Value of BCG Test and PPD Test to Assist the Diagnosis of Childhood Tuberculosis

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Abstract

Objective: According to World Health Organization (WHO) criteria we classified Turkish children with suspected pulmonary tuberculosis (TB) and tried to determine the sensitivity and specifity of PPD and BCG test in the diagnosis of childhood tuberculosis. **Study Design**: In this cross-sectional study including 78 children (mean age:6.2±4.3 y) with presumptive diagnosis of TB, parameters of age, sex, weight, height, sputum samples, gastric aspirate, tuberculin skin test, BCG test, chest radiographs and thorax computerized tomography were obtained. The patients were grouped in three with clinical and laboratory findings according to the provisional guidelines for diagnosis of childhood TB proposed by the WHO criteria. Sensitivity and specifity of PPD and BCG tests were determined. **Results:** Group I: The cases proven in bacteriologically 'confirmed tuberculosis' (27, 34.6%), Group II: Patients with probable tuberculosis (21, 26.9%), Group III: Patients with suspected TB but final diagnosis is not TB (30, 38.4%). No differences in mean age and sex ratio were observed among the three groups ($p>0.05$). Sensitivity and specifity of PPD test were 44% and 80% at confirmed tuberculosis and 46% and 100% at probable tuberculosis. Sensitivity and specifity of BCG test were %77 and %39 at confirmed tuberculosis and 79% and %53 at probable tuberculosis. **Conclusions:** In our study, we assisted the diagnosis of childhood tuberculosis with WHO criteria. BCG test was found more sensitive than PPD test.

Key Words: PPD, BCG test, diagnosis, tuberculosis, WHO

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INTRODUCTION

Tuberculosis (TB) remains a common cause of morbidity and mortality in developing countries (1). Confirmation of diagnosis in children is often cumbersome because of difficulties in obtaining adequate samples for bacteriology (2). Even in secondary or tertiary-care centers, the diagnosis is confirmed in no more than 30 to 40% of patients. Traditionally, the diagnosis of TB in childhood is based on clinical criteria, such as persistent wheezing or cough, chest radiography, history of close household contact with an adult with pulmonary TB and tuberculin skin testing. In only a minority of cases Mycobacterium tuberculosis can be obtained from gastric aspirate or sputum cultures (3,4,5). For this reason, in the diagnosis of childhood TB, World Health Organization (WHO) criteria based on clinical and radyological findings is used (6,7).

There is great need for rapid, sensitive, specific, cheap and easily performed diagnostic tests for childhood tuberculosis (8). In countries which the Bacille-Calmette-Guerin (BCG) vaccination is done routinely; the value of tuberculin skin test in the diagnosis of TB is limited. Following the publication by WHO in 1964 of it's Expert Committee report on tuberculosis the value of BCG vaccine as a diagnostic method has been widely studied. Recently several studies have been performed to determine the diagnostic value of BCG test in tuberculosis (9-13).

The aim of the study is to determine the diagnostic value of PPD and BCG skin tests to assist the diagnosis of chidhood tuberculosis with WHO criteria.

MATERIALS AND METHODS

Seventy eight patients whom ages between 90 days-14 years hospitalized at Childrens' Hospital with suspected TB during the period August 2001 to May 2004 were included in this study. Selection was based on the particular attention to the provisional guidelines for diagnosis of childhood TB proposed by the WHO(6) (Table 1). A physician investigator conducted a short questionnaire and brief physical examination of each patient at enrollment. A standardized study questionnaire was used to assess clinical symptoms, history of TB contacts, previous TB diagnosis, and demographic information. Vaccination was determined by the presence of characteristic scarring. Posteroanterior and lateral chest radiographs and thorax computerized tomography (CT) were performed in all patients. The radiographs were interpreted by an independent pulmonologist blinded to the clinical diagnosis of the patient.

Sputum samples were collected from the patients in the morning. Nasogastric aspiration (NGA) was performed in young children who are unable to expectorate sputum. Sputum, gastric aspirate, and if necessary pleural fluid, cerebrospinal fluid and biopsy specimens were studied for acid-fast bacili detection by Ziehl-Neelsen stain and microscopic evaluation. Mycobacterial cultures from the

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Table 1. WHO provisional guidelines for the diagnosis of childhood TB (6)

SUSPECTED TUBERCULOSIS

--An ill child with with a history of contact with a confirmed case of pulmonary tuberculosis.

