

AGE FOR MEASLES IMMUNIZATION SEROCONVERSION AFTER MEASLES VACCINATION AT 6-8 MONTHS OF AGE—A RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

The, objective of the study was to compare the effectiveness of measles vaccine by seroconversion in vaccinated children with non-vaccinated children of 6 to 8 months age group in a city slum community so as to study the feasibility of advancing the age of immunization. Live attenuated lyophilized Schwartz strain of measles vaccine was used. Hemagglutination inhibition (HI) antibody was estimated. Seroconversion was defined as either the conversion of negative to positive or a two fold rise in titre. One hundred and thirty two children completed the study. There was no difference in the age, sex and nutritional status between vaccinated and non-vaccinated groups ($p>0.7$). The seroconversion rate in the vaccinated group was 65% and in the non-vaccinated group was 26%. The age, sex and nutritional status did not significantly affect the seroconversion. Our data suggest that immunization with measles vaccine may be effective as early as 6 months of age. Immunization at 6 months may be needed at least for children in densely populated areas like cities and towns.

Key words: Seroconversion, Measles vaccine, Infants, Community.

The current recommended age for measles vaccination in India is after 9 months of age. About 10 to 15% of measles infection occurs in the age group of 6 to 8 months(1,2). The disease in infants has a high morbidity and case fatality. This study was conducted in the community to know the age specific effectiveness, as assessed by seroconversion to measles vaccine (Schwartz strain), at 6-8 months of age with a view to study the feasibility of immunization at an age earlier than 9 months.

Material and Methods

The study was a prospective randomized. trial conducted during 1988. All children between 6-8 months of age in an Integrated Child Development Services (ICDS) Project Area of Madras city were enumerated. Information regarding date of birth, measles immunization and infection were obtained by the Anganwadi workers and verified by one of the investigators from the records. Children with acute infections at the time of recruitment or those who had measles vaccination, measles infection or contact with measles within the past 2 weeks were excluded. Oral consent was obtained from the parents of these eligible children. Children were weighed to the nearest

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50 g. For nutritional assessment, Wellcome classification was followed. The individual centre in ICDS area was the unit of randomization.

Before immunization, 2 ml of venous blood was collected and 0.5 ml of live attenuated lyophilized Schwartz strain of measles vaccine 1000 TCID₅₀ was given to the study group. Adequate steps were taken for the maintenance of cold chain. Control group was not vaccinated at the time of recruitment. Children were observed at the end of one and two weeks for possible reactions. Second sample of blood was collected after 6 or more weeks. All control group children were vaccinated immediately after the second sample collection. Sera were coded and transported in ice box. They were stored at -20°C till they were tested at the King Institute of Preventive Medicine. Antibody titre was estimated using standard microtitration technique for hemagglutination inhibition (HI) antibody(3). Seronegatives becoming positive or a 2-fold rise in titre were considered as seroconverted and protective(2-4). Vaccine effectiveness was assessed as follows(5):

$$\text{Measles vaccine (seroconversion) effectiveness} = \frac{\text{Failure rate among non-immunized} - \text{Failure rate among immunized}}{\text{Failure rate among non-immunized}}$$

Out of 367 children enumerated in the study area, 205 were recruited, randomized and the first sample of blood was drawn. Six children, three in each group, had measles infection between first and second samples and were excluded. Fisher's exact test, Chi square test, t-test and analysis of variance were used for the analyses.

Results

The baseline characteristics: Sex, age and nutritional status do not significantly differ between the 205 who were recruited, and 162 who were not recruited (p>0.2). The second sample was collected from 92 (70%) children between 6 to 11 weeks, and 40 (30 %) between 12 and 21 weeks. Thus only 132 children completed the study. There was no significant difference in the distribution of sex, age and nutritional status between those who completed and those who failed to complete the study.

