

SEROLOGICAL EVALUATION OF 52 CHILDREN IMMUNIZED WITH THE COMBINED MEASLES, MUMPS AND RUBELLA VACCINE*

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SUMMARY: Topal B, Kanra G, Ceyhan M. (Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Serological evaluation of 52 children immunized with combined measles, mumps and rubella vaccine. *Turk J Pediatr* 33: 13-18, 1991.

Fifty-two of 298 children vaccinated with the measles-mumps-rubella (MMR) vaccine at around the age of 16 months were evaluated for antibody titres against measles, mumps, and rubella. The seropositivity rates for measles, mumps, and rubella were 86%, 92%, and 98%, respectively. While the most prominent side effects were irritability (6.04%) and fever (4.69%), 83.55% of the vaccinated children showed no undesirable reaction to the vaccine. The MMR vaccine appeared to be immunogenic and nonreactogenic for the children in the study. *Key words: measles, mumps, rubella, vaccination.*

Following the development of combined vaccines against measles, mumps and rubella, it has been unequivocally demonstrated that these diseases can be eliminated by countries which carry out well-planned vaccination programs. Their successful use has resulted in a marked change of attitude towards these diseases all over the world. Whereas the lay public, medical profession and public health authorities had previously been forced to consider rubella, mumps and measles as unavoidable childhood diseases, the effective vaccination programs mounted during the last ten years have proven that these diseases can be eliminated.

Of the three said diseases, only measles is prevented by a routine national vaccination program in Turkey. The combined measles, mumps and rubella (MMR) vaccination is not routinely administered to healthy children in Turkey. Children whose parents can afford to purchase MMR vaccine from private pharmacies are vaccinated against these three diseases. The World Health Organization (WHO) recommends that the MMR vaccine be used because it is easier to administer and less troublesome when given to 15-month-old infants¹.

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Studies show that the percentage of immunity is about the same as the application of one or both of the three vaccines. In addition, the incidence of clinical signs and symptoms is approximately the same for all three vaccines²⁻⁶.

The purpose of this study was to assess the rate of immunologic response to MMR vaccine, and the occurrence of clinical reactions in children who were vaccinated at the age of fifteen months in a private clinic.

Material and Methods

From May 1983 to September 1988, two hundred and ninety-eight healthy children were vaccinated with the MMR vaccine at our clinic. All of them had been brought to our clinic for monthly physical examinations. According to their past histories, they had never had any allergies to eggs, neomycin or kanamycin, had never received immunosuppressive drugs, had never had any symptoms or clinical signs of mumps, measles or rubella, and had never been inoculated with vaccines against mumps, measles or rubella.

The MMR combined vaccine used contained the Schwarz (measles), Urabe AM/9 (mumps) and the Wistar RA 27/3 (rubella) live attenuated virus strains. The vaccines were reconstituted immediately before use with 0.5 ml of diluent and administered into the right anterolateral aspect of the upper arm subcutaneously. Thirteen of the vaccines were produced by the Behring Institute, one by the Smith Kline Institute and 38 by Merieux.

The parents were informed of the nature and timing of any possible reactions. They made a notation if the child had fever, coryza, irritability, rash etc. and telephoned the doctor. The parents controlled the child's temperature by touch, and measured it if the child seemed feverish. Between the 7th and 10th day after injection, 30 mg/kg/day (b.i.d.) acetaminophen was given to all the children.

Measles and mumps antibody titres were determined by hemagglutination-inhibition techniques. The initial dilution was 1:5. The ELISA (enzyme-linked immunosorbent assay) technique was used for rubella antibodies. The values below 2 IU/ml were considered seronegative. The serological results for each child were sent to the child's parents and re-immunization was recommended for those who were seronegative.

Results

Even though a total 298 children were vaccinated with MMR, only fifty-two had parental consent to be enrolled in this study, and came to our clinic for an examination in January 1989. Since the vaccination, none of the children contracted measles, mumps or rubella. The mean age at immunization was 16.4

months, and blood samples were obtained at a mean age of 38.3 months. The mean value time between vaccination and obtaining blood samples was 20.5 months (minimum 3.0; maximum 67.0 months). About ninety percent of the children were vaccinated approximately at 15 months of age, considered by WHO to be the ideal age for immunization^{1,7} (Table I).

