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Comparison of hepatitis B surface antibody decay rates after vaccination between hemodialysis and peritoneal dialysis patients

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ABSTRACT

Background and objectives: The available information about maintaining effective immunity after hepatitis B virus (HBV) vaccination in dialysis patients is limited. The aim of this study was to determine whether a difference exists in the persistence of immunity between hemodialysis (HD) and peritoneal dialysis (PD) patients. We compared the decay rate of hepatitis B surface antibody (anti-HBs) titers after HBV vaccination between HD and PD patients.
Design, setting, participants, and measures: A total of 103 HD and 53 PD patients who were completely vaccinated were enrolled. We examined their anti-HBs titers at the 1st month after vaccination then annually thereafter. Changes in the anti-HBs titers were assessed by comparing annual geometric mean titers (GMTs).
Results: The slopes of the anti-HBs titer decay rates plotted on a logarithmic scale for the HD and PD groups were −23.41 and −31.48, respectively. The decay rate of the PD group was significantly faster than that of the HD group ($P = 0.0053$).
Conclusion: The decay rate of anti-HBs titers in the PD group was faster than that in the HD group. Hepatitis B vaccination could not offer long-term protection in HD or PD patients. Post-vaccination testing every 6–12 months is necessary and revaccination may be protective in dialysis patients, especially in hyper-endemic areas of hepatitis B infection.

1. Introduction

Hepatitis B virus (HBV) infection, the leading cause of cirrhosis and hepatocellular carcinoma, is a global health concern [1]. It is important and protective to recommend that dialysis patients receive hepatitis B vaccination and then undergo regular check-ups for hepatitis B surface antibody (anti-HBs) titers [2]. Compared with healthy individuals, dialysis patients show a unique immune response to HBV vaccination. Among the general population, 90–100% of vaccinated subjects acquire protective immunity and maintain protection against HBV 10–15 years later, even after vaccination in infancy [3]. Despite adopting a higher frequency immunization schedule and higher vaccine doses, the vaccination failure rate remains up to 30–60% among dialysis patients [4]. Increasing age, malnutrition, and depression are currently recognized as negative determinants of immune response among the dialysis population [5–8]. In our previous study, we demonstrated that dialysis modality has no effect on response to HBV vaccination [9]. In addition, we observed rapidly declining proportions of seroconversion in hemodialysis (HD) as well as peritoneal dialysis (PD) patients at 2-year follow up. While the unfavorable initial effect of the HBV vaccine in the dialysis groups is documented, few studies have determined the kinetics of the anti-HBs titer waning pattern and the factors affecting immune persistence in the dialysis populations. We aimed to study trends in the decay rates of anti-HBs titers in the dialysis population and compare the decay rates between PD and HD groups. We also attempted to plan an efficient screening and boosting schedule based on the observed trends.

2. Methods

We initiated data collection on dialysis patients at our dialysis center from March 2002 to March 2008, and followed-up these patients until March 2009. We enrolled dialysis subjects who tested negative for HBV surface antigen (HBs Ag) and HBV

Abbreviations: Anti-HBs, hepatitis B surface antibody; HD, hemodialysis; PD, peritoneal dialysis; GMT, geometric mean titer; HBs Ag, HBV surface antigen.

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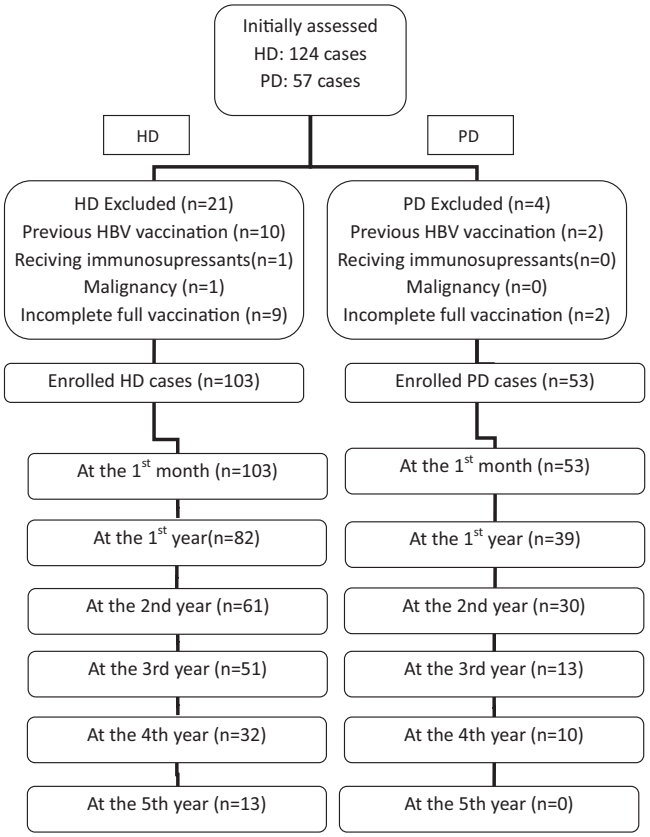

Fig. 1. The flow chart of patients enrolled in out study.

surface antibody (anti-HBs). We excluded patients who were receiving immunosuppressive agents, had malignancies, had previous HBV vaccination, or those who were unable to complete all 4 vaccinations. All patients were vaccinated with a 40 μg recommended hepatitis B vaccine (Engerix-B, GlaxoSmithKline Biologicals) injected into the deltoid muscle at 0, 1, 2, and 6 months.

