

Study of the post-vaccination anti-HBV immune response in the health staff of the Souro SANOU University Hospital in Bobo-Dioulasso.

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Abstract

Background Post immune response again VHB after immunization have been slowly reported in health personal in limited setting country. We aimed to evaluate the post-vaccination immune response against the hepatitis B virus in health personal at CHUSS Bobo-Dioulasso.

Methods This was a prospective cohort study that was conducted from March 2014 to January 2015 at CHUSS. Thus, 84 vaccinated subjects were included. Whole blood was collected from each subject for antibody determination. CMIA technology was used for the determination of anti-HBs antibodies. Subjects with a titer of less than 100 mIU / ml were considered non-protective in the hospital setting.

Results The average age of the subjects is 40.38 ± 9.82 years. The sex ratio is 2.23. Of these, 47.6% had an Ac titre greater than 100 mIU / ml, and considered very well immunized. Also, 52.4% had an Ac titer less than 100 mIU / ml; and considered as unprotected subject in a hospital setting. Of these, 27.38% had a titer of between 10 and 99 mIU / ml and 30% had a titer of less than 10 mIU / ml. Comparing the different proportions of non-responders by age, we find that there is no statistically significant difference between non-responders aged ≤ 40 years compared to those aged > 40 years ($p = 0.8$). Comparing the different proportions of non-responders by sex, we find that there is a statistically significant difference between male and female non-responders ($p = 0.044$).

Conclusion We found that about half of the subjects had satisfactory protection, which indicates a good efficacy of SHANVAC B®. Research on immunological non-responders should be pursued to identify possible causes.

Introduction

Infection with the hepatitis B virus is a major public health problem in Burkina Faso; the prevalence is 8.8% (Tao 2014, Simporé 2006). Subjects at risk for infection with the hepatitis B virus must be vaccinated. After immunization of a subject, 4 to 8 weeks after the last injection, the presence in the plasma of antibodies directed against the HBs antigen provides immunological protection against infection if the antibody level is greater than 10 mIU / mL (WHO, 2017). However, 5 to 10% of subjects are non-responders (no antibody response after vaccination or less than 10 mIU / mL) or small responders (moderate response that rapidly disappears) according to WHO. These subjects constitute true subjects at risk vis-à-vis the infection by the virus of hepatitis B. In addition to this provision, a special recommendation of titer of antibody is made for groups said to risk with regard to their socio-professional activities. These include health workers, newborns of HBsAg positive mothers, parenteral drug users, sex workers, etc. The recommendation recommends that these individuals have an anti-HBs antibody titer of at least 100 mIU / mL to be considered protected (**Haut conseil de santé publique, 2014**). Caregivers in Burkina Faso, a geographical area of high prevalence and high transmission, thus accumulate the risk of contamination as exposed to daily life. As a result, since 2013, Burkina Faso's Ministry of Health has practiced vaccination against hepatitis B on a large scale among people at risk of contamination, who

are engaged in a professional activity in health facilities. Thus, health personal of the CHU Sourô Sanou of Bobo Dioulasso has been immunized against hepatitis B (SHANVAC B® vaccine). It must be effectively protected to preserve its health and not be a source of contamination for patients. We will call non-immunological responders (NRs) subjects with an antibody titer of less than 100mIU / ml. Those with a titer greater than or equal to 100mIU / ml will be said to be good responders (**Haut conseil de santé publique, 2014**). This study aims to determine the rate of CHUSS health workers appropriately protected after vaccination. The general objective is to evaluate the proportion of good responders from CHUSS health staff who received the HBV vaccine (SHANVAC B®).

Methods And Patients

This is a cross-sectional study that included 84 subjects. This study took place over a period of 10 months at CHUSS Bobo Dioulasso. The study population is made up of the health staff of the Sourô Sanou University Hospital Center who received the SHANVAC B ® vaccine in 2013. The vaccinated subjects were included at random. The choice of these subjects is justified by the fact that the probability of having effective protection against HBV in this group is high. A non-responder at the health care staff had been defined by an anti-HBs antibody titer of less than 100 mIU / ml and a responder is defined by an anti-HBs antibody titer greater than 100 mIU / ml.

