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The Immunologic Response to Anti-Hepatitis B Vaccination Among Medical Students of Guilan University of Medical Sciences, Guilan, Iran

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Background and Aims: **An important way to prevent hepatitis B infection is vaccination especially among high-risk populations including healthcare workers. Unfortunately, immunologic response to the vaccine is not perfect. Multiple different factors such as gender, age, body mass index (BMI), smoking and underlying diseases can influence the immunologic response. So, this study was conducted to evaluate the post-vaccination immunologic response of medical students of Guilan University of Medical Sciences (GUMS).**

Methods: **In this cross-sectional study, GUMS medical students who had received complete vaccine series at zero, one, and six months were enrolled. Their demographic data and the factors which could probably alternate the immunologic response were collected by interview. The anti-HBs Ab titer was evaluated by Enzyme-Linked-Immunoassay (ELISA). Appropriate immunologic response was supposed to be HBsAb >=10 mIU/ml. The collected data were analyzed using SPSS 10.00.P value <0.05 was considered significant.**

Results: **We evaluated 233 students with mean age of 24.9±4.5 years. 74.7% were female. 4.9% did not respond properly to vaccination. Females' immunologic responses were significantly higher than males' (P=0.001). Responsiveness was significantly lower in smokers than non-smokers (P=0.02). Mean age in inappropriate and appropriate responder groups were 28.67±5.4 and 24.77±4.4 years, respectively (P=0.004).**

Conclusions: **95.1% of students had a protective level of anti-HBsAb (>10 mIU/ml). Since health-care staffs including medical students are a high risk group to be contaminated with HBV, it is preferable to be evaluated for anti-HBs titer 1-3 months after full three-dose vaccination especially when these factors are present; in this way the false sense of being immunized among them may be decreased.**

Keywords: **Medical Students, Anti-HBV Antibody, Vaccination**

Introduction

Hepatitis B virus (HBV) infection is a major public health issue throughout the world and vaccination of those at risk is the main method of containment. hepatitis B is the most important hepatic disease that can be prevented by vaccination [1-3]. Prior to hepatitis B vaccine availability, 10-30% of physicians had serologic evidence of HBV infection [4]. According to a report from University of Sydney, 71% of ward doctors, 22% of medical students, 72% of dentistry students, 50% of ward nurses, and 50% of emergency staff had received one or more needle stick injuries during the previous two years [5]. So, vaccination with a standard schedule should be given to anyone who would

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work in a health care related area but has not been vaccinated previously [6, 7]. Hepatitis B vaccination is recommended for health care workers but has a non-response rate of 5% to 32% and an unknown duration of immunity and unfortunately, immunization induced by vaccine is not complete [8]. Previous studies have shown the protective efficacy of vaccine in medical students and health care workers between 86-97% [9, 10]. Some factors such as gender, age, race, underlying diseases, smoking, and Body Mass Index (BMI) can affect the immunologic response to anti HBV vaccine [11-15].

There is no standardized post-vaccination protocol to confirm, monitor, and maintain immunity. We have three options to control or improve the immunologic response. The first option is not to follow the vaccinated person and not to control his immunologic situation. This option has just a unique advantage; it is economical. The second option is to evaluate anti-HBs Ab titer 1-2 months [16] after the third dose of vaccination. As stability of the anti-HBs titer depends on the responsiveness to the last vaccination dose [17] evaluation of anti-HBs Ab titer 1-3 months after the last dose is the best criterion for immunologic response assessment [18], and this option is the best method, especially in our high-risk group, medical students. The third option is anti-HBs tittering in different periods of time which is too expensive in developing countries like Iran, and periodic antibody concentration testing after completion of the vaccine series and assessment of the response are not recommended [19]. This study was conducted to evaluate the post-vaccination immunologic response of Guilan University of Medical Sciences (GUMS) medical students.

Materials and Methods

In this cross-sectional study, 233 medical students of GUMS with the history of three-dose vaccination were enrolled. The inclusion criteria were: 1) they should be the medical student of GUMS, 2) they should be vaccinated in three doses at 0, 1 and 6 months before entering hospital according to the GUMS schedule 3) the vaccine should be the recombinant type and injected 1 ml intramuscularly in deltoid and 4) there should be at least 2 months' and at most 2 years' time after the last vaccine dose. Participation in the study was voluntary, and all students were free to leave it. All included students were interviewed about demographic data, cigarette smoking, history of any chronic disease (such as diabetes, renal failure, lung or rheumatologic diseases, cancer or immunocompromising therapies) and vaccination history. Also some suspicious factors which are assumed to change the immunologic response such as height and weight were measured. Blood samples (5 cc venous blood) were collected from all students for tittering anti-HBsAb. For detection of the immunologic response, anti HBsAb was determined using commercially available Enzyme Linked Immunoassay (ELISA) kits (Radim anti HBsAb, Radim, Rome Italy).

