Original Article

Rate of Acquired Immunity in Dental Students after Hepatitis B Vaccination

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ABSTRACT

Background: Triple-course vaccination against hepatitis B might sometimes fail to increase antibody titers or maintain it at sufficient levels. The aim of this study was to evaluate the rate of seroprotection in dental students after receiving recombinant hepatitis B vaccine.

Methods: Anti-HBs levels of 124 dental students who had received triple-course hepatitis B vaccines (scheduled at months 0, 1, and 6) were examined. Titers ≥ 100 mIU/ml were considered as protective. Associations between age, gender and duration of being vaccinated with the titer of anti-HBs were assessed.

Results: The participants' mean age was 24 ± 1.3 years and 93% of them were female. The time passed from receiving the final dose was 3.5 ± 1.4 years. Fifty four percent of the students had protective immune response (95% CI 45.2% to 62.8%), 24.2% had positive but weak immune response (anti-HBs titer was between 10 and 100 mIU/ml), and the rest of the subjects (21.8%) were seronegative after receiving routine HBV vaccination.

Conclusion: There was a considerable rate of failure in achieving or maintaining acceptable titer levels following routine vaccination against HBV. Hence, determining serum anti-HBs titer after vaccination is recommended.

***Keywords*:** Acquired immunity, Dental students, Hepatitis B vaccines, Immunization programs.

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Introduction

Hepatitis B vaccine sometimes may fail to produce sufficient rates of seroprotection.[1-7] However, it is known as the best method for prevention against hepatitis B and is necessitated by numerous international organizations;[8] although there are certain controversies over significance of individuals' immune system competency for protection. Besides the anti-HBs titer,[9] many conditions might affect the immunocompetence state. Stress,[10] age,[3,6,11,12] excessive body mass index,[6,12] chronic diseases,[6] and smoking[6] might affect the vaccine efficacy. Male gender has been shown to have negative[6,12] and positive[11] effects on anti-HBs levels. Also age might have both negative[3,6,12] and positive[11] effects. The time duration passed since receiving the vaccine was also correlated with decreased anti-HBs titers.[3,7,11]

Diverse results have been reported regarding the intensity of immune response following triple-course vaccinations.[1-5,12-16] Since dentists are among high-risk populations, assessment of their immunity against hepatitis B is of importance. This study has evaluated the rate of proper immune response following triple-course vaccination in dental students during 2007 and 2008.

Materials and Methods

Through this descriptive cross-sectional study, an-

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ti-HBs titers of 124 dental students studying at Azad University, Dental Branch of Tehran were assessed in 2007 and 2008. The sample size was estimated by adding 20% to the size of a similar study (n = 102).[3] the participants were sequentially approved according to the inclusion criteria: them being in semester 7 or higher, receiving all vaccine doses on the exact intervals (0, 1 and 6 months) and at least one month must have been passed from the completion of the vaccination.[3] The exclusion criterion was the history of any booster doses received. All the participants signed the informed consent forms beforehand. Data were collected by filling questionnaires in addition to an examination of anti-HBs titer using available commercial enzyme immunoassay (EIA) kits.

The HBV recombinant vaccine (Euvax B, LG Chemicals, Korea) had been administered with intra-muscular (deltoid) injection method at the university in previous years. The state of immunity was considered having anti-HBs ≥ 100 mIU/ml whereas weak positive immune response was regarded as 100 > anti-HBs ≥ 10 mIU/ml.[17,18] The students' anti-HBs titers were examined in a private laboratory. Quantitative variables age, years of attending the dental school, and the time passed from the third dose) were classified into two groups, less and greater than the rounded mean value of each factor (cut-offs were determined from the means: 24 years old, 5th studying year and 2 years passed from the last dose, respectively). The rates of the good and the poor immunity responses were recorded and probable associations between immunogenicity and the students' demographic data were statically assessed by a Chi-square test.

Results

From 355 students who were asked to participate, 163 agreed. Twelve participants were excluded after filling the questionnaires. From the remaining subjects, 27 did not bring the test results. The subjects' age varied from 22 to 26 years (24 ± 1.3). They composed of 115 females; and 3.5 ± 1.4 years had passed from receiving the final dose of the vaccine.

As Figure 1 shows, 54% (95% CI 45.2% to 62.8%) of these students produced high immune response (anti-HBs ≥ 100 mIU/ml), while 24.2% showed positive but poor immune response (anti-HBs between 10 and 100 mIU/ml), and 21.8% showed no immune response (anti-HBs < 10 mIU/ml). Additionally, the Chi-square test showed a significant difference between the genders (Table 1).

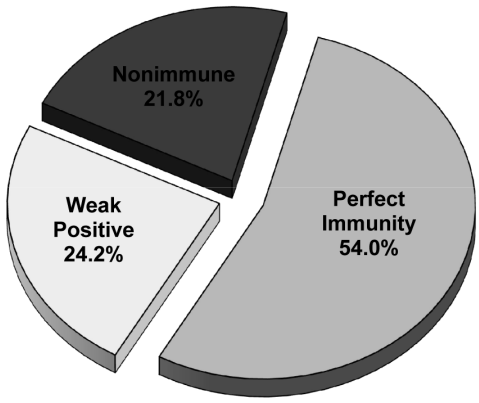

Figure 1. The prevalence of anti-HBs titers ≥ 100, between 10 and 100, and < 10 mIU/ml.