Biological analysis

Whole blood, 4 ml was collected by venipuncture at the bend of the elbow on a dry tube for the determination of anti-HBs antibodies.

The Anti-HBs antibody assay was done using Architect Ci4100®. This automated device uses CMIA technology which is a two-step immunoassay using micro particle chemiluminescence (CMIA) immunoassay technology.

In the first step, the sample and paramagnetic microparticles coated with recombinant HBsAg (rAgHBs) are brought together. The anti-HBs antibodies present in the sample bind to the microparticles coated with rAgHBs. After washing, the acridinium-labeled rAgHBs conjugate is added during the second step. After another wash cycle, the pre-activation and activation solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured in Relative Light Units (URLs). There is a direct relationship between the amount of anti-HBs antibodies in the sample and the number of URLs detected by the Architect Ci4100® optical system.

Ethic statement

Samples analyzed in our study derived from medical personal that went to laboratory for post immunization of VHB control. The results of the various examinations were given to the participants of the study. The study was approved by our National Ethic Committee for health research in Burkina Faso Ouagadougou. Patients participating in this study gave written informed consent.

Statistical analysis of data

The data and graphs were entered on the Excel 2013 software. The R version 3.2 software was used for the tables. We have made a general description of our sample by studying the distribution of all our independent variables (demographic variables: age, service origin sex, paraclinical variables: antibody titer). The tests used for the comparison of means and proportions were the tests of chi-squared and Fisher, Kruskal Wallis. P values.

Results

Socio-demographic characteristics

In this study, 84 subjects were included. The average age of the subjects in the study is 40.38 ± 9.82 years. Subjects under 40 represent 53.57% compared to 46.43% aged > 40 years. Male subjects represent 69.05% (58/84) and female subjects 30.95% (26/84); a sex ratio equal to 2.23. Also, 90.5% of subjects received 2 doses while 9.5% received 3 doses. Antibody titers ranged from 0 to 1000 mIU / mL. The geometric mean of the antibody titer is 301.20 mIU / mL (95% CI, 217.95 - 384.45 mIU / mL). Subjects with an anti-HBs antibody titer of less than 10 mIU / mL (non-responder generics) accounted for 22.62% versus 77.38% for subjects with a titer ≥ 10 mIU / mL.

For non-responders in health care settings, we found 52.4% of non-responders with an Anti-HBs antibody titer of less than 100 mIU / mL compared to 47.6% of subjects with a titer greater than or equal to 100 mIU / mL (good responders).

Factors associated with the post-vaccination immune response

Impact of age on the immunogenicity of the vaccine

Figure 1 shows the distribution of subjects by age group and vaccine immunogenicity.

Comparing the different proportions of non-responders by age, we find that there is no statistically significant difference between non-responders aged ≤ 40 years compared to those aged > 40 years ($p = 0.8$).

Figure 1: Distribution of subjects by age group and immunogenicity.

Impact of sex on the immunogenicity of the vaccine

Table I shows the distribution of subjects by sex and immunogenicity.

Table I: breakdown of subjects by sex and immunogenicity

Sex	Proportion of responders (%)	Proportion of non-responders (%)	p-value
Male	30.9 (26/84)	3809 (32/84)	0.044
Female	16.66 (14/84)	14.28 (12/84)	

Comparing the different proportions of non-responders by sex, we find that there is a statistically significant difference between male and female non-responders ($p = 0.044$).

Impact of the number of doses received on the immunogenicity of the vaccine

We found that 90.46% of the subjects underwent the 0-1 month immunization schedule. While 9.53% underwent the 0-1-6 month pattern.

Table II shows the distribution of subjects according to the number of doses received and the immunogenicity.

