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Vaccination coverage and immunity against hepatitis B among HIV-infected patients in South Brazil

Saulo Martins[a,b], *Andréa do Livramento*[a], *Michelle Andrigueti*[b], *Iara Fabricia Kretzer*[a], *Marcos José Machado*[c], *Celso Spada*[c], *Arício Treitinger*[c,*]

[a] *Health Sciences Center, Federal University of Santa Catarina, University Campus, Florianópolis, SC, Brazil*
[b] *Professor Polydoro Ernani de São Thiago University Hospital, Federal University of Santa Catarina, University Campus, Florianópolis, SC, Brazil*
[c] *Department of Clinical Analysis, Health Sciences Center, Federal University of Santa Catarina, University Campus, Florianópolis, SC, Brazil*

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ABSTRACT

Evidence-based strategies to improve the hepatitis B virus (HBV) vaccination coverage rates might help to reduce the burden caused by co-infection with HBV and human immunodeficiency virus (HIV). In this study, the aim was to evaluate the vaccination coverage and immunity against HBV among HIV-infected individuals in South Brazil, and identify factors that are associated with compliance patterns and antibody reactivity. Three hundred HIV-infected men and women were included in this survey. The patients answered a standardized questionnaire, and vaccination cards were checked in order to assess hepatitis B vaccine status. A blood sample was collected for quantitative determination of antibody to hepatitis B virus surface antigen (anti-HBs). Participants were also evaluated for their CD4 cell count and HIV viral load. The overall vaccination coverage of HBV vaccination found in this study (57.4%) was lower than that was previously reported in South Brazil. Anti-HBs levels >10 IU/L were observed in 47.0% of the studied population. A significant inequality in the coverage rates and antibody reactivity was found in favor of patients with better economic status. In conclusion, the results indicate the need for improvement in the HBV vaccination coverage among HIV carriers, in particular focusing on low-income individuals.

Introduction

Infection with hepatitis B virus (HBV) still constitutes a major public health problem in many countries. More than two billion people have been infected with HBV worldwide, resulting in 240 million chronic carriers. It is estimated that about 780,000 people die annually from complications related to hepatitis B.[1] Infection with human immunodeficiency virus (HIV) is also a serious global health problem. About 75 million

* *Corresponding author at*: Department of Clinical Analysis, Health Sciences Center, Federal University of Santa Catarina, University Campus, Florianópolis, Santa Catarina 88040-900, Brazil.
E-mail address: aricio.treitinger@ufsc.br (A. Treitinger).
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people have been infected with HIV, with 36 million deaths among individuals with acquired immune deficiency syndrome (AIDS). Globally, there are approximately 35.3 million carriers of HIV.[2]

Co-infection with HBV and HIV is common.[3–5] Both viruses share the same risk factors for infection and can be transmitted through parenteral, sexual, and vertical routes.[6] In fact, it is estimated that 10% of HIV carriers in the world have chronic hepatitis B.[4] The progression of hepatitis B-associated liver disease is particularly modified by HIV co-infection. In HBV/HIV co-infected individuals, the development of chronic hepatitis B is accelerated, with higher risk of cirrhosis and hepatocellular carcinoma development, and increased morbidity and mortality rates.[7–9] Thus, hepatitis B vaccination in the United States of America is recommended by the Advisory Committee on Immunization Practices (ACIP) for all HIV-infected individuals,[10] as a strategy to reduce the public health burden caused by co-infection with these two viruses.

Several studies have shown an impaired antibody response to the standard three doses of 20 μg HBV vaccine of HBV immunization in HIV-infected patients.[11–13] However, a significant higher seroconversion rate was associated with the administration of double dose of the classic 0, 1 and 6-month schedule hepatitis B vaccination among patients with CD4 cell counts ≥350 cells/mm^3 and HIV viral load <10,000 copies/mL.[13] A significant increase in the seroconversion rate was also demonstrated in HIV-1 patients using a rapid vaccination schedule of 40 μg HBV vaccine at weeks 0, 4, 8 and 24.[14] Furthermore, increased compliance with HBV vaccination was verified among HIV-infected patients who received the accelerated schedule.[15]

In addition to differences in compliance patterns and antibody responses found with the use of different schedules and antigen concentrations, individual factors are also associated with the success of HBV immunization among HIV carriers.[16] In this study, the aim was to evaluate the vaccination coverage and immunity against HBV among HIV-infected patients in South Brazil, as well as to identify factors that are associated with vaccination compliance and antibody reactivity in the studied population.

