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ANTIBODY LEVEL AND IMMUNITY AGAINST HEPATITIS B VIRUS INFECTION AMONG GENERAL DENTAL PRACTITIONERS

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Abstract

Introduction. *Immunization against Hepatitis B virus (HBV) is crucial for an effective control in dental healthcare settings. Nevertheless, vaccination rates among general dental practitioners (GDPs) from developed countries range between roughly 50%, as in Italy and Japan, and >90% as in US and UK. Furthermore, vaccination does not necessarily imply immunity, as serum anti-HBs antigen (Ag) level tends to decrease and booster doses are periodically required.*
Aim. *To investigate HBV vaccination and immunity rates among Italian GDPs.*
Material and methods. *195 GDPs voluntarily participated. They provided information regarding HBV vaccination in the last 10 years and underwent blood samples to detect serum anti-HBs Ag level. Immune subjects were considered subjects with anti-HBs Ag ≥10 mIU/mL. Vaccination and immunity rates were assessed with 95% confidence intervals (95CIs). Sensitivity (proportion of immune GDPs among vaccinated GDPs), Specificity (proportion non-immune GDPs among non-vaccinated GDPs) also were assessed.*
Results. *88% GDPs were vaccinated (95CI, 83-92%), but only 83% were immune (95CI, 77-88%). Sensitivity was 95.6%, suggesting that among immune GDPs, 4.4% were not recently vaccinated. Specificity was 50%, suggesting that among non-immune GDPs, 50% were recently vaccinated.*
Conclusion. *Vaccination rate among Italian GDPs was high. Nevertheless, a fraction of 5% of them was vaccinated but was not immune, thus suggesting that serum antibody level should be periodically checked because susceptible GDPs are at risk for HBV infection.*

Key words: *HBV, Hepatitis B, Vaccine, Immunity, Dentistry*

Introduction

Immunization against Hepatitis B virus (HBV) by dental healthcare workers is probably the most effective method to control the risk for infection among patients and dental staff. A narrative review of observational studies from US made in the pre-vaccination era, between 1975 and 1989, reported that the occupational risk for HBV infection among the general dental practitioners (GDPs) was between two to three times greater than in the general population. Such a risk was even doubled among oral surgeons (reviewed by 1). Using these data it was possible to estimate that the risk for HBV infection in non-immunized GDPs was 3% after 100 visits of HBV carriers[2].

Several studies, also published in the pre-vaccination era, reported HBV transmission to patients from fourteen oral surgeons and nine GDPs, including an oral surgeon who did not use gloves and transmitted HBV infection to fifty-five patients (reviewed by 3,4). Despite such a high risk for infection in dental healthcare settings, since 1987 no cases of transmission of HBV from dentist to patient has been reported, while there was only one case of patient-to-patient transmission[5]. The occupational risk in dental healthcare settings also improved. In US, for example, incidence in 2009 among healthcare workers was one hundredth the incidence in 1983[6]. Nevertheless, HBV infection risk is persistently high in endemic areas among non-immunized individuals[7-9]. The improved

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HBV control in dentistry is generally attributed to the widespread application of the guidelines released by the Centres of Disease Control and Prevention, based on the so called universal precautions which assume that all patients are potential carriers of bloodborne/airborne infections[4]. These guidelines are periodically updated, because an effective control of HBV transmission is unfeasible without an evidence-based assessment of the risk for infection in dental healthcare settings[10]. This assessment is essential to understand that, for example, HBV transmission is unlikely through dental unit waterlines, although oral fluid retraction is common during turbine use and microorganisms can be transmitted between patients through this route, despite turbine change or sterilization[11]; or that effective dental healthcare workers' immunization requires that guidelines are not imposed, but proposed, because the mere knowledge of the risk of HBV infection does not necessarily result in high compliance toward guidelines[12,13].

Barriers and immunization are, therefore, the cornerstones of hepatitis B prevention in dental healthcare settings. However, despite these measures are considered mandatory for dental healthcare workers by many professional organizations, they are not unanimously adopted by dental healthcare workers probably for the aforementioned reasons. This explains why some dentists are not immunized against HBV. For example, only 56% of interviewed dentists from Italy reported to be vaccinated against HBV[14], while another study reported that only about one half of the Italian GDPs interviewed tested their serum anti-HBs antigen (Ag) level during the last ten years[13]. Vaccination rates as low as 48% and 68% also are reported from Japan 9 and Mexico[15], respectively. Conversely, high immunization rates, higher than 90%, are reported from UK[16,17].

Aim

The aim of this study was to investigate HBV vaccination rate and the level of immunity in a sample of Italian GDPs.

Material and Methods

GDPs working in private and public offices in Rome, Italy, were considered. Details regarding their recruitment were previously described[18]. GDPs were invited to participate before registering to Continuing Medical Education (CME) courses, by signing an informed consent to interview and serological analysis. Participation was on a voluntary basis and there were no incentives. Data protection and anonymity were guaranteed. The study protocol was approved by the Review Board of the Medical and Dental Association of Rome.

