

Assessment of Immunization Rate of Hepatitis B Vaccination among Health Care Personnel in Tehran

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ABSTRACT

Background

Hepatitis B is one of the most important etiologic factors of acute and chronic hepatitis, cirrhosis of the liver and hepatocellular carcinoma. The best preventive method is vaccination. The Aim of the study was to evaluate the immunization rate against hepatitis B in medical health personnel.

Materials and Methods

This study was conducted on 331 health care workers employed in public, semiprivate, and private hospitals that had received the complete dosage of vaccination with an average duration of 0-3 years since the last dose, and had not previously received any booster or HBV - Immunoglobulin.

The Shariati (public), Imam Khomeini (public), Baqiyatallah (semi-private) and Day (private) hospitals were the sites of our research. Regarding the age and occupational status, persons were randomly selected and data relating to demographic aspects and serum anti-HBs titer were recorded in all individuals and then were evaluated.

Results

Results show that out of the 331 cases, 47 (14.2%) were non-responder (Anti-HBs titer <10 IU/L), 160 (54.4%) had low response ($10 \leq$ Anti-HBs titer ≤ 100 IU/L), and 104 persons (31.4%) were found to have good response (Anti-HBs titer >100 IU/liter). There was no significant relationship between the antibody titer and other variables including age, gender, smoking, body mass index (BMI) and duration since last dose of vaccine.

Conclusions

We suggest the assessment of Anti-HBs titer after complete vaccination in high-risk groups to find non- and low-responders in order to revaccinate them.

Keywords: Hepatitis B, vaccination, Anti-HBs titer

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INTRODUCTION

Hepatitis B infection is one of the major health problems throughout the world with the annual

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infection rate of 350 million cases.(1), According to the WHO data, 75% of this rate is related to the Asian countries.(2), The prevalence of this infection varies among different countries from 10-20% for the Far East (including China and Hong Kong)(3) to 3-5% for the middle-east countries (including Iran).(4, 5), According to the WHO statistics, the mortality rate of this infection

had reached to 700,000 cases by the year 1997.(2), Hepatitis B virus is also counted as one of the most common causes of hepatocellular carcinoma (HCC).(6-10), In endemic areas, the rate of positive HBsAg is to 78-95% in patients with HCC.(8)

Due to the high prevalence of hepatitis B and the absence of a definite treatment, vaccination against this infection has become a topic of interest.(10), Fortunately following a worldwide vaccination program against this virus, the prevalence rate of both hepatitis B and HCC has been reduced. It is even possible to eradicate this disease provided that its mode of transmission is disturbed.(11-13), Considering the number of infected persons and the excessive amount of budget required for the treatment of the disease or its complications, hepatitis B vaccination has been entered into our country's vaccination program to cover the high-risk groups and the newborns.(14), To our knowledge, although many years have passed since the execution of the vaccination project in Iran, comparative studies concerning the response rate and persistence of antibody following the vaccination, especially among the high-risk groups, are scanty. In a pilot study, the immunization rate after vaccination among the medical health workers was only 75%.(13), The immunization rate depends on numerous host factors as well as the type and method of the vaccination.(15, 16), This study was designed and conducted so as to assess the response rate to vaccination and factors affecting it.

MATERIALS AND METHODS

Population under study

Due to the high probability of exposure to HB virus among the health care workers, these personnel were enrolled in the study. In order to exclude any probable error, subjects were randomly selected from public (Shariati and Imam Khomeini), semi-private (Baqiyatallah) and private (Day) hospitals and then entered into the study considering the following criteria:

- 1- Full-time hospital employees
- 2- High-risk group personnel including those involved in the patient's care and the human products
- 3- No past history of clinical acute or chronic hepatitis B
- 4- Complete hepatitis B vaccination
- 5- Age below 50
- 6- No previous hepatitis B booster vaccination
- 7- No previous use of specific immunoglobulin against hepatitis B
- 8- Maximum duration of 36 months following the last dose of vaccination
- 9- Absence of disease or immunity affecting state

With regard to the primary study (the pilot study)(13), the specimen volume was calculated to be 323 persons for this study.

