Immune Response to Recombinant Purified Hepatitis B Surface Antigen Vaccine among Health Care Workers in Jos, North Central Nigeria

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Abstract:
Background: Seroconversion rates reported after Hepatitis B virus (HBV) vaccination globally ranges from 85–90%. Health care workers (HCW) in health institutions are at risk of acquiring hepatitis B infection. Therefore, this study determined through qualitative evaluation of immune responses to recombinant purified hepatitis B surface antigen vaccine among health care workers in Jos, North central Nigeria.

Methods: Health care workers who had received recombinant purified HBsAg vaccine at the Jos University Teaching Hospital (JUTH), AIDS Prevention in Nigeria (APIN) supported HIV were evaluated for immune response through qualitative method 6 weeks post-vaccination. Descriptive observational study design was used in this survey from April 2012 to June 2013

Results: Study subjects (HCW) were 115. Females were 68 (59.1%), males were 47(40.9%). Study participants were between the ages of 25-34 years (51.3%) regardless of gender. Out of the 115 participants examined 99(86.1%) had established HBsAb while 16(13.9%) remained seronegative after six weeks of post vaccination. The mean age of responders was 36.0 ±6.9 years.

Conclusion: Our study showed that majority of the HCW at APIN JUTH, who received the purified recombinant HBsAg vaccine had immunologic response. This response is however varied according to age groups. The study participants who are aged less than 44 years were more likely to respond satisfactorily. These underscore the importance of checking immune response to this vaccine among HCW, to ensure they are protected against nosocomial acquisition of HBV. Health care workers who fail to respond to vaccination after standard dosing should be given a fourth dose or the entire course of vaccination repeated.

Keywords: Hepatitis B virus, Vaccine, anti-HBs, Qualitative

I. Introduction

Hepatitis B virus (HBV) infection and its resulting conditions, including chronic liver disease, cirrhosis and hepatocellular carcinoma are major global health problems. It is estimated that 2 billion of the world’s population has been infected with the hepatitis B virus and about 350 million people are reported to be chronically infected with the virus worldwide and constitute the primary reservoir of infection 1.

Prevention of health care workers (HCWs) from the acquisition of hepatitis B virus (HBV) infection; especially those that are in frequent contact with blood are a major public health concern. Health care workers in health institutions especially those that cater for infectious diseases are at high risk of acquiring the HBV infection and possibly becoming chronically infected, the risk of acquisition of HBV infection after a single exposure of HBV infected blood or body fluid ranges from 6%-30%. 2, 3, 4 In addition to health education directed toward decreasing high risk behavior, vaccination is the best tool in protecting HCWs. Since the availability of HBV vaccine from 1982, the decline in the incidence of HBV infection and associated morbidity and mortality has been reported 5, 6, 7, 8. Therefore, in 1997 CDC recommended that all HCWs should be vaccinated against HBV 9. Despite the recommendation and excellent protection profile among HCWs vaccinated personnel, compliance to this recommendation remained poor in various health care settings 10, 11. Factors associated with decreased immune response to HBV vaccine include: increasing age, smoking, obesity, gender and genetic factors 12-14. Studies on HCWs published from various parts of the world have reported 12-21% non responders to HBV vaccine. Despite HBV infection being a major health care issue in both community and nosocomial settings in Nigeria, information on the qualitative immune response in HCWs is scarce. Therefore, we determined the immune responses to recombinant purified Hepatitis B surface antigen vaccine among HCWs in Jos, North central Nigeria using qualitative technique.
II. Methods

Serum samples from HCWs were screened for HBsAg those that were negative, who consented to be part of the study had HBV vaccine 1ml (20mcg) administered intramuscularly in the deltoid muscle at months 0, 1, and 6 respectively. Eight weeks later, five milliliters of their venous blood was collected into container with EDTA. The plasma separated immediately by placing the specimen EDTA bottle on a standing position in a rack. Testing for antibodies was performed using the Rapid HBV COMBO test kit Acumen Diagnostic Inc. U.S.A according to manufacturer’s instructions. Data was analyzed using SPSS version 17.

