Research Article

Immune response to hepatitis B vaccine in a group of vaccinees in the Faculty of Allied Health Sciences of the University of Peradeniya

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Abstract

Background: The risk of contracting Hepatitis B virus (HBV) infection by health care workers (HCW) is relatively high. Currently no data is available on the immune response to HBV vaccination in Allied Health Science (AHS) students of the University of Peradeniya (UoP).

Objective: The present study was undertaken to test the immune response (anti-HBs) to HBV vaccination in a group of vaccinees from the Faculty of AHS, UoP.

Method: Vaccinated AHS students (n=89) were recruited for the study with the ethical clearance obtained from the Faculty of AHS, UoP. Serum samples were tested for the presence of anti-HBs using an ELISA. Results were analyzed using MS-Excel 2010.

Results: Of the 89 AHS students tested, one student (1.12%) was a non-responder to the HBV vaccine after a single course of vaccination and 27 (30.33%) students had antibody levels between 10-100mI/mL. Most of the students (n=61) had antibody levels >100mIU/mL. The time lapse after completing the vaccination differed among students at the time of testing, but the difference between the time lapse and the levels of anti-HBs levels was not statistically significant (P=0.5). Age of the study participants ranged from 23 to 27 years with Sinhala, Tamil and Muslim students, the majority being Sinhala students (n=82).

Conclusions: Based on these findings, 1.12% of young healthy AHS students did not develop a protective immune response (anti-HBs) after a single course of vaccination. All vaccinees must test their antibody status at 6 weeks or later after completing the full course of HBV vaccination.

Keywords: HBV infection, HBsAg vaccine, anti-HBs, Allied Health Science Students, Sri Lanka.

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Introduction

Hepatitis B virus (HBV) is an enveloped double-stranded DNA virus of the *Hepadnaviridae* family.[1] It causes viral hepatitis which may progress to cirrhosis and hepatocellular carcinoma (HCC) in the chronic form of the disease.[2] HBV infection is a major global health problem. More than 2 billion people living today have been infected with HBV at some point in their life with about 400 million people estimated to be chronic carriers of the virus.[3]

HBV is present in body fluids such as blood, saliva, semen and vaginal secretions of an infected person.[4] HBV can therefore be easily transmitted from an infected person through unprotected sexual activity, sharing needles, needle prick injuries, blood transfusions, long-term renal dialysis and using non sterile needles or devices for tattoo or acupuncture.[1,2] Infected mothers can transmit HBV infection to neonates during delivery.[2] Apart from these usual routes of transmission, HBV can also be transmitted through sharing shaving razors of an infected family member or blood contact with an infected family member through abrasions or cuts.[1,2] Throughout the world, millions of healthcare professionals work in healthcare institutions and it is estimated that 80,000 to 600,000 cut and puncture injuries occur among them per year, of which approximately 50% are not documented. The risk of contracting HBV by HCW is four times greater than that of the general adult population.[3,5] The highest rates are seen among dentists, surgeons, laboratory workers, dialysis workers, cleaning service employees and nurses.[3,5]

Currently, the therapeutic options for treating chronic HBV infection are not fully effective.[2] Vaccination is an easy and cost effective measure to prevent HBV infection.[6] As Hepatitis B infection is a risk to HCW and, if a healthcare worker is infected, a risk to patients too, immunization against HBV infection provides protection to both in healthcare settings. Taking measures to avoid direct contact with blood and body fluids also reduces transmission of hepatitis B from person to person.[6] Post exposure prophylaxis of vaccination and a hepatitis immune globulin (HBIG) helps prevent infection if given within 24 hours of contact of a non immunized person with HBV.

