Original Article

Immune Response to Standard Hepatitis B Vaccination in HIV-Infected Patients

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ABSTRACT

Introduction: Due to their similar routes of transmission, human immunodeficiency virus (HIV) and hepatitis B virus (HBV) co-infection occurs considerably. HBV infection progresses more rapidly in HIV-infected patients. Therefore, HBV vaccination of all non-immune HIV infected patients is recommended. On the other hand, HIV-infected subjects have suboptimal responses to HBV vaccine. In this study, we aimed to determine the immune responses to standard HBV vaccination in HIV-infected patients. **Methods:** Fifty-six HIV infected patients who lacked evidence of either prior HBV infection or immunity were subjected to standard HBV vaccination, as 3 intramuscular injections of the standard dose (20 μg) of recombinant HBV vaccine at months 0, 1 and 6. Hepatitis B surface antibody (anti-HBs) titers were checked in all cases one month after the vaccination. A protective antibody response was defined as an anti-HBs titer of ≥10 IU/L. **Results:** HBV seroprotection was observed in 56.6% of HIV-infected patients. There was no significant difference between cases with and without seroprotection regarding age, sex, possible route of HIV acquisition, CD4 count, receiving antiretroviral therapy (and its duration) and HCV infection. **Conclusion:** Our study confirms previous reports that HIV-infected patients have a lower response rate to the standard HBV vaccination compared to general population. So other strategies are needed to improve the HBV vaccine response rate in HIV cases.

KEYWORDS: Human Immunodeficiency Virus(HIV), Hepatitis B Virus(HBV), Vaccination.

INTRODUCTION

Due to the similar routes of transmission and risk factors, the rate of human immunodeficiency virus (HIV) and hepatitis B virus (HBV) co-infection is considerable [1-3]. Chronic HBV infection affects approximately 10% of HIV-infected subjects throughout the world, with higher rates in high HBV endemicity areas and in high risk groups such as injecting drug users [2-4]. HBV infection progresses more rapidly in HIV-infected patients, with higher rates of HBV viremia, HBV reactivation, cirrhosis and hepatocellular carcinoma [5]. HBV infection has been also associated with more rapid progression of HIV infection to AIDS, by an increased expression of HIV-infected cells and a faster decrease in CD4 lymphocytes [6,7]. Moreover, the risk of hepatotoxicity from highly active antiretroviral therapy (HAART) increases in HIV/HBV co-infected patients [4, 8]. Therefore according to the current guidelines, HBV vaccine is highly recommended to all asymptomatic HIV-infected patients without evidence of prior HBV infection or the immunity to HBV, [9, 10].
In healthy adults, HBV vaccination is associated with a good protection against HBV infection and has a seroconversion rate of more than 90% [11, 12]. Due to the impaired immune responses, the success rate of HBV vaccination is lower in HIV-infected cases compared to the general population, with immunogenicity rates varying from 17.5% to 72% [13-15]. The risk factors for lower rate of responses to HBV vaccine included higher HIV viral load, hepatitis C virus antibody (anti-HCV) positivity and lower CD4 cell count prior to the vaccination [14, 16-19]. Meanwhile, achieving seroprotection rates of HBV vaccine in HIV-infected patients remains a challenge. Due to the importance of HBV prophylaxis in high-risk groups, particularly HIV infected patients; we aimed to determine the immune responses to standard HBV vaccination in HIV-infected patients and its relation to different variables such as age, sex, route of HIV acquisition and the immune status.

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MATERIALS and METHODS

In this cross-sectional study, HIV-infected patients from Iranian Research Center for HIV/AIDS in Tehran were enrolled from March to September 2014. This project was approved by the Ethics Committee of Pasteur Institute of Iran and informed consents were obtained from the patients prior to their enrollments. A questionnaire that gathered

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epidemiological, clinical and laboratory data was completed by the clinicians.

Human immunodeficiency virus antibody (anti-HIV) was determined by ELISA (MP Biomedicals, Illkirch, France) and the positive tests were confirmed by Western blot assays (Diaplus, San Francisco, USA).

All samples were tested for hepatitis B surface antigen (HBsAg), Hepatitis B surface antibody (anti-HBs), Hepatitis B core antibody (anti-HBc) and anti-HCV by ELISA. The commercial enzyme immunoassay kits used were as follows: HBsAg (Hepanosticka Biomerieux, Boxtel, the Netherlands), anti-HBs (Enzygnost, Dade Behring Marburg GmbH, Germany), anti-HBc (Enzygnost, Dade Behring Marburg GmbH, Germany) and anti-HCV (Biorad, Segrate, Italy). Recombinant immunoblot assay (RIBA Innogenetics, Ghent, Belgium) was employed to confirm anti-HCV reactivity.

Fifty-six HIV infected patients who lacked evidence of either prior HBV infection or immunity to the infection were subjected to standard HBV vaccination [3 intramuscular injections of the standard dose (20 µg) of recombinant HBV vaccine (Pasteur Institute of Iran, Tehran, Iran) at months 0, 1 and 6]. Anti-HBs titers were checked in all cases one month after the vaccination by ELISA. A protective antibody response was defined as an anti-HBs titer≥10 IU/L.

Statistical Analysis

The chi-square test was used with SPSS 16 package program for statistical analysis (Chicago, IL, USA). Data are presented as mean±SD or when indicated, as an absolute number and percentage.

