

Evaluating the Effect of Booster Dose of Hepatitis B Vaccine in Low-and Non-Responders Healthcare Workers and the Role of some Host-Related Factors

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Abstract: Problem statement: Hepatitis B comprises one of the major health problems worldwide. Health Care Workers (HCW) are a group at risk for Hepatitis B Virus (HBV) infection. Infection with hepatitis B virus has become a vaccine-preventable disease. Vaccination against Hepatitis B Virus infection (HBV) is safe and effective. The aim of this study is evaluation the immunologic response of booster dose of Hepatitis B vaccine in none and low responder health care workers and effects of some host-related factors. **Approach:** In a cross sectional descriptive analytic study carried out on the medical staff of Tabriz Shahid Madani Hospital in 2009-2010, we evaluated the immunologic response of booster dose of Hepatitis B vaccine in none and low responder health care workers and effects of some host-related factors. **Results:** Of 331 studied health care workers, 123 people (37.2%) were male and 208 people (62.8%) female. The mean antibody titer in the studied medical staff was 304.07 ± 199.98 IU L⁻¹ in the range of 0-1000 and median of 330. Dividing the antibody titer into three groups of “no response” (Titer < 10 IU L⁻¹), “Low response” (Titer 10-100 IU L⁻¹) and “Good response” (Titer > 100 IU L⁻¹) revealed that from 331 studied staff, 31 people (9.4%) were in “no response” group, 40 people (12.1%) in “Low response” group and 260 people (78.59%) in “Good response” group and after one booster dose of vaccine in none and low responder group, 7 people (2.1%) were in “no response” group, 5 people (1.5%) in “Low response” group and 319 people (96.4%) in “Good response” group. **Conclusion:** One booster dose of vaccine in people with low and none Response to hepatitis B vaccination cause to significantly increase of antibody titer so that, Good response rate increase from 78.5-96.4% and low response rate decrease from 12.1-1.5% and none response rate decrease from 9.4-2.1%. Use one booster dose of vaccine recommended in people with antibody titer blow 100.

Key words: Hepatitis B vaccines, occupational diseases, prevention and control, immunization, vaccination, booster dose, Health Care Workers (HCW), host-related factors, medical staff, immunologic response

INTRODUCTION

Hepatitis B comprises one of the major health problems worldwide (Varshochi and Mahmadian, 2011; Perez *et al.*, 1998). It may lead to chronic carrier state in 6-10% of patients (Mandell *et al.*, 2010) and chronic infection may result in various degrees of inflammation or necrosis, leading to cirrhosis and hepatocellular carcinoma. HCWs are at risk of HBV infection more than general population.

Hepatitis B vaccination is recommended for all Health Care Workers (HCW) at risk of exposure to infectious body fluids (Williams *et al.*, 2001). Testing of blood for anti-HBs one month after vaccination is

recommended to recognize non-responders as a booster dose will be beneficial in the majority of them (Perera *et al.*, 2002).

Furthermore, post vaccination antibody testing should be restricted only to high-risk subjects (Zannolli and Morgese, 1997).

Some factor such as sex, age, obesity, route of injection and smoking can influence seroconversion rate (Wood *et al.*, 1993; Mandell *et al.*, 2010).

In our country, all neonates, HCWs, medical students, accidentally exposed peoples and other high-risk groups have vaccinated routinely against hepatitis B, since 9 years ago.

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In antibody titer below 10, people become sensitive and despite having previous vaccination history, they may get infected by hepatitis B. therefore, serological examination of Hbs_ab and determination of its level in HCWs is necessary. In case of low antibody titer level, hepatitis B booster dose vaccination is inevitable.

The aim of this study is evaluation the immunologic response of booster dose of Hepatitis B vaccine in none and low responder health care workers and effects of some host-related factors.

MATERIALS AND METHODS

In a cross sectional descriptive analytic study carried out on the medical staff of Tabriz Shahid Madani Hospital in 2009-2010, we evaluated the immunologic response of the staff to vaccination against Hepatitis B and factors affecting it. In this study, HCWs, three were hepatitis B vaccine into the routine and the responses to 3 months after vaccination were studied. In our study, of 331 people, 260 of them had ideal Titer antibody titers, 40 and 31 of them had inadequate title and unacceptable antibody titer that one booster dose of hepatitis B vaccine injected for all of these and three to six months later, HBS antibody titer level was checked again in the same lab with the same kit and the effect of booster dose vaccination was examined in this group of people.

Medical staff is routinely vaccinated against hepatitis B and therefore antibody titration is essential to insure appropriate immunity.

The studied medical staffs are vaccinated by hepatitis B vaccine with following properties (entitled EUVAX B, met the WHO requirements, made in Korea, LG life sciences company) for three doses (0, 1 and 6 months) and antibody was titrated three months after vaccination. All utilized vaccines were from one brand and all tests were performed in one laboratory.

