

Original article |

EFFECTIVENESS OF BCG VACCINATION IN PREVENTION OF CHILDHOOD TUBERCULOSIS: A PROSPECTIVE STUDY FROM KISHANGANJ, BIHAR

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ABSTRACT

Introduction: BCG vaccine has shown consistently high efficacy against childhood tubercular meningitis and miliary tuberculosis and other mycobacterial diseases. It is considered to be a safe vaccine with a low incidence of adverse effects. Efficacy of BCG vaccine found in different clinical trials is variable in different geography.

Objectives: Study was done to assess the efficacy of BCG vaccine.

Materials and Methods: All the children who were less than three years of age and were previously BCG vaccinated and not-vaccinated, were included in this study. A total of sixty (60) vaccinated children and sixty non-vaccinated children were selected. These children were followed up prospectively for 24 months, at the end of which, it was seen whether they developed tuberculosis or not.

Results: Out of these 60 children in both the cases and control groups, total number of BCG vaccinated children who developed TB were 4 (i.e. 6.6%) and total number of Non-BCG vaccinated children who developed TB were 12 (i.e. 20%). Thus, the efficacy of BCG vaccine calculated in our study was 67%.

Conclusion: Most studies in different parts of the world have shown that the efficacy of BCG vaccine varies from zero to eighty percent. This study favors the efficacy of BCG vaccine. This vaccination strategy will be favorable for our children. Creation of awareness among the parents and family members for an early administration of BCG vaccine after child birth can be recommended.

Key words: BCG vaccine, efficacy, tuberculosis

INTRODUCTION

Koch believed that a successful vaccine should be a live attenuated one and several attempts were made by him. Ultimately the artificially attenuated bovine strain of Calmette and Guérin was produced by sub culturing from 1908 to 1921.¹

WHO has recommended the "Danish 1331" strain for the production of BCG vaccine.² BCG

is one of the most widely used vaccine in the world³ with 100 million doses administered every year⁴ and with more than 3 billion total doses.⁵ The BCG Laboratory of Madras, has prepared and supplied Freeze Dried BCG Vaccine from December 1967.⁶

In India, it was first tried in Madanapalle in South India in 1948.⁷ Though Initially it was given by oral route, after the Lübeck (Germany)

disaster, intra-dermal route of administration was found to be safe for mass vaccination.⁸

The rate of any adverse reaction has been reported to be between 0.1% and 19%.⁹ The protective efficacy of the vaccine in preventing pulmonary TB varied between 0-80%.¹⁰ However, its efficacy in preventing tuberculous meningitis ranged from 52/%-84%.^{11,12,13,14} A meta-analysis performed in 1994 showed that the BCG vaccine reduced the risk of pulmonary TB by 50% with greater reduction in risk of disseminated TB (78%) and TB meningitis (64%)¹⁵ The BCG vaccine has been in use for 90 years to reduce the prevalence of TB infection.

The World Health Organization currently recommends BCG vaccination for newborns in high burden countries like India.¹⁶ The vaccine is of no use in the secondary prevention of TB¹⁷ to make up for the BCG vaccine's shortfalls in preventing pulmonary TB. In 2010, 11 vaccine candidates were being evaluated in clinical trials.¹⁸ With all these background, the present study was conducted with an objective of to estimate the probability of BCG vaccination in preventing Childhood TB.

MATERIALS AND METHODS

After obtaining Institutional ethics committee approval and consent, this study was conducted in prospective comparative study design among children less than 3 years of age. The cases were taken from four medical and health service centres of Kishanganj district, Bihar. Study period was two years from Aug 2009 to July 2011. A predesigned, pretested study schedule was used to collect data. Both open and close ended questions were kept in the schedule. Privacy and anonymity of the individuals were maintained. Confidentiality thus was gained from mothers/guardians of selected children. This prospective study was done by selecting a total of 60 vaccinated children and 60 non-vaccinated children. 87% coverage of BCG vaccination (from Payne S et al)¹⁹ and 10% marginal error have been utilized to calculate the sample size. Immunization clinic attendees were recruited in this study with a random selection of four children every day from the total children who attended the clinic or less number of children when attendance of children was found poor. Two from male children and two from the female children were selected. Thus all vaccinated children (sixty) under three years

were in chance selection. Non-vaccinated children whoever were available in that age group were selected from the community keeping in mind the match for randomly selected clinic attendees. History of non-vaccination and no scar mark were criteria for selection in this group. This sample size was taken with consideration of feasibility of the work. All the vaccinated and non-vaccinated children were less than 3 years of age group. They were followed-up for 24 months, at the end of which it was seen whether they developed tuberculosis based on the following case definition (one or more of the following criteria).²⁰

Pulmonary tuberculosis suspect: Persistent Fever and / or cough for more than 2 weeks AND/OR Loss of weight / no weight gain AND/OR History of contact with suspected or diagnosed case of active tuberculosis.

