PERSISTENCE OF ANTIBODIES INDUCED BY MMR VACCINE IN INDIAN CHILDREN

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Abstract

Antibody levels were measured 6 years after MMR vaccination in 41 Indian girls. Seropositivity was 88% (measles), 95% (mumps) and 100% (rubella). MMR vaccine induces long term immunity in a majority of vaccinees; however, due to some seronegatives, the policy of second dose of MMR vaccine seems appropriate.
Measles outbreaks have been reported in immunized populations (7, 13). Similarly, mumps outbreaks have been reported in highly vaccinated populations (3, 10), including the recent large epidemic in USA (4). Both primary vaccine failure and waning immunity are responsible for the outbreaks in vaccinated populations. Infective dose and vaccine strain are important factors for long-lasting immunity (5).

In India, MMR vaccine is manufactured by the Serum Institute of India Ltd, at Pune. The vaccine contains Edmonston-Zagreb measles virus, Leningrad-Zagreb mumps virus and RA 27/2 rubella virus. Studies in Indian children using this vaccine have shown over 95% seroconversion against measles and rubella and 90% seroconversion against mumps (1, 12). The antibody persistence study would indicate the likely duration of protection afforded by the vaccine. Therefore, the present study was undertaken to assess the antibody titres persisted in a previously vaccinated pediatric population.

In November-December 1999, ninety nine healthy children aged 1 to 10 years from Kusumbai Motichand Mahila Seva Gram, Karve Road, Pune, an organization for rescue and rehabilitation of women and children, were given a single dose of MMR vaccine (Serum Institute of India Ltd), for the first time. The present study was conducted between April 2005 and August 2005 to assess the persistence of antibodies. The serological tests were conducted in the Quality Control Department of Serum Institute of India Ltd.
The study was approved by the Ethics Committee of Serum Institute of India Research Foundation. Informed written consent of legal guardian/warden of the institute and signed assent of the subjects were obtained. 41 children from this group were available for follow up in 2005. Acute febrile illness, any other infection, conditions associated with immunosuppression, receipt of immunosuppressive therapy, and participation in any other clinical trial one month before and during the course of the study, were exclusion criteria.

In 199, the batch number of vaccine used was 320-V (Expiry date – 08/2001). 0.5 ml of reconstituted vaccine was given subcutaneously. In 2005, measles and rubella IgG antibodies were assayed by ELISA technique, using Trinity Biotech kits. Mumps IgG antibodies were assayed by Calbiotech Inc. kit. For measles and rubella antibodies, the subject’s immune status ratio (ISR) values ≥ 1.1 were interpreted as seropositive. For data analysis, values below 1.1 were considered negative. For mumps antibodies, antibody index > 1.1 were seropositive. For data analysis, values ≤ 1.1 were considered negative.

Proportion of seropositives and geometric mean of IgG antibody levels were calculated, along with 95% confidence intervals. For GMT calculations, exact titres were used even for equivocal and seronegative results.

Out of 99 original vaccinated subjects, 19 were males and 66 were females. 41 subjects out of the 99 subjects were available for analysis. All the subjects met inclusion criteria and none was excluded from study. The mean age of the subjects was 14.04 years (SD
1.80 years, range 8 to 16 years). All the subjects were females. None of the males were available for follow up.

The proportion of seropositives was 36 for measles IgG (88%, 95% CI 74% to 96%), 39 for mumps IgG (95%, 95% CI 83% to 99%) and 41 for rubella IgG (100%, 91% to 100%)

The geometric means of antibody titres are given in Table 1.

A study by Boulianne N et al (2), found that at 5-6 years post immunization in children with MMR II (Merck Sharp and Dohme) and Trivirix (SmithKline Beecham), the proportion of seronegatives was as follows: Measles - 3.6% (Trivirix), and 12% (MMR II); Mumps - 7% (Trivirix), and 14.9% (MMR II); and Rubella - 3.1% (Trivirix), and 3.3% (MMR II). For measles and mumps, the proportion was significantly higher with MMR II, compared with Trivirix. The proportion of seronegatives in our study was as follows: Measles - 12.5%, Mumps - 4.82%, and Rubella – 0. Trivirix is no longer in use.

Usonis et al (9) compared mumps ELISA antibody titers 18 months after vaccination of 12-24-month-old infants with either Priorix (Glaxo SmithKline Beecham) or M-M-R II. Seropositivity rates were 80-81% with both vaccines, suggesting that both vaccines provided equivalent protection against mumps over this 18-month period.

Though statistical comparison was not possible, for measles component, our results look comparable to MMR II, as in the Boulianne study (2). For mumps and rubella antibodies,
our results look apparently better than MMR II. Similarly, the persistence of mumps antibodies in our study is higher than those reported by Usonis et al (9).

The investigators conclude that a single dose of MMR vaccine of Serum Institute of India Ltd gives a long-term seropersistence against all 3 individual diseases to a majority of vaccinees. However, some of the vaccinees may be still at risk for measles and mumps infections. It is for this reason; the World Health Organization (WHO) (6) and the Advisory Committee on Immunization Practices (ACIP) (11) recommend two doses of MMR vaccine. The Indian Academy of Pediatrics (IAP) (8) also recently updated their position to include two doses of MMR vaccine in the immunization schedule. In fact, by December 2005, 2-dose schedules were implemented in >80% of the 110 countries that have included mumps vaccine in their national immunization programmes (6). The results of the present study further reinforce this policy.

References


Table 1. Geometric Mean of Immune Status Ratios (Measles and rubella antibodies) and Antibody Index (Mumps antibodies) (n = 41)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Measles</th>
<th>Mumps</th>
<th>Rubella</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geometric Mean</td>
<td>1.8612</td>
<td>1.4484</td>
<td>2.2746</td>
</tr>
<tr>
<td>95% CI for GM</td>
<td>1.6158 to 2.1444</td>
<td>1.3508 to 1.5535</td>
<td>2.1662 to 2.3884</td>
</tr>
<tr>
<td>GSD*</td>
<td>1.5653</td>
<td>1.2482</td>
<td>1.1671</td>
</tr>
</tbody>
</table>

*Anti-log of SD of log titre values


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ERRATUM

Persistence of Antibodies Induced by Measles-Mumps-Rubella Vaccine in Children in India


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Volume 14, no. 10, p. 1370–1371, 2007. Page 1370, column 1, line 12: “... RA 27/2 rubella virus” should read “... RA 27/3 rubella virus.”