The recommended post-vaccination serum anti-HBs level is 10mIU/mL.[6] High risk groups such as HCWs should therefore be monitored after a full course of HBsAg vaccination to ensure they have protective levels of anti-HBs. If found non-immune (<10 mIU/mL), a booster or a repeat full course of vaccination must be encouraged.[7,8] The exact proportion of non-immune individuals after a single course of vaccination depends on the definition of non-responsiveness and hypo-responsiveness and are generally considered as less than 10 mIU/mL and 10 - 100 mIU/mL, respectively.[9]

The current study was carried out to assess the immune response to HBsAg vaccine in a group of immunized students in the Faculty of AHS, University of Peradeniya, Sri Lanka

Materials and methods

A cross sectional study was performed using a sample of vaccinated students, from the Faculty of Allied Health Sciences, University of Peradeniya, who consented to give blood sample to detect the immune response to HBV vacation by testing for anti-HBs levels.

Eighty nine (n=89) 23-27 year-old vaccinated AHS students were selected on convenience sampling. This sample is sufficient to draw meaningful conclusions considering the response rate to HBV vaccination in Sri Lanka[10] and the world.[5,11] After obtaining written consent for the study, the students' personal details such as age and ethnicity were recorded using a self administered short questionnaire. Vaccinated AHS students who did not consent and those >30 years were not included in the study. Venous blood samples were obtained from the study participants. Each individual blood sample was collected in a plain tube and allowed to clot at room temperature. Serum was separated by centrifugation at 2000 rpm for 5 minutes and stored at -20 ^{o}C.

An ELISA (Fortress Diagnostics Limited, United Kingdom) was used for the quantitative detection of anti-HBs levels. An internal quality control was performed using manufacturer supplied controls for <10, 10-100 and >100mIU/mL of anti-HBs. Control values and the test sample OD readings were used to calculate the cutoff values using the formula provided by the manufacturer (Fortress Diagnostics Limited, United Kingdom). All the samples were run as a single batch to avoid discrepancies.

Statistical analysis of the results was performed using the statistical software, *Graph Pad Prism Version 5.01*.

After a single course of immunization against HBV infection, vaccinees with < 10mIU/mL of anti-HBs were considered as non responders, vaccinees with anti-HBs levels between 10 and 100mIU/mL were considered as hypo-responders and vaccinees with anti-HBs levels > 100mIU/mL were considered as responders.[6,10]

Results

Table 1: Association between Anti-HBs titre, gender and ethnicity of the vaccinees

Characteristics		**< 10mIU/mL**		**10-100 mIU/mL**		**>100mIU/mL**		***p*-Value**
		n	%	n	%	n	%	
Gender	Male	0		6	27.27%	16	72.72%	0.97
	Female	1	1.49%	20	29.85%	46	68.65%	
Ethnicity								
	Sinhala	1	1.22%	24	29.26%	57	69.51%	0.67
	Tamil	0		1	25%	3	75%	
	Muslim	0		1	33.33	2	66.66%	

A total of 89 AHS students who had completed all three doses of HBsAg vaccination were tested for immunity against HBV infection. The study group had 22 males (24.7%) and 67 females (75.3%). The study participants were < 30 years old, ranging from 23-27 years with a

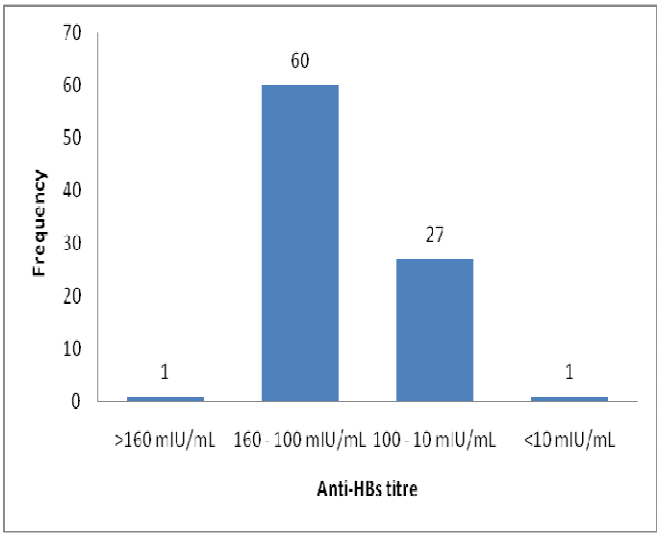

Figure 1. Anti-HBs levels in the study cohort (<10 mIU/mL to > 160 10mIU/mL).

mean age of 26.14 years. There were 82 (92.13%) sinhala students, 4 (4.49%) tamil students and 3 (3.37%) muslim students (Table 1).

