

Preventive Role of BCG Vaccination in CNS Tuberculosis

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Article History:

Submitted: 06.05.2021

Accepted: 13.05.2021

Published: 20.05.2021

ABSTRACT

Introduction: Generally, prospective randomized trials of BCG have been used to evaluate efficacy of BCG, and retrospective case-control studies of BCG have been used to compare effectiveness of different BCG vaccine strains.

Objectives of the study: The basic aim of the study is to analyze the preventive role of BCG vaccination in CNS tuberculosis.

Material and methods: This study was conducted in the Paediatric Department of Bahawal Victoria Hospital, Bahawalpur during 2019 to 2020. All suspected cases of tubercles meningitis were evaluated by taking detailed history according to the designed proforma especially considering age, sex, socioeconomic conditions of family, history of contact with tuberculosis patients, BCG status and presenting complaints of fever, headache, neck stiffness of more than 2 weeks duration along with history of fits and loss of consciousness.

Results: A total 53 patients were included in the study. Thirty seven patients (69.81%) had no BCG scar. Among this group 35(66.03%) patients had not been vaccinated with BCG. Two (3.77%) patient had history of BCG vaccination but no scar (Vaccination failure).

Conclusion: Although many studies have shown higher sensitivity of PCR on sputum but the decrease sensitivity in case of CSF. TB prevention effectiveness of BCGs varies by manufacturer. Ascertaining the relative effectiveness of BCG vaccines from different producers may have implications when setting national and global policy, as use of strains that offer superior protection may be more cost-effective.

Key words: Hematological; TB; Diseases; BCG

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INTRODUCTION

Since 1921, Bacillus Calmette-Guérin (BCG) vaccine has been given to infants to reduce the risk of tuberculosis (TB) disease, and disseminated TB. Generally, prospective randomized trials of BCG have been used to evaluate efficacy of BCG, and retrospective case-control studies of BCG have been used to compare effectiveness of different BCG vaccine strains (Connie MO, 1995). Although measures of BCG prevention effectiveness/efficacy have not been consistent, when BCG immunization of new-borns was stopped in Sweden, a circumstance that provided a non-vaccinated comparison group, a six-fold increase in TB notifications was observed in infants (Wolfgang KJ, et al, 1992). In a prospective randomized control trial in Britain in which over 50,000 older children were allocated to no vaccination or one of two vaccine groups, comparable prevention efficacy of 81% to 84% was found among those vaccinated with BCG (*Mycobacterium bovis*) or with vole bacillus (*Mycobacterium microti*), respectively, when data were compared over a 20-year period (Lurie MB, 1964).

It is recommended that BCG should be given at birth or at the time of earliest contact with the child preferably before 9 months of age and definitively by the time he is one year old (Skamene E, 1989). In one study it is shown that tuberculin conversion rates are slightly higher when it is given a little later say at 1-3 months of age. BCG can be easily given to new born above 2000 grams of weight and is effective in preterm infants also. However small for gestational age babies show poor post vaccination conversion (Lurie MB and Dannenberg Jr AM, 1965).

Contraindication to BCG vaccination

BCG should not be given in the following conditions;

- Persons who are immunocompromised due to congenital immunodeficiency, HIV, leukemia, lymphoma.

- Patients who are on steroids, chemotherapy or radiotherapy.
- It is best to avoid BCG for a period of 4-6 weeks following measles, chicken pox, and after immunoglobulin administration.

There is a lot of controversy in the efficacy of BCG in preventing tuberculosis. Different studies have shown results on the both extremes. A very famous study conducted in South India under the supervision and assistance of WHO and US center for disease control (CDC) which was published in 1979, showed no efficacy of BCG in preventing the disease. Rather there seemed more incidences in vaccinated persons (Dannenberg Jr AM, 1989). There was a lot of controversy and objections on the results of this study and this has not been accepted universally. In other studies the efficacy of BCG has been shown upto 80%. There are many factors which influence the protection efficacy of BCG, like age at the time of administration, nutritional status, potency of the vaccine and infection with non-tuberculous environmental mycobacteria. Neonatal BCG offers almost complete protection to meningitis and disseminated disease in childhood. A large number of studies which focus mostly on childhood tuberculosis showed protective efficacy ranging from 0-80% with an average over 50% (Dannenberg Jr AM, 1984).