III. Results

A total of 115 HCWs were enrolled for this study. Females were 68(59.1%) and males were 47(40.9%). The overall response rate of health care workers at the APIN center to the Hepatitis B vaccine after 3 doses and six weeks post vaccination was 99 (86.1%) (Table 1) and (Fig 1). After six weeks post vaccination, 13.9% of the HCWs did not develop HBsAb and were tagged non-respondents. (Fig1). Majority of the study participants were between the ages of 25-44 years with mean age of study participants 37.4±7.5years. The age group of workers between 25-34years and 35-44 years showed the highest response (84.3%) to the vaccine establishing HBsAb after 6weeks post vaccination. The mean age of male non responders was higher than that for females, 43±15.7 years and 34.7±2.75years respectively and also showed a significantly reduced response to the vaccine than females (P<0.05, 95%CI=4.9)

Table 1: Demographic characteristics of study subjects

<table>
<thead>
<tr>
<th></th>
<th>n after 3 doses (%)</th>
<th>n respondents (%)</th>
<th>Non-respondents (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>115</td>
<td>99(86.1)</td>
<td>16(13.9)</td>
</tr>
<tr>
<td>Males</td>
<td>47(40.9)</td>
<td>39(39.2)</td>
<td>8(6.9)</td>
</tr>
<tr>
<td>Females</td>
<td>68(59.1)</td>
<td>60(58.8)</td>
<td>8(50.0)</td>
</tr>
<tr>
<td>25-34 years</td>
<td>48(100)</td>
<td>42(87.5)</td>
<td>6(12.5)</td>
</tr>
<tr>
<td>35-44 years</td>
<td>50(100)</td>
<td>41(82.0)</td>
<td>9(18.0)</td>
</tr>
<tr>
<td>45-49 years</td>
<td>10(100)</td>
<td>10(100)</td>
<td>0</td>
</tr>
<tr>
<td>≥ 50 years</td>
<td>7(100)</td>
<td>6(85.7)</td>
<td>1(14.3)</td>
</tr>
</tbody>
</table>

Table 2: Immune Response according Age and sex distribution of study subjects

<table>
<thead>
<tr>
<th>Responders (n %)</th>
<th>25-34 yrs</th>
<th>35-44 yrs</th>
<th>45-49 yrs</th>
<th>≥50yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>n=60</td>
<td>24(24.2)</td>
<td>27(27.3)</td>
<td>6(6.1)</td>
</tr>
<tr>
<td>Male</td>
<td>n=39</td>
<td>18(18.2)</td>
<td>14(14.1)</td>
<td>4(4.0)</td>
</tr>
<tr>
<td>Non-Responders (n %)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>n=8</td>
<td>4(25.0)</td>
<td>3(18.7)</td>
<td>0</td>
</tr>
<tr>
<td>Male</td>
<td>n=8</td>
<td>2(12.5)</td>
<td>6(37.5)</td>
<td>0</td>
</tr>
</tbody>
</table>

Figure 1: Descriptive distribution of Age, sex and Response

IV. Discussion

In this study, 99 (86.1%) of study participants established HBsAb after six weeks post vaccination while 13.9% remained non-respondents failing to establish the HbsAb after recommended routine HBV vaccination. From a public health standpoint, these results indicate that a follow up test post vaccination is an
important strategy to employ in the safety of health care workers. These findings are similar to those reported by Zeeshan et al. (2007) who observed 86.2% responders and 13.2% non-responders among HCWs in Pakistan.  

Roome et al. (1993), Averhoff et al. (1998) and Saberifroozi et al. (2006) have reported 11.9%, 12% and 12.7% non-responders respectively in the USA and Iran.

In this study, age and gender were the two variables considered. Among respondents 84.3 % (86) were between the ages of 25-44years (Table 2). A study carried out in Sweden on response rates after intradermal vaccination in HCWs observed a higher response in subjects below the age of 40 and a significantly lower response in subjects older than 40 years. Similarly, the frequency of non-respondents in our study were also from study participants between the ages of 25-44 years (Table 2). While it has been shown that increase in non-respondent age increases with age, this may be explained by other risk factors such as smoking, body mass index and alcohol intake which were not evaluated by our study.