TABLE I: Age Distribution of Vaccinees

Age Group (mos.)	No. Patients (%)	Mean Vaccination Age (mos.)
All ages	52 (100.0 %)	16.4
13-18	47 (90.4 %)	14.6
19-24	3 (5.8 %)	21.0
25-48	1 (1.9 %)	26.0
49-96	1 (1.9 %)	80.0

The symptoms and clinical signs after vaccination are shown in Table II. Most of the vaccinated children were asymptomatic (83.6 percent) and did not have any clinical signs. While others were irritable and had a slight fever. Rash and parotitis were very rare.

TABLE II: Number of Children With Signs and Symptoms
Three Weeks After Immunization

Symptoms and Signs	No. Patients (%)
Irritability	18 (6.04 %)
Maculopapular rash	5 (1.67 %)
Coryza	5 (1.67 %)
Fever	14 (4.69 %)
Conjunctivitis	2 (0.67 %)
Parotitis	2 (0.67 %)
Lymphadenopathy	1 (0.33 %)
Local skin reactions	2 (0.67 %)
Asymptomatic	249 (83.55 %)

In this study, the interval between vaccination and serological evaluation was approximately two years, which is shown in Table III. Out of the 52 children, the titres that were found negative of measles, mumps, and rubella were seven (13.5%), four (8%), and one (2%), respectively (Tables IV, V, VI).

TABLE III: Interval Between Vaccination and Serological Evaluation

Age Group (mos.)	Interval (mos.)
13-18	20.0
19-24	23.3
25-48	17.0
49-96	3.0

TABLE IV: Distribution of Measles Antibody Titres

Titres	No. Patients (%)
Less than 1/5	7 (13.5 %)
1/5	7 (13.5 %)
1/10	9 (17.3 %)
1/20	4 (7.7 %)
1/40	9 (17.3 %)
1/80	13 (25.0 %)
1/160	1 (1.9 %)
1/320	2 (3.8 %)

TABLE V: Distribution of Mumps Antibody Titres

Titres	No. Patients (%)
Less than 1/5	4 (7.7 %)
1/5	3 (5.8 %)
1/10	7 (13.5 %)
1/20	6 (11.5 %)
1/40	3 (5.8 %)
1/80	9 (17.3 %)
1/160	12 (23.0 %)
1/320	8 (15.4 %)

TABLE VI: Distribution of Rubella Antibody Titres

Titres	No. Patients (%)	Mean Titres
Less than 2	1 (2.0 %)	2.0
5-20	10 (19.2 %)	14.0
21-40	10 (19.2 %)	26.3
41-80	13 (25.0 %)	53.6
81-160	12 (23.1 %)	113.9
161-320	2 (3.8 %)	211.5
321-399	— —	—
More than 400	4 (7.7 %)	400

Discussion

MMR vaccine has been used for 15 years in the USA, and ten years in the Scandinavian countries^{8,9}. On the other hand, the utilization of this vaccine in Turkey is very recent. Because of the cost of the vaccine, most of the children that we vaccinated came from families of a higher socio-economic level. Up until two years ago, families had purchased the vaccines from European countries. However, during the past two years, some companies have started importing large amounts of this vaccine.

Although infants are inoculated with the measles vaccine at nine months of age, in private clinics, the monovalent measles vaccine and MMR are given at fifteen months of age, which is the optimal age for obtaining the highest immunologic response.

According to our results, the antibody responses were as high as those reported in previous studies: 86.5% (measles) 92.3% (mumps) 98.0% (rubella)^{2,8,9}. These results were obtained by using vaccines that were transported and stored under suitable cold-chain conditions.

The subjects in our study were from families of a high socio-economic level. None of the infants were malnourished. Although their antibody responses do not reflect the whole of Turkish society, we can draw certain conclusions from these findings. On the other hand, if we could have obtained prevaccination antibody titres, it might have been possible to speculate about the actual seroconversion of these diseases.

Robertson et al² and Vesikari et al⁸ found many adverse reactions both after inoculation with MMR and the monovalent measles vaccine. Surprisingly, we found that the incidence of reactions from MMR vaccine was very low. Eighty-five

percent of the children had no symptoms or clinical signs. However, all the vaccinated children were given 30 mg/kg/day acetaminophen between the 7th and 10th day after injection as a routine procedure, which may account for this low incidence.

In this retrospective study, the results show high serum antibody levels against mumps, measles and rubella in children who were vaccinated with MMR vaccine at the age of 15 months. We suggest that all children should be vaccinated with MMR at about 15 months of age, even if they had been inoculated with the measles vaccine at 9 months of age.

We plan to conduct a prospective study to compare the immunologic response in Turkish children inoculated at nine months of age with the MMR vaccine to those inoculated at 15 months of age.

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