Tuberculin skin testing in schoolchildren with and without BCG vaccination

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Tuberculosis still continues to be a major health problem throughout the world, especially in developing countries. During 1990, 3648 Turkish schoolchildren with and without Bacillus-Calmette-Guerin (BCG) vaccination, aged 6-7 years and 10-12 years, were intradermals tested with 5 TU of Purified Protein Derivative (PPD) to investigate the rate of production of sensitivity to tuberculin in Elazığ. BCG vaccination was not documented in 820 (22.4%) children. Tuberculin positivity, representing infection with Mycobacterium tuberculosis, rates of the unvaccinated children were found as 46 per 1000 cases for the 6-7 age group and 107 per 1000 for the 10-12 age group. The overall case rate for the latter children was more than two times than that of the former children. In the two age groups, tuberculin negativity rates in the unvaccinated to vaccinated and revaccinated children were gradually decreased from 95.4%, 89.3% to 49.8%, 42.1% and 20.5%, 20.7%, respectively. Similarly, tuberculous infection rate was gradually declined as 57.3, 28.9 and 9.7 per 1000 in the unvaccinated, vaccinated and revaccinated children, respectively. Active disease was diagnosed in eight children. Of the eight children, six were unvaccinated and two were vaccinated.

Data from our study and other studies from Turkey show that routine mass BCG vaccination and revaccination should effectively be administered on a community basis in 1990s, in Turkey, because of high incidence of tuberculous infection and a highly probable protective effect of BCG vaccine. [Turk J Med Res 1993; 11 (3): 116-119]

Key Words: BCG vaccination, PPD

The incidence of tuberculosis has decreased progressively, as the general standart of living and health status of children have increased in developed countries. This is in stark contrast to the persistent high incidence today in developing countries (1). However, after years of continual decline in developed countries, the incidence of tuberculosis is increasing in the United States (2-6). Although much of this increase was attributable to immunosuppression secondary to infection with human immunodeficiency virus, other contributary causes for the rising number of cases included increased tuberculous infection among minority groups, homeless populations, incarcerated persons and recent immigrants (6). In addition to these causes, the preventive and diagnostic methods of tuberculosis are insufficient for both developed and developing countries at present. Bacillus-Calmette-Guerin (BCG) vaccination is routinely recommended as a public health measure in developing countries with a high prevalence of tuberculosis, but sufficient protective effect are not always seen, possibly because of varying vaccine potency, improper preparation, storage or administration of BCG, poor nutritional status of many vaccine recipients, the frequency and intensity of reinfection with tubercle bacilli and interference with vaccine-induced immunity by concurrent infection with nontuberculous mycobacteria (1,7). The tuberculin skin test, which is based on the detection of delayed hypersensitivity to the antigens of Mycobacterium tuberculosis, is a diagnostic technique. Purified Protein Derivative (PPD), the preferred skin test antigen, is used in the intradermal Mantoux test.

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The present study aims to evaluate the rates of production of sensitivity to tuberculin and tuberculous infection in schoolchildren with and without BCG vaccination using Mantoux test in Elazığ region.

PATIENTS AND METHODS

The study was carried out on 3648 Turkish children in two groups, aged 6-7 and 10-12 years, from several

primary schools in Elazığ, an Euphrates region during 1990. These two age groups were especially selected as they were in first and second revaccination periods. A child was accepted to be immunized if BCG vaccine had been administered within last 3 years. Various abnormal conditions affecting PPD response such as coincident clinical viral infections, immunization with an attenuated virus vaccine, treatment with immunosuppressive agents, severe malnutrition, neoplastic diseases and other chronic systemic diseases were not included in the study groups. Tuberculin skin test with 5 tuberculin units of PPD antigen was administered to children by intradermal Mantoux method and the site of antigen injection was examined for occurrence of induration after 48-72 hours. A reaction of less than 5 mm of induration was "negative". Children demon-strating either 5 to 9mm of induration or > 10 mm of erythema ("doubtful" reaction) were routinely retested. A "positive" test was defined as one manifesting 10mm or more of induration. Unvaccinated children with indurated PPD reactions of 10 mm or more were regarded as infected with M. tuberculosis (5). However, similar reactions in vaccinated and revaccinated children were attributed to BCG immunization exclusive of a history of recent close contact with active tuberculous disease and clinical and laboratory findings of tuberculosis. Children with a history and/or physical findings consistent with vaccination and revaccination with BCG were considered infected with M. tuberculosis if they had 15mm or more of induration (5). Additionally, assessment of the disease status was determined through the use of chest roentgenograms and other diagnostic procedures, namely, acid-fast stains and cultures for M. tuberculosis from gastric washings or aerolized induced sputum in children.

