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IMMUNOLOGIC EVALUATION OF HEPATITIS B VACCINE APPLICATION IN HOSPITAL STAFF

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Abstract
Objectives: The aim of our study was to assess immunological changes in hospital employees vaccinated five years ago with a recombinant hepatitis B vaccine. **Materials and Methods:** 148 hospital employees were examined at different time periods during 5 years following a three-dose schedule of intramuscular immunization with a recombinant DNA hepatitis B vaccine (Engerix-B). **Results:** At the end of a 5-year period, 20 vaccinees (13.5%) demonstrated a low level of HBs antibodies, namely < 10 mIU/ml being evaluated as lack of protection, 46 (31.1%) showed titers between 11 and 100 mIU/ml corresponding to feeble protection, 54 (36.5%) were with titers > 100 mIU/ml considered as sufficiently protected and, surprisingly, in 28 vaccinated persons (18.9%), titers of HBs Ab were over 1000 mIU/ml corresponding to high protection. The HBsAg were never detected among the entire vaccinated group. Averaged amounts of serum immunoglobulins (IgG, IgM, IgA) were lower relatively to normal values only among unprotected or feebly protected vaccinees. **Conclusions:** Our data demonstrate that postvaccinal titers are in linear dependence on the time elapsed since the vaccination and also evidence that some other immunological factors influence the outcome of vaccination.

Key words:
Hepatitis B, Vaccination, Hospital employees

INTRODUCTION

Over two billion people around the world are infected with hepatitis B virus (HBV), of whom over 350 million are chronic carriers. Approximately 25% of carriers develop progressive liver disease [1,2]. The annual mortality caused by HBV-infection and its sequels is estimated at 1–2 million people worldwide [3].

Hepatitis B virus infection is today a very important occupational hazard among medical staff. Hospital care workers belong to a high HBV-infection risk group [4–8]. Therefore, this group is recommended to a compulsory vaccination owing to the fact that modern anti-HBV vaccines are the unique efficacious method of mass protection [9–11].

Being generally very useful, an individual immune response to vaccine after primary immunization is not uniform [12,13]. HBV vaccination leads to both humoral and cellular immune response and can be evaluated by assessing HBs-specific antibodies [14]. The knowledge of immunogenecity of hepatitis B vaccine in health care workers is still insufficient [15]. This paper summarizes the results of vaccine's efficacy monitoring during five years after primary vaccination against hepatitis B.

MATERIALS AND METHODS

In all, 148 subjects working at Laniado hospital as health-care specialists, along with some members of paramedical services or administration were fully vaccinated against hepatitis B with a recombinant DNA vaccine (Engerix B). This purified HBV surface antigen used as vaccine

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was administrated intramuscularly (20 mcg in 1 ml) three times, D0, D30, and D180. For each vaccinee a detailed socio-demographic, occupational and health history questionnaire was fulfilled. The study population was assessed in 4 categories (A, B, C, D) according to the degree of protection ensured by the vaccine.

Laboratory monitoring

Laboratory tests included complete blood count, assessment of serum HBsAg and relevant antibodies (HBsAb), along with the appraisal of serum immunoglobulins (IgG, IgM, IgA).

RESULTS AND DISCUSSION

Of the 148 vaccinated hospital employees, checked 5 years after the first cycle of vaccination: 20 subjects (13.5%) with titers <10 mIU/ml demonstrated poor antibody response, being considered unprotected (category A); 46 vaccinees (31.1%) with titers ranging between 11 and 100 mIU/ml, indicated feeble protection (category B); 54 vaccinees (36.5%) with titers > 100 mIU/ml were considered sufficiently protected (category C); and 28 vaccinees (18.9%) with titers over 1000 mIU/ml) were considered highly protected (category D) (Table 1).

Our data demonstrate close links between time elapsed since vaccination and the level of antibody response (Fig. 1). The mean titer of HBsAb decreased after three years in 34.5% of subjects who had initially acquired protective antibody titers. A long term protection against hepatitis B disease is dependent on the persistence of a strong immune memory. An analysis of association between HBs antibody titers, demographic and occupational factors performed to date does not indicate that these

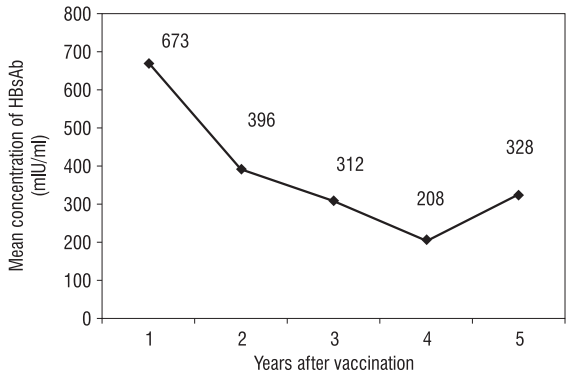

Fig. 1. Mean concentration of HbsAb and time after vaccination.

determinants predict immune response (Tables 2–5). On the other hand, hepatitis B vaccine have decreased its immunogenecity associated with increasing age, obesity, smoking and male gender.

Median concentrations of serum immunoglobulins (IgG, IgM, IgA) were detected in responders and non-responders to hepatitis B vaccine (Table 6). The immunogenecity of recombinant hepatitis B vaccine is satisfactory, but the lack of immune response to vaccination remains a problem, first of all among healthcare workers [16–18].

