JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Brief Original Article

Immune response to hepatitis B vaccine among north Iranian healthcare workers and its related factors

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Abstract

Introduction: Hepatitis B virus (HBV) is an important occupational risk among healthcare workers (HCWs). Vaccination is the most cost-effective method of preventing and controlling HBV infection. Several factors have been suggested to effect response to the vaccine. The present study aimed to evaluate vaccine response among north Iranian HCWs and to determine the factors influencing vaccine response.

Methodology: Response to the standard three-dose vaccination regimen was evaluated in term of anti-hepatitis B surface antigen level among 1,010 HCWs using an enzyme-linked immunosorbent assay (ELISA) method. Logistic regression was applied to predict antibody response, with related factors including sex, age, years of working experience, marital status, history of transfusion, smoking, history of needle stick injury, rheumatic disease, steroid use, and elapsed time from vaccination measurement.

Results: Of the 1,010 HCWs, 898 (88.9%) acquired protective levels of antibody (> 10 IU/mL). Compared with those < 30 years of age, HCWs older than 50 years and between 40 and 50 years of age were more likely to have non-protective anti-HBs levels (odds ratio = 4.48; p = 0.001 and odds ratio = 1.85; p = 0.03, respectively).

Conclusions: HBV vaccine efficacy and immune response were satisfactory among north Iranian HCWs. Since it is predicted that anti-HBs levels decrease with aging, testing for anti-HBs titer is desirable for HCWs older than 50 years of age.

Key words: Health care; virus titer; hepatitis B vaccine; immune response antigens.

J Infect Dev Ctries 2017; 11(6):501-507. doi:10.3855/jidc.8182

(Received 30 January 2016 – Accepted 05 September 2016)

Introduction

Hepatitis B virus (HBV) is an important occupational risk to health care workers (HCWs) due to their risk of exposure to infected bodily fluids and blood [1]. This infection is a major health problem that can cause chronic infection, liver failure, liver cancer, and death [2].

The World Health Organization (WHO) estimated that 2 million HCWs experience percutaneous exposure to HBV each year [3]. The parenteral exposure to known cases of HBV infection that have circulating e antigens has the highest risk of occupational HBV infection, between 19% and 37% [4]. The risk of HBV infection in HCWs is four times higher than that in the general adult population [5].

HBV surface antigen (HBsAg) vaccination is a safe, effective, and economical method of preventing and controlling HBV infection among high-risk groups; the vaccination provides at least 10 years of protection [6-9]. According to a Centers for Disease Control and Prevention report, the annual number of occupational hepatitis B infections has decreased by 95% since the hepatitis B vaccine became accessible in 1982 [10]. However, even strict obedience of the vaccination schedule does not always assure protection, and the non-response or hypo-response phenomenon is being increasingly reported [11]. Therefore, assessment of protective immunity to HBsAg vaccination is important for high-risk groups such as HCWs [12]. Antibody titers to the viral surface antigen (anti-HBs titer) < 10 mIU/mL is considered as non-responsive and < 100 mIU/mL as hypo-responsive [13]. Various studies have shown that 10% to 15% of vaccinated HCWs with an initial three-dose regimen have not developed protective level of anti-HBs titer [14-16]. Several factors have been suggested to effect response to the vaccine, such as interval after vaccination and chronic disease, two factors known to influence vaccine response [15].

There have been no vaccine efficacy studies conducted among HCWs in a north Iranian population. The present study aimed to evaluate the vaccine response among north Iranian HCWs in terms of anti-hepatitis B surface antigen level, and to determine the factors influencing vaccine response.

Table 1. Characteristics of healthcare workers evaluated for hepatitis B immune status (n = 1,010).