Based on the vaccination records, 43 (48.31%), 37 (41.57%) and 9 (10.12%) students received the last dose of vaccine 3.5, 1.5 and 1 year(s) respectively prior to testing. The mean time lapse after the last dose of the vaccine was 2.5 years.

After a course of HBV vaccination, 1 vaccinee (1.12%) was found to be a non responder, 27 vaccinees (30.33%) were hypo-responders and 61 vaccinees (68.54%) were responders (Figure 1).

There was no significant association (P=0.6) between anti-HBs levels and the time lapse from the last dose of vaccination. Moreover, there was no significant difference in anti-HBs levels between male and females (P= 0.9). There was also no significant difference in anti-HBs levels between different age groups (P= 0.7) and ethnicities (P=0.6).

Discussion

The protective immune response resulting from hepatitis B vaccination is related to the production of anti-HBs antibodies, with the induction of memory T-cells to counteract future exposure to HBV. Two to three months after the administration of the last dose of the primary vaccination series, anti-HBs concentration reaches levels more than 10mIU/mL. Hence testing for anti-HBs after allowing 2-3 months since the last dose of a complete course of vaccination is considered a method of assuring protective immunity against HBV infection.[2]

The prevalence of non responders against HBV immunization in the general population is around 5-10% in the world[5] as well as in Sri Lanka.[10] However, in this study only one of the 89 students did not develop a protective level (<10mIU/mL) and 27 (30.33%) were hypo responders. There were also 7 participants that had between 11-12 mIU/mL anti-HBs levels approximately around the cut off value (10mIU/mL). Most previous studies have been conducted in study groups of different age groups with varying time lapses from the last dose of vaccination to the time of detection.[11] In contrast, this study was conducted in a selected cohort of young vaccinees which might explain the low rate of non-responders. However, it is interesting to note that in a population of 89 young students, 30% were hypo responders. Protective immunity of such individuals after 10 years cannot be predicted. However, studies

of 20 years duration have shown that individuals with antibody levels of >100mIU/mL after a complete course of vaccination remain immune after 20 years.[6,7]

Previous studies in Italy (p=0.5) and Pakistan showed a significant association between immune response and gender,[5,11] A Netherlands based study found more than 5% of subjects from the age of 29 in men and 43 in women were non responders.[8] Compared with women, men had a higher risk of non-responsiveness and exhibited a steeper decline in production of antibody titres with increasing age.[8] In another study, the percentage of male non responders (18%) was more than twice of the female (8%) counterparts ($p=0.05$).[5] In contrast, there was no significant difference ($P= 0.7$) in anti-HBs production between male and female students in the current study. However, the small sample size (n= 89) and low number of males (24.5%) is a limitation in the current study.

A reduced immune response has been reported with vaccination of individuals over 40 years of age.[5] As the participants in the current study were <30 years, the absence of an age related effect is not surprising. Detection of a single non-responder in this relatively small population highlights the necessity of testing for anti-HBs levels after completing a whole course of Hepatitis B vaccination.

In conclusion, after a complete course of HBV vaccination, 98.88% of the vaccinees (88/89) had protective immunity level of >10mIU/mL of anti-HBs titre. However, one vaccinee out of the 89 (1.12%) was found to be a non responder after a single complete course of HBV vaccination with anti-HBs titre of <10mIU/mL. There was no significant difference in anti-HBs levels between male and female AHS students. The study highlights the necessity of testing for anti-HBs levels after completing a complete course of hepatitis B vaccination.

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