STUDY OF IMMUNE RESPONSE AFTER HEPATITIS B VACCINATION IN MEDICAL STUDENTS AND HEALTH CARE WORKERS

Sunita Tripathy¹, HC Sati², Puspa³, Seema Saha³, Ravi Shankar⁴, VK Singh⁵

ABSTRACT

Introduction- Hepatitis B Virus infection is a major public health problem and causes majority of primary liver cancer. Transmission of hepatitis B by blood transfusion and other medical intervention is well known. So medical students and health care workers are at higher risk of infection than general population. Because there is no effective treatment for Hepatitis B, it is necessary to prevent it by vaccination. Aim and Objective – (1) To evaluate the immune response after hepatitis B Vaccination in Medical Students. (2) To determine the duration of persistence of protective antibody level in Medical students and other health care workers.

Material And Method- This study was conducted in Biochemistry dept of Govt. Medical College and hospital, Haldwani, Uttarakhand, on medical students, technicians, and doctors of this medical college. All the participants had received Hepatitis B Vaccine (Engerix –B, Recombinant DNA Vaccine). Serum samples were collected from all participants for estimation of anti Hepatitis B surface antibody(HbsAb) level, after various duration of vaccination. From I year MBBS students one serum sample was collected before vaccination also. Estimation of HbsAb level was done by MINIVIDAS by immunofluorescence technique. Observation and Result – There were 100 individuals (medical students, doctors and lab technicians) included in this study. Rate of seroconversion was 100% in medical students. All were responders (HbsAb>100 mIU/ml) after 8 weeks of primary vaccination except one who was hyporesponder (HbsAb level <100mIU/ml). Majority (80%) had high response (HbsAb>1000 mIU/ml). Mean antibody titre of first year students after 8 weeks of primary vaccination was 3221 mIU/ml. While determining the persistence of protective antibody level, we found that 88.236% of participants had protective levels of antibody within 5 years of vaccination and 85% had protective levels even after 10 years. There was no significant difference of mean antibody titre between male and female participants.

Discussion- Hepatitis B is the most infectious out of HBV, HVC AND HIV Infectivity. It is well accepted that Hepatitis B vaccination induces protective level of antibody after complete course of vaccination. There are few genuine non responders .So post vaccination screening should be done in health professionals within 1-6 months of primary vaccination. Seroconversion rate of Hepatitis B vaccine globally ranges from 85-90%). In our study we found 100% seroconversion in medical students and among them 80% had high response (HbsAb > 1000 mIU/ml) after primary vaccination. Kunal Das et al showed that among seroprotected individuals there were 32.4% hyporesponders (HbsAb level 10 - 99 mIU/ml ) and 52.9% were responders (anti HbsAb >100mIU/ml). In our study there was only 5% hyporesponder and rest 95% were responders. It has been appreciated that protection may be provided for at least 25 years due to long term immunity. Our study suggested that DNA recombinant vaccine maintains protective level of HBs Ab for more than 10 years. Conclusion: Seroconversion rate is 100% in healthy young individuals. Hepatitis-B vaccine (recombinant DNA) protects for more than 10 years after primary vaccination. Probably booster dose of Hepatitis-B vaccine is not required in immunocompetent persons.

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INTRODUCTION

Hepatitis-B virus infection is a global public health problem with approximately 400 million people chronically infected. Infection due to Hepatitis B virus results wide spectrum of liver diseases ranging from fulminant hepatitis to cirrhosis and hepatocellular carcinoma. Despite advances in antiviral therapy, only a minority of chronic hepatitis B patients have a sustained response. Thus primary prevention by vaccination remains the main thrust in the control of hepatitis B infection. The health care workers and medical students are at risk of infection with hepatitis B virus through occupational exposure to blood and infectious body fluids.

Recombinant DNA Vaccine is available since 1987. Intramuscular vaccine administration at 0,1,6 month produces 85-90% seroprotection rate in adolescents. When primary vaccination produces HBsAb (hepatitis B surface antibody) level >100 mIU/ml, it is considered to be adequate response or the vaccine is called responders. If between 10-100 mIU/ml, then hypo responders and if it is <10 mIU/ml, then there is no response or non responder.

