Evaluation of Tuberculin Skin Test Four Months after BCG Vaccination at Birth

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Summary

A study was performed on 219 infants, 111 boys and 108 girls, who were completely healthy physically. Data corresponding to the samples including sex and birth weight were recorded and the tuberculin test was performed. The response was measured as the diameter of the local firmness after 48-72h. The response to tuberculin test was positive in 110 (50.2) including 57 (51.8%) boys and 53 (48.2%) girls. Positive cutaneous responses were most commonly observed 77% among infants with birth weight of 4,000 grams. Negative cutaneous responses were most common observed in 45% of infants with less than 2,500g birth weight. Adenitis was observed in 29 (13.2%) infants, 14 girls and 15 boys, after injection. Regarding the high rates of negative tuberculin responses it is recommended to revaccinate those with negative tuberculin test or initially vaccinate them after gaining appropriate weight.

***Key words*:** tuberculin test, cutaneous response, birth weight, BCG, vaccination

Introduction

Since 1921 more than 1 billion children in more than 182 countries throughout world have been vaccinated with BCG. Vaccination with BCG does not protect against itself, but rather against uncontrolled replication and dissemination of *Mycobacterium tuberculosis* from the primary foci to other parts of the lung and body. Analysis of subgroups was also done to examine the influence of other factors on BCG efficacy. Age at vaccination was found to be weakly associated with protection; vaccine

efficacy was greater in studies of children and was decreased with increasing age. The protective effect was 85% at birth and decreased to 52% for those vaccinated at 20 years old. A more stringent analysis of the effects of age on vaccine efficacy was not possible due to lake of available data on BCG vaccination in adults. The basic reaction of the tuberculosis is the immune system response as a cellular immunity. To assess of this system response to the etiologic agent of tuberculosis, we used tuberculin skin test (TST) which is according to delayed hypersensitivity (DesPrez & Hiem 1995, Chermic 1990).

Persons contacted with the etiologic agent had positive skin test and only 10-15% of them would take disease, which half of them is related to the first year of infestation. The positivity of this test after BCG vaccination is a sign of immunity in the person. A common cause of having no response to the TST is anergy due to sarcoidosis, malignancy and lymphoma especially. The other causes are acute vital infections, vaccination with living virus, corticosteroides and immune suppressive drugs and malnutrition. The duration size of TST depends on numerous factors such as the vaccine and some genetic ones. The TST's reaction after vaccination has many variations in different countries (Bates 1996). Those persons who have positive skin test should receive treatment for prevention. In developed countries, which do not carry out BCG vaccination at birth preventive treatment is carried out but in developing countries that apply BCG vaccination at birth preventive treatment with positive skin test is not recommended. In these countries, having no BCG vaccination and positive PPD, preventive treatment should be carried out before 5 years old by World Health Organization's proposal. In concern to the importance of the PPD reaction and lacking response to TST the present study was carried out in rural areas of Kashan to evaluate the immune responses of four-month infants who were vaccinated shortly after birth.

Materials and Methods

This study was considered as a descriptive analysis, which carried out on 219 in 4 month infants received BCG vaccination after birth. The number of samples was

measured in according to the induration standard deviation of 2.23 and 95% confidence. Villages choose by clustered sampling and in each cluster all the infants who were diagnosed healthy by physician were studied. After their parents agreements TST did for infants. To do the project, 0.1ml of 5 unit PPD (Razi Ins., Karaj, Iran) was injected obliquely into the volar side of the forearm. The reaction of injected site was considered 48-72h later and the results measured by health expert with ruler and were recorded in an information form.

Information pertaining to the samples such as sex, weight at birth (less than 2500g, 2501-3000g, 3001-3500g, 3501-4000g and more than 4000g), firmness diameter (less than 5mm, 5-10mm and 11-15mm) was recorded in an information sheet. Induration skin response expected to be more than 5mm reaction was considered as a positive skin test. The dermal response frequency in samples determined and confidence interval with 95% probabilities estimated for all of the four-month infants in rural areas.

