Pak Armed Forces Med J 2005; 55(4): 304-309

CLINICAL SPECTRUM OF TUBERCULOSIS IN BCG VACCINATED CHILDREN

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ABSTRACT

A descriptive study was conducted in Paediatrics department CMH Mardan to evaluate the clinical spectrum of childhood tuberculosis in BCG vaccinated children. A total of 78 cases were completely followed up and evaluated. Out of these 74.36% had intra-thoracic lesions alone, 5.13% had isolated lymph node TB, 17.95% had disseminated forms and 2.56% had hypersensitivity phenomenon. 55% cases had positive history of contact with adult case of tuberculosis. Another important finding observed in this study was that the majority of tuberculosis cases especially disseminated forms were closely associated with malnutrition and low socioeconomic conditions in affected children. In view of this study, it is recommended that most efficient ways to reduce childhood morbidity from tuberculosis is the control of transmission from adults and BCG vaccination at birth along with improving nutritional and socioeconomic conditions of paediatric population.

Keywords: Tuberculosis, BCG, BCG vaccinated children, TB.

INTRODUCTION

The world health organization estimates that the number of new cases of tuberculosis will rise from 8.8 million cases in 1995 to 10.2 million cases in the year 2000 and 11.9 million by the year 2005 [1]. Tuberculosis kills 2 million people each year [2]. It is estimated that between 2000-2020 nearly one billion people will be newly infected, 200 million will get sick and 35 million will die from tuberculosis, if control is not further strengthened [2]. Childhood tuberculosis accounts for approximately 4% of all new cases of tuberculosis each year [3]. According to WHO estimates, in 1990 there were 1.3 million new cases of tuberculosis among children age less than 15 years [4]. BCG is the most widely used vaccine in the world. In 172 countries where this strategy is applied, 85% of infants received BCG in 1993, with average coverage ranging from 62% in Africa to 92% in Asia [5]. Nonetheless, the use of BCG vaccine has been controversial due to desparate results from different clinical trials evaluating its efficacy [6,7]. A variety of explanation for the varied responses to BCG vaccines have been proposed, including methodological & statistical variations within the trials, interaction with non-tuberculous mycobacteria that either enhances or decreases the protection afforded by BCG, different potencies among the various BCG vaccines and genetic factors for BCG response within the study population. In developing countries (including Pakistan) where BCG is used routinely, it is most commonly administered at birth or in the first year of life [7]. Despite the fact of improved BCG vaccination coverage and timely revised treatment protocols the disease is still not under control. This study was undertaken to evaluate the clinical spectrum of tuberculosis and its outcome in BCG vaccinated children.

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SUBJECTS AND METHODS

This prospective study was conducted in the Department of Paediatrics Combined Military Hospital Mardan, from 15 Mar 2002

to 15 Feb 2004. This is a descriptive study. Patients in the age group from 2 months to 12 years attending the outpatient Department or admitted in the wards with symptoms suggestive of tuberculosis were subjected for detailed evaluation. Asymptomatic children having close contact with adult TB patients were also investigated and included if found to have tuberculosis. All had BCG vaccination within the first week of life and the presence of BCG scar was verified. The clinical criteria for investigation of tuberculosis were recurrent or prolonged fever, recurrent respiratory infections, chronic or persistent cough, poor weight gain, lymphadenopathy, organomegaly, meningitis, convulsions, serous effusions and arthritis. The diagnostic criteria for tuberculosis were positive Mantoux reaction along with chest skiagram findings. In Mantoux test negative clinically suspected patients, demonstration of acid fast bacilli in gastric aspirate, lymph node biopsy revealing TB pathology or CT scan appearance characteristic of tuberculoma brain were considered as diagnostic criteria. Asymptomatic Mantoux positive children with no evidence of disease, babies less than 2 months of age (Below 2 months of age clinical manifestation of TB are uncommon unless it is intrauterine infection in which tuberculin test may not be positive, which is one of the diagnostic criteria applied in the study), those who had BCG vaccination after 7 days of life (As the study was done in properly vaccinated children and ideally BCG vaccination is to be done within the first week of life), children with BCG adenitis (BCG adenitis is an accelerated reaction to the BCG vaccine and not produced by pathogenic TB bacilli, hence can not be considered as a clinical spectrum of TB), those without BCG scar and those on empirical anti-tuberculosis drugs were excluded from the study.

