

Immune Response to Hepatitis B Vaccine among Dental Students

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Abstract

Background: Hepatitis B infection is a major public health problem worldwide. Dental students who are frequently in contact with body fluids like blood and saliva are still at high risk for HBV exposure. The aim of this study was to evaluate the effectiveness of HBV vaccine and personal factors associated with serologic evidence of the immune response.

Methods: A descriptive-cross sectional study was carried out using data from Hamadan dental school students that received just three doses of HBV vaccine. The serum sample of 86 dental clinical students were examined in order to determine hepatitis B surface antigen and the level of anti-HBs using IEMA method. Logistic regression models were used to assess the relationship of vaccine response to the variables Sex, age weight, smoking status and the time lasting from the third dose of vaccine injection.

Results: Ninety-three percent had positive anti-HBs response and 7% were non-responders. No one showed HBsAg. Vaccine response was most strongly associated with age, smoking status, sex and weight. The time lasting from the third dose was unrelated to vaccine response.

Conclusion: Clinical dental students had desirable immune response to the HBV vaccine nevertheless recommended number of doses, standard protocol and early vaccination are critical to adequate protection against hepatitis infection among all health care workers, in particular dental students and dentists who are often exposed to blood and other body fluids.

Keywords: *Hepatitis B, Immunity, Vaccine, Dental students*

Introduction

The hepatitis B virus (HBV) is an important agent of hepatitis, cirrhosis and hepatocellular carcinoma in all over the world. Also this infection has been responsible for about 1 million deaths each year (1, 2). It is estimated that 3% of all people of the world are infected to the virus based on WHO reports (3). In Iran up to 3% of general populations are infected in which 200,000-300,000 individuals have chronic hepatitis (4). However the prevalence rate for hepatitis B infection in whole population in Iran has been declined since 1977 but is still the most common cause of cirrhosis and hepatocellular carcinoma in Iran (4, 5). In addition to the health recommendation programs such as application of safe and controlled blood products, use of disposable instruments and pre-marriage screening; vaccine coverage is one of the most effective ways

in preventing the hepatitis B worldwide (6). Dentists are at risk of blood borne, airborne and droplet spread transmission of infectious agents such as HBV because of their frequent and often intensive occupational exposures, so vaccination programs of dental students should not be postponed (7).

Since the levels of anti-HBs declines over time, infectious disease society of America (IDSA) recommended measuring HBs antibody levels in all high risk subjects after injection of three doses of hepatitis B vaccine (8). It has been shown that 94% of dental students that received standard vaccination program had efficient immune response (9). Cleveland et al. (10) have shown strong association between intensity of immune response and regular vaccination program. Although it has been reported hepatitis B vaccine can induce adequate immune response

in more than 90-95% subjects, the vaccination coverage among dentists as well as dental students is highly variable which considering the fact that these subjects are in continuous exposure to blood or other body fluids potentially contaminated with HBV (2).

This study presents the seropositivity and factors associated with HBV vaccine response among dental students of Hamadan University of Medical Sciences, Iran.

Material and Methods

This descriptive-cross sectional study was conducted among dental clinical students of Hamadan (the west of Iran) University of Medical Sciences during the year of 2007. Participants were explained and asked to complete an informed consent form and a questionnaire that included questions on demographics, health history and factors affecting HBV immunization including the number of vaccine doses, data vaccination, weight and smoking history were collected. All healthy students at clinical course who had received just three doses of HBV vaccine according to the standard protocol and the last dose was more than at least 1 month from the time of sampling (11), were eligible to participate in the study. The type of vaccine was the routine recombinant form (GenHepvax, Korea) which recommended by ministry of health and distributed in Iranian health centers. Also according to the standard method in schedule of 0, 1, 6 months, the injection site in adults were in the deltoid muscle (11).

Initially 89 students participated in this study and out of them three subjects were excluded because they had no history of HBV vaccination or did not complete the total course of injection. Finally 86 subjects included in the study according to the mentioned criteria.

