Study on BCG protection against leprosy in Sri Lanka

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Abstract:
BCG (Bacillus Calmette and Guerin) vaccine is known to have a protective effect against leprosy. But the degree of protection varies according to the geographical area. The aim of the study was to detect whether there is significant protection from BCG against leprosy in Sri Lanka. BCG vaccine is used as a preventive measure in countries where it has been proven to have a protective effect.

The study was carried out at Teaching Hospital Colombo South. One hundred seventy six (176) index patients with leprosy and one hundred sixty nine (169) household contacts without the disease were studied. Presence of BCG scar and reaction to Mantoux test were compared between two groups. 79.8% contacts without the disease had skin induration 5-10mm following Mantoux test while only 3.4% patients showed such a response. BCG scar was found in 95.8% contacts and 52.8% patients. Odds ratio for Mantoux response was 0.008 ($p < 0.001$). It was 0.04 ($p < 0.001$) for the BCG scar.

In our study "positive" Mantoux reaction and presence of BCG scar were detected in a higher percentage of contacts without the disease compared to leprosy patients. BCG vaccine would have protected the contacts from developing the disease by enhancing immunity.

Introduction:
Leprosy patients are frequently encountered in dermatology practice in Sri Lanka. The main control strategies now recommended are based on case finding and multi drug therapy. A protective vaccine against leprosy would provide an important additional control[1].

In 1939 Fernandez observed that a large proportion of lepromin negative children were converted to lepromin positivity when given BCG vaccine. BCG induced lepromin positivity is associated with host resistance to leprosy. Fernandez suggested that BCG vaccine might confer some protection against this disease.[1]

Several workers in different countries observed relatively small groups of vaccinated and unvaccinated subjects and found that fewer cases of leprosy arose among vaccinated subjects[2].

J. Convit *et al* found that prevalence of leprosy was higher among subjects without BCG scars and fell as the number of scars increased[2]. Studies have shown that age, sex, household contact, poor socioeconomic status and Bacillus Calmette and Guerin (BCG) vaccination are important determinants of leprosy risk[3].

Because of BCG's protective efficacy as a vaccine against leprosy the Ministry of Health of Brazil recommends vaccination of household contacts of leprosy with BCG.[4]Repeated BCG vaccination has been used as a leprosy control measure for many years in Venezuela and in endemic areas children under 15 years have also received several doses as part of the routine vaccination programme.

Clinical leprosy occurs when an appropriate antigen specific T cell response is absent in an individual infected with Mycobacterium leprae.[2]BCG vaccine induces immune granuloma formation and elimination of bacilli. Effect of vaccine wanes with time. Repeated doses of vaccine increases the protection.

Trials with BCG vaccine on human beings at different places have shown varied results. Protection was 80% in Uganda, 46% in Papua New Guinea and 28%in South India.[5]So far there are no studies done in Sri Lanka to assess the BCG protection against leprosy. If it is protective in Sri Lanka repeated doses can be given for close contacts to prevent the disease. Currently BCG vaccine is given to all newborns to prevent tuberculous meningitis and miliary TB.

Method:
A case control study was conducted at the skin clinic of Teaching Hospital Colombo South over a period of 6 months. Ethical approval was obtained from the Ethical clearance committee of the same hospital.

The objective of the study was to detect whether there is significant protection from BCG vaccine against leprosy in Sri Lanka. Patients attending the skin clinic during this period with clinical histological or microbiological evidence of leprosy and their household contacts without the disease were included. Informed written consent was obtained. Those who did not give consent and those who were on immunosuppressive drugs were excluded. Details of the patients were obtained during their normal clinic visits and the details of household contacts were taken when they came for family screening. Household contacts were examined for features of leprosy. Those who did not have leprosy were included in the control group. Data was recorded in a questionnaire. Both groups were examined for the presence of BCG scar and were subjected to Mantoux testing.

BCG scar was considered as evidence of BCG vaccination. Mantoux reaction was used as an indicator of the presence of immunity from the vaccine (after excluding other causes).

Mantoux test was done at the outpatient department of Colombo South Teaching Hospital by a specially trained nursing officer and was read after 72 hours by two independent observers. Active tuberculosis and atypical mycobacterial infections were excluded when necessary.

Mantoux test was interpreted as follows;

Transverse diameter of induration - 0-3 mm = “negative” no immunity from BCG.
Transverse diameter of induration - >3 mm = “positive” – (due to BCG)

Presence of BCG scar and Mantoux reaction was compared between two groups.

Results:
There were 176 patients and 169 controls (contacts without leprosy). Of the patient 104 (59 %) had tuberculoid leprosy; 15 (8.9%) had lepromatous leprosy and 57 (32.1%) had borderline leprosy.

BCG scar was present in 162 (95.86 %) of the control group and 93 (52.8%) of patients. The odds ratio was 0.04. ($p < 0.001$) Mantoux test was “positive” in 135 (79.88%) subjects in the control group and 6 (3.4 %) subjects in the patient group. Odds ratio was 0.008. ($P<0.001$)

Results according to the type of leprosy are given in the table.

Type of leprosy	No. with BCG scars	No. without BCG scars	NO. with positive Mantoux	No. with negative Mantoux
Tuberculoid	60 **57.7%**	44 **42.3%**	3 **2.9 %**	101 **97.1%**
Borderline Tuberculoid	15 **57.7%**	11 **42.3%**	3 **11.5%**	23 **88.5 %**
Mid borderline	1 **100%**	-	-	1 **100%**
Borderline Lepromatous	12 **40%**	18 **60%**		30 **100%**
Lepromatous	5 **33.3%**	10 **66.7%**	-	15 **100%**

During the study 37 new patients were diagnosed. Of them 4 were lepromatous, 10 were tuberculoid and 9 were indeterminate type. 14 had (unilateral) thickened greater auricular nerves.

Discussion:

There are several causes for a positive Mantoux reaction. Tuberculosis and atypical Mycobacterial infections were excluded in our participants. Sub clinical infection with Mycobacterium tuberculosis is another possibility in a country such as ours, endemic for tuberculosis. Since the control group and patients were from the same environment exposure can be considered the same. After excluding above mentioned possibilities we assumed that a positive reaction should be due to the effect of previous BCG vaccination. Mantoux reaction due to BCG vaccine is a weak reaction. Usually the induration is < 10 mm. In all the participants who had a “positive” reaction in our study induration was < 10mm.

Although there is cutaneous anergy towards Mycobacterium leprae antigens in lepromatous leprosy patients, there is no general immune suppression in leprosy patients. Hence zero mm reaction cannot be due to a Tcell defect.

93.5 % of BCG scar positive patients had a negative Mantoux reaction. These results indicate that BCG scar is not a very accurate indicator of immunity. Possible reason for this could be waning of the effect of vaccine with time. In our study there was a statistically significant difference in “positive” Mantoux reaction and presence of BCG scar between patients and control group. This shows that the immunity given by BCG vaccine is higher in contacts without the disease.

Conclusion:

Our results favour the possibility of a protective effect of BCG vaccine against leprosy in the population studied.

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