Patients were assessed by detailed history, thorough physical examination and diagnostic investigations. In the history details regarding familial and extra-familial contact with TB were enquired apart from the details of the illness. Socioeconomic status was assessed by modified method of Kuppuswami [8]. Nutritional assessment was done according to modified Gomez classification [9]. Mantoux test was done for all patients and indurations exceeding 10 mm after 48-72 hours of test was considered as positive reaction [10-13,14]. X-ray chest, hemogram and urine routine examination were done for all patients. Radiological findings were analyzed with the help of a radiologist. In relevant cases gastric aspirate for AFB smear examination for three consecutive days, lymph node biopsy, cerebrospinal, pleural and peritoneal fluid studies were done. Other diagnostic possibilities were excluded by appropriate investigations. Confirmed cases were treated according to the latest guidelines of Pakistan paediatric association on tuberculosis, also keeping in view the recommendations of American Thoracic Society & American Academy of Paediatrics [9,14-16]. Patients were followed up at fortnightly intervals for minimum period of 9-12 months. During each visit they were clinically assessed for nutritional status, clinical improvement and evidence of any drug toxicity. For all children, Serum ALT was done at the end of one month after starting therapy and chest X-ray was repeated at the end of 3, 6 and 9 months of therapy. All the family members were screened with chest X-ray to exclude intra-familial contact. Siblings of index cases were screened with Mantoux test and chest X-ray to exclude asymptomatic tuberculosis.

STATISTICAL ANALYSIS

Data was analyzed using SPSS version 10.0. Results were described through percentages.

RESULTS

One hundred and thirty eight children who fulfilled the diagnostic criteria for tuberculosis were initially included in the study but final analysis was done in only seventy eight patients who could be completely followed up. Male-Female ratio

was 1:1.2. Maximum number of cases were in the 5 to 10 years age group (53.8%); 38.5% were in 2 months to 5 years age group and 7.7% were in the age group of 10 to 12 years. 61.6% belonged to low, 34.6% to middle and 3.8% to high socioeconomic groups. Statistically significant association was observed between severe forms of TB and low socioeconomic status. More than half the cases (55%) revealed positive history of contact with confirmed case of tuberculosis. Screening the family members disclosed 6 new cases.

Clinical Presentation

The predominant symptoms were fever (68%), weight loss or poor weight gain (46%) and cough with or without wheezing (65%). Significant lymphadenopathy was observed in 33% cases and seizures as initial presentation in 4% of cases. Three patients were investigated because of positive contact history and had primary pulmonary complex. Hypersensitivity phenomenon (Poncet's disease) was observed in 2 patients.

Nutritional Status

Thirty eight percent of cases had normal nutritional status and sixty two percent had protein energy malnutrition (PEM) of which 52% had Grade I or II PEM and 10% had Grade III PEM. There was a significant relationship observed between tuberculosis and nutritional status.

Diagnostic Criteria

Seventy one (91%) patients had positive tuberculin test. Out of the tuberculin negative 7 cases, 3 had lymph node tuberculosis proved by biopsy, one had tuberculoma brain proved by CT scan and one had miliary tuberculosis proved by chest X-ray and AFB positive gastric aspirate.

Skiagram Changes

Radiological findings were observed in 75 (96%) cases. The commonest radiological abnormality was parenchymal lesion (64%), hilar adenopathy (22%) and parenchymal plus nodal lesion (18%). The 3 patients without any skiagram changes had lymph node tuberculosis proved by biopsy.

Clinical Types of Tuberculosis

Primary pulmonary complex occurring alone or in combination with other lesions (74.36%) was the most commonly observed type of tuberculosis in this study. Disseminated forms of tuberculosis were 17.95%, which included multiple organ involvement, miliary TB, tuberculous meningitis, tuberculoma and lymph nodes associated with primary complex.

Outcome

Clinical improvement observed in 94% of cases at the end of one month, 98% at the end of 2 months and 100% at the end of 3 months treatment. Radiologically 20% showed complete clearance and 76% showed moderate clearance at the end of therapy. Four percent did not revealed radiological clearance in spite of clinical recovery. None of the children revealed deterioration of illness or radiological abnormality. One case (1.3%) showed drug toxicity (joint pains and increased blood uric acid level) with Pyrazinamide, which was then stopped and replaced by Ethambutol. There was no case of drug resistance or mortality.