Five ml of venous blood sample of each subject was taken by one experienced nurse. The samples were centrifuged soon after collection and the serum was stored at -20°C . All serum samples were analyzed for HBsAg and Anti-HBs by immuno enzymometric assay (IEMA) (RADIM

kit, Italy). Antibody levels greater than 10 mUI/ml were considered protective (12). The collected data was analyzed by SPSS software version 13 and the statistical analysis was performed using Chi-square and student's test. Logistic regression models were used to assess the relationship between vaccine response and variables. Results were considered significant when $P < 0.05$.

Results

Among 86 subjects, 49(57%) were female. Their age ranged from 19 to 40 yr with a mean age of 26.1 ± 6.2 yr. Of the 86 students who were underwent the serological tests no one showed HBsAg, 80 subjects (93%) were positive for serum anti-HBs and six (7%) were non-responders. Table 1 shows the distribution of the students according to the age group, sex, weight group, and smoking status. A significant association was observed between anti-HBs titer and older age ($P = 0.016$). Subjects with age 35 yr or older were more likely to be non-responder than those younger. As shown in Table 1 woman were more likely than men to be responder. This difference was statistically significant ($P = 0.05$). The weight range of studied subjects was 45-100 kg that divided in two groups. The students with weight 60 kg or higher were more frequently to be non-responder than those lower ($P = 0.026$). Furthermore the association between smoking status and anti-HBs titer (Table 1) demonstrated that the chance of immunization among smokers is smaller than non-smokers ($P = 0.045$). The time lasting from the third injection of HBV vaccine was quite variable (1-18 months). Table 2 shows the distribution of anti-HBs titer of dental students according to the time lasting after the third dose of the vaccine. For subjects who received the third dose of the vaccine three years before the participation in this study, the vaccine response; statistically was not different with those who completed the three dose schedule in a period longer than 3-5 yr or 5 yr before. Moreover the relation between the other time lasting groups (3-5 yr and >5 yr) was similar; statistically.

Logistic regression analysis was used to evaluate the relationship (Odds Ratios) of vaccine response to the significant variables sex, age, weight and smoking status (Table 3). Vaccine response was most strongly associated with age, smoking status, sex and cigarette smoking respectively. When sex, weight and smoking status were controlled; subjects with age 35 yr or older were 4.2 times more likely to be non-responders than those younger. Compared with subjects were non-smokers, the students who currently smoked were 3.1 times more likely to be non-responders. When age, weight and smoking status were controlled; males were 2.5 times more likely than females to be non-responders. Furthermore; when age, sex and smoking status were controlled; the students with weight 60 kg or higher were 2.2 times more likely to be non-responders than those lower. It is necessary to mention that the time lasting from the third dose of vaccination was unrelated to vaccine response.

Table 1: Vaccine response of dental students according to the variables

Variable	Positive anti-HBs (%)	Negative anti-HBs (%)
Age group	<35 yr	66(97.1) 2 (2.9) 0.016
	≥35 yr	14(77.8) 4 (22.2)
Sex	Female	49 (100) 0 (0) 0.05
	Male	31 (83.8) 6 (16.2)
Age group	<35 yr	66 (97.1) 2 (2.9)
	≥35 yr	14 (77.8) 4 (22.2)
Weight group	<60 kg	43 (100) 0 (0) 0.026
	≥60 kg	37 (86) 6 (14)
Smoking	Non-Smoker	69 (95.8) 3 (4.2) 0.045
	Smoker	11 (78.6) 3 (21.4)

Table 2: Vaccine response according to the time lasting after the third dose of injection

The time lasting	Positive anti-HBs (%)	Negative anti-HBs (%)	P value
< 3 years	30 (96.7)	1 (3.3)	0.11
3-5 years	23 (95.8)	1 (4.2)	
> 5 years	27 (87.1)	4 (2.9)	
Total	80 (93)	6 (7)	