Characteristics	N	%
Gender		
Male	62	6
Female	948	94
Marital status		
Single	285	28.2
Married	725	71.8
Age (years)		
< 30	353	35
30–39	399	39.5
40–50	205	20.3
> 50	53	5.2
Anti-HBs titer (mIU/mL)		
< 10	112	11
10–100	336	33
100–200	264	26
> 200	298	30
Time elapsed from vaccination (years)		
< 5	37	3.5
5–8	320	32
9–10	653	64.5
Working experience (years)		
< 5	363	36
5–10	234	23
> 10	413	41
History of transfusion		
Negative	972	96
Positive	38	4
Smoking		
Negative	1,006	99.6
Positive	4	0.4
History of needle stick injury		
Negative	430	42.6
Positive	580	57.4
Rheumatic disease		
Negative	1,003	99.3
Positive	7	0.7
Steroid use		
Negative	975	96.5
Positive	35	3.5
BMI		
< 18.49	34	3.4
18.5–24.99	541	53.6
25–29.99	312	30.8
> 30	123	12.2

Table 2. Distribution of anti-HBs titers following HBV vaccination in healthcare workers.

Characteristics	< 10 mIU/mL		10–100 mIU/mL		100–200 mIU/mL		> 200 mIU/mL		P value*
	N	%	N	%	N	%	N	%	
	112		336		264		298		
Gender									
Male	9	14.5	19	30.6	11	17.7	23	37.2	*0.27*
Female	103	10.9	317	33.4	253	26.7	275	29	
Age (years)									
< 30	32	9.1	102	28.8	115	32.6	104	29.5	
30–39	30	7.5	131	32.8	108	27.1	130	32.6	*0.001*
40–50	34	16.6	84	41	35	17.1	52	25.3	
> 50	16	30.2	19	35.8	6	11.3	12	22.7	
Elapsed time from vaccination (years)									
< 5	2	5.7	14	34.3	10	28.6	11	31.4	
5–8	28	9.2	94	28.8	107	33.5	91	28.5	0.016
9–10	82	12.6	228	34.8	147	22.5	196	30.1	
Working experience (years)									
< 5	34	9.4	115	31.7	109	30	105	28.9	
5–10	18	7.7	79	33.9	67	28.8	69	29.6	0.01
> 10	60	14.4	142	34.3	88	21.4	124	29.9	
Marital status									
Single	27	9.5	88	30	80	28.1	90	31.5	*0.7*
Married	85	11.7	248	34.2	184	25.4	208	28.7	
History of transfusion									*0.23*
Negative	104	10.7	323	33.2	257	26.4	288	29.7	
Positive	8	21.1	13	34.2	7	18.4	10	26.3	
Smoking									
Negative	112	11.1	335	33.3	263	26.1	296	29.5	0.89
Positive	0	0	1	25	1	25	2	50	
History of needle stick injury									*0.06*
Negative	58	13.5	145	33.7	99	23	128	29.8	
Positive	54	9.3	191	32.9	165	28.5	170	29.3	
Rheumatic disease									*0.002*
Negative	108	10.8	336	33.5	262	26.1	297	29.6	
Positive	4	57.1	0	0	2	28.6	1	14.3	
Steroid use									
Negative	104	10.7	325	33.3	253	25.9	293	30.1	*0.06*
Positive	8	22.9	11	31.4	11	31.4	5	14.3	
Body mass index									
< 18.49	3	8.8	9	26.5	14	41.2	8	23.5	
18.5–24.99	48	8.9	167	30.8	155	28.7	171	31.6	*0.001*
25–29.99	43	13.8	111	35.6	70	22.4	88	28.2	
> 30	18	14.6	49	39.9	25	20.3	31	25.2	

* Chi-squared or Fisher's exact test

Methodology

This was a cross-sectional study that was carried out during 2014. This study was conducted in all hospitals in Rasht (the capital of Guilan province, located in the north of Iran). The protocol for this study was approved by the ethics committee of the gastrointestinal and liver diseases research center of Guilan University of Medical Sciences, and written informed consent (per the Helsinki declaration) was obtained from each participant.

The study population comprised all 1,010 HCWs vaccinated 1–10 years ago with hepatitis B vaccine according to the routine immunization schedule (three doses at zero, one, and six months apart), had no history of HBV infection, and had not received hepatitis B immunoglobulin prophylaxis.