GDPs were asked whether they underwent HBV vaccination during the last ten years, whether their main affiliation was public or private service and the duration of their practice. A blood sample was collected from each participant in a public health clinical laboratory by specialist healthcare workers and the level of antibody to hepatitis B surface antigen (anti-HBs Ag) was assessed with the Enzyme Immunoassay (EIA) method and was expressed in mIU/mL. A fee for service (called "ticket" in Italy) was charged to GDPs for this analysis of approximately 10 euro. GDPs who participated to the study provided the results of the analysis before the end of the CME course.

Prevalence and 95% confidence interval (95CI) of GDPs who reported to be vaccinated was estimated, as well as prevalence of HBV immune GDPs, that is, with serum level of anti-HBs Ag $\geq$10 mIU/mL, the level thought to provide protection 19 . In order to estimate the power of vaccination to predict actual immunity against HBV, the methodology to assess the predictive power of screening tests was used[20]. Namely, true positive rate (TPR, i.e., Sensitivity) was the proportion of immune individuals who declared to be vaccinated; false negative rate (FNR, i.e., "1-Sensitivity") was the proportion of immune individuals who declared not to be vaccinated; true negative rate (TNR, i.e., Specificity) was the proportion of non-immune individuals who declared not to be vaccinated; false positive rate (FPR, i.e., "1-Specificity") was the proportion of non-immune individuals who declared to be vaccinated; Accuracy (i.e., the proportion of correctly predicted as protected or non-protected). The Discriminatory Power, that is, the likelihood of vaccinated individuals to be protected against HBV relative

to the likelihood of non-vaccinated individuals to be protected against HBV. The difference in mean serum level of anti-HBs Ag in the group of those who were vaccinated and in those who were not vaccinated was assessed using the Student's t-test for unpaired samples and normalizing the antibody levels by log transformation. Undetected values were treated as log of the mean distance between 0 and the lowest detected value.

Finally, the associations between age, gender, public-private affiliation, years of practice and vaccination or HBV immunity were assessed. Unadjusted and adjusted odds ratios (ORs) were estimated with logistic regression analysis. Potential collinearity between covariates was investigated with pairwise Pearson's correlation coefficient r. If two variables yielded values higher than 0.6 they were not used together in the same regression model.

Results

The study was made between 2011 and 2012, 283 GDPs were contacted and 195 agreed to participate (participation rate, 68.9%). The majority of those who refused to participate declared that they did not want to undergo serological analysis (51 subjects), or to pay the fee for the analysis (23 subjects). Mean age of sampled GDPs was 40 years and almost two thirds were males. They were almost equally distributed between those working in the public sector and those working in the private sector. Duration of practice was, on average, fourteen years (Table 1).

88% GDPs declared to be vaccinated during the last ten years, but the proportion of those who were actually immune were 83%. The serum level of anti-HBs Ag ranged between undetected and 1000 mIU/mL (the highest limit of detection of the EIA) with a mean value of 11 mIU/mL (Table 1).

The power of vaccination to predict effective HBV protection is displayed in Table 2. With an accuracy of 88%, the large majority of those who were vaccinated were immune against HBV and vice versa. The Discriminatory Power was highly significant (DP, 22.0; 95CI, 8.0-60.6) supporting the idea that most vaccinated GDPs were immune. The data re

Table 1. *General characteristics of the sampled GDPs.*

characteristic	mean or proportion (95CI)
Mean age (years)	40.4 (39.4-41.4)
Gender (males)	65.6% (58.9%-72.3%)
Gender (females)	34.4% (27.7%-41.1%)
Affiliation (private)	51.8% (44.8%-58.8%)
Affiliation (public)	48.2% (41.2%-55.2%)
Mean duration of practice (years)	14.4 (12.6-16.2)
Vaccinated during the last 10 years	87.7% (83.1%-92.3%)
Mean serum level of anti-HBs Ag (mIU/mL)	10.9 (10.0-11.8)
Immune (serum level of anti-HBs Ag ≥10 mIU/mL)	82.6% (77.3%-87.9%)

Table 2. *Power of vaccination to predict effective HBV immunity.*

variable	parameter estimate (95CI)
True Positive Rate (Sensitivity)	95.65% (92.50%-98.80%)
False Negative Rate (1-Sensitivity)	4.35% (1.20%-7.50%)
True Negative Rate (Specificity)	50.00% (33.19%-66.81%)
False Positive Rate (1-Specificity)	50.00% (33.19%-66.81%)
Accuracy (proportion correctly predicted)	87.69% (83.08%-92.30%)
Discriminatory Power	22.0 (8.0-60.6)
*Mean serum level of anti-HBs Ag (mIU/mL)**	
Vaccinated GDPs	11.7 (10.7-12.7)
Non-vaccinated GDPs	6.5 (4.9-8.6)

*Difference between vaccinated and non-vaccinated GDPs. Student's t-test=4.89; p<0.0001

garding FNR suggest that 4% of immune GDPs did not undergo a complete vaccination cycle during the last 10 years. Regrettably, one half of GDPs who were not immune declared to be vaccinated (FPR, 50%; 95CI, 33%-67%). The mean serum level of anti-HBs Ag was significantly higher in vaccinated individuals (11.7 vs. 6.5 mIU/mL among vaccinated and non-vaccinated GDPs, respectively $p<0.0001$).

