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Accelerated versus classical hepatitis B virus vaccination programs in healthcare workers accelerated vs. classical HBV vaccination

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

Mustafa Oktay Tarhan[1 ABCDEF], **Ali İhsan Aker**[2 ABCDF], **Oguz Resat Sipahi**[3 DEF], **Gokhan Kardes**[4 B], **Kadir Biberoglu**[5 ABCDEF]

[1] Department of Internal Medicine Division of Oncology, Ataturk Training and Research Hospital, Izmir, Turkey
[2] Universal Private Hospital, Internal Medicine Clinic, Manisa, Turkey
[3] Department of Infectious Diseases and Clinical Microbiology, Ege University Faculty of Medicine, Izmir, Turkey
[4] Dokuz Eylul University Faculty of Medicine, Central Laboratory, Izmir, Turkey
[5] Department of Internal Medicine, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey

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Summary

Background: The aim of this study was to compare the efficacy of a standard hepatitis B virus vaccination program (day 0–30–60) with an accelerated vaccination program (day 0–10–21) in healthy healthcare workers.

Material/Methods: Participants were randomly assigned to a classical (group 1, days 0, 30, and 60) or an accelerated vaccination program (group 2, days 0, 10, and 21). The vaccine used was 20 µg recombinant hepatitis B vaccine (recombinant hepatitis B vaccine derived from yeast cells, Engerix B, Smith Cline Beachum). HBV markers were re-examined for the emergence of anti-HBsAg and also to detect the development of a possible acute HBV infection one, two, and three months after the last dose of vaccine. Anti-HBsAg titers >10 mIU/l were accepted as protective.

Results: The seroprotection rates were similar one, two, and three months after the last dose of vaccine in both groups. Anti-HBsAg titers in group 1 were higher than in group 2 two and three months after the last dose of vaccination ($p<0.05$).

Conclusions: Our data indicate that the accelerated HBV vaccination program was as effective as the classical vaccination program.

key words: HBV • healthcare workers • vaccination • accelerated • yeast-derived HBV vaccine • Engerix B

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Author's address: Oguz Resat Sipahi, Ege University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Izmir, Turkey, e-mail: oguz.resat.sipahi@ege.edu.tr

Background

Hepatitis B virus (HBV) affects over two billion people in the world and is a serious public health problem. It is estimated that there are over 350 million HBV carriers in the world. Chronic HBV infection is associated with higher risks of cirrhosis and hepatocellular carcinoma. Turkey has an intermediate endemicity for HBV. Hepatitis B virus surface antigen (HBsAg) and anti-HBsAg seropositivity rates are reported to be in the ranges of 3–15% and 26–69%, respectively (1994 Report of the Turkish Association for the Prevention of Viral Hepatitis). Worldwide, hepatitis B virus (HBV) infection is a major cause of acute and chronic hepatitis, cirrhosis, and hepatocellular cancer [1,3]. The most important way of preventing HBV infection is vaccination [1–7]. The seroprotection rate after the classical vaccination program (day 0–30–60) is reported to be up to 95%, but this vaccination program is not suitable for urgent vaccination [2]. The aim of this study was to compare the efficacies of standard HBV vaccination with an accelerated vaccination program in healthy healthcare workers.

Material and Methods

The study group

Fifty-eight healthy female healthcare workers (fifty-four nurses, four medical faculty students) who:

- agreed to be enrolled in the study,
- did not have a known disease and did not use any medicine regularly,
- had not received any vaccine in the previous three weeks,
- had not ever received a dose of HBV vaccine,
- had not received blood or blood products in the previous three month,
- were HBsAg, anti-HBcAg, and anti-HBsAg negative,

were included in the study.

