

Is Any Factor Influence On Hepatitis B Vaccination Response In Hemodialysis Patients?

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Citation

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Abstract

Background: Patients on hemodialysis (HD) elicit a weaker response to Hepatitis B vaccine (HBV). We aimed to determine, rate of successful immunization in HD patients and factors which could affect response to HBV vaccination.

Methods: HBV vaccination was offered to 54 patients that were negative for anti-HBc antibody and they didn't receive any dose of HBV vaccine previously. Vaccine series was given and HBsAb responses detected 1-2months after completion of vaccination. Subjects were divided into 3 groups according to the level of HBsAb: nonresponders (<10 IU/L), weak responders (10-100) and high responders (>100 IU/L). We measured some lab tests in our subjects.

Results: The patient distribution with regard to anti-HBs titers was as follows: non responders 13%, weak responders 27.7%, and high responders 59.2%. There was no significant difference between three groups in values of hemoglobin, albumin, triglyceride, cholesterol.

Conclusion: We didn't find any factors that related to HBV vaccine response on HD patients.

INTRODUCTION

Because hemodialysis (HD) patients are at high risk for contracting hepatitis B (HBV) virus, vaccination as prophylaxis is routine. Sources of infection are blood product transfusions, contamination from dialysis equipment and infections from other environmental sources. [1] The response rate to HBV vaccine in hemodialysis patients is low ranging from 50% to 80%. [2] Various strategies have been attempted to improve seroconversion antibody including adding one extra dose of vaccine for a four vaccine series and doubling the dose of vaccine to 40 µg /dose. [3] Some studies reported 80% seroconversion by this route. [4]

Previous studies have examined the influence of various inherited and acquired factors, on the response to HBV vaccination in HD patients. Age, poor nutrition, infection with hepatitis C virus and presence of certain HLA haplotypes have been associated with a lower vaccine response in this population [5, 6, 7]. The influence of other factors such as diabetes mellitus (DM) and adequacy measures of HD remains controversial. It has previously been shown that HBV vaccine response was weaker in HD

with inefficient dialysis and older age. [8]

In order to address this paucity of information on why hemodialysis patients may or may not respond to the HBV vaccine, we measured levels of various hormones, inflammatory markers, immune markers, and lipids in hemodialysis patients. Our goal was to identify which of these factors are associated with responsiveness to HBV vaccine in hemodialysis patients. We measured the levels of factors that may impact on the effectiveness of vaccination program including parathyroid hormone (PTH), albumin, fasting blood sugar (FBS), quantitative C reactive proteins (CRP), complements (c3, c4), hemoglobin, triglyceride, cholesterol, hepatitis C virus antibody (HCV-Ab) by routine laboratory technique. We chose these factors because there is some controversy about their role on responsiveness to HBV vaccine. Our hypothesis is that most of these factors can't influence on response to HBV vaccine in hemodialysis patients.

METHODS

This is a prospective study. This study performed from

February to October 2005. HBV vaccine was offered to patients who were negative for antibody against hepatitis B core antibody (anti-HBc), HBV antigen and antibody, and they didn't receive any dose of HBV vaccine previously. This project was approved by the Pasteur Institute of IRAN ethics committee and informed consent was obtained from patients prior to their enrollment.

54 patients were enrolled in our study. All patients had been on a 4 hour, three times weekly dialysis schedule; with a blood flow rate of 300ml/min. Patients received four doses vaccination schedule (Heberbiovac Cuba) 40 µg injections intramuscularly in the deltoid muscle at 0,1,2,6 months. We measured the patient's Hepatitis B surface antibody (anti-HBs titers) by ELISA using commercial Kits (Hepanostika Biomerieux Nederland) 1-2 months after the last injection. Subjects were divided into 3 groups according to the level of Hepatitis B surface antibody (HBsAb): nonresponders (<10 IU/L), weak responders (10-100 IU/L) and high responder (>100 IU/L). We measured the levels of factors may impact on the effectiveness of vaccination program in 3 groups including parathyroid hormone (PTH), albumin, fasting blood sugar(FBS), quantitative CRP, c3, c4, hemoglobin, triglyceride, cholesterol, Anti HCV Ab by routine laboratory technique. Kruskal Wallis and chi-square test were used for statistical analysis. We utilized these methods to determine factors that predicted a response to vaccination. A p value of <0.05 was considered significant.

RESULTS

A total of 54 patients enrolled in our study include 28 men and 26 women aged 56± 17(minimum 20 and maximum 85 years), 52 were of Persian race, 11% had a history of tobacco use (see table 1).

Figure 1

Table 1: Distribution of hemodialysis patients according to response to hepatitis B vaccine and some variables. NS=Non significant

Variables	Non responder =10	Weak responder=15	High responder=38	P value
Diabetes mellitus	2	7	10	NS
Anti HCV Ab	0	1	1	NS
Male/female	5/2	8/7	15/17	NS
Iranian/non Iranian	6/1	15/0	31/1	NS
Smoking	2	3	1	NS

Only two of our patients were HCV Ab positive (3.7%). Mean weight of our patients was 63.5±12.9 kilogram. They had been on HD for 33.5±37.3 months. Mean Efficiency of

dialysis (KT/V) was 1.21±323.7 IU/ml. History of diabetes mellitus (DM) was found in 19 (35%) of our patients. Mean antibody level after 1.5 month of completion of vaccination was 271.6±323.7. The patient distribution with regard to anti-HBs titers after 1-2 months of vaccination was as follows: non responder 7(13%), weak responder 15(27.7%); high responder 32(59.2%). Distribution of our patients according to their response to 4 doses of vaccine and values of hemoglobin, serum albumin, triglyceride cholesterol... is shown in table 2.