Initially, there were 124 HD patients and 57 PD patients assessed. We excluded patients who were receiving immunosuppressive agents (1 HD case of frequent acute exacerbation of chronic obstructive lung disease), had malignancies (1 HD case of lung cancer), had previous HBV vaccination (10 HD cases and 2 PD cases, respectively), or those who were unable to complete all 4 vaccinations (9 HD cases and 2 PD cases, who transferred to other dialysis units) (Fig. 1). A total of 156 patients (64 male and 92 female) were enrolled. Serial blood samples were obtained from each available subject at the first month after the final vaccination (time t_0), the first year (time t_1), and second year (time t_2) after the final vaccination, and annually thereafter (time t_n). Anti-HBs titers were checked with an ELISA kit (AUSAB-EIA, Abbot Labs, USA). A total of 156 subjects were enrolled; 156 t_0 samples, 121 t_1 samples, 91 t_2 samples, 64 t_3 samples, 42 t_4 samples, and 13 t_5 samples were obtained from these patients. Anti-HBs titers ≥ 10 mIU/ml were regarded as protective in both HD and PD patients. The lower and upper limits of detection using this quantitative method were 0.1 mIU/ml and 1000 mIU/ml, respectively. In the case of undetectable titers, values of 0.05 mIU/ml and 1000 mIU/ml were assigned.

We calculated the geometric mean titers (GMTs) of anti-HBs from the available patients to determine the central tendency of the anti-HBs titers given the skewed distribution of the anti-HBs levels. We traced the trends in the decay rates of anti-HBs titers among the dialysis subjects. We also compared the decay rates of anti-HBs titers between the HD and PD groups.

Table 1
Patient characteristics.

Characteristics	HD	PD	*P* value
Number	103	53	
Age	60.89 ± 11.52	51.74 ± 15.10	<0.001
Gender (M:F)	45:58	19:34	0.393
Duration of dialysis	41.25 ± 41.39	35.64 ± 28.0	0.522
DM	37	13	0.205
Hemoglobin (g/dl)	9.71 ± 1.40	9.19 ± 1.32	0.041
Albumin (g/dl)	3.50 ± 0.37	3.48 ± 0.40	0.958
Responders (proportion)	71 (68.63%)	38 (71.69%)	0.854

Note: Data are shown as the number (%) or mean ± S.D. as appropriate. *Abbreviation*: DM, diabetes mellitus.

Comparisons of categorical data were performed by means of the Chi-square test. Continuous data were compared by the non-parametric Wilcoxon rank-sum test. The annual decay pattern of the log anti-HBs level in both HD and PD patients is assessed using the repeated measures ANOVA with the first-order auto-regressive variance-covariance structure. We also examined the association between anti-HBs titers and post-vaccination time lapse. A P value < 0.05 was considered statistically significant. The GMT for the anti-HBs levels was computed by the following model: GMT at time t_n = GMT at time t_0 + (β_1 log[time]), where 10 is the base of the natural logarithmic function and β_1 is the coefficient of this logarithmic function. We examined the differences between the slopes of the logarithmic functions of the HD and PD groups. To take into account the fact that many factors such as gender, age, albumin, and hematocrit levels might influence immune persistence, we used the regression function "titer at time t_n = titer at time t_0 + (β_1 log[time])" to identify the slope for each patient. A multiple linear regression model was then adapted to examine the effects of age, albumin, gender, modality, and hemoglobin on the slope.

3. Results

3.1. Patient characteristics and response rate

A total of 156 participants (103 HD and 53 PD individuals) were included in our study. Patient characteristics are summarized in Table 1. The GMT of the 156 vaccines checked at the first month after the fourth dose was 42.52 mIU/ml. Among all dialysis patients vaccinated, there were 110 responders and the overall seroconversion rate after primary vaccination was 70.5%. Among patients younger than 40 years of age, 93.7% responded compared with 83.3% of those aged 41–50 years, and 66.1% of those older than 50 years.

3.2. Anti-HBs GMT during 5-year follow-up

The log anti-HBs level is significantly different over time in both HD and PD groups (P = 0.0011 and P < 0.0001, respectively).

The GMT among both dialysis groups was 43.30 mIU/ml at time t_0, 13.9 mIU/ml at time t_1, 11.3 mIU/ml at time t_2, 5.8 mIU/ml at time t_3, 4.2 mIU/ml at time t_4, and 0.7 mIU/ml at time$_5$. During annual follow-up after the final injection, the PD group had a higher anti-HBs GMT than the HD group in the first 2 years (Table 2).

Table 2
Serial geometric mean times from 5-year follow-up of hemodialysis and peritoneal analysis patients.

	GMTs					
	1st month	1st year	2nd year	3rd year	4th year	5th year
HD	43.3	13.9	11.3	5.8	4.2	0.7
PD	55.2	16.7	12.7	3.07	1.5	

GMT, geometric mean titers.