Method of study

Individuals were randomly selected from a list of medical health care workers (as the high risk group) employed in public (Shariati, Imam Khomeini), semi-private (Baghiatallah Azam) and private (Day) hospitals considering the inclusion criteria. All the subjects had been vaccinated by a recombinant HB vaccine produced in yeast (Heberbiovac, S.A. Havana, Cuba). Afterwards, trained individuals filled out the questionnaire planned for this study. A total number of 347 persons were enrolled and 5 ml of blood was taken from each one and sent to the referral laboratory. In the laboratory, the sera were separated and assessed for Anti-HBC and Anti-HBs titer (quantitative and titration study) using the Elisa technique with Organon kits produced in Holland. All Anti-HBc positive sera were excluded, thereby leaving a total of 331 subjects as the population entered the study, then the required evaluations conducted regarding to their age, gender, duration since last dose of vaccine, location of the employment, BMI*, smoking habit and Anti-HBs titer. All data were analyzed by the SPSS software.

* Body Mass Index

RESULTS

At the end of the specimen collection and appropriate laboratory tests, individuals were divided into 3 groups according to their Anti-HBs titer; non-responders (serum level <10 IU/liter), low responders (serum level=10-100 IU/liter) and good responders (serum level >100 IU/liter).(17), The following results were then obtained:

Mean and frequency distribution of persons under study according to serum antibody titer

Of the 331 cases, 47 (14.2%) had no response to the vaccination, 180 (54.4%) and 104 (31.4%) were in low responder and good responder groups, respectively (Table 1). With an estimation of 95% of the medical health care workers having characteristics similar to the population under study, we found that 10.4-18% was non-responder, 49-59.8% was low and 26.4-36.4% was good responder. The mean serum antibody level in this population was 70.8 IU/liter and the distribution was compatible with the normal curve.

Table 1. Frequency distribution according to antibody titer and gender

Antibody titer (IU/L)	Gender		
	0-9	10-100	>100
Male	18 (14.5%)	64 (51.6%)	42 (33.9%)
Female	29 (14%)	116 (56%)	62 (30%)
Total	47 (14.2%)	180 (54.4%)	104 (31.4%)

Mean and frequency distribution of serum antibody level according to gender

There were 124 (37.5%) male and 207 (62.5%) female among 331 cases (Table 1). 14.5% of men and 14% of women were non-responder, 51.6% of men and 56% of women were in low and 33.9% of men and 30% of women were in good responder groups. A significant difference therefore, was not seen between the two groups of men and women.

Mean and frequency distribution of serum antibody level according to age

The population under study (331 subjects) were classified into three age groups, 20-30 years, 31-40 years and 41-50 years which made up of 210 (63.4%), 96 (29%) and 25 (7.6%) persons in each group, respectively. Obviously, because of the constitution of the study there was no case under 20 years. Within these three age groups, 13.8%, 14.6% and 16% of subjects were non-responder, 54.3%, 52.1% and 64% were low responder and 31.9% , 33.3% and 20% were good responder which means that no significant difference existed among these three age groups.

Mean and distribution of serum antibody level according to the duration following the last dose of vaccination

331 cases were divided into three groups of which 147 persons (44.4%) had received the last dose of vaccine between 0-12 months, 79 persons (23.9%) between 13-24 months, and 105 persons (31.7%) between 25-36 months before the beginning of study. In each of the three groups, 9.5%, 24.1% and 13.3% were non-responder, 56.5%, 48.1% and 56.2% were low responder and 34%, 27.8% and 30.5% were good responder (Table 2). There was no significant difference with regard to the Anti-HBS titer among these three groups.