DISCUSSION

From 1927 through 1968, 21 controlled clinical trials of the efficacy of BCG vaccines were initiated in 10 countries, of which 19 were completed and evaluated. The protective benefit was found to be extremely variable, ranging from zero to 80% [17]. In trials evaluating specific morbidities, protection against meningitis or miliary tuberculosis in children ranged from 46% to 100% [5]. In the past decade or so, there have been 14 case control studies in 12 countries, comparing tuberculosis cases to controls by BCG vaccination status. Efficacy has ranged from 2% to 83%, and against meningitis or

Clinical Types	No. of Patients	Percentage
I. Primary pulmonary complex (PPC)	58	74.36
II. Lymph node tuberculosis	4	5.13
III. Disseminated forms	14	17.95
Miliary TB	2	14.28
Disseminated TB	4	28.57
TB meningitis	4	28.57
Tuberculoma	1	71.43
Lymph node TB associated with PPC	3	21.43
IV. Hypersensitivity phenomenon (Poncet's disease)	2	2.56
TOTAL	78	100

miliary tuberculosis in children from 58% to 100%. Evaluation of house hold contacts of known cases also has shown a protective efficacy of 53% to 74% in those receiving BCG vaccine [5]. Paediatric tuberculosis is an important public health marker. A child exposed to a source of tuberculosis may develop an infection which progress to active disease or remains silent. In some western studies 65% to 75% children with active tuberculosis the localization is intra-thoracic. Other common presentations of childhood disease are lymphadenitis, miliary tuberculosis or TB meningitis [18-23].

In regional studies, Udani in his study in 2000 BCG vaccinated children with tuberculosis has observed that 91% had intra-thoracic lesions with majority having mediastinal lymph node tuberculosis. The incidence of neurotuberculosis and other types of disseminated tuberculosis were 45% each in this study. Other forms like isolated splenomegaly, hepatomegaly, single organ involvement, bone & joint tuberculosis were also observed [24-26]. Mathur et al in a comparative study between BCG vaccinated and non-vaccinated groups of patients could not find any significant difference in clinical pattern or mortality rate. In his study, the incidence of thoracic tuberculosis and TB meningitis were 24.4% & 68.6% respectively with mortality rate of 27%, in BCG vaccinated group [27]. In a recent Indian study in BCG vaccinated children, it has been observed that 72.6% had intra-thoracic lesions, 16.8% had disseminated TB, 6.32% had isolated lymph node TB and 4.2% had hypersensitivity phenomenon [28].

In the present study, 74.36% had intra-thoracic lesions alone, 5.13% had isolated lymph node tuberculosis, 17.95% had disseminated forms and 2.56% had hypersensitivity phenomenon (Poncet's disease). A control study to compare the percentage of different forms of tuberculosis in BCG non-vaccinated group was not possible due to very few numbers of such cases in the area.

Another important finding in the present study is that the majority of tuberculosis cases, especially disseminated forms were observed in children with malnutrition (62%) and in those belonging to low socioeconomic group (61.6%). This association was also seen in various other studies in past [28-30]. This association is explained by the fact that BCG vaccine enhances protection against dissemination of tuberculosis through T-Cell mediated cellular immunity which is greatly impaired in malnourished children. So the efficacy of BCG vaccination decreases markedly in the malnourished children, which usually belongs to low socioeconomic groups [31-33].

CONCLUSION

Although the protection by BCG vaccination against all forms of tuberculosis varies tremendously and is largely unpredictable in diverse settings, there is little doubt from both clinical trials and case controlled studies that BCG vaccination reduces the frequency of and deaths from such serious complications of primary tuberculosis, as TB meningitis and miliary tuberculosis.

From the present study it is concluded that almost all types of tuberculosis occur in BCG vaccinated children and 17.95% progress

to disseminated forms. Fifty five percent cases of childhood tuberculosis revealed positive history of contact with confirmed adult case of tuberculosis in the family or community. This study also revealed the low protective value of BCG vaccination against the tuberculosis in children having malnutrition and belonging to low socioeconomic status.

RECOMMENDATIONS

As deterioration in the control of tuberculosis, immediately hurts the youngest generation. So the most efficient way to reduce the childhood morbidity from tuberculosis is the control and arresting of transmission from adults with infectious disease.

Because BCG vaccination contributes to the protection of children against unnecessary deaths from some serious complications of tuberculosis like TB meningitis and miliary tuberculosis in countries (like Pakistan) where tuberculosis is frequent, access to health care is limited, and the diagnosis of infected children is difficult. Depending on the epidemiological situation this must be complimented by BCG vaccination at birth or as early in life as possible.

By improving nutritional status and socioeconomic conditions of paediatric population the protective benefits of BCG vaccination can be enhanced.

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