Brief Report

The Immune Response of Vaccination Against Hepatitis B virus in Iranian Patients Undergoing Chemotherapy

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Abstract

Introduction: Hepatitis B virus (HBV) infection and its complications are major public health problems. As it is hard to treat and control the chronic state, control of disease depends on the prevention especially by vaccination. There is an impaired immune response to vaccinations including HBV in patients with some malignancies. The aim of this study is to assess the response rate of patients undergoing chemotherapy to HBV vaccination. **Materials and Methods:** All patients from two hematology/oncology clinics in Isfahan, Iran with the history of at least 1 month chemotherapy who had the inclusion criteria were enrolled in a case control study. Also a sex- and age-matched control group from healthy population was selected. They were vaccinated in a schedule of 0, 1, and 6 months and were examined for antibody titers 1 month after the last dose. The titers more than 10 mIU/ml were determined as positive response to vaccination. **Results:** In this study, 50 patients and 50 healthy subjects were enrolled. The two groups were age and sex matched ($P > 0.05$). Frequency of negative responses to HBV vaccination in case and control groups were 9 (18%) and 1 (2%), respectively (OR = 10.75, CI = 1.30–88.47, $P = 0.027$). Of 50 patients, 54%, 12%, 22%, and 12% had breast cancer, lymphoma, gastrointestinal, and genitourinary cancers, respectively, and frequency of negative responses were 3 (11%), 1 (16%), 4 (36.4%), and 1 (16%), respectively ($P = 0.167$). **Conclusion:** According to our results, malignancy and chemotherapy will have an important effect on the immune system and cause negative response to HBV vaccination. Our results revealed the importance of passive immunity and screening for HBV infection in patients undergoing chemotherapy. Also more studies for better vaccination schedules in this group of patients are recommended.

Keywords: *Chemotherapy, hepatitis B virus, malignancy, response, vaccination*

Introduction

Hepatitis B virus (HBV) infection and its complications are major public health problems. It is reported that more than 2 billion people are infected with HBV in the world. In 6% to 10% of patients, acute hepatitis B leads to chronicity and 15% to 25% of them die from chronic liver diseases.[1-3] The prevalence of chronic carriers in the patients with defective immune system is higher than the general population.[2] As is hard to treat and control the chronic state, control of disease depends on prevention. HBV infections can be prevented by the host immune response stimulated either naturally or by vaccination. A three-dose series of vaccination (administered at 0, 1, and 6 months) against HBV is used to prevent the infection.[4] A response to HBV vaccination is determined by the development of hepatitis B virus surface antigen antibodies (HBs-Ab).[5] About 90% to 95% of healthy subjects achieve a protective titer of antibodies after vaccination. But the response will reduce in some individuals such as older people, males, smokers, overweight individuals, and immunocompromised patients.[6-9] Also the level of seroprotection will reduce during the time. Some factors such as age and time of the last vaccination are important.[10] The seropositive of 89.4% for healthcares and 87% for children have been reported in 30 and 11 years followup after vaccination, respectively.[11,12]

The prevalence of HBsAg positivity is less than 1% in general population but 10% to 20% in individuals with cancer.[13,14] Studies have reported an impaired immune response to vaccinations including HBV in patients with malignancies.[15,16] Anticancer therapy causes an immunosuppressive state

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and increases susceptibility to viral infections such as HBV. Also bacterial and fungal infections are more probable in this group of patients.[13] The aim of this study is to assess the response rate of patients undergoing chemotherapy to HBV vaccination.

Materials and Methods

A case-control study was conducted from March 2011 till March 2012. All the patients from two hematology/oncology clinics in the Isfahan city of Iran that were receiving chemotherapy (for at least one month) who did not receive HBV vaccination or did not have HBV infections in the past were enrolled and the final case group was selected considering the exclusion criteria. The control group was selected from healthy people without any immune diseases and history of chemotherapy who did not receive HBV vaccination or did not have HBV infections. The data were obtained from interview, medical history and blood testing. Participants who took any immunosuppressive drugs were excluded from the control group. Also patients with incomplete or suspicious medical documents were excluded. Fifteen patients with malignancies undergoing chemotherapy completed our criteria and were enrolled as a case group. Also 50 healthy subjects (control group) were involved.

The participants were advised that participation in the study is on a voluntary basis and an informed consent was obtained. Demographic characteristics such as sex and age were obtained through interview. A type of malignancy and duration of chemotherapy were obtained from medical documents of the patients.

Screening for antihepatitis B antibody (HBsAb) was done by performing enzyme-linked immunosorbent assay (ELISA) method and positive subjects were excluded. The negative individuals were vaccinated by HBV vaccine intramuscularly in the deltoid muscle by fallowing a schedule of 0, 1, and 6 months. The antibody titer was tested after one month (seven months after the first dose) by ELISA method and the titers more than 10mIU/ml were determined as positive response to vaccination.

Data analysis

Statistical analysis was performed using SPSS for windows (Version 16.0, 2007, SPSS Inc, Chicago, IL, USA). The Student *t*-test (for comparison of age) and Chi-square test (for other variables) were used to compare variables. Univariate analysis was done to estimate odds ratio (OR) and 95% confidence intervals (CI). Statistical significance was assessed at the 0.05 probability level in all analyses and the data are given as mean ± standard deviation (SD) or frequency.