The study was performed between 1996–1997. Oral informed consent was obtained from each participant. Initial body mass index and cigarette smoking history of all cases were recorded. The participants were randomly assigned to the classical (group 1, days 0, 30, and 60) or the accelerated vaccination program (group 2, days 0, 10, and 21). The vaccine used was 20 µg of recombinant hepatitis B vaccine (recombinant hepatitis B vaccine derived from yeast cells, Engerix B, Smith Cline Beachum) and it was administered to each patient by the intramuscular route into the deltoid muscle. All patients were requested to record any kind of side-effect.

HBV markers were re-examined to search for the emergence of anti-HBsAg and also to detect the development of a possible acute HBV infection one, two, and three months after the last dose of vaccine. Anti-HBsAg levels were assayed through titrimetric analysis by enzyme-linked immunoassay (Monolisa anti-HBs ELISA kits, Pasteur Diagnostics, France), and titers >10 mIU/l were accepted as protective. Since the upper limit of the ELISA was 150 mIU/mm^3, the results were not compared as geometric means; however, conversion of the anti-HBs titers to ordinal variables (0–9 mIU/ml=1, 10–19 mIU/ml=2, 20–29 mIU/ml=3, etc.) was helpful in analyzing the differences in the antibody titers.

Data were analyzed with the SPSS 5.0 package program using the Mann-Whitney U and chi-square tests. A p value less than 0.05 was considered significant.

Results

Group 1 and group 2 were similar in terms of age, body mass index, and cigarette smoking (p>0.05, Table 1) The seroprotection rates were similar one, two, and three months after the last dose of vaccine. Anti HBsAg titers in group 1 were higher than in group 2 two and three months after the last dose of vaccine (Table 2). Overall, fatigue (12.2%) was the most common side effect, followed by induration around the injection side (5.4%), fever (3.2%), and headache (1.6%). One case (0.5%) reported diarrhea. There was no difference between the groups in terms of side effects.

Discussion

Parenteral exposure to blood-borne infectious agents is a relevant risk among healthcare workers [3–9]. Job-related risk factors for nurses, medical doctors, and other healthcare workers are of crucial importance for the wellbeing of patients as well as their own. The most important way of preventing HBV infection is vaccination [9–13]. Vaccination against HBV is still low among Turkish nurses. In a study from Eskisehir, Turkey [7], 32.4% of 139 nurses were not vaccinated for HBV and 1.4% had evidence of HBV infection. In addition to vaccination, proper educational programs for certain risk groups have been shown to be beneficial for prevention [6,14]. Turk et al. [6] reported that educational programs for healthcare workers about methods of preventing hepatitis B virus infection are effective in terms of knowledge and in developing appropriate attitudes. HBV vaccination is effective in decreasing HBV incidence and cost-effective in preventing chronic HBV infection, cirrhosis, and hepatocellular carcinoma [15,16].

To our knowledge, there is no study comparing the day 0–10–21 regimen and the day 0–30–60 regimen with a vaccine without pre-S_2 antigen in healthy adults. Bock et al. [13] compared day 0–7–21, 0–14–21, and 0–28–56 regimens with the same vaccine used in the presented study. They reported a significantly higher seroprotection rate in 0–7–21 and 0–14–21 groups than in the 0–28–56 group 30 days after the first dose of vaccination. In contrast to their study, we checked the anti-HBs titers not during the vaccination period, but after the last dose of vaccine and after the same time periods in both study arms, so we do not have antibody response data 30 days after the first dose of vaccination. Bock et al. reported a higher seroprotection rate in a 0–28–56 group than the 0–7–21 group (89% vs. 76.4%), but there was no significant difference between 0–7–21 and 0–14–28 groups (89% vs. 78.5%) and 0–28–56 and 0–14–21 groups (78.5% vs. 76.5%) 30 days after the last dose of the vaccination program. Contrary to their findings, there was no difference in terms of seroprotection rate between the two groups 30 days after the last dose of vaccination in our study. Marchou et al. [2] compared the day 0–10–21 regimen vs. the day 0–30–60 regimen with recombinant vaccine with pre-S_2 antigen produced in mammalian cells (Genhevac B).

Table 1. General characteristics of groups 1 and 2*.