A data collection sheet was used to collect information about gender; age; occupational characteristics; date of vaccination; marital status; and history of drug use, disease, transfusion, smoking, and needle stick injury (NSI).

The anti-HBs level was measured using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (Diapro Diagnotic Bioprobes Milano, Italy). Positive response or sero-protection was defined as anti HBs > 10 mIU/mL. Anti-HBs titer of < 10 mIU/mL are considered to be non-responsiveness to HBsAg vaccination; anti-HBs levels between 10 and 100 mIU/mL are considered to be hypo-responsiveness, and levels > 100 mIU/mL are regarded as a high level of immunity [10].

Table 3. Association between anti-HBs antibody status and characteristics of healthcare workers, using logistic regression.

Characteristics	HBsAb titer, mIU/mL				Odds ratio (95% CI)	P Value *
	0-10 N 112	%	> 10 N 898	%		
Age (years)						
< 30	32	9.1	321	90.9	Ref.	
30–39	30	7.5	369	92.5	0.79 (0.46–1.37)	0.41
40–50	34	16.6	171	83.4	1.95 (1.13–3.3)	0.01
> 50	16	30.2	37	69.8	5.14 (2.49–10.61)	0.001
Working experience (years)						
< 5	34	9.4	329	90.6	Ref.	
5–10	18	7.7	215	92.3	0.751 (0.408–1.383)	0.35
> 10	60	14.5	354	85.5	1.583 (0.96–2.492)	0.06
Rheumatic disease						
Negative	108	10.8	895	89.2	Ref.	
Positive	4	57.1	3	42.9	4.7 (0.92–24.5)	0.06
Elapsed time from vaccination (years)						
< 5	2	5.4	35	94.6	Ref.	
5–8	28	8.7	292	91.3	1.64 (0.76–2.98)	0.23
9–10	82	12.6	571	87.4	2.33 (0.94–5.38)	0.07
Body mass index						
< 18.49	3	8.8	31	91.2	Ref	
18.5–24.99	48	8.9	493	91.1	0.9 (0.5–2.9)	0.43
25–29.99	43	13.8	269	86.2	1.5 (0.8–3.1)	0.09
> 30	18	14.5	105	85.4	1.7 (0.9–4.7)	0.07

* Logistic regression test

All analyses were performed using SPSS version 20 (IBM, Armonk, USA). Data were analyzed categorically for antibody titer as the dependent variable, and the independent variables were grouped as follows: gender; age; body mass index (BMI); years of working experience; marital status; history of transfusion, smoking, NSI, rheumatic disease, and steroid use; and elapsed time from vaccination. Comparisons were made using cross-tabulation with the Chi-square test, and logistic regression was used to evaluate the relationship between the antibody response to HBV vaccines and independent variables. All tests were two-sided and P values ≤ 0.05 were considered significant.

Results

Of the 1,010 HCWs, 949 (94%) were females. The mean age of the participants was 35.03 (standard deviation = 8.21). Characteristics of HCWs are described in Table 1.

As shown in Table 1, 112 (11%) of the participants who received all three doses of vaccination did not develop a sufficient anti-HBs response; 336 (33%) had an anti-HBs titer between 10 and 100 mIU/mL, 264 (26%) had an anti-HBs titer between 100 and 200 mIU/mL, and the remaining 298 (30%) had an anti-HBs titer of > 200 mIU/mL (Table 1).

There was a significant association between anti-HBs level and age, BMI, elapsed time from vaccination, years of working experience, and having a rheumatic disease (Table 2). In this study, no significant association was found between gender, marital status, and history of transfusion, NSI, steroid use, smoking, and anti-HBs level (Table 2).

As presented in Table 3, in regression analyses (after adjusting the effect of variables), only age was a significant predictor of response to vaccine. HCWs older than 50 years and between 40 to 50 years of age were significantly more likely to have non-protective anti-HBs level than were HCWs < 30 years of age (odds ratio [OR] = 5.14; 95% confidence interval [CI] = 2.49–10.61, and OR = 1.95; 95% CI = 1.13–3.3, respectively). Other related factors, such as elapsed time from vaccination, years of work experience, history of NSI, having a rheumatic disease, BMI, and steroid use, were not significant predictors of response to vaccine after they were entered into a logistic regression model (Table 3).