BCG as diagnostic modality

BCG can be used for the diagnosis of tuberculosis in place of mantoux test. It has been recommended by WHO expert committee on tuberculosis. Classically a positive BCG test is appearance of a papule with induration within 24-48 hours followed in 3-5 days by enlargement in size of the papule and pustule formation. By day 7 there is ulcer formation followed by scab formation. Total duration of reaction is 7-10 days (Inove T, et al., 1991). It is useful especially in undernourished children. There is no adverse effect of BCG on the tuberculous

disease (Lefford MJ, 1975).

Objectives of the study

The basic aim of the study is to analyze the preventive role of BCG vaccination in CNS tuberculosis.

MATERIAL and METHODS

This study was conducted in the Paediatric Department of Bahawal Victoria Hospital, Bahawalpur during 2019 to 2020. In this study 53 children aged from 6 month to 13 years suspected of having tuberculous meningitis from 3 different teaching hospital, including Mayo Hospital Lahore, Jinnah hospital and Shaikh Zayed Hospital Lahore were included in the study.

The selected cases were divided into 3 groups as following (Figure 1):

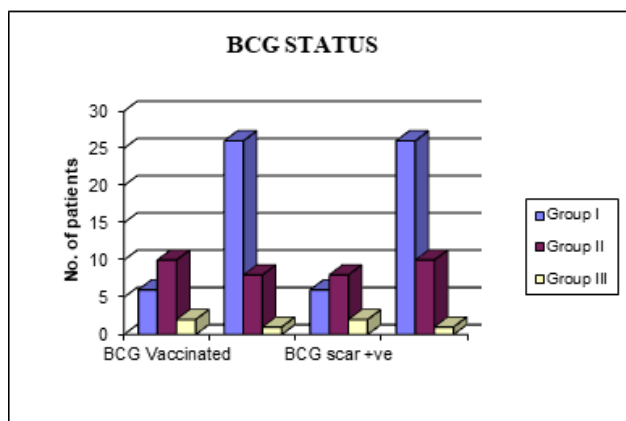


Figure 1: Graphical representation of BCG status of patients

- **Group I: Highly probable TBM:** Meeting 3 out of 5 clinical criteria and positive for at least 3 supporting tests.
- **Group II: Probable TBM:** Meeting three out of five clinical criteria and positive for 2 supporting tests.
- **Group III: Possible TBM:** Meeting three of five clinical criteria and positive for one supporting test:

All suspected cases of tuberculous meningitis were evaluated by taking detailed history according to the designed proforma especially considering age, sex, socioeconomic conditions of family, history of contact with tuberculous patients, BCG status and presenting complaints of fever, headache, neck stiffness of more than 2 weeks duration along with history of fits and loss of consciousness. These children were also evaluated for the evidence tuberculosis outside the central nervous system, and a clinical response to antituberculous therapy. Supporting evidence was obtained by examination of cerebrospinal fluid. ESR, Montoux test, X-ray chest, CT scan as mentioned in the inclusion criteria.

All patients who were suspected as cases of tuberculous meningitis were put on antituberculous treatment without waiting for the results and treatment was continued even if all these three specific test were negative, only on the bases of clinical response of the patient. Some patients who presented in stage III of TBM expired during the brief stay in the hospital some patient did survive and responded to treatment and were discharged and regularly followed. Majority of them had residual sequelae like mental retardation, hemiplegia, quadriplegia, blindness, deafness, behaviour disorders and learning disability. About half of the patients required surgical intervention and ventriculo peritoneal shunt operations were done.

RESULTS

A total 53 patients were included in the study. Out of these 53 patients 32 patients were in highly probable TBM group and 18 cases in group II (Probable TBM) and 3 patients belonged to group III (Possible TBM). Out of these 53 patients 27(50.94%) patients were male and 26 (49.05%) were females with male to female ratio of 1.03:1. Thirty seven patients (69.81%) had no BCG scar. Among this group 35(66.03%) patients had not been vaccinated with BCG. Two (3.77%) patient had history of BCG vaccination but no scar (Vaccination failure) (Table 1).

