OPTIMUM AGE OF A CHILD FOR BCG VACCINATION

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ABSTRACT

The objectives of this study were to evaluate whether a newborn or a neonate is capable of responding immunologically after BCG vaccination and to find out if this immunity persists for one year. Normal infants aged between 0 days-3 months brought to immunization centre were included in the study. In vitro leukocyte migration inhibition test was performed in these children using Phytohemagglutinin and purified protein derivative (PPD). They were grouped based on their age at vaccination, their LMI values and on the time interval after vaccination. The mean values of % LMI (PPD) in all the age groups were positive and there were no significant differences between the newborns, the neonates and other groups. The values were positive and comparable even after 12 months in all the groups. The percentage of infants with positive or negative values to LMI (PHA) and negative values to LMI (PPD) were also comparable at different time intervals in different age groups. The results suggest that newborns or neonates are as capable of eliciting a positive immune response after BCG vaccination, as older infants and the practise of vaccinating a child at birth could be continued.

Key words: *BCG, Immunization.*

In India, BCG vaccine is administered to majority of the infants at birth or in the neonatal period, the main reason for this being a good rate of compliance. However, doubts have been expressed regarding a newborn's capacity to acquire immunity when vaccinated with BCG(l). Also, the rate of BCG complications are thought to be high in these infants. The main objectives, of the present study were to evaluate whether a newborn or a neonate is capable of responding to BCG vaccination and to find out if BCG-induced immunity persists for atleast a year in these infants.

Material and Methods

Infants who were brought to the immunization centres of *(a)* State Tuberculosis Centre; *(b)* Tuberculosis Association of Andhra Pradesh and (c) Niloufer Hospital for Women and Children in Hyderabad during the period March 1990 to February 1994, and for whom an informed consent was obtained from the parents, were included in the study. The parents were given a reference card and were asked to report to the clinic 3 (±1) months, 6 (±1) months and 12 (±2) months after the vaccination. A detailed history of the child was recorded during each visit.

Blood was collected during any one of the visits; sampling was done only once for each child, except in subjects with negative responses during the first visit. Leukocyte

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migration inhibition test (LMIT) was per formed using one step capillary method, with PHA-P as the mitogen and PPD as the antigen(2).

$$\%LMI = 100\left[\frac{\text{area of fan in test well}}{\text{area of fan in control well}}\right] \times 100$$

% LMI ≥ 20% is considered to be positive.

For statistical analysis children were classified into different groups' based (a) on their age at the time of vaccination (0-7 days; >7 days - 1 mo; >1 mo - 2 mo and >2 mo - 3 mo; (b) on their LMI values (≥20% and <20%) and (c) on the time-interval after vaccination (3 mo, 6 mo and 12 mo). The mean values between different groups were compared using the T test.

Results

The mean values of % LMI (PPD) in all the age-groups were positive (≥20%) and there were no significant differences between different groups *(Table I).* The mean values at different time intervals after the vaccination are also shown in *Table I.* The percentages and mean values were similar in all the groups.

The percentage of infants with positive and negative LMI (PHA) but negative LMI (PPD) at different time-intervals are shown in *Table II.* In the first two age-groups 6.4% of the children had negative responses both general and specific at the end of 3 months and 4.2% and 6.7%, respectively had negative responses one year after vaccination. The percentage of children who had positive general responses but had negative responses specific to tuberculin were comparable.

Discussion

Although BCG vaccination is recommended in many countries in the Expanded Programme on Immunization, the policies vary in different countries. In England a child is vaccinated only at the age of 13 years(3), whereas EPI recommends vaccination at birth(4). Information available on the efficacy of BCG vaccination in the newborn is scanty (5). On the other hand, complications are thought to be more common in these infants (5-8). As a result, some authors recommend a lower dose of BCG, leading to further reduction in the response to tuberculin(8).