Table 3: Odds Ratios for vaccine non-responders (Logistic Regression Models)

Variable	Standard Error	Odds Ratio	95% Confidence Interval
Age (≥35: <35*)	0.53	4.25	2.12 – 6.18
Smoking (Yes: No*)	0.32	3.12	1.75 – 6.42
Sex (M: F*)	0.29	2.52	1.83 – 4.55
Weight (≥ 60 kg: < 60 kg*)	0.25	2.21	1.5 – 6.20

* Reference group

Discussion

The present study showed that among 86 dental students who reported receiving 3 dose of HBV vaccine, 93% presented antibody titer > 10 mUI/ml (responders) and 7% were non-responders. Some authors believe that hepatitis B vaccine can in-

duce adequate immune response in about 90-95% individuals (13, 14). In a large cohort study conducted by Brian et al. (15) revealed that protection induced by hepatitis B vaccine remains robust for at least 15 yr, as 88% of participants had anti-HBs present and responded to the initial vac-

cine series. In a study (16), of the 89 Medical students, 100% had adequate antibody response 6 months after injection of the third dose of HBV vaccine. Several other studies about HBV vaccine response carried out that had similar results with our study (9, 17-19).

In the present study, although the difference between the times lasting from the third dose of vaccine were not statistically significant, some authors mentioned that the antibody titers decline over the time. As an example, in a follow up study (14), 15-50% of vaccinees had lost protective anti-HBs levels after 9-15 yr of vaccination. However the exact duration of immunity after vaccination against HBV is not known, it has been shown seven percent of dental students who receive and completely respond to vaccination lose anti-HBs after 32 months (17, 20). Also El-Reshaid et al. (21) showed that 30% of antibody titers decrease after two years of vaccination. Although the relationship of hepatitis B vaccination response with age is controversial (22), the association between increasing age and diminished vaccine response reported in our study is consisted with previous studies (22-26). Vaccine failure rate for subjects older than 35, in this study was 22% compared with 3% for students under 35 yr of age. It was reported previously that it can be due to the immunological changes because of the aging process (27). Logistic regression analysis revealed increasing age to be the strongest variable associated with lower response of vaccine which is consistent with result of William et al. (11). The results of our study suggest that females are more likely than males to demonstrate a vaccine response. There is contradiction about gender differences in vaccine immunization rates. Sezer et al. (28) and Tomasiewicz et al. (29) stated that male sexuality may play a significant part in declining antibody titer, whereas there were no significant differences in HBV vaccine response between males and females (2, 22). It has been shown that the immunity rates after vaccination in obese subjects are lower than the controls and the exact mechanism is not clear (14, 23).

Kovacic et al. (30) and Cleveland et al. (10) had believed that hormonal effects in overweight persons can decrease antibody titers. They also stated that in the obese individuals the vaccine may be deposited in fat tissue rather than muscle and this causes diminished immunity response. Gamage et al. (31) mentioned that there were no statistical difference between antibody titer and weight. Although our study in direction of mentioned evidences suggests that subjects with lower weight have more chance to be responders, it should be noticed that the weight of the participants at the time of study might be different compared with the time of vaccination.

Despite the small number of smokers in this study, the results suggest that non-smokers are more likely to demonstrate vaccine response statistically. This finding confirms the results made by Bock et al. (32). It has been supposed, the diminished response in smokers may be due to the increasing of T suppressor lymphocytes (33).

In summery, post vaccination tests of hepatitis B should be considered for all health care workers who may be at risk for exposures from injuries with sharp instruments, Furthermore the test should be conducted between 1 and 6 months after completion of vaccination program to ensure attainment of adequate protective antibody levels (10).

Despite considering universal precautions; optimal vaccine response provides long term protection of dental students who are often exposed to blood and other body fluids. Thus follow up studies are suggested to provide additional information about duration of immunity especially among dental students and dentists.

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The authors declare that there is no conflict of interests.

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