Hepatitis B surface antibody titre >10mIU/ml is considered to be a marker of sustained immunity. Seroprotection persists for 10-15 years and so booster vaccination may not be necessary for 15 years post vaccination.

AIM–
1. To evaluate the immune response after hepatitis B vaccination in Medical Students.
2. To determine the duration of persistence of protective antibody level in Medical students and other health care workers.

MATERIAL AND METHOD

This study was conducted in the dept. of biochemistry Govt. Medical college Haldwani, Uttaranchal, during 2007-2008. The subjects included were 1st year to 4th year MBBS students of the medical college and doctors and lab technicians working in STM hospital, which is the teaching hospital of this medical college. As a matter of policy followed in our medical college, all the students joining MBBS course are vaccinated against Hepatitis-B, irrespective of their immunity status. So to start with we selected 20 students of 1st year randomly and collected 2-blood samples for HBsAb, one before vaccination to know their immunity status and second sample 8 weeks after complete course of vaccination, to see the immune response or sero-conversion. They had received 3-doses schedule of Hepatitis B -Recombinant vaccine (Engerix) intramuscularly at 0, 1, 6 months duration.

Then we collected one blood samples from 2nd year, 3rd year and 4th year MBBS students (20 each) who were vaccinated during their admission to MBBS course and also from 20 other students, doctors and lab technicians who were vaccinated for more than 5 or 10 years ago, to know the period of persistence of antibody after primary vaccination. Blood samples were analyzed for Hepatitis B surface antibody (HBsAb) level by ELFA (Enzyme linked Fluorescent Assay) by Mini Vidas (Biomeureux) by a local pathology lab by outsourcing.
OBSERVATION

100 subjects included in this study were divided into four groups according to duration of post primary vaccination.

Group I- Students of First MBBS who were vaccinated in Sept-2007 and antibody level estimated after 8 weeks of primary vaccination.

Group II- Students of 2nd year to 4th year MBBS, vaccinated for less than 5 years.

Group III- Students and Lab technicians vaccinated for more than 5 years and less than 10 yrs

Group IV- Doctors and technicians vaccinated for more than 10 years

Table- 1 shows age and sex distribution of study group. Out of 100 participants 47 % were male and 53% were female. Majority of them were in the age group of 20 to 24 years. Only 6% individuals were more than 40 years.

The seroconversion rate was 100% (HBsAb>10 mIU/ml). Among them 80% had high response (HBsAb >1000 mIU/ml), 20% were hypo-responders (HBsAb=10 mIU/ml -100 mIU/ml)

Nobody was non-responder in our study. There was no significant difference of immune response between male and female participant

From this table we can say that antibody decay occurs with time. In our study mean antibody level after 8 weeks of post vaccination was 3221 mIU/ml, where as it was 1298 mIU/ml, up to 5 years and antibody level was 289 mIU/ml in Gr-III (5-10 yrs post vaccination). We didn’t find decreasing tendency in Gr-IV in comparison to Gr-III. Even after 10 yrs antibody level was in the protective rang.

Table 1: Age and Sex distribution

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-19</td>
<td>9</td>
<td>13</td>
<td>22</td>
</tr>
<tr>
<td>20-24</td>
<td>21</td>
<td>29</td>
<td>50</td>
</tr>
<tr>
<td>25-29</td>
<td>6</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>30-34</td>
<td>6</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>35-39</td>
<td>-</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>40 &amp; above</td>
<td>5</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Grand total</td>
<td>47</td>
<td>53</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 2: Antibody titer of 1st year MBBS students before and after vaccination

No. | Sex | Mean Age (yrs) | Mean Ab titre (mIU/ml) | Mean HBsAb titre (mIU/ml)
---|-----|----------------|------------------------|------------------------|
| 10 | Female | 19.4 | Undetectable | 2809 |
| 10 | Male | 20.0 | Undetectable | 3633 |
| Mean | 19.7 | | 3221 |

Table 3: Group wise distribution of individuals with mean age and mean antibody titre

