Effectiveness of BCG Vaccination in Children in the Gorkha District

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Abstract

Studies of the effectiveness of BCG in various countries over the past 50 years have resulted in a wide range of results. In an attempt to disclose the possible reasons for the great variation in the results of the major prospective trials the World Health Organization has recommended that retrospective case-control BCG efficacy studies be done in a number of varying countries. (WHO Weekly Epidemiological Record, 1983). During a three month period from December 1983 through March 1984 at Amp Pipal Hospital, Gorkha District, we compared the frequency of BCG scars in 100 tuberculosis cases under 5 years of age and 100 controls matched for age and sex. Thirty percent of the case group had a BCG scar at the time of diagnosis while 79% of the disease-free control subjects had a BCG scar. Using these findings, the effectiveness of BCG vaccination in children under 5 years of age in the Gorkha District is 88.5%. A few unavoidable potential biases inherent in the case-control study design may be partly responsible for the encouraging results.

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Introduction

BCG vaccination has been used for tuberculosis prevention for more than 50 years; however the study of its effectiveness has been clouded with controversy. The eight major BCG trials, recently reviewed in the Journal of the American Medical Association (Clemens et al, 1983), show a range of efficacy from 75% - 80% in the U.K. and in American Indians to 50% efficacy in American School children (Clemens et al, 1983). The most recent results from the Chingleput trial in South India, the largest BCG trial to date with 270,000 participants and 7.5 years follow-up, show no protective effect overall. However, among children initially aged 0-14 years BCG showed some protective effect (Tuberculosis prevention Trial, Madras, 1979).

For this reason, the World Health Organization has recommended that retrospective case-control efficacy studies be done in a number of developing countries to examine the frequency of BCG scars in child cases and in disease free control subjects (WHO Weekly Epidemiological Record, 1983). P. G. Smith points out that case-control studies would have a number of advantages in studying BCG efficacy: 1) the cost would be small, 2) the study could be completed in a short period of time, and 3) case-control studies done in a number of varying areas could possibly help to disclose the reasons for the great variation in the results of the major prospective trials (Smith, 1982).

In Nepal, BCG has been used for tuberculosis control since the mid-1960's, first in Kathmandu and then in the hill and Terai regions (Worth and Shah, 1969). This study estimates the effectiveness of BCG in the Gorkha district.

Tuberculosis cases were selected from a chart review of all the children under five years of age (at the beginning of tuberculosis treatment) who were under treatment or had begun treatment for tuberculosis at Ampipal Hospital in the past three years. Charts with consistent diagnostic criteria as outlined below were selected and then it was noted from the chart whether the patient has a BCG scar or not on initial presentation. Ideally, each tuberculosis case should have been examined personally for a BCG scar, but this was impossible for two reasons: 1) BCG vaccination was sometimes used as a diagnostic tool at the time of presentation, and 2) villages are spread out over such a large walking distance that visiting each village where the cases come from was technically impossible.

Methods

100 tuberculosis cases were identified and controls were matched for age and sex. After

finding the rate of BCG scars in each group an odds ratio (i. e. the relative risk of not having a BCG vaccination) was calculated in the following manner:

		TB no TB	
no	BCG	A	B
	BCG	C	D

odds ratio = $A \times D / C \times B$

Effectiveness would then be $100 (1 - \frac{1}{\text{odds ratio}})$ (Smith, 1982).

Ninety five percent confidence limits were then obtained using the method presented by P. G. Smith, which allows calculation of confidence limits on the efficacy found knowing the number of cases and matched controls and the percent of the population vaccinated (Smith-1982).

The record system at Amp Pipal Hospital is very good, especially concerning the records of children under 5 years old. An essential part of the examination of every child, and especially of those suspected of having tuberculosis, is the presence or absence of a BCG scar, which by convention in Nepal, is given on the right deltoid region. In each case selected the presence or absence of a scar had been confirmed by both a nurse and a physician.