Mantoux test was positive in 25 of 32 (78.12%) highly probable cases and 10 of 18 (55.55%) probable cases and 1 of 3(33.33%) possible cases. Total 36 of 53 (67.92%) cases had mantoux test positive. Mantoux test was negative in 17 of 53 (32.07%) patients who had presented in advanced stage and were malnourished. ESR was raised in 30 of 32 (93.75%) highly probable cases and 15 of 18(83.33%) probable cases and 2 of 3 (66.66%) possible cases and total 47 of 53 (88.67%) cases had raised ESR (Table 2).

Table 1: BCG status of patients

BCG status	No. of patients	%age	Group I	Group II	Group III
BCG vaccinated	18	33.96	6	10	2
Non vaccinated	35	66.03	26	8	1
BCG scar +ve	16	30.18	6	8	2
BCG scar -ve	37	69.81	26	10	1

Table 2: Results of Mantoux test and ESR

Symptoms of patients	No of patients	Mantoux test positive % age	No of patients	Raised ESR %age
Highly probable TBM	25	75.12%	30	93.75%
Probable TBM	10	55.55%	15	83.33%
Possible TBM	1	33.33%	2	66.66%
total	36	67.92%	47	88.67%

DISCUSSION

The study data demonstrate positive but differing prevention effectiveness for clinical TB for BCG vaccines. The prevention effectiveness hierarchy of manufacturers for clinical TB was the same whether one were evaluating areas of high-or low-TB prevalence (Bothamley G and Hand Grange JM, 1991). All three BCG vaccines were also protective but with differing effectiveness observed for culture-confirmed TB and for TB meningitis. Tuberculosis is the world's leading cause of death from a single infections agent. In developing countries like Pakistan tuberculosis continuous to be major health problem. The factors responsible for failure to control tuberculosis in Pakistan are low socioeconomic conditions, lack of health education, non-compliance and drug resistance (Unanue ER, 1983). For the same reason mortality is high in developing countries. The reported tuberculosis rates among children less than 15 years of age in the United States increased by 40% from 1985 to 1993. The most severe complication of tuberculosis is infection of the central nervous system, which is invariably fatal if appropriate therapy is not administered promptly (Orme IM, 1987).

Outcome of tuberculous meningitis is strongly associated with the stage of disease at presentation. 47% among them mainly those who presented in Stage III. Our findings correspond too many other authors. In this study the median age of tuberculous meningitis is 3 years which is higher than 12 month in USA. Male to female ratio was 1.03:1 in our study in comparison to 1.38:1 according to the data collected at Baylor College of Medicines Houston, Texas (John M and Grange, 1990).

In this study 33.96% children were vaccinated with no difference in survival rate. The protective efficacy of BCG was found to be low in the moderately and severely malnourished group. It has been found that 2 patients had history of BCG vaccination but no BCG scar (Rook GAW, 1998). It points out either the faulty administration or the decreased potency of vaccine due to improper storage. In our study 66.03% patients had positive history of contact with tuberculous patients. Out of these 35.84% had adult cases of pulmonary tuberculosis with in the house (Rook GAW and Al-Attayah R, 1991). 33.96% did not disclose any history of contact. Among them were 2 patients who had received antituberculous therapy for 1 month and even then only PCR was positive and rest of the tests were negative (Khomenko AG, *et al.*, 1990). 4 patients included in the study had received ATT for more than 4 weeks and there CSF was negative for all tests including PCR. This observation is consistent with that of Lin and Harm department of neurology, Tri Service General Hospital Taipei, Taiwan China 1995.99 (Moreno C, *et al.*, 1989; Ridley DS and Ridley MJ, 1992).

CONCLUSION

Although many studies have shown higher sensitivity of PCR on sputum but the decrease sensitivity in case of CSF. The reason for this is poor yield of T. Bacillus in the specimen and secondly many patients who came to these tertiary care centers had already received anti tuberculous therapy which further reduced the chance of detecting mycobacterium Bacillus in the CSF. TB prevention effectiveness of BCGs varies by manufacturer. Ascertaining the relative effectiveness of BCG vaccines from different producers may have implications when setting national and global policy, as use of strains that offer superior protection may be more cost-effective.

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