ELISA test was used to evaluate the samples used kit in this study was the Anti-HBs kit, made by ROCHE Company entitled "COBAS". Methods of this kit was ELISA, in which ELISA micro plates in this method ELISA micro plates are covered by antigen S so that after adding serum containing antibodies against antigen S, antigens would bind with antibodies. In the next step, antigen S conjugated with peroxides enzyme is added which attaches to the part of the antibodies not bound to antigens. Later, adding chromo gene and substrate dies the solution whose color can be read by ELISA reader.

After performing tests and reading the plates by ELISA reader, standard curves were provided using standard samples. Later using these curves, the concentration of antibodies in the tested sample were

calculated. Based on the instructions of the kit manufacturer, antibody level less than 10 units per mL was considered negative and amounts higher as positive.

RESULTS

This study was carried out on 331 people from the medical staff and HBs_Ag titers were measured after three dose vaccination (0, 1 and 6 months), the following results were obtained.

123 people (37.2%) from the studied staff were male and 208 people (62.8%) female. Demographic data of the studied medical staff are presented in Table 1.

The mean antibody titer in the studied medical staff was 304.07 ± 199.98 IU L⁻¹ in the range of 0-1000 IU L⁻¹ and median of 330 IU L⁻¹.

Antibody titer before and after booster dose of vaccine of the studied staff according to gender, smoking and hyperlipidemia are presented in Table 2. Repose to Vaccination in studied health workers at the base of smoking and hyperlipidemia are presented in Table 3. Repose to Vaccination in studied health workers with and without booster dose of vaccine was showed in Fig. 1. Titer of antibody of HCWs with and without booster dose of vaccine was showed in Fig. 2.

Table 1: demographic factors of health care workers

	Sex		P_Value
	Male	Female	
Age (year)	35±9	31±6	<0.001
Length (m)	1.72±0.061	0.59±0.05	<0.001
Weight (Kg)	73±12	63±11	<0.001
BMI	25.65±4.12	24.13±3.86	0.002
Smoker	15	1	<0.001
HLP	30	10	<0.001

Table 2: Antibody titer before and after booster dose of vaccine of the studied staff according to gender, smoking and hyperlipidemia

		Titer antibody without booster dose (IU/L)		Titer antibody with booster dose (IU/L)	
		Mean ± Std Deviation	P_V	Mean ± Std Deviation	P_V
Sex	Male	340±205	0.013	387±175	0.137
	Female	283±195		359±164	
Smoking	No	307±199	0.588	371±167	0.501
	Yes	252±224		341±207	
Hyperlipidemia	Yes	318±214	0.640	382±177	0.617
	No	302±198		367±168	

Table 3: Repose to Vaccination in studied health workers at the base of smoking and hyperlipidemia

		Smoking			Hyperlipidemia		
		No	Yes	P_V	Yes	No	P_V
Titer antibody	Non responders	27	4		4	27	
Without booster	Low responders	37	3	0.020	5	35	0.859
Dose (IU/L)	Good responders	251	9		31	229	
Titer antibody	Non responders	5	2	<0.001	2	5	0.601
With booster	Low responders	3	2			5	
Dose (IU/L)	Good responders	307	12		38	281	

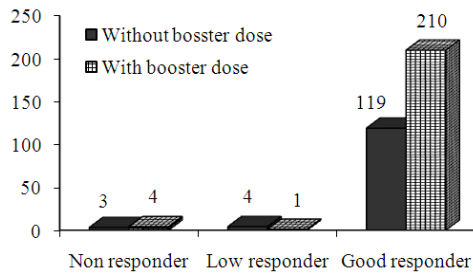


Fig. 1: Repose to vaccination in studied health workers with and without booster dose of vaccine

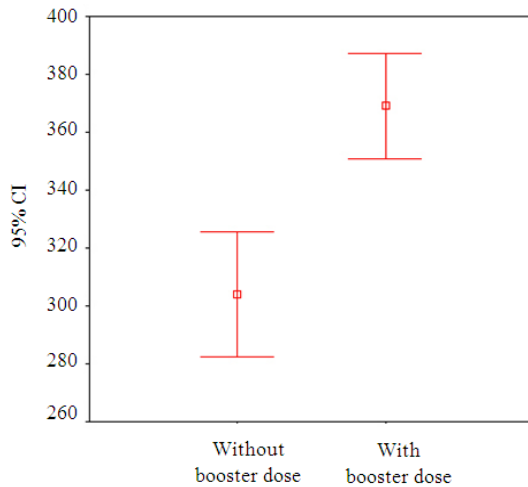


Fig. 2: Titer of antibody of HCWs with and without booster dose of vaccine

Dividing the antibody titer into three groups of “no response” (Titer 10 IU L^{-1}), “Low response” (Titer $10\text{--}100 \text{ IU L}^{-1}</math>) and “Good response” (Titer $>100 \text{ IU L}^{-1}</math>) revealed that from 331 studied staff, 31 people (9.4%) were in “no response” group, 40 people (12.1%) in “Low response” group and 260 people (78.5%) in “Good response” group and after booster dose of vaccine, 7 people (2.1%) were in “no response” group, 5 people (1.5%) in “Low response” group and 319 people (96.4%) in “Good response” group.$$

