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BCG Vaccination and Active Tuberculosis Prevention: A Three-Year Study

Masoomeh Alimagham [1], Saeid Aminiafshar [1], Siamak Farahmand [2], Parviz Vahdani [3], Mostafa Alavi Moghadam [4], Kamran Sharafi [1]

[1] Department of Infectious Disease, Labaffinejad Hospital, [2] Department of General Surgery, Imam Hossein Hospital, [3] Department of Infections Diseases, Loghman Hakim Hospital, [4] Department of Infections Diseases, Imam Hossein Hospital, Shaheed Beheshti University of Medical Sciences, TEHRAN-IRAN

ABSTRACT

Background: *Six to eight million people are infected with tuberculosis (TB) annually throughout the world, out of which 2 to 3 million die. BCG vaccination and its efficacy are always used in tuberculosis control planning. There are different rates of BCG vaccination efficacy in the world from 0 to 80%. BCG vaccine has different efficacy in endemic and non-endemic areas. The prevalence of tuberculosis in Iran is high; therefore it was necessary to perform a study in this regard.*

Materials and Methods: *This was a case-control descriptive study conducted from 2001- 2003. There were 50 cases of active pulmonary tuberculosis (according to WHO definitions), and 100 controls without tuberculosis admitted for other reasons.*

Results: *Vaccination was done in 10 (20%) people in the case group and 36 (36%) people in the control group (OR: 43%).Thus vaccine efficacy was calculated to be 57% in this study from the equation VE=1-OR (CI: 95% between 0.04-0.81). Twenty percent of vaccinated people have been protected from active tuberculosis in this study.*

Conclusion: *In this study vaccine efficacy was 57% (CI: 95% between 4-81%), and protection rate of vaccinated people against active tuberculosis was 20%. The effectiveness of BCG vaccine is not constant in all situations and old age and past history of contact with TB patients are confounding factors causing the low efficacy of the vaccine. While case control studies have limitations; thus, similar studies should be planned in different parts of our country for more accurate results.* ***(Tanaffos 2007; 6(2): 63-67)***

Key words: *Tuberculosis, BCG vaccine, Active tuberculosis*

INTRODUCTION

Tuberculosis (TB) is a chronic infectious disease caused by *Mycobacterium Tuberculosis*. The most important clinical manifestations are pulmonary and central nervous system involvements (e.g. meningitis and tuberculoma). Six to eight million people are infected with TB annually in the world. Two to 3 million die due to TB. In developing and undeveloped countries, 85% of mortalities are in patients between 15-59 years of age (1). Tuberculosis is the cause of 26% of preventable deaths in adults. Poverty and HIV epidemics have a profound effect

Correspondence to: Alimagham M
Address: Department of Infectious Disease, Labaffinejad Hospital, Tehran-Iran
Email address: taomani@gmail.com
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on control planning of tuberculosis. It is estimated that the disease will be controlled in the 70th decade of the 20th century but just the opposite occurred in the 80th decade with the appearance of multi-drug resistant strains (MDR) (2, 3, 4). Iran is an endemic area with a high prevalence of TB; therefore tuberculosis control should be implemented. Vaccination is an important measure for controlling tuberculosis and after World War II it was recommended by WHO for all countries. There are different rates of BCG efficacy in different parts of the world from 0 to 80%. (5). BCG vaccine has different efficacies in endemic and non-endemic areas (2, 5, 6). Prevalence of tuberculosis in Iran is high; therefore, it was necessary to plan such a study to evaluate BCG efficacy.

