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EVALUATION OF BCG IMMUNIZATION WITHIN THE FIRST 60 DAYS OF LIFE

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ABSTRACT

The purpose of this study was to evaluate the efficacy of the BCG vaccine in the first 60 days of life in inducing delayed-type hypersensitivity (DTH), and to evaluate the reliability of the Mantoux test in comparison with the BCG test for detecting DTH.

A study was done in 885 healthy, well nourished infants 5 to 7 months old from rural areas of the Urumieh province, who received BCG immunization in the first 60 days of life. The subjects were evaluated in two random groups; the first group underwent the BCG test and for the second group a Mantoux test was performed (with 5TU).

A total of 84.2% of infants had BCG vaccine scars. Cases who had received the BCG test had a positive reaction in more than 90% and those who had scars showed increased positivity. In the second group, 63% had a negative PPD reaction (0-4 mm induration), 23.8% were weakly positive (i.e., 5-9 mm induration), and only in 13.2% was a positive reaction (10 mm or more induration) found. So in spite of successful induction of DTH by BCG vaccination at birth, the tuberculin test is not a reliable method for detecting hypersensitivity.
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INTRODUCTION

In order to protect children against the serious forms of tuberculosis (miliary and tuberculous meningitis),[6] the policy of the Ministry of Health of the Islamic Republic of Iran is to immunize infants with BCG vaccine as early as possible within the first 60 days of life, preferably at birth. The vaccine is injected intradermally in the upper portion of the left arm, at a dose of 0.05 ml. At school entry age the PPD test is carried out and if negative (induration less than 5 mm), the BCG vaccine is injected (0.1 ml) for a second time.

There were 3 studies that somehow had a point to this subject. In one of them, tuberculin tests (2 TU strength) were performed on 228 infants under 2 years of age who had been vaccinated with BCG at birth. A positive PPD reaction (greater than 6 mm induration) was found in only 8.8% and 16.2% had no BCG scar on examination; 14.9% of the studied infants had a negative PPD reaction (0-5 mm induration) together with absent BCG scars.

Another study was done in 322 infants, 3 to 18 months old who had undergone BCG immunization in their neonatal period. 99.4% of them showed BCG scars. However, in 60.5% of cases with scars, tuberculin reactions were negative (less than or equal to 10 mm induration). In the 3rd study 387 infants who had received BCG vaccination at birth were evaluated by the PPD test at 6-8 weeks postvaccination, and a total of 92% of these infants had visible BCG scars at that time. All infants were tested with PPD, but only 68% returned for the test to be read and the tuberculin test was negative (0-4 mm induration) in 14 (37%) of them. Therefore, it is important to know the fate of these large numbers of tuberculin negative cases. Is their sensitization not detectable with the tuberculin test? If not, what should be done?

Table I. Results of the tuberculin test in relation to presence or absence of BCG vaccine scars in 446 infants tested.

Test Result	Negative		Weakly Positive		Positive		Strongly Positive		Total positives		Total	
Induration (mm)	0 - 4		5 - 9		10 - 15		>15					
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Scar Present	221	49.5	101	22.6	52	11.7	4	0.9	157	35.2	378	84.7
Scar Absent	60	13.5	4	0.9	0		0		4	0.9	64	14.4
Lost data	4 (0.9%)									4	0.9	
Total	281	63	105	23.5	52	11.7	4	0.9	161	36.1	446	100

Table II. Comparison of tuberculin test results in the presence and absence of BCG vaccine scars.

Test Result	Negative		Weakly Positive		Positive		Strongly Positive		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
Scar Present	221	58.5	101	26.7	52	137	4	101	378	100
Scar Absent	60	93.75	4	6.25	0	-	0	-	64	100

MATERIAL AND METHODS

A total of 885 healthy, well nourished infants, 5 to 7 months old who had received BCG vaccination (0.05ml intradermally, on the upper portion of the left arm within the first 60 days of life) were divided randomly into 2 selected groups. The first group underwent the BCG test (0.1ml) and the second group received the tuberculin test (5 TU). Both tests were done on the volar aspect of the forearm using a short, bevelled no. 26 needle.[4,5,7] The tuberculin test was read at 68-72 hours and the BCG test was read on days one, two, three, five, seven, fourteen, twenty-one, forty-five, and seventy-five by measuring the maximum transverse induration in millimeters.[8]

RESULTS AND DISCUSSION

In this study a total of 84.2% showed BCG scars, 50.4% received the tuberculin test, and 49.6% the BCG test. 46% were female and 54% were males.