Extra-pulmonary tuberculosis suspect: 1. Lymphnode enlargement of > 2 cm in one or more sites with or without periadenitis, with or without Evidence of tuberculosis; 2. Presence of an abscess with or without discharging sinus.

Confirmed Tuberculosis: The detection of AFB by sputum smear microscopy and culture examination of tissues and aspirated fluids

Study variables: Age, sex, BCG immunization status, development of TB after 24 months follow-up. The observations in this study and control groups were then compiled and results were analyzed. Tables with proportion and efficacy of BCG vaccine were described.

RESULTS

This prospective study was done by using children of the age group of 0 – 3 years. A total of 60 vaccinated and 60 non-vaccinated children were selected. They were followed up for 24 months. Age distribution of children was from 0 to 1 year, more than 1year to 2 years and more than 2 years to 3 years and each group was made of 20 children. [Table 1]. Distribution of children according to gender was 10 in each sex of the different age groups.

Four vaccines developed tuberculosis among the study population and twelve controls (non vaccinated) developed tuberculosis among the same number of population. Proportion of tuberculosis development was 6.66% and 20.00% respectively. [Table 1 & 2]. The difference was found statistically significant ($Z=-2.1483, p<0.05$).

Table 1: Distribution of children according to incidence of TB after follow-up for 24 months as per age and sex (n=120)

Age (yrs)	Sex	Vaccinees (Vaccinated)	Controls (Non vaccinated)	Vaccines developed TB (n1=60)	Controls developed TB (n2=60)
0 - 1	Male	10	10	0	1
	Female	10	10	0	2
>1- 2	Male	10	10	0	2
	Female	10	10	0	2
>2-3	Male	10	10	2	2
	Female	10	10	2	3
Total		60	60	4 (6.66%)	12 (20.0%)

Efficacy of vaccine was the concern of this study. This was determined utilizing the formula for efficacy measurement. Efficacy of BCG Vaccine in this study was found to be 67%.

Table 2: Distribution of children according to development of Tuberculosis (n=120)

Children	Developed TB	Not developed TB	Total
BCG vaccinated	04	56	60
BCG non vaccinated	12	48	60

Z=-2.1483; p<0.05

DISCUSSION

In the present study, vaccine efficacy of BCG was found to be 67% which showed the protective role of BCG in Tuberculosis. This observation was consistent with some other studies. A sixty years follow up study for long term efficacy of BCG vaccine in American Indians and Alaska Natives revealed BCG vaccine efficacy was 52% (95% confidence interval, 27%-69) which persisted for 50 to 60 years, suggesting that a single dose of an effective BCG vaccine can have a long duration of protection.¹⁵

A meta-analysis revealed that the protective effect of BCG against miliary or meningeal TB in randomized controlled trials was 86% and in case-control studies was 75%.²¹

Another meta-analysis revealed that BCG induces protective efficacy against tuberculous meningitis of 73% (67 - 79%) and against miliary disease of 77% (58 - 87%) in HIV-uninfected children.²² A case-control study was conducted in Madras to assess the efficacy of BCG in preventing tuberculous meningitis in Children which showed the protective efficacy of BCG was 77%.¹¹

A study of effectiveness of BCG vaccination among school age children at Brazil showed

that the overall vaccine effectiveness of a first BCG vaccination at school age was 25% (3-43%).²³

A study at England showed the estimate of vaccine efficacy was 52 % (95% confidence interval, 27%-69%) for bot pulmonary and extra pulmonary TB. A similar protection was observed for pulmonary tuberculosis alone. Efficacy during 10-years intervals shows a tendency to a slight but not significant waning of the protective effect over time, waning being significant for men only. This study demonstrates substantial protection by BCG lasting more than 60 years. In addition, this study suggests that BCG can provide durable protective immunity against both pulmonary and extrapulmonary disease.²⁴

One study investigated risk factors for tuberculosis infection in 979 child household contacts of 414 adult index patients with sputum smear - positive pulmonary tuberculosis in Istanbul. Contrary to the prevailing theory that BCG vaccination protects only against tuberculosis disease, this results suggest that the vaccine also protects against tuberculosis infection. This finding has important implications for understanding of the biology of tuberculosis infection and development of improved tuberculosis vaccines.²⁵

Haile M.et al (2005 June) reviewed findings related to the use of BCG vaccine, focusing on its limitations and benefits in controlling TB. Several trials showed that the protective efficacy of BCG vaccine varied between different populations. A 60 year follow-up study of American Indians reported the long term efficacy of BCG to be 52%.²⁶

Conclusion: The present study showed moderate efficacy of BCG vaccine.

Recommendations: Further studies needed in different parts of the country for different forms of tuberculosis.

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