

Seropositivity for Hepatitis B Virus, Vaccination Status and Response to Vaccine in a Cohort of Dental Students

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Abstract

Background: The development of a vaccine against hepatitis B virus (HBV) has been a major achievement in terms of prevention of HBV infection. To evaluate the immunological status against HBV of dental-profession students, we analysed the long-term immunogenicity and effectiveness of HBV vaccination in Italian dental students with different work seniorities, determining the influence of epidemiological variables on the immune response. **Methods:** This study, carried out from January 2014 to April 2016, involved 361 under- and post-graduate dental students attending the Second University of Naples. HBV serum markers were determined and multivariate logistic regression analysis was used to identify factors associated with the level of long-term immunogenicity. **Results:** Of the 361 subjects evaluated, 15 (4.2%) declared no history of vaccination. All vaccinated subjects were HBsAg/anti-HBc negative, with 86 (24.9%) having an anti-HBs titre <10 IU/L. The latter were younger, more likely to be attending undergraduate dental school, and more likely to have been vaccinated in infancy. **Conclusion:** The findings of this study suggest that assessment of HBV serum markers in workers potentially exposed to hospital infections is useful to identify small numbers of unvaccinated subjects or vaccinated subjects with low antibody titre, all of whom should be referred for a booster series of vaccinations.

Keywords

HBV Infection, HBV Vaccination, Anti-HBs Titre, Dental Students

*These authors contributed equally to this work.

1. Introduction

Hepatitis B virus (HBV) is a major global health problem [1]. Infection can be asymptomatic or symptomatic, and can take the form of acute or chronic liver disease, and is potentially fatal. The World Health Organisation (WHO) estimates that, globally, about 2 billion people have been infected with HBV, and more than 350 million are chronically infected, and nearly one million per year die from its acute or chronic sequelae [2]. The risk run by healthcare personnel (HCP) of contracting HBV is four times greater than that of the general adult population [3]. The most common routes of transmission from patients to HCP are needle stick and other sharps injuries, followed by mucocutaneous exposure [4]. The risk of transmission of the virus per needle stick injury from a patient infected with HBV is 37% - 62%, among the highest risk rates for a virus [5]. The use of drills and scalers in the presence of bodily fluids, such as blood and saliva, and dental plaque, generates aerosols of oral micro-organisms and blood with consequent infection risk. Thus, dental workers are a high-risk group for HBV infection given their frequent exposure to blood or body fluids containing HBV [6].

A range of different measures and interventions, such as the use of safety devices, has helped to reduce the risk of HBV transmission to HCP, but the development of HBV vaccines must consider the major achievement in terms of prevention of HBV infection [4]. Since 1992, there has been a compulsory vaccination programme in Italy for infants: the procedure is reported on a vaccination card, a document designed exclusively to record basic identifying information and the immunization services received. The vaccination coverage has been high (94%), and the programme has greatly reduced the incidence of HBV infection [7]. All babies are vaccinated (at month 3, 5 and 11) to prevent the risk of acquiring HBV infection by perinatal and familial transmission; moreover, during the first 12 years of application of the programme, all children at the age of 12 were also vaccinated to prevent HBV transmission by unsafe sexual activity or intravenous drug use. This strategy permitted the programme to cover the Italian population aged 0 - 24 years by 2003 [8].

It is generally observed that antibody titres decline over time following immunization, resulting in an increased rate of infection, especially when the titre of the antibody to hepatitis B surface antigen (HBsAg) falls below the protective cut-off level of ≥ 10 mIU/mL [9]. The present study was therefore carried out to determinate the level of anti-HBs and other HBV serum markers as well as associated factors in under- and post-graduate dental profession students in an Italian university.

2. Methods

2.1. Setting and Study Population

The study was carried out from January 2014 to April 2016 and involved dental hygiene students, dental school students, and post-graduate dental student attending the Second University of Naples.

