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Original Research Article

Evaluation of BCG test in diagnosis of tuberculosis in BCG vaccinated children and its comparison with Mantoux test

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ABSTRACT

Background: The prevalence of active disease in India is 15-25 per thousand population, 1/4th of them being open cases. The incidence of disease is 2-3% per year. The children are particularly susceptible because of malnutrition, overcrowding and lowered imunity. The infection in children is primary whereas adults have reactivation or secondary tuberculosis which is characterized by hypersensitivity and immunity to previous exposure. Mantoux test has been a useful diagnostic test for tuberculosis since long, but it could be false negative in proved cases of milliary tuberculosis, tubercular meningitis and disseminated forms especially in malnourished children.
Methods: The prospective study was conducted in a tertiary hospital of Northern India, included 100 children admitted in hospital with clinical suspicion of tuberculosis and having been previously and immunized with bacillus calmette-guerin (BCG) in infancy as evidenced by BCG scar.
Results: BCG test was positive in all 100 children (using modified Kenneth Jones criteria), 71% cases showed an induration of more than 10 mm while 29% showed induration of 7-9 mm. Most of case with 7-9 mm induration were either severely malnourished, having preceding history of pertussis/measles or longer vaccination intervals .The mean induration size observed was 11.0 mm.
Conclusions: Induration more than 10 mm with BCG or mantoux test can well be taken as indicative of fresh tubercular infection even in vaccinated children. The modified Keneth Jones criteria are useful clinical criteria for screening of suspected cases of tuberculosis.

Keywords: BCG test, Mantoux test, Tuberculosis, Vaccination

INTRODUCTION

Humanity shall forever remain indebted to Robert Koch for unraveling the mystery of tuberculosis rightly called consumption in those times as it slowly consumed the victim. His discovery paved the way for further insight into the problem and made possible advances in control and management of the disease. The prevalence of active disease in India is 15-25 per thousand population, 1/4th of them being open cases.[1] The incidence of disease is 2-3% per year.[2] The children are particularly susceptible because of malnutrition, overcrowding and lowered imunity.[1,3-8] The infection in children is primary whereas adults have reactivation or secondary tuberculosis which is characterized by hypersensitivity and immunity to previous exposure. Dissemination in children can result in dangerous forms like CNS or military tuberculosis.[9] Mantoux test has been a useful diagnostic test for tuberculosis since long ,but it could be false negative in proved cases of milliary tuberculosis, tubercular meningitis and disseminated forms especially in malnourished children.[2,10] This led Udani et al to propose

accelerated reaction to bacillus calmette-guerin (BCG) as an alternative diagnostic test.[11] High sensitivity of BCG test as compared with mantoux test has been proved by various studies.[12] BCG vaccine developed by Calmette and Guerine of Pasteur institute, Paris in 1924 was first introduced for prevention of tuberculosis in 1948. But over years it has been observed that BCG vaccination does not provide complete protection against tuberculosis and disease is possible and prevalent among vaccinated individuals also.[1,311,13-15] The occurrence of tuberculosis in BCG vaccinated children could be because of natural waning of of BCG induced immunity, because of close contact with open cases of tuberculosis, malnutrition and concurrent infections.[1,4,16-20] Though BCG and mantoux test continue to be important tools in the diagnosis of TB, questions have been raised about their utility in previously vaccinated children.[21] Mantoux test more than 10mm 3 years after BCG vaccination and especially more than 15 mm have been suggested to be taken as indicative of fresh infection rather than previous immunization.[18,22] Similarly BCG test positive more than 10 mm have been suggested to be indicative of tubercular infection even in previously vaccinated children.[12,22] In view of these factors, the present study was undertaken for evaluation of BCG test in diagnosis of tuberculosis in BCG vaccinated children and to compare the results with mantoux test.

METHODS

This prospective study, conducted in a tertiary hospital of Northern India, included 100 children admitted in hospital with clinical suspicion of tuberculosis and having been previously immunized with BCG in infancy as evidenced by BCG scar. Children without scar were excluded even if there was history of BCG vaccination. In addition, detailed history about contact with tuberculosis patient, history of infectious diseases in the preceding 6 months, investigations like x-rays, biopsy/FNAC, ascitic/pleural fluid, CSF analysis, sputum/gastric aspirate for AFB were undertaken wherever indicated. Control study group included the children attending hospital for reasons other than suspicion of tuberculosis and having BCG scar indicative of immunization during infancy. Children aging one year, three year and five years having a previous BCG scar formed 3 subgroups in control study group. Both the groups were simultaneously subjected to BCG and mantoux test and induration sizes were noted to know the effect of previous BCG on subsequent testing in the form of induration as an evidence of vaccine induced immunity with passage of time.