Table II: distribution of subjects by number of doses and immunogenicity

Number of doses received	Proportion of responders (%)	Proportion of non-responders (%)	p-value
2	44.04 (37/84)	46.42 (39/84)	0.55
3	3.57 (3/84)	5.95 (5/84)	

By comparing the different proportions of non-responders according to the vaccination schedule, it was found that there was no statistically significant difference between subjects who received two doses of those who received three doses ($p = 0.55$).

Discussion

We found in our study that subjects with an anti-HBs antibody titer of less than 10 mIU / mL (non-responder generals) accounted for 22.62% compared to 77.38% for subjects with a titre greater than 10 mIU / ml. Regarding non-responders in care settings, we found that 52.4% of the subjects in the study had an anti-HBs antibody titre of less than 100 mIU / ml (non-responders) compared to 47.6% of subjects with titre greater than or equal to 100 mIU / ml (good responders).

In most immunocompetent studies, 5% to 10% of vaccines did not respond to HBV vaccination (**Barin, 1982**). Our results corroborate those of some authors who found high proportions of non-responders such as **Gargouri, 2011** (12.1%) and **Abiteboul, 1990** (15.4%).

This higher rate of non-responders obtained in the study may be explained by the fact that the protective threshold for neutralizing antibodies in the personnel of the recommended care settings is ten times that recommended by the WHO (antibody titer < 10 mIU / mL). To this must be added the influence of the anti-HBs antibody assay time. Indeed, we performed the anti-HBs antibody assay one year after immunization. And, it is possible that the decrease in Ac titers over time is an additional argument for our results because sample collection was done on average 12 months after the last dose (**Bruce, 2013**). In sum, the ability of SHANVAC B® vaccine to induce, in vaccinated health personnel, the production and persistence of specific neutralizing antibodies beyond a threshold considered protective has been proven.

In our study, we find that there is no statistically significant difference between non-responders aged ≤ 40 years compared with those of non-responders age > 40 years ($p = 0.8$). Our results corroborate those of Treadwell, 1993 and Goldwater, 1997 which showed that one of the factors of less good response to vaccination is age (> 30 years for men and > 40 years for women). Thus, the average age of subjects is 40.38 years. These show that most of the vaccines in our study have reached the age at which the immune system does not respond to HBV immunization or poorly. We suggest that early immunization in health care settings in resource-limited settings could improve the post-vaccination immune response against HBV.

In addition, we found that there is a statistically significant difference between male and non-female responders ($p = 0.044$). The possible reasons for a large proportion of non-responders to hepatitis B vaccination in males are still poorly studied. Associated factors such as overweight, smoking, excessive alcohol consumption, HLA DRB1 and DQB1 alleles, and comorbidity: diabetes, renal failure, cirrhosis, immune deficiency (transplantation, infection with HIV, immunosuppressive therapies) may explain the poorer response to hepatitis B vaccination (**Treadwell 1993, Goldwater 1997**). However, our study did not explore these factors in subjects.

By comparing the different proportions of non-responders according to the vaccination schedule, it was found that there was no statistically significant difference between subjects who received two doses of those who received three doses ($p = 0.55$).

Carlsson obtained quite similar results in 1999. They vaccinated some medical staff and compared the effects of the intramuscular and intradermal routes. On the other hand, several other studies aimed at analyzing the possibility of reducing the doses required for vaccination against hepatitis B have given different results. In adults (> 40 years), a 2-dose schedule is clearly inferior to a 3-dose regimen (**Gellin, 1997**). Nevertheless, with a rapid vaccination plan (0-1-2 months) using SHANVAC B® vaccine, it could be possible to protect the health care staff with a better rate of completeness (**Young, 1996**). A study on the evaluation of the developmental potential of rapid seroprotection was carried out; the beneficial results of a reduced duration vaccine regimen with a new triple antigen vaccine (Hepacare) have been achieved (**Jeune, 2001**). These results confirmed that accelerated vaccination could be achieved with appropriate protocols. Clearly, protection against hepatitis B could be improved if a shorter vaccination regimen could achieve levels of protection with anti-HBs antibodies.