Table 2. Antibody titer according to last dose of vaccination

Time (months)	Anti HBs titer (IU/L)		
	0-9	10-100	>100
0-12	9.5%	56.5%	34%
13-24	24.1%	48.1%	27.8%
25-36	13.3%	56.2%	30.5%
Total	14.2%	54.4%	31.4%

Mean and frequency distribution of antibody level according to smoking habit

Only 10% of this population was smokers and the other 90% (298) had no history of smoking. Among smokers and non-smokers 15.1% and

14.1% were non-responder, 60.7% and 53.7% were low responder and 24.2% and 32.2% were good responder, respectively. No significant difference was found between the smokers and non-smokers according to the Anti-HBS titer.

Mean and frequency distribution of antibody level according to BMI

According to the body weight, all the cases were divided into two groups. A group with normal body weight (BMI \leq 25) and an overweight group which comprised of 253 (76.3%) and 78 persons (23.7%) respectively. Of these, 14% and 15% were reported to be non-responder, 52.5% and 60% were low responder, and 33.5% and 25% were good responder respectively. No significant difference established between these two groups.

Mean and frequency distribution of antibody level according to the staff's work place

Among 331 persons entered the study, there were 145 (33.8%) cases in public hospitals, 96 (29%) in semi-private, and 90 (27.2%) in private hospitals. Of these three groups, 18.6%, 9.4% and 12.2% were found to be non-responder, 67.6%, 61.4% and 25.5% were low responder and 13.8%, 29.2% and 62.3% were in good response state respectively (Table 3). According to the Anti-HBS titer, a significant difference was found to exist among the personnel employed in the three different types of hospitals ($p<0.0001$).

Table 3. Antibody titer according to the place of employment ($p<0.0001$)

Place of employment	Anti HBs titer (IU/L)		
	0-9	10-100	>100
Public hospitals	18.6%	67.6%	13.8%
Semi-private hospitals	9.4%	61.4%	29.2%
Private hospitals	12.2%	25.5%	62.3%

DISCUSSION

According to the WHO report; the rate of the hepatitis B infection has reached 350 million cases per year.(1), This infection is the major etiologic factor of cirrhosis and carcinoma of the

liver(5-7) and the probability of developing HCC is 200 times more frequent in the cases with hepatitis B infection compared to normal subjects.(8,9), Health care workers are at high risk for exposure to HBV virus. There are estimated 100-200 health care workers who die each year from complications of chronic hepatitis B infection, therefore vaccination against this disease is of a particular importance in this high risk group.(18)

Chub-uppakarn found a significant reducing rate of this infection following hepatitis B vaccination of 180 children (2 month - 15 years old) in the South of Thailand.(19)

On the other hand, Lee MS performed a cohort study to determine the efficacy of hepatitis B vaccination on the prevalence of HCC. In this study, a total of 370,285 persons aged 30 or above who initially had a healthy liver were enrolled. These individuals were divided into three groups of HBsAg positive (18,914 persons), HBsAb positive (78,094 persons) and HBsAg and HBsAb negative (273,277). In the third group, 13.21% of individuals were vaccinated by 1985. After the average follow-up of 3.8 years, the rate of HCC development in the three groups were: 0.58 (95% CI: 0.31-1.09) in the vaccinated group, 18.1 (95% CI: 14.2-22.9) in the group with chronic infection and 0.34 (95% CI: 0.19-9.6) in unvaccinated group who later developed infection.(20), Therefore vaccination leads to decreased risk of development of HCC in adults.

In Iran a recombinant HB vaccine produced in yeast (Heberbiovac, S.A. Havana, Cuba) has been used for general vaccination since 1992.(21)

The result of the present study demonstrated that out of the 331 specimens collected from various health care workers, 14.2% had Anti-HBs titer <10 IU/L, 54.4% had $10<$ anti-HBs titer <100 IU/L and 31.4% had Anti-HBs titer >100 IU/L.