TABLE I– *Mean Values (± 1SD) of % LMI (PPD) in Children Tested at Different Time-Intervals after BCG Vaccination*

Age at vaccination	Time interval after vaccination					
	3 months		6 months		12 months	
	n	$\bar{x}$ (1 SD)	n	$\bar{x}$ (1 SD)	n	$\bar{x}$ (1SD)
0-7 days	38	30.4 (10.7)	26	30.1 (10.0)	43	35.0 (9.6)
>7 days - 1 mo	67	28.0 (8.6)	49	28.7 (9.3)	58	33.6 (10.2)
>1 mo - 2 mo	61	27.2 (9.2)	37	29.7 (10.8)	36	33.9 (10.7)
>2 mo - 3 mo	61	27.8 (9.8)	29	33.1 (10.3)	30	34. 1 (9.0)

TABLE II– *Percentage of Infants/Children with Positive/Negative LMI (PHA) and Negative LMI (PPD) Values at Different Time Intervals*

Age at vaccination	Time interval after vaccination					
	3 months		6 months		12 months	
	PHA+ PPD–	PHA– PPD–	PHA+ PPD–	PHA– PPD–	PHA+ PPD–	PHA– PPD–
0-7 days	21.1	6.4	19.2	10.3	7.0	4.2
>7 days - 1 mo	14.9	6.4	20.4	5.5	5.2	6.7
>1 mo - 2 mo	19.7	8.3	18.9	2.7	5.6	5.4
>2 mo - 3 mo	21.3	10.8	6.9	3.1	3.3	Nil

Whether a child acquires immunity after vaccination at birth, is questioned by some authors(l,9,10). Immune responses to BCG in the neonate are thought to be influenced by maternally transmitted antimycobacterial antibodies(9), which are present in high titres in neonates(ll). An earlier report suggested that there was no transplacental transfer of antigen in normal, sensitised mothers(12), but our studies (unpublished data) indicated that anti-mycobacterial IgG antibodies do cross the placenta.

However, if vaccination, is delayed, the child is needlessly exposed to environmental mycobacteria. An earlier study suggested a high rate of sensitisation of children (11 years and older) to non-tuberculous mycobacteria(13). Many of these children had antibodies to the Koch's type of mycobacteria, which are detrimental to the effect of BCG(14). Geographical differences were reported, both in the prevalence of these bacteria and in the efficacy of BCG. In Agra, BCG had to be given within the first two years for it to be optimally effective, where as in Ahmednagar the same vaccine given to teenagers could be expected to be efficacious(15).

Most of the earlier studies on this aspect were based on tuberculin reactivity. However, since tuberculin skin test responses are not reliable as a post-vaccination check in this region(16), *in vitro* immune responses were assessed in the present study. The results suggest that a newborn is as capable of eliciting positive *in vitro* immune responses as the older child, when vaccinated with BCG. There were no significant differences between* the numbers of children in different age-groups with negative responses. Though 21% children in the first age-group had negative specific responses, the incidence dropped to 10% at the end of one year suggesting that some of the children picked-up eventually. Similar observations were reported earlier(17). A study in mice has indicated that BCG-specific T cells are present as early as day 7 after inoculation at birth(18). However in a study, by Ildirim *et al.(5)* it was reported that BCG given at the end of the 3rd month provides a higher rate of response than when given during the first three days of life.

In one study, a quarter of the children who received BCG at birth had no scar(9). In the present study, 4.2% of the children vaccinated at birth had negative specific

responses at the end of one year. The general immune responses of these children were also low.

Neonatal BCG was reported to offer complete protection in children to meningitis and other disseminated forms of tuberculosis and about 65% against pulmonary tuberculosis(7). Tuberculin sensitivity confirmed high effectiveness not only six to nine weeks after BCG, but also 4 years later(19). On the contrary, in another study by Grindulus *et al.(9)* a low percentage of children were tuberculin positive 22 months after neonatal BCG vaccination.

The results, therefore, suggest that though there is a need to evaluate the specific cell-mediated immune responses of newborns and neonates after BCG vaccination by adopting more sensitive techniques, till such time, the practise of vaccinating a child at birth or in the neonatal period could be continued.

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