Methods

Patients

This cross-sectional study was conducted at Professor Polydoro Ernani de São Thiago University Hospital located in Santa Catarina, South Brazil, between October 2012 and March 2013. The sample consisted of HIV-infected men and women receiving free antiretroviral therapy and laboratory monitoring. Universal antiretroviral drugs distribution program was introduced in Brazil in 1996 aiming to ensure free access to essential regimens, including protease inhibitors, for all people living with HIV. In addition, the Brazilian Ministry of Health has established the National CD4+/CD8+ T Lymphocyte Count and Viral Load Laboratory Network to monitor patient therapeutic response.[17]

This study was approved by the Ethics Committee of the Federal University of Santa Catarina (Protocol 94.398). Informed written consent was obtained from all participants after having received written information.

All the patients in this study were evaluated for their HIV viral load and CD4 cell count. Patients were stratified according to viral load into three groups (<50 copies/mL, 50–10,000 copies/mL and >10,000 copies/mL) and according to their CD4 cell count into two groups (<500 cells/μL and ≥500 cells/μL). The cut-off of 500 cells/mm^3 for the CD4 count was taken according to the Brazilian Therapeutic Guidelines for Clinical Management of HIV Infection in Adults.[18]

The patients answered a self-administered questionnaire, which comprised the following modules: socio-demographic characteristics (including sex, age, ethnicity, and socioeconomic status), transmission route of HIV infection, time since HIV infection diagnosis, and time since initiation of antiretroviral therapy. The surrogate variables for socioeconomic inequalities were monthly income and highest level of education in the household.

The study was conducted in order to determine the vaccination coverage based on the evaluation of vaccination cards and to investigate the association of anti-HBs titers with different socio-demographic aspects. The study sample was divided into three groups (vaccinated, unvaccinated, and possibly unvaccinated) to estimate the effect of the analyzed variables on compliance with vaccination schedules.

Patients who had received the hepatitis B vaccine in the classic three-dose or four double-dose schedules were included in the vaccinated group. Patients vaccinated before the HIV diagnosis received the classic three doses of HBV vaccine. However, it is not possible to know if those patients who had received the three-dose schedule (normal regimen) were HIV-infected at the time of vaccination. On the other hand, patients vaccinated after HIV diagnosis received the four double-dose schedule vaccine.

Patients with no vaccination records who had anti-HBs levels higher than 10.0 IU/L and tested negative for HBsAg and/or antibody to hepatitis B core (anti-HBc) serological markers were classified as vaccinated. Those with no vaccination records who tested positive only for anti-HBc were included in the unvaccinated group.

Subjects were also tested for their immune status against HBV, and were classified according to anti-HBs levels: ≤2.0 IU/L, 2.1–10.0 IU/L, and >10.0 IU/L.

Assessments

A blood sample was collected from each subject for the determination of anti-HBs concentration. After serum separation, anti-HBs antibodies were detected by Chemiluminescence Microparticle Imunoassay (CMIA) using a commercial kit (ARCHITECT®, Abbott Diagnostics, Sligo, Ireland), according to the manufacturer's instructions. CD4 cell count was determined with BD FACSCalibur flow cytometer (Biosciences, San Jose, CA, USA) in units of cells/μL. Plasma HIV RNA was quantified with a branched DNA technique [VERSANT HIV-1 RNA 3.0 (bDNA), Siemens Tarrytown, New York, USA].

Statistical analysis

Pearson's chi-square test was carried out to examine the association between categorical variables, and a value of $p < 0.05$