ORIGINAL ARTICLE

Tuberculin Test on Infants and Children Who Had Been Given BCG Vaccination During Neonatal Period

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ABSTRACT On one hundred and seven children 3 months to 5 years old who had received BCG vaccination during neonatal period were reviewed with tuberculin test. This study were conducted at the children's and maternity Hospital Sri Ratu Medan for 4 months. They comprised 61 males and 46 females with moderate to well nourished. Tuberculin test was seen at 72 hours after the injection. Tuberculin test was said positive if the induration was >5 mm was found. Positive tuberculin test were found on 58 children (54.2%), out of which 49 children (84.5%) were <1 year old and 9 children (15.5%) were 1 year old. Significant difference was found in positive tuberculin test between child group of <1 year old compared to those of >1 year old ($p < 0.001$). Diameter of induration was between 0-10 mm. Most of the children (51= 47.7%) were having diameter of 5-9 mm. Median diameter of induration of tuberculin test was significant difference between child group of <1 year with those of >1-2 years, >2-3 years, >3-4 years and >4-5 years old respectively ($p<0.01$). BCG scar did not show significant relationship with tuberculin test result and age. **[Paediatr Indones 1996; 36:160-168]**

Introduction

The role of BCG vaccination and tuberculin test can not be separated from child tuberculosis. Up to now, BCG vaccination has been used to prevent child tuberculosis even though its effectiveness differs in various countries, ranging between 0-80%.[1,2] It is reported that conversion reaction following BCG vaccination only reaches 0-30%.[2]

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Putrali et al[1] stated, that it seems BCG vaccination cannot protect children from lung tuberculosis, but it is still given to infants to protect the infants and children from serious tuberculosis and disability that causes death.[1] Ten Dam[3] reported, that even though BCG vaccination at birth will give protective power, it is still needed further evaluation.

Nation-wide BCG vaccination has been carried out since 1969 as the follow up of Ciloto workshop which aimed at children of 0-14 years old without previous tuberculin test being given. Now the aim of BCG vaccination is infants of 0-11 months old.[1] WHO recommend that BCG vaccination be given since birth even though the response is not so good as when it is delayed a few months after birth.[4] BCG effectiveness in preventing tuberculosis in influenced by the use of vaccine such as strain, effectiveness, and dosage, genetic variation or immunodeficiency, age nutrition and other infections.[5,6] The scientists have the opinion that the effectiveness of BCG generally for three years which is know through tuberculin test conversion from positive to negative. Other view states that the immunity lasts for nine years, even if tuberculin test is negative, immunity still prevails.[7]

Tuberculin test is the cheapest, most accurate and secured and reliable. Other than to make tuberculosis diagnosis it is also used to evaluate individual or group immunity whom have been given BCG vaccination.[2,8] The purpose of this study is to have general picture of BCG vaccination during neonatal period.

Methods

This study was carried out cross sectionally since November 1st 1992 to February 28th 1993 at Child Policlinic in the Children's and Maternity Hospital Sri Ratu Medan. All children who have been given BCG vaccination during neonatal period at the age 3 months to years who came for brief medication or other treatment are taken into this study. Those who are suspected anergy (such as having infection, having and virus vaccination, corticosteroid, and bad nutrition) and were not present during reading were taken out of this study. Children who had been given BCG vaccination were proved by the presence of scar on right deltoid area or from the note of Policlinic report and Road-to-Health Card. Those who had been vaccinated but had no scar on right deltoid were also included in this study. The scar transversal diameter was measured in millimeters. Weight and height were measured and recorded, physical examination was carried out. Nutrition status is based on Semi Loka Antropometri result 1991 with anthropometry index of BW/A, BL/A and BW/BL with tolerance limit >- 2SD.[9]