<table>
<thead>
<tr>
<th>Groups</th>
<th>Male</th>
<th>Female</th>
<th>Mean Age</th>
<th>Mean HBsAb titre (mIU/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (8 weeks post Primary vaccination)</td>
<td>10</td>
<td>10</td>
<td>19.7</td>
<td>3221.00</td>
</tr>
<tr>
<td>II (9 weeks to 5 years post Primary vaccination.)</td>
<td>28</td>
<td>32</td>
<td>21.88</td>
<td>1298.94</td>
</tr>
<tr>
<td>III (&gt; 5 to &lt;10 years of vaccination)</td>
<td>5</td>
<td>5</td>
<td>25.67</td>
<td>289.42</td>
</tr>
<tr>
<td>IV IV (10 years or more of vaccination)</td>
<td>4</td>
<td>6</td>
<td>30.7</td>
<td>344.50</td>
</tr>
</tbody>
</table>
Table 4 shows the difference in mean antibody titre in relation to different sex. There was no significant difference of mean antibody titre in between male and female (p=0.499).

Table 5 shows the relationship between mean antibody titre with age. According to the age we divided 100 individuals into 2 groups . Group A < 25 years and group B > 25 years. There was significant difference of mean antibody titre in these groups. (P=0.05)

Table 6 shows rate of decay in 2-groups, by comparing mean antibody titre with post vaccination duration < 5 years and > 5 years, irrespective of age. Our study showed that there was significant difference in Mean antibody titre of those individuals who were vaccinated for < 5 years duration than those vaccinated for > 5 years.

Table-7 comparing mean antibody titre in different age groups (when duration of vaccination >10).There was statistically significant difference in mean antibody in individuals of age group <25 years than those who were >25 years of age (p= 0.004) when post vaccination period is more than 10 years in both groups.

Table 8 shows relation of antibody titre with different age groups (< 25 years and > 25 years) when duration of vaccination is more than 5 years in both. There was no significant difference (p= 0.103)

RESULT

There were 100 individuals (medical students, doctors and lab technicians) included in this study .Out of which 47% were male and 53% were female. 50 % were in the age group of 20-24 years. Rate of seroconversion was 100% in medical students. All were responders (HBsAb>100 mIU/ml) after 8 weeks of primary vaccination except one who was hyporesponder (HBsAb level <100mIU/ml). Majority (80%) had high response (HBsAb>1000 mIU/ml).Mean antibody titre of first year students after 8 weeks of primary vaccination was 3221 mIU/ml.
While determining the persistence of protective antibody level, we found that 88.236% of participants had protective levels of antibody within 5 years of vaccination and 85% had protective levels even after 10 years. There was no significant difference of mean antibody titre between male and female participants. There was significant decrease in mean antibody titre (antibody decay) with the increase in the duration of post primary vaccination. HBsAb titre was 3221 mIU/ml just after 8 weeks of vaccination where as it was 289.42 mIU/ml within 5-10 years. Protective level of HBs-Ab titre persisted even after 10 years.

We found a significant difference of mean antibody level between younger and older age group. There was significant difference in antibody titre below and above 25 years of age where the duration of vaccination was more than 10 years (p<0.05). Where as it was non-significant and when duration of vaccination was 5-10 years (p=0.103).

DISCUSSION

Hepatitis B is the most infectious out of HBV, HVC AND HIV Infectivity. It is well accepted that Hepatitis B vaccination induces protective level of antibody after complete course of vaccination. There are few genuine non responders (11, 12, 13, 14). So post vaccination screening should be done in health professionals within 1-6 months of primary vaccination. In UK evidence of HBsAb titre of >100 mIU/ml is required before medical students are allowed access to patient. Students with serum level of HBsAb < 10 mIU/ml have to repeat the full vaccination and those with 10-99 mIU/ml are required to receive a single booster vaccination (15,16,17).

