Comparison of the accelerated and standard vaccination schedules against hepatitis B in healthcare workers

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Background: For healthcare workers, sometimes the conventional hepatitis-B virus (HBV) vaccination schedule might not provide seroconversion rapidly enough. The aim of this study was to compare the efficacy of conventional HBV vaccination with an accelerated schedule (days 0-1-21). **Materials and Methods:** In this randomized clinical trial, 161 healthcare workers were divided into two vaccination groups; group A underwent the conventional schedule (0-1-6 months) and group B received the accelerated program (0-10-21 days) of hepatitis B virus vaccine. The anti-HBs antibody was determined 30 days after completion of the third vaccine injection in both groups by enzyme immunoassay (EIA) (Abbot, Aux SYMsys). By using the Fisher's exact and Wilcoxon tests, the results were analyzed. The protective level of anti-HBS was defined as titer ≥10 MIU/ml. **Results:** The seroprotection rate, 30 days after vaccination, were similar in both groups A and B; 96.3% of the participants in group A and 92.6% in group B had anti-HBS antibody ≥10 MIU/ml. **Conclusion:** Our data indicated that compared to the classic HBS vaccination program an accelerated schedule could also be effective and achieve seroprotection more rapidly.

Key words: HBS, healthcare workers, hepatitis-B, vaccination

INTRODUCTION

Hepatitis-B virus (HBV) infection is a worldwide health problem especially in healthcare workers. It is estimated that about 400 – 500 million chronically infected patients are present in the world.[1] The prevalence of chronic HBV infection in the general population of Iran is estimated to be about 1.7%.[2] In endemic areas hepatitis B virus is the main cause of hepatocellular carcinoma and cirrhosis. As effective treatment for the cure of chronic hepatitis B infection has not yet been established worldwide, and the best way to protect if is by vaccination. Monovalent, safe, and effective vaccine against hepatitis B virus is available globally.[3] At present, the classic immunization schedule recommends repeated doses at months 0, 1, and 6,[4] which provides a seroprotective rate of 95 – 99%.[5] Sometimes there is a need to complete the immunization program in a shorter duration, for example, in healthcare workers, travelers

to endemic areas, or prisoners who are not immune. This schedule is also given a higher compliance.[6-9] The National hepatitis B vaccination program has reduced the prevalence of HBV infection and its carriers and it is also associated with a decrease in the incidence of hepatocellular carcinoma and cirrhosis.[10,11] The aim of our study is to compare the effectiveness of the standard hepatitis B vaccination program (0, 1, and 6 months) with an accelerated schedule (0, 10, and 21 days).

MATERIALS AND METHODS

This study was carried out in the Imam Reza Hospital of the Kermanshah University of Medical Sciences, Iran, from January to September 2009. One hundred and sixty- one healthcare workers, who were negative for HBS Ag, anti-HBS, and anti-HBC antibodies, were enrolled and randomized into two groups. Prior data indicated that the seroconversion rate among people receiving the standard vaccination schedule was 85%, and a sample size of 161 healthcare workers would enable us to detect a seroconversion rate of 98% among people who received vaccine in an accelerated method, with a probability (power) of 80%. Type I error probability associated with the null hypothesis of equal seroconversion rate for experiment and control group is 0.05. The exclusion criteria were: A history of vaccination for HBV, Immune deficiency conditions,

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diabetes mellitus, chronic renal failure, pregnancy, age above 60 years, occupational or non-occupational exposure to HBV, and those who had received any vaccination in the last three months. The participants were assigned either an accelerated or standard HBV vaccination schedule randomly. The recombinant hepatitis B vaccine (Gen-Hevac B, Pasteur) was given as 20 µg intramuscular injections via the deltoid muscle. Thirty days after the third vaccination, serum samples of the subjects were obtained and anti-HBS antibody levels were detected by EIA (Abbot, Aux SYMsys). The protective level of anti-HBS was defined as titer ≥10 MIU/ml. By using the Fisher's exact and Wilcoxon tests, the results were analyzed and the geometric mean titers were determined. In order to investigate the association between age and the body mass index (BMI) with the Ab level, we used linear regression. In addition, we classified the subjects to four groups based on the BMI and compared the Ab titer using the Kruskal–Wallis non-parametric method. The data were analyzed using Stata 10 and the level of significance was defined as less than 0.05. All subjects signed the informed consent.

RESULTS

Of the 161 participants in our study, 81 subjects received the conventional HBV vaccination and 80 subjects, the accelerated schedule. All baseline characteristics of the participants in both groups were with a similar distribution, except for smoking [See Table 1]. There were no statistical differences between the titer of the anti-HBS antibody in both groups 30 days after the last injection of the HBV vaccine [Table 1]. In the accelerated group, eight participants were current smokers, but the data on smoking was missing for 34 subjects in the control group. In 152 participants the titer of the anti-HBS antibody reached 10 IU / L or over (94.4%). The values for the accelerated group was 97.6% and in the classic group was 96.3% ($P = 0.31$). As shown in Table 2 and Figure 1 the titer of the antibody was not associated with age, sex, and smoking, but inversely, it was associated with the BMI.

Among those with the accelerated method, the values for the seroconversion rate were 94.4% and 87.5% among non-smokers and smokers, respectively ($P = 0.42$).

By using the Kruskal–Wallis analysis, a difference was revealed among the four groups of BMI ($P < 0.001$). The seroconversion rates among obese subjects were significantly lower than others (71.4 and 50% for accelerated and standard methods, respectively).