Results

The study showed that positive dermal reaction was 51.4% in boys and 49% in girls. 110 (50.2%) person had positive TST that estimated 43.6-56.8 with 95% confidence interval. The results of tuberculin test response according to sex and weight at birth are showed in tables 1 and 2.

Table 1. *Frequency of distribution of induration diameter due to BCG vaccination according to sex*

Firmness diameter (mm)	**Tuberculin response**			
	Boy	**Girl**	**Total**	**Cumulative**
No firmness	34 (30.7)	40 (37)	74 (33.8)	74 (33.8)
<5	19 (17.7)	16 (14.8)	35 (16)	109 (49.8)
5-10	50 (45)	47 (43.6)	97 (44.3)	206 (94)
11-15	8 (7.2)	5 (4.6)	13 (5.9)	219 (100)
Total	111 (100)	108 (100)	219 (100)	219 (100)

Table 2. *Frequency of distribution of tuberculin test response according to weight at birth*

Weight (gr)	Tuberculin response					
	Positive	%	Negative	%	Total	%
≤2500	7	(31.8)	15	(68.2)	22	(100)
2501-3000	30	(54.5)	25	(45.5)	55	(100)
3001-3500	43	(47.8)	47	(52.2)	90	(100)
≥3501	31	(59.6)	21	(40.4)	52	(100)
Total	110	(50.2)	109	(49.8)	219	(100)

The research findings showed that the induration diameter due to BCG vaccination was 6.8±2.9ml in boys and 6.7±2.7ml in girls. We also found adenitis in 29 vaccinated infants, 14 (48.3%) girl and 15 (51.7%) boys, and in induration diameter of 5-10mm the most adenitis observed.

Discussion

One of our important findings was negative response to TST (75%) in infants with at birth weight of less than 2,500gr and more positive response to TST (77%) in infants with at birth weight of more than 4,000gr. Such this study was carried out by Sedaghatian in United Arab Emirates (Sedaghatian *et al* 1998). This research indicated that positive tuberculin test in term infants was more than pre-term ones (less than 33 gestational weeks). The researcher did not recommend BCG vaccination at birth in pre-term infants, which had consistent with this study. They showed that the TST response in 101 pre-term infants (up to 31 gestational weeks) at 2-4 months after BCG vaccination at birth was negative in 312 percent cases and there was the induration diameter of less than 5mm in 47 percent of cases. It was recommended that BCG vaccination should not be injected in pre-term infants at birth (Sedaghatian & Kardouni 1993), which was consistent with his study.

In a study was carried out by Koohnavard, the TST response four months after BCG vaccination at birth was positive in 97% of cases in Kashan urban areas (Koohnavard 1993). Daei Parizi reported that the positive response to TST three

months after BCG vaccination at birth was 92.7% (Daei Parizi 1989). The Lidrim's study showed more positive response to TST in infants who had BCG vaccination three months after birth than infants did with BCG vaccination at birth (Lidirim & Cavusoglu 1992). The study of Chantwal indicated that the TST response was positive in 95.3% infants three months after BCG vaccination at birth in India (Chantwal *et al* 1994). Also, the 19% decrease in the positive reaction to TST in three years old child was recorded.

As it observed the result of the four recent researches was not consistent with our study. So, the causes of differences should be found in nutritive status and immunologic deficiencies. Such a relation in scientific sources has been suggested (Hydarnejad 1990). In contrast with these studies Mussipinhata showed an equal positive TST in term and pre-term infants (Mussipinhata & Goncalves 1993).

The other finding of our study was the diameter of induration at injection site. The size of induration was 5-10mm in 44.3% of cases and more than 10mm in 16% of cases. No induration with more than 15mm diameter was observed (Table 1). The results of our research indicate that infants with at birth weight of less than 2,500gr had lower frequency of positive TST therefore, it recommends that vaccination of them should be carried out at higher age (Table 2).

Regarding the high rates of negative tuberculin responses among infants with the birth weight of less than 2,500g it is recommended to revaccinatrd those with negative tuberculin test or initially vaccinate them after gaining an appropriate weight.

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