Antibody responses after hepatitis B vaccination among maintenance haemodialysis patients

Nahar K¹, Jahan M², Nessa A², Tabassum S²

¹Department of Pathology & Microbiology, Islamia Eye Hospital & Mirza Ahmed Ispahani Institute of Ophthalmology, ²Department of Virology, Bangabandhu Sheikh Mujib Medical University, Dhaka.

Abstracts

In haemodialysis patients, hepatitis B virus infection has higher mortality and is more likely to result in the carrier state. Although Hepatitis B vaccine is effective in producing protection against HBV infection, the antibody response may be variable. In this study, seroprotection rate of hepatitis B vaccine in maintenance haemodialysis patients was studied after primary vaccination and after completion of the full vaccine regime. 50 unvaccinated patients on maintenance haemodialysis were included in this study. Patients negative for HBsAg, Anti-HBc (total) and Anti-HCV were vaccinated with 40µg of Engerix B following a schedule of 0, 1, and 2 months. The antibody titer was tested at 3rd month and if the titer was <10 or between 10-100 mIU/ml, they were given another 4th dose of vaccine at 6th month, and their antibody titer was tested again at 7th month. In maintenance haemodialysis patients, the response rate to HBV vaccine was 44% after the primary vaccination and 80% after completion of the full vaccine regime.

Introduction

Worldwide, hepatitis B virus (HBV) infection and its sequelae are a major public health concern. It is estimated that more than 2 billion people are infected with HBV globally, of whom 350 million are chronically infected; 15%-25% of the chronically infected persons die from chronic liver diseases¹. HBV infections are common and poses major threat to patients treated with long-term haemodialysis (HD), and have a tendency to become chronic carriers of HBV due to defective immune system³. Once infected, 50 to 60% of HD patients are likely to become chronic carriers of HBV and may also increase the risk of transmission of HBV to other HD patients, medical personnel’s, and family members. HBV infections can be prevented or controlled by the host humoral immune response (anti-HBs) directed against the major surface antigen (HBsAg), elicited either naturally or by vaccination⁴. Fortunately, hepatitis B vaccine has been available since 1982². Patients with chronic kidney disease (CKD), especially if diabetic, have a reduced response to vaccination because of the general immune suppression associated with uremia³. As a result of decreased cellular responses, there are also various disturbances in humoral innate immunity e.g. low complement IV factor, decreased cytokine response after stimulation⁶. Thus, hepatitis B vaccination is recommended for all maintenance HD patients and for all pre-end-stage renal disease patients before they become dialysis dependent⁷. The recommended primary series of hepatitis B vaccine induces a protective anti-HBs response in 90%-95% adults with normal immune status⁸. However, the response rate is lower in chronic kidney disease (CKD) patients and may vary from 66-84%⁹,10,12. Our study reports the response rates of hepatitis B vaccine among maintenance haemodialysis patients.

Materials and Methods

The study was carried out among 50 patients with chronic kidney disease at the Department of Virology, Bangabandhu Sheikh Mujib Medical University (BSMMU). The patients were recruited from the Haemodialysis unit of BSMMU, Renaissance Hospital & Research Institute Limited and the Kidney Hospital & Dialysis Centre, Dhaka. A total of 50 patients (20 males and 30 females) were included in this study. Their ages ranged from 20 to 70 years (mean age: 46.52 ± 12.36 years). Among them, 18 (36%) patients were diabetic and 32(64%) patients were non-diabetic. The mean serum creatinine level of the patients was 8.53 ± 2.14 (Table I).

Screening for hepatitis B surface antigen (HBsAg) and total antibody to core antigen (Anti-HBc total) and Anti-HCV were performed by ELISA method (4th generation, Diasarion, Lot no. ETI-MAK-4
Patients negative for HBsAg, Anti-HBc (total) and Anti-HCV were vaccinated with 40µg of Engerix B intramuscularly in the deltoid muscle by following a schedule of 0, 1, and 2 months. Seroconversion was defined as an antibody titer equal to or more than 10 mIU/ml. The antibody titer was tested at 3rd month and if the titer was <10 or 10-100 mIU/ml (non-responder or poor responder) they were given another 4th dose (40µg) of vaccine at 6th month, and their antibody titer was tested again at 7th month. Chi-square test was used for analysis of data.

Statistical analysis: The data obtained from this study were entered into SPSS 11.5 for windows and analyzed. Test of significance was estimated using the statistical method. Values were expressed as mean ±SD. Antibody responses among the variables were compared by Chi-square test. P value <0.05 was considered as significant.

Results
After completion of primary vaccination (0, 1, 2 months), 22(44%) patients became responders to HBV vaccine and 28(56%) remain non-responders. However, among the responders 19(38%) were poor responders and only 3(6%) patients were good responders (Table II).

On the other hand, after completion of the full vaccine regime (0, 1, 2 and 6 months) the number of responders were 40(80%) and non-responders were 10(20%). Of the 40 responders, 16(32%) were poor responders and 24(48%) were good responders (Table III). The response rate was higher (80%) after completion of the full regime than after primary vaccination (44%) and this difference was highly significant.

Table III shows the association of antibody response after vaccination with the age and sex of haemodialysis patients. Among male patients, 6(30%) were good responders, 8(40%) were poor responders and 6(30%) were non-responders. In case of female patients, 17(56.7%) were good responders, 9(30%) were poor responders and 4(13.3%) were non-responders. However, the seroconversion rate was higher (86.7%) among female patients than male patients and it was highly statistically significant (p=0.0001). In younger patients below 40 years of age, 14(93.3%) were responders while only 1(6.7%) was non-responder. However, in patients aged above 40 years, 26(74.3%) were responders and 9(25.7%) were non responders. The antibody response rate of younger patients was comparatively higher than older patients and this difference was highly statistically significant (p= 0.0001).

Discussion
HBV had a high prevalence among dialysis patients and health care professionals in the 1970’s. In many parts of Europe, universal precautions, reduced use of blood products, and erythropoietin (Epo) treatment played an important role in reducing the prevalence of HBV to less than 5% among dialysis patients. With the introduction of hepatitis B vaccine in the 1980s, it was hoped that HBV would be eliminated from the dialysis population. Although HBV has not been eradicated yet, the vaccine has helped to reduce the incidence further, but with suboptimal efficacy in patients with chronic renal failure.
The response rate to HBV vaccine in haemodialysis patients is low, ranging from 50% to 80%.

Variations in the immune response to HBV vaccine have been observed, with some studies reporting a higher response rate among female subjects. In a study from the UK, 67% of women responded successfully to the vaccine, while only 50% of men did so.

In this study, the vaccine response rate was higher in younger patients than older ones. Other studies have also observed that immune response decreases with increasing age. In a study from Egypt, the response rate was 84.2% in patients below 40 years of age, which decreased to 33.3% at 60 years or above. Both humoral and cellular immune response usually diminishes with age.

In some of the studies it was observed that antibody response rates increases with increasing length of time on dialysis but duration of dialysis has no association. This association was not observed in the present study due to some potential limitations.

Majority of our haemodialysis patients had history of vaccination (84%) but analysis found that only 19% have good response, 59% have poor response and 42% have no response. These data indicate that approximately half of the dialysis patients had no protection despite vaccination which may probably be due to immunosuppression. Thus, the present study concluded that in haemodialysis patients, the antibody response to the primary vaccine series comprising of three doses of hepatitis B vaccine increased subsequently after administration of an extra fourth dose.

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References


