vaccine. Sera were stored at -20°C until assayed at the same time at University laboratory. Antipertussis specific IgG antibodies (antipertussis toxin and anti-filamentous hemagglutinin antibodies together) against pertussis were measured by quantitatively enzyme immunoassays using Bordetella pertussis IgG ELISA kit based on sandwich principle (IBL

Immunobiological Laboratories, IBL, Hamburg, Germany) according to the instructions of the manufacturer. The cut-off values of less than 25 U/mL was considered negative and more than 25 U/mL positive for antipertussis antibody. Immunologic response to the pertussis component of the vaccine was defined as changing seronegative sera at before vaccination to positive and or 4-fold increases in antibodies titers after vaccination. Mean concentration of antibodies (MCA) titers were calculated for mothers and, also, for infants before and after vaccination to assess the role of infants passive immunity on immune response to the vaccine. The infants were categorized into two groups based on their antibodies titers before vaccination (seronegative vs seropositive). The immunologic responses rate and MCA levels were compared between two groups by unpaired t-test. Statistical analyses were performed by using SPSS 11 software and $P < 0.05$ was considered significant.

Results

For the first stage of the study 110 mother-infant pairs were enrolled. Mean age of mothers was 26 (5) years, and infants 64.8 (24.8) days. Seroprevalence rates and MCA titers for mothers and infants before vaccination were 78.9%, 67 (SD 48.1) U/mL and 45.3%, 33.5 (SD 34.7) U/mL respectively. For the second stage of the study, 69 infants with the mean age 220 (SD 24.8) days were brought to complete the study. Of these 69 infants, 37 belonged to seronegative and 32 to seropositive group. The MCA titers of seroprotected and susceptible infants were 56.6 (SD 40.6) and 12.3 (SD 6.4) U/mL, respectively. The major reason for dropout was parental refusing to allow further blood sampling. From 69 infants, 55 were seroprotected, two of whom continued their prevaccination immunity without increasing the antibodies titers, because of poor immune response to vaccination, or by continuing of passive immunity, therefore, the true seroconversion rate will be 53 out of 69 (76.8%). Based on prevaccination antipertussis antibody status, there was no statistically significant difference between the two groups of infants (with and without passive immunity at before vaccination) regarding their immune response to pertusis immunization

[seroconversion rate: 81.1% vs 71.9%, $P = 0.36$ and MCA titers: 90.1 (SD 48.1) U/mL vs 83.6 (SD 55.7) U/mL, $P = 0.59$, for sero-negative vs seropositive infants, respectively].

Discussion

In our study, antipertussis seroprevalence rate and MCA titers in mothers were 78.9% and 67 (SD 48.1) U/mL, respectively. These levels seem much higher than that reported in a recent study by Healy, *et al.*(5) and is comparable with two older studies from a highly vaccinated population(6,7). Natural infection-induced immunity and repeated natural boosting in a new well vaccinated community with shorter history of high vaccine coverage may be the most probable explanation for these high sero-prevalence rates and titers observed in our study.

All subclasses of IgG are transported actively from mother to her infant predominantly during the third trimester of pregnancy. In a study on the placenta transfer and decay rate of pertussis antibodies in infants, Van Savage, *et al.*(7) showed that antibodies concentration in infants were comparable with their mothers. However, maternally originated antipertussis antibodies have a half-life of 5-6 weeks and drop to undetectable levels by 4-6 months of age, based on the antibody titers acquired at birth. Cord-blood samples were not available for our study, so, it was not possible to evaluate the placenta efficacy in transferring and decaying rates of antibodies in infants, "this is a limitation for our study". However, results showed that pertussis seroprevalence rate and MCA titers in two months old infants were 45.3% and 33.5 (SD 34.7) U/mL respectively. This finding suggested that most probably cord-blood levels of antibodies were proportional to maternal titers and expected half-life of antibodies were ~ 6-8 weeks. However, the high rates of seroprevalence at two months of age is in accordance with the findings that the higher maternal antibodies titers correlate with longer duration of passive immunity in her infants(1-4).

The inhibitory influence of maternal antibodies on infant immune response to wP vaccine was reported previously(3,4), however, this effect was

What this Study Adds

- Maternal antipertussis antibodies did not affect the infant final immune response to wP vaccine.

not seen in our study. To determine the mechanisms by which maternal antibodies influence infant vaccine response, Siegrist(8) showed that the influence of passive immunity on infant immune responses depend upon the maternal antibody-vaccine antigen ratio at the time of immunization, and inhibition will not occur if maternal antibody titers do not persist until completion of the infant immunization schedule. Also, passive immunity does not prevent T-cell priming, and subsequent vaccine doses will induce infant antibody response as soon as maternal antibody titers decline below the infant response threshold. The similarity of the final immune responses to 3 doses of wP vaccine between the two groups of infants in our study are in accordance with Siegrist conclusion.

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