Conclusion

This study that we conducted to determine the effective protection of staff shows that 77.38% of vaccinated persons are protected, according to WHO criteria, with an antibody titer of ≥ 10 mIU / mL. Care staff is a target group that requires better protection with a higher antibody titer (≥ 100 mIU / mL). In this specific group the seroprotection rate is 47.61%. Although satisfying this rate can be improved.

Declarations

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Contributions of the authors

Design and implementation of experimental protocols: SY SS GMK OSM TY. Analyze the data: SY SS GMK TY. Contribution in reagents / materials: SY SS GMK SG TY. Article writing: SY FF TY SS SG OSM.

Conflict of interest

We declare here that there is no conflict of interest

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Figures

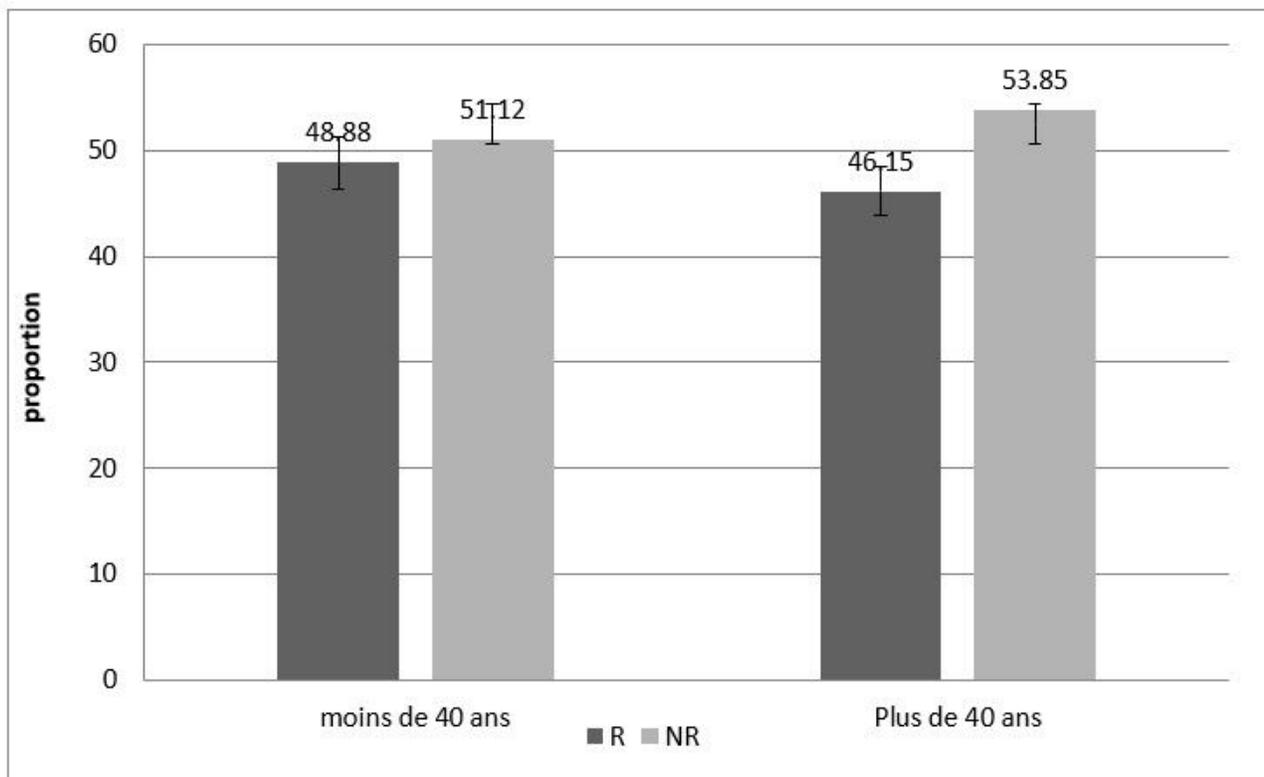


Figure 1

shows the distribution of subjects by age group and vaccine immunogenicity