	N	Age	Cigarette consumption**	Body mass index***
Group 1	30	26.1±4.9	5±6.3	19.9±2.6
Group 2	28	24.8±4.7	3.9±5.1	21.2±2.5

* ± standard deviation; ** n/day; *** kg/m^2.

Table 2. Seroprotection rates (anti-HBs >10 IU/ml) and median anti-HBs titers (As converted to ordinals 0–9 mIU/ml: 1, 10–19 mIU/ml: 2, 20–29 mIU/ml: 3, etc.) of the groups one, two, and three months after the last dose of vaccine.

1 month				2 months				3 months			
Gr 1	%	Gr 2	%	Gr 1	%	Gr 2	%	Gr 1	%	Gr 2	%
12*	80*	7*	71*	16**	90*	9.5**	89*	16***	97*	16***	100*

* p>0.05; ** p=0.014; *** p=0.026.

They reported a seroprotection rate of 70% one month after the last dose of Genhevac B, in the 0–10–21 group, which is comparable with the 71% seroprotection rate achieved in our study. The fact that anti-HBsAg titers were found to be lower in the accelerated vaccination program in our study is in concordance with the results of Marchou et al. [2] in the above-mentioned study. The 71% seroprotection rate in the accelerated vaccination program suggests that this method may be an alternative in post-exposure prophylaxis.

The 89% seroprotection rate achieved three months after the last dose of the accelerated vaccination group is comparable with the results of Marchou et al. [17] in a study in which they compared a day 0–21 regimen with a 0–10–21 regimen with Genhevac B, reporting a geometric mean titer of 77.6 mIU/ml, which concords with the 80–89 mIU/ml anti-HBs titer achieved in our study (our results were not compared as geometric means, as mentioned above).

Shortening the intervals between the priming doses of HBV vaccine was reported to improve compliance and increase response in a study performed in a Catalonian prison [18].

Conclusions

Our data indicate that an accelerated HBV vaccination program is as effective as the classical vaccination program and can be used as an alternative for the vaccination of healthcare workers, travelers to risky areas, family members or sexual partners of patients with acute or chronic HBV infections, some immunocompromised patients, or adolescents in whom urgent vaccination is needed.

Appendix 1. Anti-HBs titers one, two, and three months after vaccination in groups 1 and 2 (values as mIU/ml).

Case no	1st month		2nd month		3rd month	
	Group 2	Group 1	Group 2	Group 1	Group 2	Group 1
1	1	0	9	0	15	12
2	2	0	16	1	20	5
3	1	1	8	3	14	31
4	0	1	1	24	21	>150
5	2	4	10	57	21	125
6	1	4	12	23	23	100
7	4	25	12	87	25	>150
8	7	34	13	>150	112	>150
9	25	39	56	138	119	>150
10	27	51	57	58	120	>150

Appendix 1 Continious. Anti-HBs titers one, two, and three months after vaccination in groups 1 and 2 (values as mIU/ml).

Case no	1st month		2nd month		3rd month	
	Group 2	Group 1	Group 2	Group 1	Group 2	Group 1
11	31	56	59	>150	135	>150
12	31	60	60	>150	138	>150
13	38	102	61	>150	148	>150
U	61	112	87	136	>150	>150
15	62	117	91	145	>150	>150
16	69	117	93	>150	>150	>150
17	69	118	100	>150	>150	>150
18	73	126	102	>150	>150	>150
19	78	130	108	>150	>150	>150
20	86	131	109	>150	>150	>150
21	>150	131	>150	>150	>150	>150
22	>150	133	>150	>150	>150	>150
23	>150	138	>150	>150	>150	>150
24	>150	140	>150	>150	>150	>150
25	>150	143	>150	>150	>150	>150
26	>150	144	>150	>150	>150	>150
27	>150	>150	>150	>150	>150	>150
28	>150	>150	>150	>150	>150	>150
29	–	>150	–	>150	–	>150
30	–	>150	–	>150	–	>150

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