Statistical evaluation was made using the chi-square test.

RESULTS

Table 1 summarizes tuberculin testing results for the 3648 schoolchildren, aged 6-7 and 10-12 years, with or without BCG vaccination. BCG vaccination was not documented in 820 (22.4%) children of which 660 (34.1%) were in the 6-7 age group and 160 (9.3%) were in the 10-12 age group. Tuberculin positivity, representing infection with M. tuberculosis, rates of the unvaccinated children were found as 46 per 1000 cases for the 6-7 age group and 107 per 1000 for the 10-12 age group. Case rate for the latter children was more than two times higher than for the former children.

The rates of tuberculin negativity in the children of two age groups with a history and/or physical findings consistent with BCG vaccination and revaccination were gradually decreased (49.8% for the 6-7 age group, 42.1% for 10-12 age group and 20.5% for the 6-7 age group, 20.7% for the 10-12 age group respectively) when compared with that of the unvaccinated children (95.4% for the 6-7 age group, 89.3% for the 10-12 age group). These decreasing rates were significantly different ($p<0.001$). Additionally, in the two age groups the rates for percent positive PPD, representing infection with M. tuberculosis, appear different from the unvaccinated to vaccinated (significantly, $p<0.001$) and revaccinated (insignificantly, $p>0.05$) children.

Tuberculous infection rate and status in children with or without BCG vaccination are shown in Table 2. According to unvaccination, vaccination and revaccination status, tuberculous infection rate were gradually decreased to 57.3, 28.9 and 9.7 per 1000 population, respectively ($p<0.001$). Active disease was diagnosed in six unvaccinated and two vaccinated children. None of the revaccinated children had infection with disease.

Table 1. Tuberculin reaction according to history of BCG vaccination

Vaccination Status	6-7 age group (n=1934) n	%	10-12 age group (n=1714) n	5
Unvaccinated (n=820)	660		160	
PPD: Negative	630	95.4	143	89.3
10mm or more	30	4.6	17	10.7
Vaccinated (n=2211)	1186		1025	
PPD: Negative	590	49.7	437	42.1
10 to 14mm	571	48.2	554	54.6
15mm or more	25	2.1	34	3.3
Revaccinated (n=617)	88		529	
PPD: Negative	18	20.5	109	20.7
10 to 14mm	69	78.4	417	78.7
15mm or more	1	1.1	3	0.6

* Unvaccinated children with indurated PPD reactions of 10 mir or more were regarded as infected with M. tuberculosis (5).

Table 2. Tuberculous infection rate and status in children with or without BCG vaccination

Vaccination status	Tuberculin positivity representing infection with M.tuberculosis	Total infection rate[a]	Infection without disease	Infection with disease
Unvaccinated (n=820)	Total : 47 Examined : 26	57.3	20	6[b]
Vaccinated[c] (n=2211)	Total : 64 Examined : 27	28.9	25	2[d]
Revaccinated[c] (n-617)	Total : 6 Examined : 4	9.7	4	

a. Per 1000 population.
b. Primary pulmonary tuberculosis was present in three cases, cervical adenitis in two and progressive (cavitary) disease in one.
c. Five vaccinated and two revaccinated children had close contact history and/or clinical and laboratory findings of tuberculosis.
d. Primary pulmoner tuberculosis was present in one case and cervical adenitis in one.

