BCG vaccine in children and development of tuberculosis: it has a real protective effect in endemic population?

JULIANA FIGUEIRÊDO DA COSTA LIMA SUASSUNA MONTEIRO[1*]; LÍLIAN MARIA LAPA MONTENEGRO; MARTA MACIEL LYRA CABRAL[2]; ALINE DOS SANTOS PEIXOTO[1]; MARCELA PEREIRA SALAZAR[1]; ROSANA DE ALBUQUERQUE MONTENEGRO[1]; HAIANA CHARIFKER SCHINDLER[1].

1. AGGEU MAGALHÃES INSTITUTE/FIOCRUZ, RECIFE - PE - BRAZIL 2. FEDERAL UNIVERSITY OF PERNAMBUCO, RECIFE – PE - BRAZIL;

[*]juliana.figueiredo@fiocruz.br / jujufig@hotmail.com

BACKGROUND

Tuberculosis (TB) is a neglected disease which estimates one-third of world's population to be infected. The incidence of pediatric TB is 6% of total incident cases (8.6 millions) and the mortality 8% (74.000) of total deaths among HIV negative. Children are more vulnerable to develop severe forms of TB and the diagnosis is subjective and not easy to confirm, as so, people living with HIV have a risk 30 times higher to be infected with TB than population HIV negative. In Brazil, BCG's vaccination is mandatory at birth. Vaccines are considered safe, preventive and cost-effective. However, World strategies for decrease TB haven't effectively succeeded, because of difficulties in precise diagnosis and delay on beginning treatment, despite vaccination. Recife (Pernambuco State, Brazil), is an endemic region for tuberculosis (78.3 cases/100.000hab) and has high taxes of coinfection TB/HIV. Beside the majority vaccination of all birth children, the cases of childhood TB and in adults is still very high. This study evaluated the protective action of BCG on vaccinated patients (children and adults).

METHODS

Two different groups of children (≥15 years of age), from hospitals of Recife, Pernambuco, Brazil were analyzed for tuberculosis: Group A (data collected between 2003-2006) and Group B (data collected between 2011-2016). A third group, of adults (data collected between 2011-2016) was also analyzed. To confirm the disease, the gold-standard was clinical criteria and specific treatment response, according to WHO guidelines for TB. All statistical conclusion was made on 5% of significance and data were analyzed on SPSS by X^2 test and Binary logistic regression. The reference-test to confirm TB was a criteria based on clinical symptoms, radiological profile, epidemiological history or laboratorial exams and therapeutic response. Statistical analyses were done on SPSS20.0 and on OpenEpi. All the conclusions were taken on 5% of significance. The study were developed at Immunoepidemiology Laboratory at Institute Aggeu Magalhães/FIOCRUZ, in Recife-Pernambuco, Brazil.

OBJECTIVES

Evaluate the real protect effect of BCG vaccine in children who lives in endemic region of TB. To compare the protective effect of BCG between children and adults with TB.

RESULTS

Two database of different chronological studies were compared. The first study was performed between 2003-2007 including only children (Group A); the second study was performed between 2009 and 2014 with children and adults (Group B). Were included 295 children (Group A = 198; Group B = 97), whose 3 of them were HIV positive. And 159 adults were included from group B database, where 83 of them were known HIV positive. Evaluating all groups together by epidemiological data, follow are the results: on adult's group, the majority was men (55.4%) and the mean age of this group was 40.9 ± 15.5 years of age. The mean age on group A was 6.6 ± 3.9 years old and, on group B, it was 7.51±4.9. The kind of TB, *per* group, on patients with scar of BCG are detailed on table 1.

In both children groups, there were no statistical difference (p=0,26) between have scar of BCG and developed TB (latent or active), even in kids with contact with bacillipherous adult. The variables "to have BCG´s scar" and "have or not TB" in adult's group, were statistically different: p=0,02 (Table 2). The variable "having contact with bacillipherous TB" was also measured on groups associated with TB diagnosis.

Table 1: Frequency of clinical forms of TB in for BCG vaccinated patients.

Clinical form of TB	Frequency (%)		
	Group A	Group B	Adults
Pulmonary	52 (65.8)	18 (54.5)	34 (63)
Pleural	3 (3.8)	3 (9.1)	4 (7.4)
Ganglionary	13 (16.5)	6 (18.2)	2 (3.7)
Meningititis	1 (1.3)	1 (3)	0 (0)
Miliary	3 (3.8)	1 (3)	6 (11.1)
Bone	2 (2.5)	1 (3)	2 (3.7)
Other EPTB	5 (6.3)	3 (9.1)	6 (11.1)
Total	79 (100)	33 (100)	54 (100)

Table 2: Binary logistic regression for skin test result and BCG's scar *versus* diagnosis of TB (latent or active) or not TB (Group A and B, respectively).

Variables in the Equation – GROUP A

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1[a]	Scar of BCG	-1,137	0,832	1,867	1	0,172	0,321
	Constant	1,099	0,816	1,810	1	0,178	3

a. Variable(s) entered on step 1: scar of BCG.

Variables in the Equation – GROUP B

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1[a]	Scar of BCG	1,508	1,126	1,793	1	0,181	4,516
	Constant	-1,609	1,095	2,159	1	0,142	0,200

a. Variable(s) entered on step 1: Scar of BCG.

region) is interfering on conclusion of res… protects against more several forms of TB (mainly in early childhood). The presence of HIV was not analyzed related to protective effect on BCG against TB. This analyze must be done to minimize possible bias, especially in adults. Further studies with more patients and in other endemic regions should be performed, as so for a more effective vaccine against all forms of TB should be done.

REFERENCES

1. Kirimuhuzya C. Peadiatric Tuberculosis: Is the World Doing Enough? In: Mahboub BH & Vats MG, editors. Tuberculosis - Current Issues in Diagnosis and Management. ISBN: 978-953-51-1049-1, InTech, DOI: 10.5772/54953. Available from: http://www.intechopen.com/books/tuberculosis-current-issues-in-diagnosis-and-management/peadiatric-tuberculosis-is-the-world-doing-enough-
2. Costa-Lima, JF, Guedes GMR, Lima JFA, et al. Single-tube nested PCR assay with in-house DNA extraction for ***Mycobacterium tuberculosis*** detection in blood and urine. *Rev Soc Bras Med Trop*. 2015;48(6):731-738. DOI: http://dx.doi.org/10.1590/0037-8682-0210-2015.
3. WHO. Global Tuberculosis Report 2017. France. 2017. Available on: file:///C:/Users/jujuf/Documents/Aggeu/Global%20TB%20report%202017.pdf
4. Roy A, Eisenhut M, Harris R J, Rodrigues L C, Sridhar S, Habermann S et al. Effect of BCG vaccination against *Mycobacterium tuberculosis* infection in children: systematic review and meta-analysis *BMJ* 2014; 349 :g4643.

Financial Support: CNPq Conselho Nacional de Desenvolvimento Científico e Tecnológico; CAPES; FACEPE Fundação de Amparo à Ciência e Tecnologia do Estado de Pernambuco; Ministério da Saúde FIOCRUZ Fundação Oswaldo Cruz Instituto Aggeu Magalhães; ICOHRTA International Clinical Operational Health Services Research Training Award