DISCUSSION

The seroconversion rate after an accelerated hepatitis B vaccination schedule at 0, 10, and 21 days was similar to the classic schedule (0, 1, and 6 months) in the healthcare workers.

### Table 1: The baseline characteristics* in participants of HB vaccination

Characteristics	Accelerated N = 81	Routine N = 80	*P* value
Age (mean ± standard deviation)	30.30 ± 6.49	30.25 ± 5.99	0.96
Sex* (male)	47.50	46.91	0.94
BMI (mean ± standard deviation)	24.20 ± 3.89	25.04 ± 2.38	0.10
Smoking*†	9.9	0.0	0.03
Anti-HBS level			0.97
25 percentile	58.0	43.3	
50 percentile	117.0	128.0	
75 percentile	190.1	200.8	
95 percentile	568.1	574.5	

*Values show the percentages, †Data were missing for 34 participants, who received vaccination under the routine (0, 1, and 6 month) schedule

Table 2: Association between the Ab titer and explanatory variables

Characteristics	Ab level	
	Median	*P* value
Age	- 0.01*	0.43*
Sex		
Female	118.0	0.75
Male	121.8	
BMI	- 0.10*	< 0.001*
Smoking†		
Yes	69.2	0.28
No	118.0	
Method of vaccination		
Rapid	117.0	0.97
Routine	128.0	

*The values show the slope estimate for age and BMI with the corresponding *P* values, †Data were missing for 34 controls
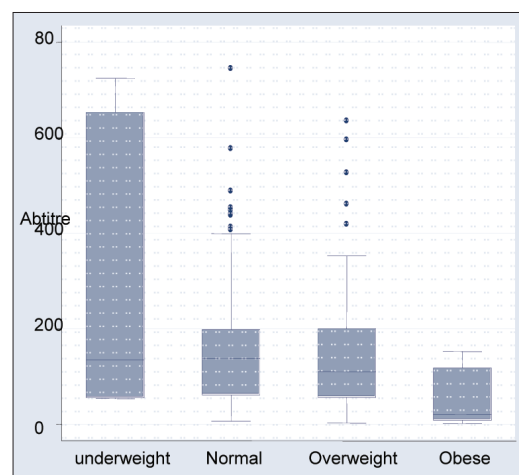
Figure 1: Box plot of antibody titer according to the BMI of the participants

Due to job-related risk factors, nurses, doctors, and other healthcare workers are at risk for exposure to blood-borne infection agents like hepatitis B virus.[12] The most important manner in which hepatitis B vaccine infections and their

complications like hepatocellular carcinoma and cirrhosis can be prevented is through vaccination.[10,11,13]

The classic HBV vaccination program includes three injections at 0, 1, and 6 months. Sometimes there may be a problem in the completion of this schedule, like in the case of travelers, prisoners, drug users, and healthcare workers.[12,14,15] Seroconversion to the protective level of antibody against hepatitis B at shorter intervals is optimal in these groups. Another schedule is the accelerated regimen that vaccine injected on days 0, 10, and 21. Some studies have shown a good immune response when using the accelerated schedule. Hernandez-Bernal F reported a rapid and good immune response in healthy adults.[16] Also, Asli A A showed early protection in prisoners by using the accelerated program,[17] however, Janbakhsh A reported that the serological response rate to the HBV vaccine may be lower in healthcare workers using the classic schedule.[18]

The Hepatitis B vaccine induces immunological memory as a function of memory B cells and the third dose induces a secondary immunological response that increases anti-HBS titers, which are neutralizing antibodies that provide protection against HBV infection.[19,20] Similar to our study, according to Tarhan *et al* (2006), the accelerated HBV vaccination program is as effective as the classical vaccination program and is an acceptable alternative for vaccination of healthcare workers.[12] Mehmet Bosnak and co-workers have also shown that the accelerated vaccination program elicits protective levels of anti-HBS antibody more rapidly than the classical schedule, without any significant difference in the seroprotection rate after one year.[14] These studies and ours show that accelerated vaccination schedules against hepatitis B virus induce a high rate of seroconversion. Therefore, if the near-term risk of infection is high, for example, a traveler leaving for an endemic country within a month or in new care health workers, who are not immune, it is suitable alternative.[21] Also, the accelerated vaccine series may optimize vaccination compliance in homeless adults and drug users.[15,22] Harries *et al.* has also shown that the accelerated schedule is effective, with similar side effects, at a similar rate as those on the conventional schedule.[23] The accelerated schedule is also effective, practical, and well-tolerated during pregnancy.[24]

The Food and Drug Administration (FDA) has approved the accelerated schedule for Twinrix, that is, a combined Hepatitis A and Hepatitis B vaccine, license for persons 18 years of age or older, but not for the Monovalent hepatitis B vaccine yet.[25] Hans L *et al*. have shown that accelerated schedule at months 0, 1, and 2 is effective enough to elicits a high rate of seroprotection, which is persistent at least for 12 months.[26]

CONCLUSION

Our data indicate that an accelerated hepatitis B vaccination schedule on days 1, 10, and 21 provide a protective antibody titer within a shorter time compared to the classical schedule on months 0, 1, and 6. The accelerated schedule can be used for persons under high risk, such as, family members of hepatitis B virus carrier, or healthcare workers who may have direct contact with a patient's blood or bloody fluid, or those who travel to endemic areas with hepatitis B.

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