RESULTS

In this study, 56 HIV-infected patients were enrolled. The mean age of the patients was 36.91±7 years. Among them, 53.6% were male and 46.4% were female. The mean CD4 count of the HIV subjects was 467.54±218.93 cells/mm^3. The presumed routes of HIV transmission were heterosexual contact (53.6%), intravenous drug use (41.1%), infected blood and blood products transfusion (1.8%), and in 3.6% of the cases, the route of HIV acquisition was not identified. Patients who had received antiretroviral therapy (ART) were 98.1% and the mean duration of their ART was 32.5±21.05 months. The anti-HCV positives were 69.6% of the cases. HBV seroprotection was observed in 56.6% of the HIV-infected patients. There was no significant difference between the cases with or without seroprotection, with regard to sex, possible route of HIV acquisition, CD4 count, receiving ART, duration of their ART and HCV infection.

DISCUSSION

The present study investigated the immune responses to standard HBV vaccination in HIV-infected patients and its relation to different variables. We found a response rate of 56.6% in HIV-infected patients. Our survey showed a lower rate of HBV seroprotection after standard HBV vaccination in case of infected people with HIV, compared to the general population, regardless of their age, sex, possible route of HIV acquisition, CD4 count, receiving ART (and its duration) and HCV infection. Approximately 90-97% of healthy adults will show protective anti-HBs titers after vaccination with recombinant HBV vaccine [11, 12]. It is recommended that all HIV positive adults be screened for prior HBV infection. Any person who is, HBsAg, anti-HBs and anti-HBc negative should receive the three-dose HBV vaccination series, regardless of his/her CD4 count or HIV viral load [20, 21]. Prior studies of the immune responses to HBV vaccine in HIV infected patients have indicated varying response rates from 0% to 87%. [15, 16, 18, 19, 22-25].

Cornejo-Juárez *et al*. [26] found 60.7% response rate in HIV-infected patients vaccinated with HBV recombinant vaccine. In Bailey *et al*. study [27], the response rate to HBV vaccination was 47%. Higher CD4 counts and lower HIV viral loads were significantly associated with seroconversion. In another investigation by Paitoonpong *et al*. [28], the overall response rate to HBV vaccination was 71.4%. The responder group had a significantly higher CD4 counts than the non-responder group. In a survey in Iran on 48 HIV-positive patients, 29.1% of the vaccinated HIV-infected patients had positive anti-HBs titers [29]. In another study performed in Kermanshah, Iran, HBV immune responses were detected in 52.7% of the cases [30]. Studies comparing seroprotection rate of standard hepatitis B vaccination in HIV-positive patients were shown in Table 1. The association of HBV seroprotection rates and CD4 counts is controversial. Some studies have shown higher response rates associated with higher CD4 counts while others have obtained contrary data [15, 16, 18, 19, 22-25]. Our study showed that CD4 counts had no influence on the immune response to HBV vaccination and accords with Wilson [16] and Overton [22] studies.

Table. 1. Studies comparing seroprotection rates of standard Hepatitis B vaccination in HIV-positive patients.

Publications	Seroprotection Rates
Collier *et al*. (1988) [24]	CD4 >500 : 87.5% CD4 <500: 33.2%
Hess *et al*. (1989) [23]	0%
Rey *et al*. (2000) [15]	CD4 >500: 87.5% CD4 200-500: 33.3%
Wilson *et al*. (2001) [22]	37.1%
Alaei *et al*.(2003) [29]	29.1%
Tedaldi *et al*. (2004) [19]	37.2%
Gandhi *et al*. (2005) [18]	62.3%
Overton *et al*. (2005) [16]	17.5%
Fonseca *et al*.(2005) [13]	34%
Cornejo-Juárez *et al*. (2006) [26]	60.7%
Janbakhsh *et al*. (2006) [30]	52.7%
Veiga *et al*. (2006) [31]	59%
Ungulkraiwit *et al*. (2007) [32]	46%
Bailey *et al*.(2008) [27]	47%
Paitoonpong *et al*.(2008) [28]	71.4%
Landrum *et al*. (2009) [33]	35%
Psevdos *et al*. (2010) [34]	34.7%
Launay *et al*.(2011) [35]	65%
Kaech *et al*. (2012) [36]	22%

In this study, there was no significant difference in response rates to HBV vaccination in cases with or without HCV co-infection, as shown in other studies [30, 36]. However, few studies have indicated that HCV infection can reduce the responsiveness to HBV vaccination [18]. These discrepancies may be due to the different rates of HCV co-infection in the studied subjects. The lack of association between age or gender and HBV vaccine responsiveness was not unexpected which was in accordance with some previous studies [30, 37]. The association between the HBV vaccine response rates and antiretroviral therapy and its duration has been shown in some

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studies [2, 30]; however, other investigations have failed to establish a link between these variables and HBV vaccine seroprotection [32, 38]. We also could not find the influence of antiretroviral therapy and its duration on the immune response rate to HBV vaccine. A major limitation of our study was the relatively small sample sizes which might have led to the non-significant results of the variables. In conclusion, our study confirms the previous reports that had indicated HIV-infected patients have a lower response rate to the standard HBV vaccination, compared to the general population. So, other strategies such as increasing the number of HBV immunizations, higher vaccine doses or use of different vaccination routes need to improve the HBV vaccine response rate in HIV cases.

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CONFLICT OF INTEREST:

All of the authors have declared that no competing interests exist.

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