MATERIALS AND METHODS

This was a case-control study conducted on patients in the age range of 15-60 years with a definite diagnosis of tuberculosis from 2001 to 2003. Fifty patients with active pulmonary tuberculosis (according to WHO definition)(6) were admitted to infectious disease wards of the Shaheed Beheshti Medical University Hospitals and controls were 100 patients without tuberculosis admitted to hospitals for other reasons at the same time and had no documents for tuberculosis infection in their clinical, laboratory and radiographic examinations. Cases and controls were matched for sex and age ($\alpha = 0.05$ and $\beta = 0.1$). The parameters in this study were age, sex, past history of vaccination, close contact with a known case of active tuberculosis, marital status, number of family members living with each other and level of education. BCG vaccination was confirmed by interview and observing the scar of vaccine in the arms as well as and vaccination card. (7, 9, 10, 17)

RESULTS

In the case group 24 (48%) were males and 26 (52%) were females, and in the control group 48 (48%) were males and 52 (52%) were females. In the case group 34 patients (68%) were living in the city and 16 (32%) were living in villages. In the control group 83 (83%) were living in the city and 17 (17%) were living in villages. Vaccination was done in 10 (20%) patients in the case group and 36 (36%) in the control group. A significant correlation was found between the place of residence and vaccination but no significant difference was seen between other parameters (p=0.03). Also, a significant correlation was found between age and close contact with a case of active tuberculosis. It means that those in contact with cases of active tuberculosis have been in lower age groups (p=0.03). In this study OR was 43%; thus, vaccine efficacy from the equation (VE= 1-OR) was calculated to be 57% (CI: 95% between 0.04-0.81), and by using Chi-square test, the difference between age, sex and close contact with a case of known active tuberculosis was significant. Specific OR in males was 21 and VE was 79% and specific OR in females was 60% and VE was 40%. Specific OR in those who had close contact with a case of known active tuberculosis was 13% and VE was 73% and specific OR in those who had no close contact with cases of known active tuberculosis was 34% and VE was 66%.

Table 1. Partial and complete distribution of characters in control and case groups.

Characters	N = 50 Case (%)	N =100 Control (%)	Result
Male	24 (48)	48 (48)	Chi2 (1) =0
Female	26 (52)	52 (52)	NS
Single	41 (82)	68 (68)	Chi2 (1) =3.29
Married	9 (0.18)	32 (32)	NS
With contact	7 (14)	7 (7)	Chi2(1)= 1.14
Without contact	43 (86)	93 (93)	NS
Not literature	24 (48)	41 (41)	
Primary school	12 (24)	20 (20)	Chi 2(4)= 7.12
Secondary school	8 (16)	9 (9)	NS
Diploma	4 (8)	25 (25)	
University degree	2 (4)	5 (5)	
Urban	34 (68)	83 (83)	Chi (1) =4.37
Rural	16 (32)	17 (17)	P=0.037
Vaccinated	10 (20)	36 (36)	Chi2(1)= 4.17
Unvaccinated	40 (80)	64 (64)	P= 0.041

*NS: Not Significant

Table 2. Crude and matched odds ratio BCG vaccine effectiveness on tuberculosis according to sex.

Sex group	Odds ratio
Male	0.2 VE= 79%
Female	0.6 VE= 40%
Crude	0.4
Matched	0.4
Test for heterogeneity	Chi2 (1)= 1.2 P1> Chi2=0.3
Mantel-Haenszel	Chi2 (1)= 4.2 P1.Chi2= 0.04

Table 3. Crude and matched odds ratio BCG vaccine effectiveness on Tuberculosis according to contact.

Contact history	Odds ratio	CI=95%
With contact	1.33 VE= 0.3%	0.16-0.81
Without contact	0.34 VE=0.6	0.14-0.85
Crude	0.43	0.19-0.96
Matched	0.41	0.18-0.95
Test for heterogeneity	Chi2 (1)= 1.2 P1. Chi2=0.26	
Mantel-Haenszel	Chi2 (1)= 4.32 P1.Chi2= 0.03	

Table 4. Crude and matched odds ratio BCG vaccine effectivness on tuberculosis according to age.