Based on the risk assessment document, we carried out a health surveillance programme during the study period on first, third, and fifth year dental school students; first and third year health profession school students (dental hygienists); and first and third year students of the university's specialization schools. All were actively recruited before any possible exposure to risky patients or procedures connected with the university courses, as established by our health protocol [10] [11].

2.2. HBV Serum Markers

After obtaining informed written consent, all students visited medically for the first time were asked to complete a pre-coded questionnaire, stating their age, gender, hepatitis B vaccination status, previous exposure to HBV, smoking behaviour, BMI and educational level. The information on HBV vaccination given by the students was always checked against their vaccination cards. A blood sample was taken from each participant under strict aseptic conditions with a plain vacutainer. Blood was allowed to clot and serum was separated and stored at -20°C until testing. HBV serum markers (HBsAg, anti-HBs and total anti-HBc) were determined using commercial immunoenzymatic assays (Abbott Laboratories, North Chicago, IL, USA). Anti-HBs titres were extrapolated from a calibration curve generated using the WHO reference standard and are expressed in IU/L. In particular, actual values were obtained for anti-HBs titres between 10 and 400 IU/mL, and for this interval the geometric mean was calculated using standard procedures; for values <10 IU/mL or >400 IU/mL, the laboratory readout indicated only either “under 10 IU/mL” or “over 400 IU/mL”, respectively.

2.3. Ethics

According to Italian legal guidelines for observational studies, ethical approval for conducting this survey was unnecessary and, accordingly, cross-sectional studies did not require formal approval by local institutional review boards [12]. Personal information on the subjects included in the study was protected according to Italian law [13].

2.4. Statistical Analysis

Statistical analysis of data was performed using SPSS v.20.0 software. Continuous variables are given as mean \pm standard deviation, and categorical variables as the absolute value and relative frequency. Differences in mean were evaluated using an unpaired Student t-test, and the chi-squared test was applied to categorical variables. A p-value of <0.05 was considered to be statistically significant.

3. Results

In total, 361 under- and post-graduate dental-profession students attending the Second University of Naples were screened from January 2014 to April 2016

(**Table 1**). Only 15 (4.2%) declared no history of vaccination: they were all born in Italy and were HBsAg/anti-HBs/anti-HBc negative; 6 were attending the dental hygienist school, 6 the undergraduate dental school, and 3 were specializing doctors. All were being evaluated for HBV for the first time.

All vaccinated subjects were also HBsAg/anti-HBc negative, but only 86 (24.9%) had an anti-HBs titre <10 IU/L, the majority (75.1%) having a titre >10 IU/L. 163 (47.1%) were female and 0.28% were foreign students; 201 had received a course of 3 paediatric doses (10 µg) of recombinant hepatitis B vaccine at their 3rd, 5th and 11th month of postnatal life, and 145 had received a course of 3 adult doses (20 µg) of the same vaccine when 12 years old. Only 49 students were sure that their mothers were HBV negative at the time of giving birth to them.

The subjects with an anti-HBs titre <10 IU/L were younger, more frequently of lower student seniority, were frequently non-smokers, and had more frequently been vaccinated in infancy (**Table 2**). They were recommended for a booster series of HBV vaccinations. The 15 unvaccinated HBsAg/anti-HBs/anti-HBc negative subjects were required to undergo the complete HBV prophylaxis programme.

4. Discussion

In 2013, the incidence of HBV infection in Italy was only 1 per 100,000 individuals; 20% were immigrants from areas highly endemic for HBV [14].

In our study, we found no positivity to serum HBsAg or anti-HBc in any of the vaccinated students, indicative of an excellent vaccination programme. However, we found that almost one quarter of them had an anti-HBs titer <10 IU/L. This group was younger, had lower student seniority (they were attending their first year of dental studies) and, therefore, had the highest number of subjects who had received compulsory vaccination in infancy. Indeed, they were all born after 1992.

Table 1. Demographics of under- and post-graduate dental-profession students.