The recombinant hepatitis B vaccine provides immunity in approximately 95% of vaccinated healthcare personnel, but there is a certain percentage of employees who respond insufficiently [19]. In healthcare workers, the overall percentage with inadequate levels of anti-HBsAb (less than 10 mIU/ml), reported by Marinho et al. [20] was 5.2%, and the percentage of individuals with low response (10–100 mIU/ml) was 27.5%. Among vaccinated emergency physicians, the levels of anti-HBsAb after three years of monitoring were found to be protective in 81%, at borderline in 5%, and not reactive in 14% of physicians [21]. Among healthy adult volunteers who received a full

Table 1. Serum concentration of HbsAb 5 years after vaccination

Category	HBsAb level (mIU/ml)	Number of persons, P = 0.95
		Abs (%)
A	<10	20 ± 4.5 (13.5 ± 3.6)
B	11–100	46 ± 6.8 (31.1 ± 5.6)
C	101–1000	54 ± 7.3 (36.5 ± 6)
D	>1000	28 ± 5.3 (18.9 ± 4.3)
Total		148 (100.0)

Table 2. Serum concentration of HbsAb (mIU/ml) and gender of the vaccinees

Category	HBsAb level (mIU/ml)	Gender, P = 0.95	
		Males (%)	Females (%)
A	<10	14.3 ± 3.8	11.6 ± 3.4
B	11–100	47.6 ± 6.9	28.3 ± 5.3
C	101–1000	33.3 ± 5.8	37.4 ± 6.1
D	>1000	4.8 ± 2.2	24.2 ± 4.9

vaccination course with recombinant DNA yeast-derived hepatitis B vaccine, 40% had a blood positive sample taken 8 years after the first vaccination [22]. A ten-year period following the vaccination against HBV indicates that 57% of hospital employees show protective antibody titers [23].

Hepatitis B surface antigen (HBsAg) was not detected in any of the examined hospital workers. In the adult

Table 3. Serum concentration of HbsAb (mIU/ml) and age of the vaccinees

Category	HBsAb level (mIU/ml)	Age at the time of vaccination, P = 0.95	
		Aged 20–40 years (%)	Aged 41–56 years (%)
A	<10	10.4 ± 3.2	11.6 ± 3.4
B	11–100	29.9 ± 5.4	34.9 ± 5.9
C	101–1000	37.7 ± 6.1	37.9 ± 6.1
D	>1000	22.0 ± 4.7	18.6 ± 4.3

Table 4. Serum concentration of HbsAb (MIU/ml) and place of birth of the vaccinees

Category	HBsAb level (mIU/ml)	Place of birth, P = 0.95		
		Israel (%)	Euro-America (%)	Asia-Africa (%)
A	<10	11.1 ± 3.3	7.4 ± 2.7	13.3 ± 3.6
B	11–100	36.5 ± 6	25.9 ± 5.1	23.3 ± 4.8
C	101–1000	33.3 ± 5.8	55.6 ± 7.5	26.7 ± 5.2
D	>1000	19.1 ± 4.4	11.1 ± 3.3	36.7 ± 6.1

Table 5. Serum concentration of HbsAb (MIU/ml) and occupation of the vaccinees

Category	HBsAb level (mIU/ml)	Occupation, P = 0.95		
		Physician (%)	Nurse (%)	Paramedical (%)
A	<10	–	12.0 ± 3.5	6.2 ± 2.5
B	11–100	25.0 ± 5	30.0 ± 5.5	43.8 ± 6.6
C	101–1000	75.0 ± 8.7	34.0 ± 5.8	43.8 ± 6.6
D	>1000	–	24.0 ± 4.9	6.2 ± 2.5

Table 6. Category and HbsAb level (mIU/ml) and serum concentration of immunglobulins

Category and HBsAb level	IgM(mg/ml), P = 0.95		IgC (mg/ml), P = 0.95		IgA (mg/ml), P = 0.95	
	Median quantity	Range	Median quantity	Range	Median quantity	Range
A <10	1.38 ± 1.17	0.10–2.33	10.6 ± 3.3	6.1–12.2	1.82 ± 1.35	0.17–3.39
B 11–100	1.48 ± 1.22	0.40–4.39	11.1 ± 3.3	7.5–17.4	1.89 ± 1.37	0.13–4.50
C 101–1000	1.68 ± 1.30	0.43–4.67	13.2 ± 3.6	7.7–28.2	2.35 ± 1.53	1.02–5.95
D >1000	1.85 ± 1.36	0.69–4.67	14.8 ± 3.8	9.2–23.0	2.76 ± 1.66	1.51–4.21

German population, the percentage of HBsAg carriers showed a maximum of 1.12% in the 41–50 age group [24]. Preventive antibody levels were obtained after HBV vaccination in most of HBsAg/anti-HBs negative and anti-HBs positive persons [25]. A mathematical model predicts anti-hepatitis B virus surface antigen decay after vaccination against hepatitis B [26].

CONCLUSIONS

Studies of the correlation between HBsAb titers, occupational and demographic factors, performed to date, do not indicate that these factors have a predictive value in terms of the immune status of healthcare workers. A gradual lowering of antibody titers depends only on the time elapsed since vaccination.

Our data also suggest that the outcome of vaccination is a consequence of the validity of host facilities and the immune system of the vaccinee.

A high prevalence of unprotected individuals who have received the complete standard vaccination against HBV is of concern and warrants review of current vaccination strategies.

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