Tuberculin test was done by Mantoux method by injecting 5 TU of PPD RT23 with 0.005% Tween 80 and 0.01% chinosol made by Biofarma, 1 flacon containing 1.5 ml as such as 0.1 ml with tuberculin disposable having dividing line with content of 1.00 ml and disposable syringe no 26 G on volar one third upper left lower arm, if failed was repeated on volar one third upper right lower arm. Reading was taken 72 hours

after injection by the researcher under good lighting in which the lower arm were slightly folded, by was or requesting the children to visit the hospital. They were excluded from the study if they did not come to the hospital. The induration occurred was measured on transversal diameter in millimeter by using transparent soft plastic ruler. Erythema, vesicle and bullous were also recorded. The tuberculin was considered positive if diameter of induration of >5 mm and negative if <5 mm. The results obtained were statistically tested by Chi-square test, Fisher exact or Kruskal-Wallis Anova using computer program (True Epistat) on level significant of $p<0.05$.

Results

Out of 110 children given tuberculin test, 107 (97.3%) children showed up for result reading and 3 children were not present during reading were taken out of this study. All the subjects had nutrition status moderate to well nourished.

Table 1. Age and sex distribution

Age (yr)	Male	Female	Total	%
< 1	38	29	67	62.6
1 -	9	5	14	13.1
2 -	5	3	8	7.5
3 -	6	3	9	8.4
4 -	3	6	9	8.4

Table 2. Tuberculin test result per age

Age (yr)	Tuberculin test		Total	%
	Negative	Positive		
<1	18	49	67	62.6
1 -	12	2	14	13.1
2 -	5	3	8	7.5
3 -	7	2	9	8.4
4 -	7	2	9	8.4
Total	49 (45.8%)	58 (54.2%)	107	100.0

Table 3. Induration diameter of tuberculin test per age

Age (yr)	Induration diameter (mm)			Total
	0 - 4	5 - 9	≥10	
< 1	18	42	7	67
1 -	12	2	-	14
2 -	5	3	-	8
3 -	7	2	-	9
4 -	7	2	-	9
Total	49 (45.8%)	58 (54.2%)	107	100.0

Not any subject showed erythema, vesicle, or bulla at the injection site

Table 4. Tuberculin test on child group of < 1 year old and > 1 year old

Age (yr)	Tuberculin test				Total	%
	Negative	%	Positive	%		
≤ 1r	18	36.7	49	84.5	67	62.2
> 1	31	63.3	9	15.5	40	37.4
Total	49	45.8	58	54.2	107	100

$X^2 = 23.869$ df = 1 p <0.001

Table 5. Relationship of tuberculin induration diameter with age

Age	Median (mm)	Variance	p
< 1	7.00	8.249	<0.001
1 -	2.00	4.533	0.010
2 -	4.00	2.982	0.002
3 -	0.00	11.028	0.003
4 -	3.00	8.5	0.002

H = 33.3061 df = 4 p < 0.01

Table 6. Relationship of BCG with tuberculin test

Tuberculin test	BCG scar				Total	%
	Absent	%	Present	%		
Negative	5	62.5	44	44.4	49	45.8
Positive	3	37.5	55	55.6	58	54.2
Total	8	7.5	99	92.5	107	100.0
Fisher's exact test				p > 0.05		

Table 7. BCG scar relationship with age

A g e	BCG scar				Total	%
	Absent	%	Present	%		
≤ 3 year	5	62.5	84	84.8	89	83.2
> 3 year	3	37.5	15	15.2	18	16.8
Total	8	7.5	99	92.5	107	100.0
Fisher's exact test				p > 0.05		

Discussion

Tuberculin test is the most effective way to view the result of BCG vaccination and is very successful in helping tuberculosis diagnose on children under five years old[8] The correct and successful vaccination of BCG will change tuberculin conversion into 95%.[2]

Moodie et al (1962), as cited by Lin[10] obtained positive tuberculin test (diameter of induration of >5 mm) 96.5% for the group vaccinated with BCG vaccine 3 days after birth, 94.8% for the group vaccinated with BCG vaccine and Smallpox vaccine within 3 days after birth and 96.5% for the group vaccinated with BCG vaccine within 3 days after birth and Smallpox vaccine 3 weeks later.[10]