Male non-respondents showed a significantly reduced response to the vaccine than female non-responders (P<0.035). Smoking and other genetic factors which could contribute to poor response in men have not been explored in this study. In Pakistan, a study among HCWs showed that the frequency of male non-responders was higher than female non-responders 18% and 9% respectively (P=0.001).

The frequency of occurrence for male non-responders in this study was 6.9% and 6.9% for females. The results of this study suggest that both male and female health care workers are at equal risk of exposure to HBV. This result differs from the findings reported by Wood et al 1993 and Zeeshan et al (2007) who observed a response rate of 18% and 9% respectively of male and female (P=0.006 and 0.00) respectively. A recent study showed lower response in healthy homosexual men compared to healthy workers also an association with different HLA-DR alleles has been found in different studies, those with HLA phenotype of B44, DRB1*0701, DQB1 *0201 were nearly four times likely to be non-respondents compared to respondents. It is possible that the response may be specific to HBV surface antigen recognition. The ability to produce antibody in response to a specific protein is controlled by dominant autosomal class II genes of the major histocompatibility complex (MHC). Smoking and certain genetic factors have been reported as probable reasons of decreased immune response in male. Uppermost rate of immune response was observed among those with age group of 25-44years and started decline with increasing in age (p=0.0001). Among HCWs >50 years of age, only 6.9% developed to HBV vaccine, though the sample size in this group was small, the findings are more or less in agreement with Roome et al’s (1993) observation of inadequate levels of antibodies in relation to increasing age, from 2.8% among those younger than 30years to 42.1% among those older than 60 years (p<0.0001) of age. This finding has great clinical significance as non-responders remain susceptible to HBV infections. Therefore, from an infection control perspective, the post vaccination HbsAb establishment should be determined for all HCWs. In Nigeria, there is limited data regarding immune response after HBV vaccination in HCWs, this study therefore adds to the growing body of reports on immune responses to HBV vaccine in HCWs from different parts of the world.

A limitation of this study was the absence of a quantitative determination of anti-HBs titres. However, in a resource limited setting our results provide a baseline for future epidemiological studies in this area. Also we did not evaluate the association of decreased immune response with risk factors other than age and gender. Struve et al (1992) and Winter et al (1994) have suggested smoking as a risk factor in poor response to HBV vaccine. Obesity defined as a BMI>30 has been suggested to increase the risk of vaccine failure as observed in the very obese with BMI over thirty five. Immunosuppression has also been reported by some authors to result in reduced response rates to vaccination. The response to vaccine in HIV infected patients has been shown to be related to low CD4+ counts and high HIV-RNA levels. Other factors that have been mentioned are nutritional status, site of administration of vaccine, and immunogenetic make up also contributed to reduced immune response.

V. Conclusion

The use of qualitative method to determine the immunological response among HCWs can be adopted among health institution bearing in mind the economic burden when using the quantitative technique. In this study we were able to establish that HCWs with HbsAb responded well to the establishment of HbsAb using the qualitative technique. There is a need to strictly implement the policy of hepatitis B immunization in every health care location as recommended by CDC. It is also imperative to check the post vaccination status of all HCWs after 6-8 weeks of vaccination as it not ensure safety of employees but also reduces rate of transmission hence functioning as a cost effective exercise at individual as well as national level. This is the first qualitative study that provides the local epidemiological information assessing the immune response to HBV vaccine among HCWs in Nigeria.

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VI. Recommendation

Post vaccination testing is recommended for high risk person, including health-care and public safety workers; chronic hemodialysis patients, HIV-infected persons, and other immunocompromised persons, and sex or needle-sharing partners of HBsAg-positive persons. Though, in majority of health institutions in Nigeria this practice is usually not followed 20. The importance of pre-exposure vaccination cannot be over emphasize because of the cost effectiveness that the post exposure which cost more and the extra cost burden could either be on the HHCWs or the institution especially in the developing world.

VII. Conflict of Interest

None

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References