Tuberculin tests were performed on 446 infants 5-7 months of age; 84.2% of our cases had post-vaccine scars, while others have reported rates of 94.4%[2] and 92%[3]. In our study 63% had an induration of 0-4 mm (negative) in response to the tuberculin test while others reported a negative response in 37%[3]. 14.4% had no BCG scar and 13.5% of the infants had a negative tuberculin test reaction together with absent BCG scars. These results are very similar to the findings of Mallol et al.[1] (16.2% and 14.9%, respectively).

58.5% of infants who had undergone BCG vaccination had negative tuberculin tests and another 26.7% had an induration of 5-9 mm. In other words, 85.2% of infants had an induration of less than 10 mm, which differs from the 60.5% reported by O'Ryan et al.[2]

In this study the tuberculin test was negative in 63%, weakly positive in 23.5% (5-9 mm); and 10 mm or more in only 12.6% (Table I). There was a significant correlation between the presence of a BCG scar and the percent of positive tuberculin tests ($P < 0.001$).

In cases with post BCG vaccine scars 58.5% had negative tuberculin tests, but in those without scars 93.5% had a negative reaction (Table II).

Tuberculin reactions sized 10mm or more were recorded only in infants with scars pertaining to previous BCG vaccination (Table I).

An overall review of these results shows that in spite of a significant increase in the number of positive tuberculin tests and in the presence of BCG scars a high proportion of cases had a negative post BCG vaccine tuberculin reaction. Therefore, the tuberculin test is not a reliable method for detecting vaccine-induced delayed-type hypersensitivity.

The BCG test was performed on 439 infants 5-7 months

Table III. Results of the BCG test in relation to the presence and absence of scars in 439 infants tested.

Test Result	Negative		* Positive		Total	
Induration (mm)	0 - 4		> 5			
	No.	%	No.	%	No.	%
Scar Present	18	4.1	345	78.6	363	82.7
Scar Absent	12	2.7	64	14.6	76	17.3
Total	30	6.8	409	93.2	439	100

* A positive BCG test means an induration of 5 mm or more within the first 7 days of immunization at the injection site.

Table IV. Comparison of BCG test results in the presence and absence of BCG vaccine scars.

Test Result	Negative		* Positive		Total	
Induration (mm)	0 - 4		> 5			
	No.	%	No.	%	No.	%
Scar Present	18	5	345	95	363	%
Scar Absent	12	15.8	64	84.2	76	%

* A positive BCG test means an induration of 5 mm or more within the first 7 days of immunization at the injection site.

of age, 82.7% of which had post BCG vaccine scars, and a total of 93.2% had a positive reaction (i.e. an induration of 5 mm or more within the first seven days of immunization at the injection site) while only 6.8% had a negative reaction (Table III). The rate of positive tests increased to 95% in infants with scars and decreased to 84.2% in those without scars (Table IV).

We found that 77% of all infants who underwent the BCG test had a positive reaction within 24 hours; this rate increased to 90% and 92.5% after 48 and 72 hours, respectively. Only 1% was added to the number of positive reactions within 4-7 days after the test (Table V), so it seems that the appropriate time for interpretation of the BCG test is 48-72 hours later, which is similar to the tuberculin test. 65% of cases attained an induration of 5-10mm and another 27.6% had 11-20 mm induration.

In summary, the presence of a BCG vaccination scar increases the rate of positivity both in BCG and especially in tuberculin tests.

However the tuberculin test in comparison with the BCG test has a very high rate of failure in detecting delayed-type hypersensitivity (at least in the first 60 days of life) or 3 months after BCG immunization. In other words, a negative tuberculin test does not necessarily mean failure of BCG immunization and in such cases, if indicated, a BCG test is recommended. Follow up of BCG tests for 75 days revealed no side effects. A proportion of cases (6.8%) had negative BCG tests and therefore need more investigation, especially in developing countries where BCG immunization remains one of the main strategies in the control of tuberculosis.

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Table V. Induration produced in 439 BCG tested infants in relation to the time period following the test.

Test Result/ Induration (mm) / Time After Test	Negative 0 - 4	Weakly Positive 5 - 10	Positive 11 - 20	Strongly Positive 20 +	Total Positive	% Positive
one day	101	224	112	2	338	77
two days	44	51	6	-	395	90
three days	33	8	3	-	406	92.5
five days	33	-	-	-	406	92.5
seven days	30	3	-	-	409	93.5
total no (%)	30 (6.8)	286 (65.1)	121 (27.6)	2 (0.5)	409 (93.2)	93.2

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