Age group	Odds ratio	CI=95%
15-29	0.29 VE= 80 %	0.46-0.87
30-44	0.65 VE=32	0.16-2.34
45-60	0.2986 VE=72	2.49
Crude	0.43	0.19-0.96
Matched	0.36	0.14-0.88
Test for heterogeneity	Chi2 (1)= 1.2 P1. Chi2=0.54	
Mantel-Haenszel	Chi2 (1)= 5.10 P1.Chi2= 0.02	

DISCUSSION

There are 14 case-control studies on the efficacy of BCG vaccinations to date and only 5 of them were accepted by the World Health Organization. BCG vaccine effectiveness was between 89% in San Paulo and 2% in Argentina (6, 7, 8, 9, 10). Since the BCG vaccination is a mass campaign in governmental programs, we can not perform an interventional study in this regard; thus, a case control study is a useful method for assessing the effectiveness of BCG vaccination (11, 12). In studies reporting a low efficacy of vaccine, the cases' information were derived from the records of patients with tuberculosis, thus we can not make a correct estimation regarding BCG vaccination. (13, 14) One of the important factors in assessing the effectiveness of BCG vaccination is the definition of cases. In this study the disease was confirmed by clinical, laboratory (sputum smear and culture) and radiographic examinations. For evaluation of the past history of vaccination we checked vaccination cards or we checked the scar of vaccination and interviewed patients and their family members. In one study in Chili after vaccination of 635 neonates only 3 of them did not have scar, so this phenomenon has no significant effect on this study (15) Vaccine effectiveness can be contributed by some factors including Vaccine preparation, handling, cold chain, injection technique, immune system status of cases and history of past sensitivity to atypical mycobacteria (16).

In this study, we considered different factors that may contribute in vaccine immunity. Other parameters in this study were as follows: age, sex, past history of vaccination, close contact with a known case of active tuberculosis, marital status, number of family members living with each other and level of education. There were no significant differences between cases and controls in age, sex,

close contact with a known case of active tuberculosis, marital status, number of family members living with each other and the level of education and vaccine effectiveness. But there were significant differences between cases and controls in regard to close contact with a known case of active tuberculosis and place of residence. In our study the effectiveness of vaccine in older age groups was lower than in younger ones. In a study in Chili, TB cases had lower levels of education, lower weight, and lower socioeconomic income than controls (15, 17). In some studies performed in Bangkok and Barcelona the protective effect of vaccine was higher in neonates than adults (8, 9, 11, 18). In a study conducted in England, the protective effect of vaccine diminished 10 to 12 years after vaccination, therefore the BCG booster vaccine has to be injected at age 10 or more rather than in 6 year olds (11).

In our study BCG vaccine efficacy in cases with no close contact to a known case of active tuberculosis diminished 66%. This rate was 0.3% in those with close contact to a TB patient. Therefore when the cases have contact with sources of infections the efficacy of vaccine diminishes and may have no protective effect anymore.

In the study conducted in Bangkok, the efficacy of BCG vaccine in a group of patients without close contact with a known case of active tuberculosis was 95%, while this rate was 50% in those with a history of close contact with TB patients (11). Protective effects of vaccine are high in severe forms of disease (e.g. meningitis). In a study in San Paulo, the risk of meningitis in unvaccinated children was 12.5 times greater than in vaccinated ones; on the other hand, in children with close contact with infected cases the risk of tuberculous meningitis was 61.3 times greater than in children without contact (7, 19).

In our study the effectiveness of BCG vaccine was 79% in males and 40% in females, which shows the effect of sex on vaccine efficacy. Similar studies in Barcelona have shown the effectiveness of vaccine to be about 41% in males and 22% in females. Similar results have been reported in Bangkok and Queens- land studies (18).

CONCLUSION

BCG vaccination is a mass campaign in governmental health programs; as a consequence we cannot have interventional studies in this way. Based on the results of this study, there was a significant difference between place of residence and vaccination, but there were no significant differences among other parameters. In this study vaccine efficacy was 57% (CI: 95% between 0.04-0.81), and protection of vaccinated people against active tuberculosis was 20%. Effectiveness of BCG vaccine is not steady in different situations. Advanced age and past history of contact with TB patients are confounders that can cause low efficacy of the vaccine. Despite the fact that case-control studies have limitations in conduction and may have selection bias, as a consequence similar studies should be planned in different parts of our country to reach more accurate results.

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