Variable	Value (%)
No. of subjects	361
Age in years	26.1 (5.4)
Female	173 (47.9)
Place of birth	
Italy	348 (96.7)
Elsewhere	13 (3.3)
School Attended	
School of dental medicine	129 (35.7)
Healthcare profession school (dental hygienists)	145 (40.2)
postgraduate dental school	87 (24.1)

Continuous variables are given as mean (SD); categorical variables are given as n° (%).

Table 2. Characteristics of vaccinated students stratified by anti-HBs titre (n = 346).

Variable	<10 IU/L	≥10 IU/L	P
No. of subjects	86 (24.9)	260 (75.1)	
Age in years	24.3 (7.1)	27.2 (6.3)	<0.001
Males	57 (66.3)	126 (48.5)	
School Attended			
School of dental medicine	35 (40.7)	88 (33.9)	
Healthcare profession school (dental hygienists)	44 (51.2)	95 (36.5)	
Postgraduate dental school	7 (8.1)	77 (29.6)	
Vaccinated			
In infancy	55 (64.0)	142 (54.6)	<0.001
At 12 years of age	31 (36.0)	118 (45.4)	
Time in School (years)	1.8 (2.2)	2.9 (2.7)	<0.001
Boby Mass Index	23.9 (2.4)	22.8 (3.5)	<0.001

Continuous variables are given as mean (SD); categorical variables are given as n° (%).

In accordance with other authors, we found that factors associated with decreased immunogenicity were older age, sex and obesity, while we did not find any close relationship with smoking [8] [15].

Several studies have reported that 85% - 90% of people vaccinated as adolescents have anti-HBs levels >10 mIU/mL when measured 10 years after vaccination. This percentage was 40% - 60% for those vaccinated as infants, as measured 15 - 20 years after vaccination [16] [17]. The possible causes of the low anti-HBs titres in adult subjects vaccinated in infancy could be due to lower interaction between B and T cells in babies, and in some cases, the presence of anti-HBs in mothers might affect the response to the HBV vaccine in their children [18] [19].

Testing HCP as well as medical and dental students for anti-HBs levels may be warranted, as these categories of workers represent a high-risk population: indeed, there are approximately 66,000 HBV infections per year worldwide [20] [21] [22]. This is particularly relevant in countries such as Italy where there is no post-vaccination serological testing, making it impossible to identify unvaccinated subjects [23] [24]. In our study, 14 students had not been vaccinated; as prescribed by Italian law (Article 279 of Legislative Decree n. 8, 19 April 2008), they were referred for vaccination and re-evaluation of anti-HBs titre [25].

For dental profession students, it is necessary to assess anti-HBs titre either at matriculation or at the start of employment in order to identify subjects with levels <10 IU/L. In fact, although the current WHO and Centers for Disease Control view is that subjects with an anti-HBs titre <10 IU/L still retain memory immunity and that no booster dose is necessary as part of a routine immunization programme, a more protective approach should be adopted for workers under continuous risk of exposure to HBV [26] [27] [28]. To distinguish between non-responsive subjects and those whose titres have waned over time but

who are still protected, a “challenge” or “booster” dose should be administered and titres rechecked 1 - 2 months later. Those presenting with titres ≥ 10 IU/L can be considered protected and not needing additional testing or vaccination, whereas those presenting with titres that are still < 10 IU/L after the challenge dose should be referred to a vaccination programme. For subjects in which the negative result persists-considered non-responders by the WHO-the possible risk of infection with the virus should be evaluated.

Strengths and Limitations

This study has limitations, including the fact that the sample size was small and some data could not be confirmed, such as the vaccination status of students without a vaccination card and anti-HBs level immediately following vaccination.

5. Conclusion

The present study evaluates the efficacy and immunogenicity of HBV vaccination in a series of subjects with a high risk of being exposed to HBV. The results suggest that assessment of HBV markers is worthwhile to identify the small number of dental students and HCP that may not have been vaccinated, such as immigrants from countries without universal immunization, and HBV carriers that exist for various reasons, including rare failure in protection or uptake after immunization.

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