Table 1. The contingency table between the two levels of immune response and demographic data

Variables	Compared groups	Anti-HBs ≥ 100 mIU/ml (%) n = 67	Anti-HBs < 100 mIU/ml (%) n = 57	P value
Age	< 24 yr old	35.8	36.8	> 0.9
	≥ 24 yr old	64.2	63.2	
Gender	Female	97	87.7	< 0.05
	Male	3	12.3	
Studying years	< 5th year	16.4	19.3	> 0.7
	≥ 5th year	83.6	80.7	
Duration passed from the 3rd dose	< 2 years	3	8.8	> 0.2
	≥ 2 years	97	91.2	

The Chi-square test was used to calculate the P value. For every variable, the total sum of each column makes 100%.

Discussion

Although some studies have stated that the decline in anti-HBs titer does not necessarily indicate a lack of protection against hepatitis B,[9,19] evaluating anti-HBs is still the most cost-effective protection predictor. The findings of this study might indicate a considerable rate of failure to acquire (or maintain long after vaccination) necessary levels of immune response among dental students (anti-HBs in 46% of students < 100 mIU/ml and in 21.8% < 10 mIU/ml). This is in harmony with the results of Rajabipour[4] which reported 44% failure to produce necessary rates of immune response, Talebi[3] who reported 63.7% failure (34.3% weak, and 29.4% no response), Chan et al.[13] with 57.1% failure rate, Ramezani et al.[15] and Sivarajasingam et al.[2] who reported 13% to 15% rates for titers < 10 mIU/ml respectively. However, Koff et al.[5] reported a higher rate of anti-HBs < 10 mIU/ml (67%). This might be attributable to the different timings in receiving the third doses. In addition, Estevez et al.,[12] Velu et al.,[14] and Van Damme et al. [16] reported much lower rates of failure (≤ 3%), which might be rooted in short-term evaluations of anti-HBs titer in those studies. However, Zanetti[1] reported 5% prevalence of less than 10 mIU/ml titers after 10 years, which differed from the findings of this and several other studies.

Although controversies exist, this is now accepted that anti-HBs antibody titers greater than 10 mIU/ml may suffice to protect against hepatitis B infection.[19] The present study considered titers ≥ 100 mIU/ml a sufficient seropositivity for dental students; however, the percentage of the sample with immune responses between 10 and 100 mIU/ml was also reported to increase the comparability of the results with those studies in which titers ≥ 10 had been defined as proper seroprotection. Nevertheless, the cut-off point used to dichotomize the immune response was 100 mIU/ml. Therefore, the results of this study regarding the significance of corresponding variables should be cautiously interpreted and compared with the other studies which had used other cut-off points such as 10 mIU/ml.[20]

The finding of this study concerning the negative association between gender and seroprotection was consistent with other studies.[6,12] Nevertheless, because of the small number of male participants, this should be approached with caution. The females were 93% of the sample which might reduce the impact of the male gender on the findings. However, the male gender had a relatively strong effect on immune response which was detected even through such a sample; although 12.3% of the subjects with < 100 mIU/ml titer rates were male, only 3% of those with ≥ 100 mIU/ml were male, which implies that the male gender might negatively affect the immune response.

No significant relationship was found between the level of anti-HBs and the other two parameters, age and the duration of being vaccinated. It was probably because of small differences in participants' age and the duration of being vaccinated in the present study. Moreover, due to the absence of a significant association between the duration of being vaccinated and the level of titer, probably it might be concluded that this brand of vaccine might produce stable levels of seroprotection during two years.

This study was limited by some factors. Only two male participants confirmed that they smoked cigarettes; hence, the variable smoking was omitted. Also, since most of the data pieces were collected by filling the questionnaires, there might be bias factors such as forgetting the exact vaccination times. However, since the dental school at which this study was established obliges the students to receive all the vaccine doses on a regular basis, there might be a low possibility to forget a dose. On the other hand, because the university did not forbid previously vaccinated students to receive it again, there was a possibility for students to have boosters. Furthermore, the university did not provide any written vaccination record to the students to confirm their state of vaccination on the exact intervals. Last but not the least, quality standards for hepatitis B vaccines require at least 95% seroprotection in vaccinated healthy adults (defined as >10 mIU/ml, if measured 1-3 months after the last dose full schedule).[20] Therefore, in this population of healthy young adults this was certainly to be expected. However, only 78.2% of the sample produced such a response to the used vaccine. This might be due to probable unfavorable storage conditions, possible near expiration dates of vaccines, probable HBsAg positivity (implying acute/chronic infection) or anti-HBc positivity (implying previous infection) in the students which might negatively affect antibody production after vaccination, and that such titer waning after few years might be natural in many cases, because a comparatively long time had been passed since the last dose of the vaccine.[3,7,11,15,19]

These results may accentuate on the need to receive additional doses to achieve acceptable levels of anti-HBs titer after few years.[20]

Conclusion

Since the results showed a significant decline in the anti-HBs titer of the dental students, along with understanding that anti-HBs may reach acceptable levels by receiving extra doses, measuring anti-HBs and receiving additional doses (if necessary) is recommended.