None of the investigated explanatory variables were associated with the vaccination status (Table 3), thus suggesting that age, gender, years of practice and public or private practice did not affect the probability of being vaccinated. Conversely, the probability to be immune was partly affected by gender, since males were less likely to be immune than females and years of practice, since the likelihood to be immune decreased progressively with the years of practice (Table 4). However, these associations were no longer significant after the adjustment for covariates.

Table 3. *Unadjusted and adjusted odds ratios (ORs) of the associations between age, gender, public-private affiliation, years of practice and HBV vaccination.*

variable	Unadjusted OR (95CI)	Adjusted OR (95CI)
Age (continuous variable)	0.97 (0.92-1.03)	0.95 (0.89-1.01)
Gender (reference, female)	0.46 (0.16-1.30)	0.38 (0.12-1.18)
Affiliation (reference, private)	1.65 (0.68-3.97)	2.77 (0.93-8.30)
Years of practice (continuous variable)	0.96 (0.91-1.01)	0.94 (0.88-1.02)

Table 4. *Unadjusted and adjusted odds ratios (ORs) of the associations between age, gender, public-private affiliation, years of practice on HBV immunity.*

variable	Unadjusted OR (95CI)	Adjusted OR (95CI)
Age (continuous variable)	0.96 (0.91-1.01)	0.99 (0.92-1.06)
Gender (reference, female)	0.35 (0.14-0.90)*	0.42 (0.13-1.29)
Affiliation (reference, private)	0.69 (0.33-1.45)	0.56 (0.19-1.68)
Years of practice (continuous variable)	0.94 (0.90-0.98)*	0.97 (0.91-1.03)

*$p<0.05$

Discussion

The present study is one of the papers presented at the workshop "Advances in Infection Epidemiology and Control in Dental Healthcare Settings", Department of Public Health and Infectious Diseases, Sapienza University, Rome, Italy on February 9th, 2013[21-27].

The most important shortcoming of this study was that almost one third of the contacted GDPs did not participate to this study and it is not possible to estimate whether non-participating subjects had similar or different levels of HBV immunization, thus making it impossible to predict the overall protection rate of all the contacted GDPs. Anyway, the present vaccination rate, close to 90% (Table 1) was high enough and similar to rates reported from US and UK[16,17] and considerably higher than the rate reported from Italy in 2007[14]. Thus, the most important issue in Italian GDPs, does not seem to be whether they were vaccinated or not, but whether they periodically check their immunization level. Indeed, a previous study reported that only one half of the sampled GDPs tested their serum level of anti-HBs Ag during the last ten years[13]. This is a serious problem associated with the results of the present study that as many as 50% of GDPs with anti-HBs Ag levels lower than the critical threshold of 10 mIU/mL were actually vaccinated against HBV during the last ten years (Table 2). In other words, these subjects believed to be immune, because of vaccination, but they were actually not protected. Therefore, the present study found that almost 10% of regularly vaccinated GDPs were not immune (data not in Table). Other studies reported that among regularly vaccinated GDPs, those who were not immune were 25% from Japan 9 , 24.2% from South Korea[7], 18.9% from Brazil[8]. These data globally considered, suggest that approximately 16% dental healthcare workers who are vaccinated, or declare to be vaccinated are not HBV immune. Therefore, although vaccination rate could be as high as 90% or greater, the effective rate of protection may be roughly 80%.

This high proportion of vaccinated and non-immune dentists is a serious problem from the point of view of occupational risk among dental healthcare workers. As already noted, the risk

for HBV infection in non-immunized GDPs is 3% after 100 visits of HBV carrier patients[2]. However, such a risk was minimized in recent years because of the high vaccination rate among dentists from highly developed countries and the decreasing prevalence of HBV carriers in the general population. The problem that protection rate among dental healthcare workers is lower than expected is particularly important in areas where HBV is endemic. For example, in Romania, 36% (200/563) dental patients resulted anti-HBc Ag positive -HBc Ag is a marker of HBV infection. Consequently and unfortunately, 43% dentists were anti-HBc Ag positive[28]. This worryingly high hepatitis B prevalence among Romanian dentists was not surprising and was not only due to high hepatitis B prevalence in the general population, since almost three fourth of dental healthcare workers from Romania were not vaccinated against HBV[29]. Thus, low immunity rate (despite high immunization rate) among GDPs in HBV endemic areas is responsible for high infection rates among dental healthcare workers, which are inacceptable nowadays, when infection control guidelines are readily available.

Conclusion

The data from the present study suggest that HBV vaccination rate among Italian GDPs from public and private sectors was high. Nevertheless, the level of immunity was lower than expected, probably because GDPs did not check their immunization status periodically. This result was corroborated by similar data from other developed countries. If this shortcoming is not likely to produce any additional risk for HBV infection among patients, it could be an important occupational risk among dentists who work in areas or countries where HBV is highly endemic.

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