DISCUSSION

BCG vaccination is commonly used in many countries, especially in developing countries to prevent tuberculosis. BCG vaccination, when effective, does not reliably prevent disease, but interferes with the hematogenous spread of M. tuberculosis, thus reducing the risk of severe primary disease and its complications such as miliary tuberculosis and meningitis (7). Many studies from various countries of BCG vaccine efficacy among newborns and children have reported a protective effect againts all forms of tuberculosis ranging from 17 to 90% (8-18). However, protection against tuberculous meningitis and against cavitary, miliary and bone and joint tuberculosis has been estimated to be 75% or greater. The reasons for this variable protective effect have never been explained adequately (10,16,17).

Tuberculosis continues to be a major health problem in developing countries. Although morbidity and mortality rates for Turkey have declined from 350 per 100.000 and 8.8 per 100.000 population in 1980 to 58 per 100.000 and 3.7 per 100.000 population in 1987, respectively (19,20). These rates are more than approximately 3-10 times higher than for developed countries (5,7,18,21,22). Because of the high incidence of tuberculosis in our country mass BCG vaccination has routinely continued today on a community basis. However, unvaccinated children rates of 22.4% from this study and 31.3-32.2% from other studies (23,24). [35% for Turkey (20,25)] demonstrated that routine BCG vaccination of newborns and children has been neglected, thus resulting in the high rate of tuberculin positivity, representing infection with M. tuberculosis (57.3 per 1000 cases). Higher tuberculous infection rate in the 10-12 age group than in the 6-7 age group suggests that natural exposure to tubercle bacilli of children from environment increases definitely with ages. Other data from Turkey also projected high tuberculous infection rate of 35 to 45 per 1000 cases in unvaccinated children (19).

Gradual decreasing in both tuberculin negativity, associated with a possibly increased risk of tuberculous infection, and tuberculin positivity, representing infection with M. tuberculosis, from the unvaccinated to vaccinated and revaccinated children clearly indicated efficacy of BCG vaccination and revaccination. Graudal decreasing rate of tuberculosis infection with and without disease in the same children also demonstrated efficacy of BCG administration. Therefore, BCG vaccine should effectively be administrated as a method of prevention of tuberculosis on a community basis in the 1990s in Turkey and similar developing countries. BCG scheme should include first vaccination for newborn infants and revaccination for tuberculin negative children during first and second 4 to 5 year periods.

BCG aşısı olan ve olmayan okul çocuklarında tüberkülin deri testi

Tüberküloz halen bütün dünyada, özellikle gelişmekte olan ülkelerde büyük bir sağlık sorunu olarak devam etmektedir. 1990 yılında Elazığ'da tüberküline duyarlılık oranını belirlemek amacıyla BCG aşısı olan ve olmayan, 6-7 ve 10-12 yaşlarındaki 3648 okul çocuğunda 5 TU PPD ile intradermal tüberkülin testi yapıldı. 820 (%22.4) çocuğun BCG siz olduğu görüldü. Aşılanmamış çocuklarda M. Tuberculosis ile infeksiyon oranını gösteren tüberkülin pozitifliği oranı, 6-7 yaş grubunda 46/1000 ve 10-12 yaş grubunda 107/1000 olarak bulundu. Sonraki çocuklardaki infeksiyon oranının, önceki çocuklardakinin iki katından fazla olduğu dikkati çekti. İki yaş grubundaki tüberkülin negatiftik oranının; aşılanmamış, bir defa aşılanmış ve birden fazla aşılanmış çocuklarda sırasıyla: %95.4, %89.3'ten %49.8, %42.1 ve %20.5, %20.7'ye düştüğü görüldü. Benzer şekilde tüberküloz infeksiyonu oranı aşılanmamış, bir defa aşılanmış ve birdan fazla aşılanmış çocuklarda sırasıyla 57.3/1000, 28,9/1000, 9,7/1000 olarak azaldı. Sekiz çocukta aktif hasta'' tanısı konuldu. Bu sekiz

çocuktan altısı aşılanmamış, ikisi bir defa aşılanmış idi- Bu çalışma ve Türkiye'den diğer çalışmaların verileri; BCG kitle aşılamaları ve aşı rapellerinin, tüberküloz infeksiyonunun yüksek insidansı ve BCG aşısının yeterli koruyucu etkisi nedeniyle, gelişen bir ülke olan Türkiye'de 1990'larda da toplum bazında etkin olarak uygulanması gerektiğini göstermektedir.

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