Ethics

The research protocol was approved by the Ethical committee of Isfahan University of Medical Sciences in Iran.

Results

The mean age of study sample was 39.62 ± 7.81 (mean ± SD). Of all participants, 30 and 70 subjects were male and female, respectively. The mean age of case and control groups were not statistically significant different (40.44 ± 8.56 and 38.80 ± 6.96, respectively, P = 0.296). In each group 15 subjects were male and 35 were female. Table one reports the frequency of malignancies. Because of the small sample size, some groups are merged and new classification is also shown in the Table 1.

Frequency of the negative responses to HBV vaccination 6 months after last dose of vaccine injection were nine (18%) and one (2%) in the case and control groups, respectively (OR = 10.75, confidence interval = 1.30–88.47, P = 0.027). Table 2 shows the negative response frequencies of patients undergoing chemotherapy in each malignancy type. We classified GI, GU, and breast cancers as solid cancers and lymphoma as hematologic malignancy. Frequency of positive response in patients with solid cancers and hematologic malignancies were 81.8% (36 of 44 patients) and 83.3% (5 of 6 patients), respectively (P = 0.916).

Discussion

This study was conducted to evaluate the effect of chemotherapy on the human response to HBV vaccination. Of the participants, 18% of case and 2% of control group had negative response to vaccination. In comparison to study of Ramesh *et al*.,[13] who showed that 28.6% of

Table 1: Frequency classification of different types of malignancies in the case group (n=50)

Malignancy type	Number (%)	New classification*	Number (%)
Breast cancer	27 (54)	Breast cancer	27 (54)
Lymphoma	6 (12)	Lymphoma	6 (12)
Rectal cancer	5 (10)	Gastrointestinal (GI) cancer	11 (22)
Colon cancer	4 (8)		
Esophagus cancer	2 (4)		
Prostate cancer	2 (4)	Genitourinary (GU) cancer	6 (12)
Ovarian cancer	2 (4)		
Bladder cancer	2 (4)		

*New classification is done because of low sample size in some groups to make the groups capable of further analysis

Table 2: Negative response frequency of patients undergoing chemotherapy divided by the malignancy type

Malignancy type	Negative response*	*P*
Breast cancer	3 (11%)	0.167
Lymphoma	1 (16%)	
Gastrointestinal (GI) cancer	4 (36.4%)	
Genitourinary (GU) cancer	1 (16%)	

*Data is given as number (%)

children receiving chemotherapy had protective antibody titers and also study of Entacher *et al*.,[16] who showed 32% positive response to vaccination, our results revealed a higher response (82%). Entecher *et al.* showed that the vaccination response in patients undergoing chemotherapy with solid malignancies is higher than hematologic malignancies (28.5% vs 0%). our results revealed that 81.8% of subjects with solid tumors and 83.3% of patients with hematologic malignancy had a positive response and are statistically equal ($P > 0.05$). Another study conducted by Hovi *et al*.[17] showed that 45.4% and 88% of patients with solid tumors and hematological malignancies, respectively, had a positive response to HBV vaccination.

The results showed that subjects with malignancy undergoing chemotherapy had 10.75 fold risk of negative response to HBV vaccination in comparison to healthy people. Hovi *et al.* reported that children receiving chemotherapy have weaker responses to HBV vaccine than children not receiving chemotherapy.[17] Berberoglu *et al.* showed that 6 months after first dose of vaccination in children with cancers, 56% were positive for antibody titration. They also reported that 67.5% and 70.5% were positive after nine and 12 months, respectively.[18] Rosen *et al.* in a study reported that six out of seven healthy controls had protective antibody titers but six out of 32 patients with breast cancer responded to HBV vaccination.[19]

There are some possible reasons in addition to chemotherapy for the weaker response in the case group such as immunodeficiency after malignancy, genetic factors, malnutrition, associated life styles and environmental factors in some malignancies and possible effect of chemotherapy on vaccine directly. As our results showed that there is a higher risk of weak response to HBV vaccination in patients with malignancies undergoing chemotherapy in comparison to healthy population. As 82% of patients with malignancies undergoing chemotherapy showed a positive response to HBV vaccination we think it is better to vaccinate them all for HBV and then screen them. The vaccination and screening are worth doing because of higher risk of negative response in these patients than normal population. Because of sever damages caused by hepatitis B infection, passive immunity will be helpful when we find not responding patients. Our results showed a profound immune deficiency after chemotherapy and more studies on HBV vaccination schedule in this group is necessary. Studies with a higher sample size and also study of comparison of patients with malignancy without chemotherapy with patients with malignancy undergoing chemotherapy will be helpful.

Conclusion

In concussion, according to our results, malignancy and chemotherapy will have an important effect on the immune system and cause negative response to HBV vaccination. Our results revealed the importance of passive immunity and screening for HBV infection in patients undergoing chemotherapy. Also more studies for better vaccination schedules are recommended.

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Conflicts of interest

There are no conflicts of interest.

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