In a study performed in Italy on medical students, the immunity caused by vaccination (Anti-HBs titer >10) was 70-79% after 5 years.(11)

In another study conducted in China on 1,087 completely vaccinated persons, the immunization rate (Anti-HBs titer >10) was found to be 65.3%

as compared to 28.3% of the control group.(22), Another study carried out on a total number of 3,112 children (0-4 year old) from Ethiopia, indicated that after two years 11% of the individuals had an antibody titer below immunization values (Anti-HBs titer <10).(23), In another study conducted by Lin DB in Taiwan on a total of 2,130 healthy children aged between 2-6 years, HBsAb was positive (titer >10) in 100% and 75% of cases after 3 and 6 years respectively.(24)

Using the same vaccine type in Iran but considering a different responding value to HBV vaccine Shokrgozar *et al.* found that of the total number of 252 healthy adults, 12 subjects were non-responder (Anti-HBs titer<10 IU/L), 30 adults were low responder (Anti-HBs titer>10 and <500 IU/L) and 210 subjects had a high response rate (Anti-HBs titer>500 IU/L), representing a total percentage of 95.2% responder (Anti-HBs titer>10 IU/L) one month following the last dose.(25), Comparing to their result, ours demonstrated that 90.5% of those who had their antibody assessed within 12 months of the last injection had achieved a good response rate.

According to Amini study, about 8% of adults who had been vaccinated with Cuban recombinant HB vaccine were non-responder after 24 month of the third dose of injection(21), while that of our study was about 4% within 20 month following the last dose of vaccine. This indicates a favorable response rate of our study comparing Amini's (92% vs. 96% Anti-HBs antibody>10 IU/L respectively).

Then again our study showed that 86.7% of the cases who received their last dose of vaccination within the last 25-36 months had Anti-HBs titer >10, this was an approving result comparing Janbakhsh's which indicated an immunization rate of 70.4% within 3 years after the last dose.(26), In another study done on the nurses in Gaemshahr* the reported immunization rate (Anti-HBs titer >10) within the first year of vaccination was 94.1% which was almost compatible to that of our

* a city located in the North of Iran.

study (90.5%).(27)

We also found that the response rate (Anti-HBs titer >10) was 85.8% after an average of 20 months following the last dose of injection. This finding compares favorably with the values had been reported throughout the world. On the other hand, since values above 100 denote a good response, statistics obtained during this study show that good response rate was 31.4% after 20 months, which is different from values seen in study conducted on 4,791 children (1-12 years old) in Saudi Arabia to determine the hepatitis B immunization level which showed that 28% of individuals had titers of Anti-HBs titer > 100 after eight years of follow-up.(28), Since immune-compromising factors and age above 50 years that are considered as confounding had been excluded from our study, factors such as improper storage and injection of the vaccine must be considered.

Although in this study significant difference was not demonstrated between the number of responders and the duration since the last dose, there has been found a rise in responders 25-36 months after the last dose (86.7%) comparing to that of 13-24 months following the last injection (75.9%), this might be as a result of their frequent exposure to this virus during their career period.

Additionally in our study, a significant relationship was not found to exist between the antibody titer and other variables such as age, gender, smoking habit, BMI and duration since the last dose of vaccine, this was almost compatible with the result of study done by Havilichek *et al.*, which demonstrated that race, sex, and duration of the antibody titer since the last dose of vaccination did not affect the rates of seroconversion, but in their study age greater than 50 years was associated with significantly decreased seroconversion rates compared with seroconversion rates of those younger than 50 years old ($p = 0.02$).⁽¹⁴⁾, This was also found by other studies^(26, 27), which indicated that the age above 40 had a negative effect on antibody formation. However, ours didn't suggest the age as a factor influencing the response rate, this is also explained by the fact that since cases above 50 years had been excluded in our study no significance difference was able to be detected in

this regard.

This study demonstrates that only a significant relationship was found between antibody titer and the place of the employment.

CONCLUSION

With regard to the importance of health-care employees immunization against hepatitis B, we suggest the assessment of Anti-HBs titer in this high risk group after completion of hepatitis B vaccination. This can give an insight into the actual status of their response to define individuals with anti-HBs titer <10 IU who should receive another course of vaccination and those with anti-HBs titer (10-100 IU) whose one booster dose of vaccine is strongly recommended.

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