Figure 2

Table 2: Values of variables (Mean±2SD) according to patients' response to HBV vaccine in 3 groups: non responder, weak responder, high responder (confidence interval 95% of variables). NS=Non significant

Variables	Non responder	Weak responder	High responder	P value
Serum albumin(g/dl)	4.39±0.42	4.36±0.41	4.28±0.4	NS
Hemoglobin(g/dl)	9.5±1.7	9.7±1.2	9.7±1.7	NS
Parathyroid hormone(PTH)	152.8±107.1	200.1±219.3	240.3±395.5	NS
C-Reactive protein(mg/l)	11.2±17.5	5.8±5.7	7.8±9.6	NS
Fasting blood sugar	133±94/1	95.7±19.7	114±58.05	NS
Cholesterol	141.7±41.3	139.6±35.5	146.3±42.3	NS
Triglycerides	152.8±105.3	166.3±77.9	140±68.6	NS
C3	107.6±39.6	115.6±28.7	110.1±26.5	NS
C4	31.9±14.9	33.1±11.2	35.9±15.1	NS
weight	63.2±9.4	70.3±10.5	70.3±10.5	NS
Duration of dialysis (month)	15.6±13.5	28.1±29.1	33.5±37.3	NS
Efficiency of dialysis(KT/V)	1.1±0.2	1.1±0.2	1.3±0.3	NS
Age	51.3±15.1	59.9±7.9	54.6±19.2	NS

There was no significant difference between three groups (weak responder, high responder and non responder) in values of following: hemoglobin, serum albumin, triglycerides, cholesterol, fasting blood sugar (FBS), C3, C4, CRP, PTH, efficiency of dialysis (Kt/V), duration of dialysis treatment, weight by Kruskal Wallis analysis. There was no significant difference between anti-HCV (+) and none infected individuals with regard to post vaccination response too. Our data did not reveal differences in gender, sex, smoking, percentage of subjects with DM between 3 groups by chi-square test [Table 1]. When we collapsed weak and high responders into one group (Anti HBsAb>10 IU/L) we showed a high response rate 87% to 4 doses of HBV vaccine (>10 IU/L), but 7 patients didn't show any response.

DISCUSSION

Prior studies have shown that unresponsiveness to HBV vaccine is multifactorial, and related to the presence of several modulators. [4, 9]. Several factors have known to reduce response to HBV vaccine in different ethnic groups.

Identifying potential nonresponders to the HBV vaccine at the start of HD may allow the use of a different HBV vaccination protocol or adjuvant therapy at the onset of vaccination. This may maximize the chances of seroconversion and minimize the time required to achieve a protective antibody titer in this subset of the HD population.

For a precise determination of factors influencing on hepatitis B vaccine response, this study performed. We examined the level of numerous hormonal, inflammatory, immune, and lipid modulators in patients on hemodialysis, and did not find that any of them could predict a response to hepatitis B vaccine in HD patients. Some studies showed that older age, low albumin level, infection with HCV virus in the HD population associated with a poorer vaccination response [4, 9]. Other researchers have had conflicting findings - Urbanowicz et al. did not observe significant difference of age, sex and HCV infection between responders and non-responders [10]; but Navarro suggested that infection with HCV infection decreases the response rate to HBV vaccine. [11] We did not find significant relation between HCV infection and HBV vaccine response, but with only 2 HCV positive patients our power to determine this relationship is low.

The association between C4 gene and HBV vaccine non-responsiveness has been observed by Stachowski, de Silvestre and Hatae [12, 13]. This is contrast with our findings.

Kovacic showed that HBV vaccination response was weaker in hemodialysis patients with inefficient dialysis and older age but we didn't find such correlation. [8].

Other findings in this study included the fact that DM was not a significant predictor of nonresponse in HD patients. We had hypothesized that it would be significant because patients with diabetes mellitus have immune compromise from renal failure. Chin et al showed that DM has an independent association with a poor vaccination response rate [2]. But our finding corroborates previous work that the presence of DM in HD patients has not been associated with HBV vaccine response [2]. In our study we had only 19 diabetic mellitus patients and only 9 patients need to take insulin, so we may have failed to show an association because of low power. Chronic renal failure diabetic patients commonly have impaired insulin clearance and they require less exogenous insulin because of diminished degradation by renal insulinase. Therefore many of them don't need exogenous insulin and they can maintain their blood glucose in normal level. Diabetics appear to have a lower degree of

antigen presentation and T cell function too. [2].

Hepatitis B virus infection has higher mortality and is more likely to result in a carrier state in uremic patients. The introduction of universal precautions and the reduced use of blood products facilitated by the widespread use of Epo have contributed significantly bringing the prevalence of hepatitis B down in dialyzed patients. With the introduction of Hepatitis B vaccine in 1980 it was hoped that hepatitis B would be eliminated from dialyzed patients but vaccine showed suboptimal efficacy. The lower response rate to the HBV vaccine in HD patients has prompted clinicians to use a higher dose (40µg) and more frequent injections (0, 1, 2, 6 months). Using this schedule Sezer and Peces reported that 80% and 77.5% of HD patients seroconverted retrospectively [11]. Nonetheless, there is still a vaccination success rate lower than that of the general population. In our study after following this schedule, we recorded seroconversion rates of 87% after completion of vaccination and this is a higher response rate than in prior studies but for others didn't response to vaccine we should forced on infection control measures.

Our study had some potential limitations because of Low power in HCV positive cases and diabetic patients, but we should considered that in different ethnic groups, factors related to HBV vaccine unresponsiveness were different and may be unknown factors were responsible for this disagreement, and this is the first study on hemodialysis patients of Iran and further study with more patients is necessary to confirm our data.

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