If one or more of the following diagnostic criteria were met the child was selected as a tuberculosis case; 1) fever $\pm$ cough for more than 1 week + positive chest x-ray, 2) Gibbus spinal deformity by x-ray, 3) chronic, large, non-tender cervical adenopathy + (fever for more than 2 weeks or positive case in the family or response to only tuberculosis treatment) or 4) chronic meningitis (more than 1 week)

Controls were selected from children attending the under five clinic with presenting complaint, history and examination that could not be attributed to tuberculosis. The presenting complaint could not include cough of any duration, fever for more than 2 days (all patients with fever had to have a probable non-tuberculous cause for the fever such as otitis media or upper respiratory infection), neck adenopathy, spinal deformity, signs or symptoms of meningitis, psoas abscess or skin tuberculosis. Also, any past history of cough or fever for more than 3 days or any of the above signs or symptom excluded the patient from the control group.

Each control child was examined by the author for the presence or absence of a BCG scar and then each control was matched with a tuberculosis case of the same sex and age (within + or - 2 months). Unfortunately, it was impossible to match for village of residence because patients come from such a vast number of villages which are spread out over a very large area and it was impossible in the 3 month duration of the study to visit each village.

Discussion

This result is the highest value for efficacy ever obtained in a study of BCG efficacy. A few unavoidable potential biases may be responsible for this:

1) The case group and the control group may actually be from two different populations. Relatively healthy children who are regular visitors to the under five clinic will probably have a BCG scar simply because they had been to the clinic previously. These children may also be better nourished and generally better cared for than those who had not been to the clinic previously. Forty-four out of the 100 controls had never been to the clinic before and 29 (65.9%) of these children had BCG scars. However, the remaining 56 controls had been to the clinic at least one time previously and 50 (89.3%) of these children had BCG scars. This confirms that the children who had been to the clinic at least one time previously had a higher rate of BCG vaccination (89.3%) than those who were first-time visitors and received their BCG elsewhere (65.9%).

Unfortunately, it was impossible to discover from the tuberculosis case's records whether they had been regular visitors to the clinic before diagnosis or whether they presented for the first time to the clinic with tuberculosis, which made it impossible to match for this factor.

If one uses only the 44 first-time visitor controls (65.9% scar rate) with their matched cases the odds ratio becomes 4.5 and efficacy becomes 77.8%. Unfortunately, 100 first-time visitors controls were not available in the three month time span of the study so that the entire control group could consist of first-time visitors. Ideally the tuberculosis cases should be selected on the day they appear at the clinic and not from a chart review. This would allow for diagnosis and analysis of BCG scar by the same doctor, and it would also make it possible to know whether the tuberculosis cases were first-time visitors and would allow for matching for that as well. In addition, examination and matching for varying levels of gene-

ral health such as malnutrition could be done. If feasible, control should be selected from a visit to each case's village instead of from the clinic. This was impossible in the short amount of time available.

2 Another problem that biases in favor of efficacy is that in diagnostic decision making in Amp Pipal the presence of a BCG scar biases against making the diagnosis of tuberculosis and the absence of a BCG scar biases in favor of making the diagnosis of tuberculosis. This would falsely increase the efficacy of BCG.

3) A problem that biases against efficacy, but is accounted for in the term "overall protective effect": or "effectiveness" (Smith, 1982), is that children may have been infected (i.e., PPD+) before BCG vaccination and therefore would gain no protection from BCG (no PPD testing is done before vaccination). Very few children are born in the Amp Pipal Hospital (100 deliveries in the past year). Therefore, very few children are vaccinated at birth (one in this study). Children are vaccinated either at birth (one in this study). Children are vaccinated either by government or charity BCG campaigns or by the Amp Pipal Community Health programme clinics in the hospital and outlying villages.

The potential biases involved in such a retrospective study of BCG efficacy could be minimized by spending more time in the study setting. This would allow time to select cases at the time of diagnosis instead of from a chart review and to select controls from the case's village matched for age, sex, nutritive status, and economic status.

Table 1

	TB		no TB	
no BCG	70	21	91	
BCG	30	79	109	
	100	100	200	

$$\text{Odds ratio} = (70)(79)/(30)(21) = 8.7$$

$$\text{Effectiveness} = 100 \left(1 - \frac{1}{8.7} \right) = 88.5\%$$

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