References

1. Zanetti AR. Update on hepatitis B vaccination in Italy 10 years after its implementation. Vaccine 2001; 19(17-19): 2380-3.
2. Sivarajasingam V, Ogden GR. Hepatitis B vaccination: knowledge among clinical dental staff and students in Dundee. Br Dent J 1995; 178(3): 105-7.
3. Talebi Taher M. Determining immunogenicity rate after receiving hepatitis B vaccine, in personnel of Firoozgar hospital in Tehran, autumn 2003. Journal of Iran University of Medical Sciences. 2003; 39: 919-27.[Persian]
4. Rajabipour F. Evaluating Hbs Ab levels of interns studying in Lorestan University of Medical Sciences. Journal of Lorestan University of Medical Sciences (Sogand). 2002; 5: 1-5.[Persian]
5. Koff RS. Immunogenicity of hepatitis B vaccines: implications of immune memory. Vaccine 2002; 20(31-32): 3695-701.
6. Averhoff F, Mahoney F, Coleman P, Schatz G, Hurwitz E, Margolis H. Immunogenicity of hepatitis B Vaccines. Implications for persons at occupational risk of hepatitis B virus infection. Am J Prev Med 1998; 15(1): 1-8.
7. Whittle H, Jaffar S, Wansbrough M, Mendy M, Dumpis U, Collinson A, et al. Observational study of vaccine efficacy 14 years after trial of hepatitis B vaccination in Gambian children. BMJ 2002; 325(7364): 569.
8. Brotherton JM, Bartlett MJ, Muscatello DJ, Campbell-Lloyd S, Stewart K, McAnulty JM. Do we practice what we preach? Health care worker screening and vaccination. Am J Infect Control 2003; 31(3): 144-50.
9. Boland GJ, de Gast GC, Italiaander E, van der Reijden J, van Hattum J. Long-term immunity to hepatitis B infection after vaccination with recombinant hepatitis B vaccine. The Netherlands Journal of Medicine 1996; 48(1): 23.
10. Glaser R, Kiecolt-Glaser JK, Bonneau RH, Malarkey W, Kennedy S, Hughes J. Stress-induced modulation of the immune response to recombinant hepatitis B vaccine. Psychosom Med 1992; 54(1): 22-9.
11. McMahon BJ, Bruden DL, Petersen KM, Bulkow LR, Parkinson AJ, Nainan O, et al. Antibody levels and protection after hepatitis B vaccination: results of a 15-year follow-up. Ann Intern Med 2005; 142(5): 333-41.
12. Estevez ZC, Betancourt AA, Muzio G, V, Baile NF, Silva CV, Bernal FH, et al. Immunogenicity and safety assessment of the Cuban recombinant hepatitis B vaccine in healthy adults. Biologicals 2007; 35(2): 115-22.
13. Chan CY, Lee SD, Tsai YT, Lo KJ. Long-term follow-up of hepatitis B vaccination in susceptible hospital personnel. J Gastroenterol Hepatol 1992; 7(3): 266-9.
14. Velu V, Nandakumar S, Shanmugam S, Shankar EM, Thangavel S, Kulkarni PS, et al. Comparative efficacy of two dosages of recombinant hepatitis B vaccine in healthy adolescents in India. Pediatr Infect Dis J 2007; 26(11): 1038-41.
15. Ramezani A, Eslamifar A, Banifazl M, Ahmadi F, Maziar S, Razeghi E, et al. Efficacy and long-term immunogenicity of hepatitis B vaccine in haemodialysis patients. Int J Clin Pract 2009; 63(3): 394-7.
16. Van Damme P, Minervini G, Liss CL, McCarson B, Vesikari T, Boslego JW, et al. Safety, tolerability and immunogenicity of a recombinant hepatitis B vaccine manufactured by a modified process in healthy young adults. Hum Vaccin 2009; 5(2): 92-7.
17. Fagan EA, Harrison TJ. Viral Hepatitis: A Handbook for clinicians and scientists. 1st ed. Philadelphia: Springer; 2000. p. 125-6.
18. Das S, Brassington M, Drake SM, Boxall E. Response to hepatitis-B vaccination in healthy homosexual individuals: retrospective case control study. Vaccine 2003; 21(25-26): 3701-5.
19. Hepatitis B vaccines. Weekly Epidemiological Record 2009; 84(40): 405-20.
20. Clemens R, Sanger R, Kruppenbacher J, Hobel W, Stanbury W, Bock HL, et al. Booster immunization of low- and non-responders after a standard three dose hepatitis B vaccine schedule--results of a post-marketing surveillance. Vaccine 1997; 15(4): 349-52.