Mantoux test was done with 1 TU contained in 0.1 ml of PPD R23 with tween 80 solution obtained from BCG vaccine laboratory Guindy Madras (India). It was injected intradermally to the volar surface of left forearm with tubercular syringe and reaction was recorded as induration, after 72 hours and extent of induration was measured in transverse diameter with a ruler by PEN method and interpreted as:

- 0-5 mm negative
- 6-9mm doubtful
- More than 10 mm positive.

BCG test was done using a heat stable freeze dried vaccine, obtained from Japan BCG laboratory, stored at 2 to 8 degrees in refrigerator, after fresh reconstitution and injected intradermally in left deltoid region with a tuberculin syringe and 27 G hypodermic needle. Reaction was observed for one week especially 24-72 hours and again on 5th-6th day for maximum induration size and results were interpreted as:

- 0-5 mm negative
- 5-10 mm mildly positive +
- 10-20 mm moderately positive ++
- More than 20mm strongly positive +++.

The readings of induration sizes were compared in symptomatic and control groups to estabilish diagnostic induration sizes of BCG test in previously vaccinated children. The results were also compared with mantoux test.

RESULTS

The study included 100 children admitted in hospital with clinical suspicion of tuberculosis and having been previously immunized with BCG in infancy as evidenced by BCG scar. Children without scar were excluded even if there was history of BCG vaccination. Of total number, 65% of the children were preschoolers and males outnumbered (63%) females (Table 1).

Table 1: Age and sex distribution.

Age group (years)	Male	Female	Total
0-2 years	14	04	18
2-4 years	13	09	22
4-6 years	13	12	25
6-8 years	10	05	15
8-10 years	06	03	09
10-12 years	07	04	11
Total	**63**	**37**	**100**

Among factors affecting BCG induced immunity, 80% of the children had history of contact with tubercular case out of which 50% had close contact. Malnutrition was observed in 70% (PEM) of total number of children. In present study, 72% patients belonged to rural areas with low socioeconomic status and poor housing conditions. Overwhelming infections like measles and pertussis in preceding 3-6 months were noted in 16% of cases in present study (Table 2). Among different types of tuberculosis, pulmonary tuberculosis was the most common form in all age groups, 58% being primary

complex and 14% being progressive pulmonary disease (Table 3). Tubercular lymphadenitis and abdominal tuberculosis accounted for 12% and 11% of the total patients respectively.

In present study, BCG test was positive in all 100 children (using modified Kenneth Jones criteria), 71% cases showed an induration of more than 10 mm while 29% showed induration of 7-9 mm. Most of the cases with 7-9 mm induration were either severely malnourished, having preceding history of pertussis/measles or longer vaccination intervals. The mean induration size observed was 11.0 mm (Table 4). Regarding size of induration with Mantoux test and BCG test in case of tuberculosis among previously vaccinated children, the mean induration sizes for Mantoux test and BCG test were 11.2 mm and 11.0 mm respectively (Table 5).

Table 2: Factors associated with tubeculosis among vaccinated children.

Associated factors	No. of cases (n)	Percentage	Remarks
H/O contact	80	80	50% close contacts
PEM	70	70	30% GR 3- 4
BCG> 3 years	72	72	-
Rural population	72	72	-
Infections	16	16	pertussis 10 measles 06

Table 3: Age wise distribution of tuberculosis.

Age group (years)							
0-2 years		**2-4 years**	**4-6 years**	**6-8 years**	**8-10 years**	**10-12 years**	
Type of tuberculosis	**No. of cases (percentage)**						**Total**
Primary pulmonary tuberculosis(ppc)	13	14	14	07	04	06	58
Progressive pulmonary disease(ppd)	03	03	04	02	01	01	14
Abdominal tuberculosis	01	01	03	02	02	02	11
Tubercular lymphadenitis	01	02	03	02	02	02	12
Skeletal tuberculosis (spinal)	00	02	00	01	00	00	03
CNS tuberculosis	00	00	01	01	00	00	02
Total	**18**	**22**	**25**	**15**	**09**	**11**	**100**

Table 4: Mantoux and BCG induration sizes in different age groups among tuberculosis patients.

