

BCG scar diameter and asthma: A case-control study

Emanuel Sarinho, PhD, Deborah Schor, MD, Marco Veloso, MD, and Marilia Lima, PhD
Recife, Brazil

Recent research has shown that an inverse relationship may exist between the delayed-type cutaneous hypersensitivity reaction to *Mycobacterium tuberculosis* and the atopic state,¹ such that a strongly positive tuberculin response is associated with a lower incidence of allergic disease, lower levels of serum IgE, and higher levels of clone T_H1 cell cytokines.¹ Supporting this, animal models have shown that the BCG vaccine is able to suppress allergic sensitization and the development of bronchial hyperactivity.² Using scar size as an indicator of BCG vaccine response³⁻⁵ and therefore of atopic resistance, this case-control study was designed to assess whether an association exists between it and asthma. This study was conducted to test the hypothesis that there is a significant difference in vaccine scar diameter in children with asthma when compared with a control group. In Recife, Brazil, because of the high prevalence of tuberculosis, 95% of children receive the BCG vaccine shortly after birth.

METHODS AND SUBJECTS

Patient selection

The study was performed from May to July 1999. In total, 264 children attending a local public health center (age range, 2-9 years), all from the low-income population that the health center serves, were selected for entry into the study. Consent was obtained from the parents of each child, all of whom agreed to participate in the data collection.

Control subjects (70 boys and 64 girls) were selected from those children attending the health center who had not had, according to the parents, any history of episodes of dyspnea in the previous 2 years. Cases (74 boys and 60 girls) were selected from children attending the health center who had a history of 3 or more episodes of dyspnea in the previous 2 years and who had responded well to oral or inhaled bronchodilator therapy. These children were considered to have asthma but were not having symptoms at the time of inclusion into the study. Any child whose asthma status was in doubt was excluded from the study.

The weights and heights of the children in each group were distributed between the 10th and 90th percentiles, and there was no matching for age and sex. The study was designed as a case-control trial, with asthma the dependent variable and scar diameter the exposure factor.

It was calculated that 214 children would need to be included in the study group to find that 60% of children without asthma and 40% of children with asthma have scars larger than 5 mm ($\alpha = .20$ and $\beta = .05$). We included 268 children in the study group, 134 in each group, to increase the CIs.

Study protocol

We used a simple millimeter ruler to measure the BCG scar sizes in 2 planes, the largest vertical and horizontal readings, and an average of the 2 results was taken for each child. Measurements were taken by 1 person to avoid interobserver bias and were taken blind (ie, the observer was unaware of the diagnosis of the child). Similarly, a different team member who was unaware of the size of the child's BCG scar determined asthmatic status.

Statistical analysis

The odds ratio and χ^2 were calculated with EPI INFO 6.0. A *P* value < .05 was considered significant.

RESULTS

The median age for the control, nonasthma group was 4 years, and for the case, asthma group was 4.1 years. The children with asthma were not having symptoms at the time of inclusion into the study.

The data showed that 57.5% (77/134) of the children with asthma had scars larger than 5 mm but that 76.1% (102/134) of the nonasthmatic control children had scars larger than 5 mm ($\chi^2 = 10.51$, $P < .01$; Table I). The odds ratio was calculated to be 0.42.

Fig 1 shows that the prevalence of BCG scars smaller than 5 mm in diameter was higher among the children with asthma than the children without asthma.

DISCUSSION

Shirakawa et al¹ have recently demonstrated the existence of an inverse relationship between tuberculin positivity and atopy in which a positive tuberculin response was linked to a lower frequency of allergic diseases. Based on the recent identification of molecules that lead to the activation and maturation of T cells, it has been suggested that it is possible to suppress T_H2 activity in inflamed airways of atopic patients. The molecules with the potential to suppress T_H2 activity include local stimulators of T_H1 cytokine subclasses, such as the BCG vaccine.⁶ In addition, in animal models, immunization with this vaccine suppresses allergic sensitization and the development of airway hypersensitivity.²

The resulting scar diameter is considered to be the best reflection of response to the BCG vaccine, and it is likely to reflect the production of a secondary cytokine, such

From the Department of Pediatrics, Section of Allergy, Asthma and Immunology, Federal University of Pernambuco, Recife.

Reprint requests: Emanuel Sarinho, PhD, Av. Parnamirim, 373/202-Parnamirim, Recife-PE-CEP 52060-000, Brazil.

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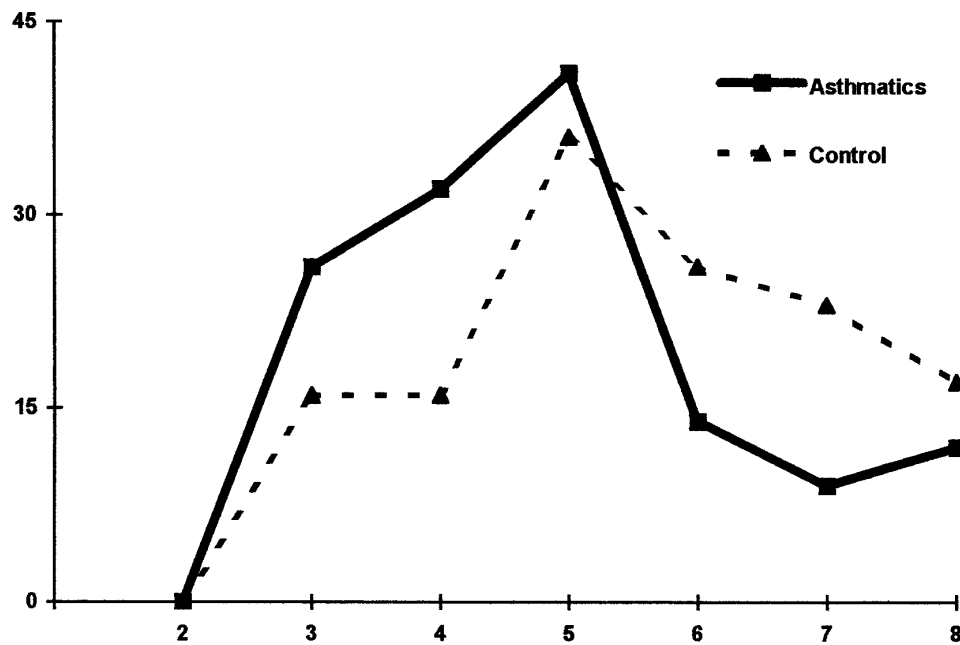


FIG 1. BCG scar frequency among children with asthma and control subjects ($P < .01$).

TABLE I. Medium diameter of BCG scar in children with asthma and control subjects

Group	Scar size	
	≥ 5 mm (%)	< 5 mm (%)
Case	77 (57.5)	57 (42.5)
Control	102 (76.1)	32 (23.9)

Odds ratio = 0.42 (95% CI = 0.24-0.74). $\chi^2 = 10.51$ ($P < .01$).

as IFN- γ .³⁻⁵ Recent research has demonstrated that the amount of IFN- γ produced by purified protein derivative-specific lymphocytes in atopic patients is less than the amount produced in a healthy control group, indicating that T_H2 response in atopic patients is not only for allergens but also for bacterial antigens.⁷ This study has demonstrated that children with asthma produce smaller vaccine scar diameters than the control group, for a 5-mm reference value ($P < .01$).

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