Lin et al[10] on a study using 5 TU of tuberculin obtained positive tuberculin test (diameter of induration of >5 mm) on 94.9% infants. Carvenka et al[11] started with 2 TU and 5 TU tuberculin (if the result was negative tuberculin dosage would be raised into 10 TU and 20 TU or even 40 TU) on infants obtained positive tuberculin test (diameter of induration of >6 mm) with Danish, Swedish and Czechoslovakia vaccines respectively 84.6%, 82.5% and 19.5%. Rivai et al[12] on their study on infants who had been

given Biofarma BCG vaccination 1-7 days after birth, after 3-6 months of test by using 100 TU old Tuberculin, positive tuberculin test (diameter of induration of > 5 mm) on 94.45%.

Kurniawan[13] found that 25.9% positive tuberculin test (diameter of induration of > 5 mm) on children 0-5 years after Bio Farma BCG vaccination by using 2TU of PPD RT23. On group 1-2, 2-3, 3-4, 4-5 years after vaccination respectively 31.5%, 21.1%, 24.7%, 23.3% and 30.6%. Chhatwal et al[14] found that 95.3% positive tuberculin test (diameter of induration of >5 mm) at 3 months after vaccination on infants who had been given BCG vaccination during neonatal period by using 5TU of PPD. The positive rate declined significantly ($p < 0.01$) to 19% by 3 years of age. Isbagio et al[15] found that 85% and 70% positive tuberculin test (diameter of induration of >5 mm) on infants 0-9 months of age after 12-16 weeks of Bio Farma BCG vaccination and Pasteur by using 5TU of PPD RT23 with mean diameter of induration 9.94 mm and 8.62 mm.

This study used 5TU of PPD RT23 made by Biofarma. Positive tuberculin test was found on 58 children (54.2%) out of which 49 children (84.5%) were <1 year old and 9 children (15.5%) >1 year old. If diameter of tuberculin test was regarded as conversion from negative to positive, only 54.2% on children of 3 months to 5 years old conversion was found, while on children of <1 year was 84.5%. This difference may be caused by using different of BCG vaccine (strain, mode of production, concentration), tuberculin factor (type, strength and mode), limit of positive tuberculin test, sample variation age and different number of sample.

Horwitz,[16] using 11 different of BCG vaccine, after 8 to 10 weeks tuberculin test was done with 2TU of PPD RT23 greatest diameter of induration (>18 mm) on reference International vaccine, UNICEF Japan and Denmark vaccine, smallest reaction on Czechoslovakia vaccine (< 8 mm). Sutaryo,[17] compared Bio Farma BCG vaccine and Japan BCG vaccine mean diameter of induration 17.2 mm and 17.4 mm was found whereas tuberculin conversion respectively 91.9% and 87.7%. According to Brewer et al,[18] BCG strain used for vaccination is not a significant determinant of the overall efficacy in the prevention of tuberculosis. Mehta et al (1972), as cited by Miller[5] diameter of induration of >5 mm respectively 90.6%, 93.9% and 95.3% was found, if tuberculin test in 6, 8 and 12 weeks after BCG vaccination was done. If compared positive tuberculin test of child group of <1 years old with those of >1 years old, there is significant difference ($p<0.001$).

Interpretation of tuberculin test on previously given BCG infants is quite a problem to Solve.[8] According to Kendig, tuberculin test induration diameter after BCG vaccination is 5-9 mm, seldom more than 12-14 mm and if >15 mm was found superinfection is suspected.[19] Lifshit[20] reported that infants who had been given BCG vaccination during neonatal period, after 1 year tuberculin test induration >5 mm was only 10% and they have not induration of >10 mm. Horwitz[16] found that 10% had induration of >5 mm and not one reached 10 mm on infants who had been given BCG vaccination during neonatal period.