--With loss of weight, cough (> 2 weeks) and wheeze not responding to antibiotic therapy for respiratory disease

PROBABLE TUBERCULOSİS

A suspect case and any of the following:

--Positive induration on tuberculin testing

--Suggestive appearance on chest radiograph

--Histological appearance of biopsy material

--Favourable response to specific antituberculous therapy

CONFIRMED TUBERCULOSİS

--Detection by microscopy or culture of tubercle bacili from secretions or tissues

--Identification of tubercle bacili as Mycobacterium tuberculosis by culture characteristics

same specimens were performed by inoculation in Lowenstein-Jensen medium.

Tuberculin skin test

Tuberculin skin test was performed by injecting 0.1 ml 5TU RT 23 Tween 80 of purified protein derivative (PPD) solution intradermally and the dose was 0.05 ml for patients younger than 12 months. The reaction was measured with millimeters of induration after 48 to 72 hours and evaluated according to the criteria of national guideline (14).

BCG Test

The BCG solution was injected 0.1 ml intradermally. The BCG solution was Pasteur vaccine containing 800.000-3.200.000 unit 1077 stain. Indurations of 5 mm or greater were considered as positive reactions. BCG reactions were categorized as accelerated, classical and delayed reaction according to the time of appearance of the papule and induration. Accelerated reaction was defined as induration formation developing within 0-24 h and classical reaction with 24-48 h of injection. Induration formation after the third day of injection was considered as delayed reaction. The later course was defined as normal vaccine reaction. In our study the classical reaction was evaluated as BCG test positivity.

The patients' microbiological and radiological data were collected. Then patients were divided into three groups in according to WHO criteria. We tried to determine the sensitivity and the specifity of PPD and BCG tests.

The Statistical Package for Social Sciences version 11.0 (SPSS Inc, Chicago III Illinois) was used for all analyses.

Table 2. General Characteristics of Children Suspected of Having Tuberculosis

	Definitive TB (%)	Probable TB (%)	Negative TB (%)
Mean age (y)	5.2±1.8	7.5±2.1	5.0±3.0
Sex male (%)	12/27 (44)	10/21 (48)	17/30 (46)
Clinical characteristics			
PPD positivity *	12/27 (44)	10/21 (47)	-
Malnutrition	9/27 (33)	4/21 (19)	5/30 (16)
Tuberculous contact	9/27 (33)	10/21 (47)	10/30 (33)
Cough (> 2 weeks)	26/27 (96)	18/21 (85)	24/30 (80)
Radiographic findings			
Atelectasis	1/27 (3)	2/21 (9)	4/30 (13)
Parenchymal consolidation*	17/27 (62)	13/21 (61)	10/30 (33)
Mediastinal lymphadenopathy or hilar lymphadenopathy *	14/27 (51)	13/21 (61)	-
Extrapulmonary TB			
Pleurisy	5/27(18)	-	-
Meningitis	-	4/21 (19)	-
Pericarditis	2/27 (7)	-	-
Lymphadenitis	-	2/21 (9)	-

* ($p<0.05$)

The comparisons between categorized variables was made using chi-square test, $p< 0.05$ was considered significant.

RESULTS

78 patients whose ages varied between 90 days and 14 years with 56% aged under 6 years. *Mycobacterium tuberculosis* was isolated from 27 (34.6%) children, and these children were classified as confirmed TB (Group I). Twenty-one (26.9%) of patients who had positive PPD and specific radiological features were designed as probable tuberculosis (Group 2). The remain of patients 30(38.4%) were Group 3.

In the group with the diagnosis of TB (Group I and II) the mean age was 6.2± 4.3 years and 54.1% of them were girls. No differences in mean age, sex ratio, and index cases, were observed between the three groups ($p>0.05$). The demographic, clinical and radiological characteristics of these 3 groups are presented in Table 2. The documentation of bacteriological findings of Group 1 is shown in Table 3.

