

RESEARCH NOTE

Hepatitis B Vaccination in Leprosy Patients

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Key words: leprosy - HBV - HBV vaccine

Immunodepression is a well known condition in leprosy patients, and the association of this disease with HBsAg has been claimed in multitudinous reports since the first BS Blumberg's et al. paper (1967 *Lancet* 1: 173-176). In that paper the authors concluded that Australia antigen was more common in lepromatous leprosy (confined ones) than in tuberculoid form (outpatients). Recently we presented a study in which the prevalence for any HBV-markers in leprosy patients was 64.9% and 22.9% in institutionalized and outpatients respectively (H Rosa 1992 *Rev Inst Med trop São Paulo* 34: 421-426). This high prevalence was a motivational decision for a vaccination programme in the leprosy population still not infected by HBV.

To our knowledge a vaccination programme against hepatitis B in leprosy was not reported.

For this study we used the same leprosy population reported in our previous paper (Rosa *loc.cit.*) which was screened for HBV markers. Briefly, 171 lepromatous and borderline adults long-time institutionalized and 83 outpatients were studied. A standard questionnaire was applied to them, and age, sex, years of residence in the colony, years of disease (for outpatients), and history of blood transfusion was recorded. In the case of institutionalized patients, the data about the disease duration was missed because the majority of patients was unable to precise date marks; thus, we consider the "years of institutionalization or residence" as surrogate markers of disease onset. All leprosy patients were screened for HBsAg, anti-HBs and anti-

HBc markers by RIA and classified into the following categories of exposure to HBV: (1) HBsAg positive; (2) any positive HBV-marker (HBsAg, anti-HBc and/or anti-HBs) as prior HBV infection or exposure to virus and, (3) absence of HBV-marker as without prior HBV infection or not exposure to virus. As inclusion criteria only patients under 65 years of age and without HBV serum marker were considered for. Twenty-three out of 60 institutionalized patients and 49 out of 64 outpatients were eligible. Twenty inpatients and 21 outpatients accepted to be vaccinated; all but seven outpatient concluded vaccination schedule. The vaccinated leprosy patients were compared with healthy volunteers members of our Hospital of Clinics in Laboratories, Blood Bank and Obstetrics. The results are shown in the Table.

TABLE

One year follow-up of a vaccinated leprosy population with Hepatitis B vaccine and compared with healthy volunteers controls

	Control	Inpatients	Outpatients
n	21	20	14
M/F	10/11	13/7	7/7
Age	39 ± 11	42 ± 9	38 ± 10
Yrs dis	-	9.9 ± 5.7	4.9 ± 3
Med	-	-	Sulph
Seroconv	18 (86%) ^a	2 (10%) ^a	1 (7%) ^a

Age (\bar{X} SD); Med (medications); Sulph (sulphone); Seroconv (seroconversion or anti-HBs); ^a: p<0.01.

The vaccine used was Engerix-B (Smith Kline Biologicals, Belgium) a recombinant DNA hepatitis B vaccine, in a dose of 20mcg by intramuscular route (deltoid) at one and six months respectively. Both groups of patients received the same schedule of vaccination. No booster was given. International and manufacturers requirements on safety and protective efficacy were carefully followed. An informed consent of each patient was obtained.

Institutionalized patients were vaccinated in their homes at leprosy colony. Outpatients received vaccine at the ambulatory of a clinic for leprosy control; in this case an explanatory letter and a vaccination schedule was sent to each selected patient. Response to vaccine was investigated by monitoring two HBV markers: anti-HBs at the end of the 1st, 2nd, 7th and 12th months, and anti-HBc (total) at the end of 12th month after vaccination, respectively.

Tests for anti-HBs and anti-HBc detection were performed by ELISA technique. Biological

reagents for these antibodies detection were prepared and supplied by the Centro de Referência Nacional para Hepatites Virais - FIOCRUZ - Rio de Janeiro, Brasil (National Referência Center for Viral Hepatitis); tests were carried out at Department of Virology of the Instituto de Patologia Tropical e Saúde Pública da Universidade Federal de Goiás.

Vaccine failure was defined as the absence of surface antibody or the presence of core antibody after 12 months of vaccination.

Data analysis were performed by calculating the percentage of positivity to anti-HBs in the total population who finished the vaccine schedule in the 12 months follow-up period. Chi-squared test and chi-squared test for trend were used to compare the proportion of seroconverters leprosy patients in this study with the proportion of patients found naturally HBV infected as reported in our previous paper (Rosa *loc. cit.*)

Two among the institutionalized patients (10%) and one among the outpatients (7%) presented seroconversion to anti-HBs (Table). The present study pointed out striking low levels of antibody response among lepromatous patients after a standard HBV vaccine schedule without

booster. This seems a very interesting result considering that we found high prevalence of antibodies to hepatitis B virus in the screened leprosy population, suggesting that they mount antibody responses to natural virus infection. In the sense the vaccinated group seems to have failed to acquire levels of protection in a significant proportion in relation to the naturally infected group of patients. We can speculate that because the Engerix vaccine does not have all necessary epitopes, an adequate immune response was not obtained in these group. Probably, these leprosy patients should be considered as adequate candidates to pre-S2 vaccines to increase the vaccine immunogenicity promoting the seroconversion with higher levels of anti-HBs.

Nevertheless, we are aware that this study was not designed as vaccine trial, the sample size was rather small, and there were several drop-outs in the outpatient group probably due to internal migration and not related to the vaccination field organization.

The responsiveness of HBV vaccine in leprosy patients is an exciting question that we are trying to answer in ongoing studies.