Seroconversion rate of Hepatitis B vaccine globally ranges from 85-90% (18). A K Jain et al found seroconversion rate of 98.45%. (19). Kruman.S et al found 99% of subjects developed protective level of HBsAb after vaccination with Recombivax HB (Merck) after 1 month of last dose in his study (20). In our study we found 100% seroconversion in medical students and among them 80% had high response (HBsAb > 1000 mIU/ml) after primary vaccination with Engerix-B vaccine. But we could not evaluate seroconversion rate in other groups (doctors and technicians) because individuals in these groups were vaccinated 5-10 years back. The US Public Health Service Advisory Committee On Immunization Practice (ACPI) recommendation issued in 1987 defined the protective level of anti HBs-Ab as greater than or equal to 10 mIU/ml, measured 1-2 months after completion of hepatitis b vaccine series (21,22). An Indian study conducted by Kunal Das showed that among seroprotected individuals there were 32.4% hyporesponders (HBsAb level 10-99 mIU/ml) and 52.9% were responders (anti HBsAb >100mIU/ml). (23). In our study there was only 5% hyporesponder and rest 95% were responders.

There are some known factors like gender, smoking and obesity which influence immune response. Brian J Mac Mohan reported males had higher antibody level than females (24). Where as Jane W.S Fang et al found that female children responded with a significantly higher antibody level than male children. (25). In the study conducted by Mohd.Abdul in Bangladesh had protective level of anti HBs antibody in 85.88% males and 92.31% of females. (26). Glaser et al found in his study that antibody level becomes less in persons undergoing more stress than less stress one. (27). Dr Hayley Willecy also found that those above 40 years, obese and smokers are more likely to fail to respond (28). In the study conducted by Ann P. Winter, higher proportion of smokers failed to seroconvert after 3 doses of hepatitis vaccine. (29) But we did not find such difference, may be due to same level of stress in both male & female medical students and also because there was no smoker or obese individual in our study group which parameters usually affects antibody level.
It has been reported that antibody response decreases with age. R. John Looney found that antibody response was dramatically different between young and elderly group. In his study, 35 / 35 young developed protective titre versus 19 / 45 elderly. (30). We did not find the significant difference in mean antibody titre in different age groups, when duration of vaccination was less than 5 years. But there was significant difference in antibody level between age group < 25 years and > 25 years when duration of vaccination was more than 10 years. Study conducted by Kunal das et al', Seroprotection (HBsAb >10 mIU/ml) after primary vaccination was achieved in 85.3% volunteers who were more than 40 years of age. Surg Cdr C N Choudhury et al concluded in his study that higher age at vaccination is a risk factor for low antibody response. (31) we could not compare elderly group for seroconversion with young medical students because participants of more than 40 years had their primary vaccination 5-10 years back.

There are few long term studies which suggest that hepatitis B vaccine protects an individual for more than 15 years (32, 33). Jafar zadeh et al evaluated persistence of antibody level in healthy Iranian children at 10 years after primary vaccination and found that 47.9% of children had protective level of HBsAb >10 mIU/ml. (34) It has been seen that approximately 20% geometric mean titre decay occurs per year (35). We did not estimate geometric mean titre decay. We studied persistence of antibody level in different individuals, where we found that, antibody level decreases with time. In our study mean Ab titer was 3321 mIU/ml 8 weeks after vaccination, 1298.94 mIU/ml within 5 years and 289.42 mIU/ml within 10 years.

Although initially it was thought that Hepatitis B vaccination does not provide indefinite protection. This is no longer considered. Previous reports suggested that primary vaccination would provide protection between 5-7 years (36,37). But subsequently it has been appreciated that protection may be provided for at least 25 years due to long term immunity derived from immunological memory in those individuals who showed adequate response to primary Hepatitis vaccination (38). Our study suggested that DNA recombinant vaccine maintains protective level of HBs Ab for more than 10 years. Gabbuti et al suggested that booster dose is not required in immunocompetent individuals. (39).

CONCLUSION.

Seroconversion rate is 100% in healthy young individuals. HBsAb level decreases after certain period as age advances. Hepatitis-B vaccine (recombinant DNA) protects for more than 10 years after primary vaccination. Probably booster dose of Hepatitis-B vaccine is not required in immunocompetent persons after 5 years of primary vaccination which is a usual practice.

LIMITATION-Persistence of protective level of antibody against HBV infection was studied in different individuals for different post vaccination duration. It needs a long term continuous monitoring of same study group over 10-15 years.

REFERENCES

14. SS Chious et al. Nature of Immunological non responsiveness to Hepatitis B vaccine in healthy individuals. Journal Immunology, 1988 July; 64(3).545-50

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