The baseline characteristics between the study and control groups are compared in *Table I*. There was no significant difference between the groups in the distribution of the age, sex and nutritional status. The distribution of post-immunization titre values of the study and control

TABLE I -Comparison of Baseline Characteristics Between Study and Control Groups

Characteristics	Study group (71)		control group (61)*	
	n	(%)	n	(%)
<i>Sex</i>				
Male	32	(45.1)	30	(49.2)
Female	39	(54.9)	31	(50.8)
<i>Age</i>				
6 mo	21	(29.6)	18	(29.5)
7 mo	23	(32.4)	23	(37.7)
8 mo	27	(38.0)	20	(32.8)
<i>Nutritional status</i>				
Normal	23	(32.4)	20	(32.8)
Under-nutrition+	48	(67.6)	42	(67.2)

*p>0.05 for all variables.

+Includes Marasmus, Study group 1 and Control group 3.

TABLE III– Comparison of Seroconversion Rates and Changes in GMT to Measles Vaccine Between Study and Control Groups

Age (mo)	Study group				Control group			
	n	Seroconverted (%)	Pre imm GMT	Post-imm GMT	n	Seroconverted (%)	Pre-imm GMT	Post-imm GMT
6	21	14 (67)	8.00	16.54*	18	3 (17)	10.08	5.9*
7	23	13 (56)	8.24	16.49*	23	5 (22)	12.96	8.5*
8	27	19 (20)	7.80	18.19*	20	8 (40)	8.00	10.2**
Total	71	46 (65)	8.00	17.13*	61	16 (26)	10.27	8.1**

p<0.0001.

**p>0.05 (paired t-test)

and in 36 and 25 among control group after an interval of 6-11 and 12-21 weeks, respectively. The number of children seroconverted for the corresponding time intervals were 28 and 18 in the study group and 6 and 10 in the control group. There was no difference in the seroconversion rates between, the two different time intervals of blood collection in either group. There was no significant difference in the post-immunization GMT values between two time intervals in study group ($p>0.05$) but there was a difference in the control group.

Discussion

This study was done in the community. The laboratory personnel were not provided the clinical details to avoid expectation bias(6). The control group was used to assess the significance. The seroconversion was clinically significant as the conversion rate was 65 %. Measles vaccine effectiveness observed in our study in the field was $(45/61-25/71)/(45/61)=52\%$. Seroconversion rates in vaccine efficacy studies (4,7,8) (seroconversion at ideal conditions and/or for those who have been initially seronegative) are likely to be

higher than the rates in vaccine effectiveness studies (2,9-11) (studies carried out in actual settings and include all children for analysis).

Our data is comparable to that of few studies for the age group of 6-8 months: Latin America (65%) and Halsey (63%)(7,8). However, our finding is different from that of others: lower rates were reported by Katiyar (52%), Dick (45%), Saha (34%) and Ruiz (47%) (9,10,12,13); higher rates were reported from South India (87%). Latin America (65% to 85%) and Kenya (87%) (4,7,14). Apart from other factors, the differences in the observations could be due to variations in the design, measurement and analysis of the studies. In the present study, if vaccine efficacy by seroconversion among seronegatives is alone considered, then the seroconversion rate in the study group was 29/35, i.e., 83 %, in the control group it was 9/24, i.e., 37% and the vaccine effectiveness in the field was 73 %.

If the interval between first and second blood sample collection, is too long, the possibility of subclinical infection contributing to enhanced seroconversion effect is a possible bias. This may be more so

in the control group and thereby reduce the *effectiveness* of the vaccine. There was a high increase in the GMT level among 8-months-old, in both the study and control groups. This could probably be due to sub-clinical infection. This study confirms the finding of others that seroconversion to measles is not influenced by the nutritional status (2,4,15,16).

Though the vaccine effectiveness is not high, it suggested that immunization in India may have to be considered as early as 6 months, at least for children living in densely populated areas like cities and towns where the outbreaks are more and spread of measles is rapid (17). They need another dose after 15 months of age, probably at 18 months of age, along with DPT and OPV (18,19). Close supervision is necessary to ensure that children immunized before the age of 9 months do in fact receive a second dose(20). It has been shown by many studies that low level of immune response in infants do not interfere with subsequent (second) dose of immunization (21-23).

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