Discussion

HCWs are high risk for infection with hepatitis B worldwide [17]. NSIs are serious occupational hazards in the transmission of a variety of bloodborne pathogens, such as hepatitis B virus, among HCWs [18]. The WHO estimates 66,000 cases and 261 deaths annually from hepatitis B infection in HCWs from injuries caused by needles [19]. The best way to prevent and control hepatitis B infection is the use of the hepatitis B vaccine [20]. Unfortunately, some vaccinated people fail to develop protective antibody to the vaccine related to several factors, including genetics, age, immune system impairment, and high BMI [21].

The present study evaluated the vaccine response among 1,010 north Iranian HCWs in terms of anti-hepatitis B surface antigen level and determined the factors influencing the vaccine response.

Our results revealed a high protective level of HBV antibody among north Iranian HCWs who received the complete three-dose vaccination course; 898 (88.9%) of the participants acquired antibody titers higher than 10 IU/mL and are compatible with global levels.

These findings were similar to the protective levels found among HCWs in Egypt (96%) [22], southern Iran (87.3%) [23], and Pakistan (86%) [24].

In our study, a significant association between age and seroconversion rate was found. HBV antibody titer decreased significantly with increasing age of participants. The insufficient anti-HBs response was nearly five times (OR = 4.48) higher in HCWs > 50 years of age than in HCWs < 30 years of age. Also, previous studies have demonstrated that when age at vaccination was > 40 years, the seroconversion rate was lower [24-27].

Previous studies have shown that the protection given by the HBV vaccine lasts at least 15–20 years [28,29]. Our findings showed anti-HBs titers declined with time, but when adjusted for age, this decline was not significant. In agreement with these findings, 30% of participants in our study had anti-HBs titers > 200 IU/mL after more than 10 years following vaccination.

Years of working experience were inversely related to the anti-HBs level. The highest years of working experience were associated with lower anti-HBs levels, but when adjusted for age, this association was not significant. Years of working experience, therefore, was not an independent predictor of seroconversion rate; its effect was due to aging.

Several studies have shown that obesity is an important factor associated with decreased vaccine-induced immune response [30-33]. Our findings revealed that BMI over 30 kg/m^2 was associated with an increased risk of non-responsiveness to the HBV vaccine, but on multivariate regression analysis, the

independent role of BMI on vaccine-induced immune response was not significant. This might be due to predominance of BMI over 30 kg/m^2 in the older group.

In our study, 57% of individuals who experienced a rheumatic disease had non-protective levels of anti-HBs (titers < 10 IU/mL). Rheumatic patients were nearly five times more likely to not respond to the vaccine compared with healthy individuals, but this was not significant, perhaps due to the small number of patients. This finding was in agreement with other studies [26,34].

Our findings demonstrated that the rate of seroconversion was not associated with gender. Some studies found that females had higher seroconversion rates than males [26,35-38]. Other studies were consistent with our finding [15,24,27,39]; however, because the majority (94%) of our participants were female, this finding should be interpreted with caution. Though 22% of our participants who had used steroids did not develop seroprotective levels of anti-HBs, this finding was not significant. A small number of steroid users justifies this result.

Conclusions

HBV vaccine efficacy and immune response were satisfactory among north Iranian HCWs. Early full-dose vaccination should be administered to all non-vaccinated HCWs. Although HCWs are hired after graduation, usually when they are 25 years of age and are vaccinated at the time of entrance, the Ab titer is not controlled most of the time during aging and gaining work experience. Since it is predicted that anti-HBs level decrease with aging, testing for anti-HBs titer is desirable for HCWs older than 50 years of age.

Acknowledgements

This study is a part of PHD research thesis. We would like to thank all members of Gastrointestinal & Liver Diseases Research Center (GLDRC). Also, we would like to thank all the hospitals staves that assisted us in this study.

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Conflict of interests: No conflict of interests is declared.