Response of the staff according to gender, smoking and hyperlipidemia with and without booster dose of vaccine are presented in Table 2 and 3 which shows that response in the smoking staff was significantly less ($p < 0.001$) but no significant difference was observed in the response between genders ($p = 0.129$) and no case of hyperlipidemia ($p = 0.601$) was reported.

There was a significant reverse linear relation between age and antibody titer in the studied staff and

antibody titer decreased significantly as age increased ($p = 0.003$, $R = -0.161$) but no significant linear relation was observed between weight, height and BMI and antibody titer.

DISCUSSION

Use of the vaccine in high-risk health care professions has been modest, despite widespread participation in the establishment of vaccination programs among these institutions.

Postvaccination antibody testing and regular testing for antibodies is recommended only to high-risk subjects, especially to health care workers and subjects with immunodeficiency. In these cases, the booster dose should be administered in none responders and might include double doses (Alvarez *et al.*, 2000). Although a high percentage of HCWs have been fully vaccinated with hepatitis B vaccine, efforts need to be made to improve this coverage (Mahoney *et al.*, 1997). Testing of blood for anti-HBs one month after vaccination is recommended to recognize non-responders as a booster dose will be beneficial in the majority of them (Perera *et al.*, 2000).

In the study of 2.5% also received the booster dose of the HBV vaccine (Duseja *et al.*, 2002).

In our study of 331 HCWS, 71 (21.45%) received booster dose of HB vaccine due to none or inadequate coverage.

In the study of Lok *et al.* (1988), age is considered as an effective factor in determining the response to the vaccine therefore highest response to the vaccine had achieved in the early patients and serum antibody titer had indirect correlation with age that good response rate was decreased from 86% in the fourth to 47% in sixth decade.

In our study, the antibody was reduced in patients with age but these changes were not significant.

In the studies of Shaw *et al.* (1989) and Minana (1996) the response rates in men were lower.

In our study, unlike the results of these studies, response rate in women was lower than men and mean of antibody titer was significantly higher in men than women.

In the study of Shaw *et al.* (1989) and Shapiro and Margolis (1992) immunological response in obese patients was low.

In our study, titer of antibody was reduced with increasing of weight and BMI, but these changes were not significant.

Tomasiewicz *et al.* (1994) propose that timing of booster vaccination should be scheduled on the basis of anti-HBs level. It seems to be necessary to control the level of anti-HBs at least 3 years after the last dose of vaccination (Tomasiewicz *et al.*, 1994).

Das *et al.* (2003) recommended that a single booster dose after 6 months in primary non-responders leads to good seroprotective anti-HBs antibody titers.

Although most participants responded to a booster dose of hepatitis B vaccine, the significance of the increased proportion of none responses among older adolescents might indicate waning immune memory (Samandari *et al.*, 2007).

Although body mass index affected the response to the first hepatitis B booster, when full compliance to regular revaccination was ensured, all non- and low-responders eventually reached sufficient anti-HBs levels (Clemens *et al.*, 1997).

Overall, 73/76 (96%) of students in the second group had protective concentrations of antibody after the booster dose (Bryan *et al.*, 1992).

In our study, the ideal response to routine vaccination with three doses was 78.5% which increased to 96.4% with use a booster dose in the 71 people who had no acceptable response that this increase in response rate was significant.

CONCLUSION

Of 331 studied health care workers, 123 people (37.2%) were male and 208 people (62.8%) female. The mean antibody titer in the studied medical staff was 304.07 ± 199.98 IU L⁻¹ in the range of 0-1000 and median of 330. Dividing the antibody titer into three groups of “no response” (Titer < 10 IU L⁻¹), “Low response” (Titer 10-100 IU L⁻¹) and “Good response” (Titer > 100 IU L⁻¹) revealed that from 331 studied staff, 31 people (9.4%) were in “no response” group, 40 people (12.1%) in “Low response” group and 260 people (78.59%) in “Good response” group and after one booster dose of vaccine in none and low responder group, 7 people (2.1%) were in “no response” group, 5 people (1.5%) in “Low response” group and 319 people (96.4%) in “Good response” group. One booster dose of vaccine in people with low and none Response to hepatitis B vaccination cause to significantly increase of antibody titer so that, Good response rate increase from 78.5-96.4% and low response rate decrease from 12.1-1.5% and none response rate decrease from 9.4-2.1%. Use one booster dose of vaccine recommended in people with antibody titer blow 100.

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