Of the cases 72.9% had only pulmonary tuberculosis. Together with the pulmonary tuberculosis 10.4% had tuberculosis pleurisy, 8.3% had tuberculosis meningitis, 4.1% had tuberculosis pericarditis and 4.1% had tuberculosis lymphadenitis (Table 2) . Positivity of PPD test

Table 3. Bacteriologic Results of Confirmed TB

	Ziehl-Nielsen Stains	Lowenstein-Jensen Culture
Sputum	2/23(8)	1/4 (25)
Gastric washing	19/23 (83)	2/4(50)
Spinal fluid	1/23(4)	1/4 (25)
Pleural fluid	1/23(4)	-
Total	23/23(100)	4/4 (100)

Table 4. The validity of BCG and PPD

	BCG TEST		PPD TEST	
	Confirmed TB	Probable TB	Confirmed TB	Probable TB
Sensitivity (%)	77	79	44	46
Specificity (%)	39	53	80	100
Positive Predictivity (%)	60	73	55	100
Negative Predictivity (%)	77	62	73	54

in extrapulmonary TB is 31% (4/13) and is evaluated as one case among five patients with pleurisy, one case among two patients with pericarditis. We observed two PPD pozitivity in two patients with lymphadenitis. No pozitivity has been occured in 4 patients with menengitis. We observed BCG test as positive in 9 of 13 patients with extrapulmonary TB (3/5 pleurisy, 2/4 meningitis, 2/2 pericarditis, 2/2 lymphadenitis).

We found the positivity of BCG test in 27 confirmed tuberculosisis as 21(%77) and 17 in 21 probable tuberculosis (%81). Sensitivity and specifity of PPD test were 44% and 80% in confirmed tuberculosis and 46% and 100% in probable tuberculosis. Sensitivity and specifity of BCG test were %77 and %39 in confirmed tuberculosis and 79% and %53 in probable tuberculosis (Table 4). No complication due to BCG test and tuberculin test was observed.

DISCUSSION

Although more rapid and sensitive laboratory techniques are being developed, in developing countries the diagnosis of tuberculosis in children is still made on the basis of positive tuberculin skin test, clinical and radiographic findings and history of contact with an adult source case. Tuberculosis is particularly difficult to diagnose in children because of the poor yield of standard laboratory testing and the lack of characteristic symptoms(8). Bacteriologic results were available for 45 to 83.6% of cases in previously reported series (15,16). The yield of sputum and NGA cultures and smears in children often is reported to be very low and varies greatly depending on frequency of sampling, techniques used, and stringency of criteria used to define true positive cases. In our study group, only four patients (4/78, 5.1%) were culture positive and twenty three patients (23/78, 29.5%) had positive results in Ziehl-Neelsen stains. A total of 34.6 (%27/78) were confirmed TB cases.

Radiographic evidence of pulmonary disease is often observed in pediatric patients with TB, but such findings are neither sensitive nor specific (17,18). Indeed, although the majority of our patients' chest radiographs were abnormal, only 89% of confirmed TB cases and 50% of probable TB cases demonstrated patterns highly characteristic of TB such as lymphadenopathy, primary complex, consolidation and atelectasis.

In our study no significant differences in age, sex, close household contact, malnutrition, were observed between patients with a confirmed or probable diagnosis of TB and those who were classified as negative for TB. Also no significant difference was found in respect to the presence of extrapulmonary TB between patients with confirmed and probable TB.

There is a great need for rapid, sensitive, specific, cheap and easily performed diagnostic tests for childhood tuberculosis. Recently several studies had been performed to determine the diagnostic value of BCG test in TB in addition to PPD test (9-13). In our study BCG test was found to be 77% and PPD test 44% positive in patients with confirmed tuberculosis. But the specifity of BCG and PPD tests were 39% and 80% respectively. Similar results were obtained in probable TB cases. We found higher BCG test positivity than PPD positivity in tuberculosis cases. Göçmen et al. (13) found 100% BCG test positivity and 45% PPD test positivity in 50 children with tuberculosis. Udani (11) had also observed BCG test to be 100% positive in culture proven tuberculosis. Shrivastava et al (9) found positive BCG and PPD test as 87% and 19%, respectively. When we consider the confirmed and probable TB cases together positivity of BCG test was higher.

As a conclusion, BCG is a rapid and safe test for the diagnosis of TB. BCG test is more sensitive than the PPD test but the specifity of the PPD test is higher than the BCG test. If BCG and PPD tests are applied simultaneusly, they may be more useful for the diagnosis of pulmonary TB. Additionally WHO criteria which we used in that study are practicaly useful for the diagnosis of TB.

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