Ab levels ≥10 mIU/ml were considered appropriate immunologic response and levels <10 mIU/ml were considered inappropriate. Finally, the collected data were analyzed through SPSS version 10.00 software. The association between quantitative factors that would possibly interfere in immunologic response was evaluated through independent t-test. P values less than 0.05 were considered statistically significant.

Results

233 students had our inclusion criteria and were enrolled in the study. Their ages were between 20 and 35 years old with mean of 24.9 4.5 years.

Among them, 179 individuals (74.7 %) were female. The number of females was much more than that of males; it probably reflects the majority of female medical students in these years, or it can be a selection bias.

5 students (2 %) were smoker. They smoked 0.2 to 0.7 pack-years. 3 students (1.2 %) had lung diseases and 98.8% (230 cases) had no specific chronic diseases. 221students (95.1%) did properly respond to anti HBV vaccine.

The mean age among responders and non-responders were 24.77 4.4 years and 28.67 5.4 years, respectively (P= 0.004). 179 females (97.8%) and 54 males (87.9 %) had adequate immunologic response (P=0.001). 3 cases (60%) of smokers and 230 cases (95.83 %) of non-smokers were in appropriate response group (P=0.02). So, in our study, there was statistically significant relation between age, gender and smoking with appropriate immunologic response (table 1).

Discussion

According to WHO recommendation, HBV infection can be prevented by vaccination [20]. On the other hand, we know the immunologic response differs in various races and different cultures and some other factors [21]. Evaluation of the high-risk

Table 1. Adequate immunologic response frequency after Anti-HBV vaccination according to gender, BMI, smoking status and underlying diseases

		Number	Relative frequency	
Gender	Female	179	%97.81	P=0/001
	Male	54	% 87.09	
BMI	<20	59	%96.72	P>0/05
	20-25	137	% 96.48	
	25-30	33	% 86.84	
	30-40	1	% 100	
	>40	0	% 0	
Smoking status	+	3	%60	P=0/02
	-	230	% 95.83	
History of chronic disease	+	3	% 100	P>0/05
	-	230	% 95.04	

groups' immunologic response to vaccination will help us to plan and select an effectual vaccination programs well and compare it with international standards, and reach WHO goals.

In our study, 95.1% of medical students had protective level of anti-HBs (≥10 mIU/ml). This result is almost similar to that of other studies performed among Iranian adults [13, 22]. The standard immunologic response rate is declared 95% (between 80-100%) [16]. That has been surpassed in this study.

The maximum response rate in Iran has been achieved in our study; it is probably because of the young age of our subjects and also because they were medical students and had not begun their professional job. One of the other factors in this regard has been the high percentage of the girls. In addition, there are more girls in this study than boys, which can increase the response rate. In one study, only 81% of emergency physicians had responded to anti HBV vaccine [23]. Some researchers believe that the HBV vaccines are unable to induce an adequate immune response in 5-11.9% of healthy adults [24, 25]. Another study demonstrated that 29% of healthcare staffs had not responded to HBV vaccine [8].

In our study, similar to other Iranian researches [13], there was a significant correlation between low immunologic response and some factors such as agedness. In other words, age is an important factor in immunologic response to vaccine. It seems that weakness of immune reaction in adults is a result of age-dependent alterations, such as malnutrition, insufficient blood supply, metabolic changes, drug, etc. [24].

In our study, females responded to anti HBV vaccine higher than males (P=0.01). Other studies did not detect any significant differences between genders [8, 26].

In our study similar to other studies, cigarette smoking had a significant relation with immunologic response (P<0.05)[12, 27 and 28]; although this correlation was not significant in another research carried out among healthcare staff [8]. The low rate of smokers in our study can be due to high percentage of girls compared to boys.

In our study, the same as other studies, [27, 28] BMI rising had no significant relation with adequate seroconversion. We surpassed this goal in this study. However, some studies showed a significant correlation between these two variables [12]. Although this discordance may be the result of fewer obese and severely obese samples in our BMI groups.

Chronic diseases such as renal failure and celiac disease are risk factors for vaccine non-responsiveness [27, 28]; however, in our study there was no significant relationship between the history of any chronic disease and immunologic response. It is probably because our subjects were younger, so chronic diseases were not common among them. Another factor in this regard has been the small number of cases with chronic diseases.

To sum up, anti HBV vaccination is an efficient protective way for high risk people especially healthcare staff including medical students and it is preferable to evaluate their immune response.

Conclusion

Hepatitis B vaccines are highly immunogenic, but have decreased immunogenicity associated with increasing age, smoking, and male gender. On the other hand, as medical students are a high-risk group to be contaminated by HBV, it is preferable to be evaluated for anti-HBs titer 1-3 months after full three- dose (0, 1, and 6) vaccination especially when these factors are present.

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