Kurniawan et al[13] found that diameter of induration of > 5 mm, > 10 mm and >15 mm respectively 25.9%, 12.2% and 6.3% on children 0-5 years after BCG vaccination. On group 0-1, 1-2, 2-3, 3-4 and 4-5 years after vaccination mean diameter of induration respectively 4.24 mm, 3.32 mm, 3.82 mm, 4.35 mm and 4.87 mm. Mean diameter of induration between group is not significant difference.

Dalimunthe et al,[21] found that 21.7% induration of tuberculin test > 5 mm on infants who had been given BCG vaccination during neonatal period after the children were 1 year old. Ildirim et al[22] reported that BCG vaccination was given to healthy full-term infants 3 days after birth compared with 3 months old, tuberculin test at age 1 year indicated significantly greater response in infants vaccinated at 3 months. Kebede,[23] investigated in 86 infants aged 6 to 24 months who had been given BCG vaccination during neonatal period, the overall conversion rate was 59%, of whom 75% showed induration not exceeding 10 mm, while Chhatwal[14] reported that infants who had been given BCG vaccination during neonatal period, at 3 months the mean diameter of induration was 10.68 mm but by 3 years it had decreased to 3.86 mm and none of the children had an induration of >10 mm.

In this study diameter of induration found varies between 0-10 mm, most of which with the diameter of 5-9 mm (51 = 47.7%), 10 mm diameter 6.5% and those of diameter >10 mm is not found. Although median diameter of induration of >1 year old group were smaller than those of <1 year old group, but induration is not waning because the subject each group is different. If compared median diameter of induration of child group of <1 years old with those of >1-2 years, >2-3 years, > 3-4 years and >4-5 years old, there is significant different ($p<0.01$).

Grindulis[24] found that 75% had BCG scar at aged 22 months who received BCG vaccine shortly after birth, 50% of those children negative response to 10 TU. Siregar et al[25] found that 34.2% of infants in Mobil Oil Indonesia Policlinic and 19.6% in Lhok Seumawe Hospital Policlinic had been given BCG vaccination know through BCG scar presence. Tuberculin test on children who had received BCG vaccination, both with and without scar were compared with those who had not received BCG is no significant difference. Young[28] investigated 701 children 1-15 year of age, showed that 82% had a documented history of BCG vaccination while only 78% had a visible scar. The prevalence of ≥5 mm induration on Mantoux testing varied from 6-26%.[28] In this study 99 (92.5%) of children have BCG scar, most of which (55.6%) shows positive tuberculin test. There is no significant difference ($p>0.05$) if BCG scar presence or not is compared with tuberculin test.

BCG scar has been mostly used as sign on having been given BCG vaccination the first two years of birth. According to WHO the proportion of children with BCG scar decreased by time increase after vaccination. Only 60% of children who have been given BCG vaccination at birth still show any scar at the age of 3 years old.[26]

According to Amrane, as cited by Suraatmaja[2] BCG scar can absence after BCG vaccination and presence of BCG scar can be used as indication on child has been

given BCG vaccination. Ildirim[22] found that mean scar diameter significantly smaller on infant who received BCG vaccination 3 days after birth compared with 3 months after birth at age 1 year. In this study, those who have BCG scar are mostly (84 = 84.8%) found among children of < 3 years old and 15.2% children > 3 years old. There is no significant difference ($p>0.05$) if the presence or absence of BCG scar is compared between children < 3 years old with those of > 3 years old.

We can conclude that on children who had received BCG vaccination during neonatal period:

1. The positive tuberculin test result were 54.2%, out of which 84.5% were < 1 year old;
2. The diameter of induration of tuberculin test was 0-10 mm; most of the children (51 = 47.7%) had 5-9 mm diameter, and no one had diameter of > 10 mm.
3. The percentage of positive tuberculin test and the median diameter of induration were significantly difference between child of <1 years old with those of >1 year old.
4. There is no relationship between BCG scar with tuberculin test result and age.

Our data also suggest that tuberculin test is better performed 3 months to 1 year after BCG vaccination. Further study is needed to rule out the relationship of tuberculin test result of children who received BCG vaccination during neonatal period with protection against tuberculosis to determine revaccination on children with negative tuberculin test.

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