		BCG test +ve		Mantoux test +ve	
Age group (years)	**No.of cases**	**Cases (percentage)**	**Mean induration**	**Cases (percentage)**	**Mean induration**
0-2	18	18	12.5 mm	06	11.6 mm
2-4	22	22	12.0 mm	14	10.7 mm
4-6	25	25	10.7 mm	08	12.1 mm
6-8	15	15	10.4 mm	04	10.5 mm
8-10	09	09	10.4 mm	02	10.0 mm
10-12	11	11	10.2 mm	04	12.5 mm
Total	**100**	**100**	**11.0 mm**	**38**	**11.2 mm**

Table 5: Mantoux and BCG induration sizes observed

Induration size (mm)	Mantoux test (percentage)	BCG test (percentage)
0-5	48	0
5-10	14	29
10-20	38	62
20-30	00	09
>30	00	00

DISCUSSION

Tuberculosis is widely prevalent throughout the world. Though its incidence has declined in the developed countries due to improved living standards, tuberculosis is still a major health problem in underprivileged African and Asian countries including India. BCG vaccine which was introduced to prevent disease did not prove to provide complete protection though it does modify the course of disease and lowers the incidence of severe forms of tuberculosis like CNS tuberculosis, milliary

tuberculosis and disseminated forms.[1,3,13-15] Moreover the BCG induced immunity is known to wane off with passage of time and thus there is possibility of tuberculosis in BCG vaccinated children especially where factors like malnutrition, overcrowding, concurrent infections, longer intervals since BCG vaccination and close contact with tuberculosis patients are operative.[16-20] Thus to evaluate the efficacy of BCG test and Mantoux test in diagnosis of tuberculosis among previously vaccinated children, this study was conducted and formed the basis of following observations:

The incidence of tuberculosis is known to be higher during first few years of life. In present study, 65% of children were preschoolers as also observed by other workers like Chandra P (85%), Jain (66%), Chandra and Harilal (58%) and Bhandari (63.3%).[3,4,6,7] Male children outnumbered females in all age groups forming 63% of the patients which was in consistence with findings of Jain (62.8%) and Bhandari (63.3%). This predilection for males as observed may be a reflection of the fact that male children get more attention. In our study, history of contact was found in 80% with 50% having a reference case in family members. In different studies, history of contact was traceable in 9-88% with most cases showing a reference case in family. The observation correspond with those of Bhandari (88%).[6]

Malnutrition has been observed among tuberculosis patients by most of the workers with prevalence of 60 to 100%.Reported figures include Chandra (90%), Chandra and Harilal(60%), Gh. Nabi (89%), Jain (86.8%).[3,4,7,8] In present study, PEM was observed in 70% cases with 44% being PEM grade 3-4 as per IAP classification.

In present study, 72% patients belonged to rural areas with poor socioeconomic status and poor housing conditions. 71% patients had received BCG more than 3 years back by which time the BCG induced immunity is known to wane off.[18] Overwhelming infections like measles and pertussis in preceding 6 months are well known to lower immunity and flare up even quiescent tuberculosis infection.[16-20] 16% cases in present study showed infections in the preceding 6 months.

Among different types of tuberculosis in the present study, pulmonary tuberculosis was the most common among all age groups. Similar results were found in studies conducted by Narmada (50%), Chandra (85%), Gh. Nabi (47.5%), Bhandari et al (78%) and Deshpande (79%).[4,6,8,15] The relative efficacy of BCG test ranges from 73.3% to 100%. In present study, there was 100% positivity with BCG test is consistent with the observations of Udani et al (100%), Udhani and Kandhari (100%), Choudhary et al (46.1%).[12,23,24]

CONCLUSION

At the end of the study, it was concluded that an induration more than 10 mm with BCG or Mantoux test can well be taken as indicative of fresh tubercular infection even in vaccinated children. BCG vaccine does not provide complete protection against tuberculosis and disease is prevalent even among vaccinated children. The BCG induced immunity wanes off with time and does not interfere with subsequent testing especially after 2 years. Furthermore the diagnosis of tuberculosis cannot be based on a single test. Furthermore the modified Keneth Jones criteria are useful for screening of suspected cases of tuberculosis.

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