Impact of a Nurse Vaccination Program on Hepatitis B Immunity in a Swiss HIV Clinic

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Abstract: We evaluated the impact of a nurse program for hepatitis B virus vaccination in a center from the Swiss HIV Cohort Study. Immunity (anti-HBs > 10 IU/mL) increased from 32% to 76% in the intervention center (n = 238) where vaccine management was endorsed by nurses, but only from 33% to 39% in control centers (n = 2712, P < 0.001) where management remained in charge of physicians. Immunity against HBV in the HIV population is insufficient in Switzerland. Specific nurse vaccination program may efficiently improve health care.

Key Words: Hepatitis B, HIV, nurse intervention, vaccination, vaccination coverage

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INTRODUCTION

Hepatitis B virus (HBV) can cause acute infection ranging from asymptomatic to fulminating hepatitis (<1%) depending on various host and viral factors. Chronic infection leading to cirrhosis and hepatocellular carcinoma occurs in a minority of patients. The incidence of acute HBV infection is higher in HIV-positive patients than in the general population (12.2 versus 0.33 cases/1000 person-years). Similarly, the prevalence of chronic HBV infection is higher in HIV-positive patients than in the general population (4%-10% versus <1%).

The most efficient way to prevent HBV infection is vaccination, which is recommended by the Centers for Disease Control and Prevention for every HIV-positive patient. HBV vaccine is safe and efficient. However, its immunogenicity is lower in HIV-positive patients (18%-61%) compared with immunocompetent subjects (90%-95%). Risk factors for nonresponse to vaccination include older age, alcohol abuse, high HIV RNA, low CD4 T-cell count, and absence of combination antiretroviral therapy. The number of vaccinated HIV-positive patients is largely insufficient in most countries, with 14%-62% of patients receiving at least 3 doses of vaccine.

Strategies to improve the rate of HBV vaccination among high-risk populations included mainly free vaccination programs delivered to sex workers, men having sex with men, intravenous drug users or homeless. To our knowledge, no studies have evaluated the efficacy of HBV vaccination programs in clinical practice among HIV-positive patients, population with a better follow-up than the population included in the aforementioned studies.

In 2006, an external audit in the Lausanne HIV center of the Swiss HIV Cohort Study (SHCS) showed that the medical files failed to report HBV vaccination coverage and immunity. We investigated the effectiveness of a nurse intervention program for systematic chart review and HBV vaccine management in our center.

METHODS

Patients recorded in the SHCS on January 1, 2007, were eligible for the study. The SHCS is an ongoing, continuous enrollment prospective observational cohort of HIV-infected patients followed at 7 medical centers in Switzerland. Patients have been enrolled since 1988 and signed written consent for data collection and blood sampling. Ethical approval for this research was obtained from the institutional review boards. P.Y.B. is supported by the Swiss National Science Foundation (32003B_127613 / 1), the Leenaards Foundation, and the Santos-Suarez Foundation. The authors N.B.B., A.P., M.C., and P.Y.B. contributed equally to this work. The authors have no conflicts of interest to disclose. Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal’s Web site (www.jaids.com).

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addition, nonimmune patients (anti-HBs <10 IU/L) and patients with unknown immunity were eligible for nurse vaccination program in the intervention center. Six other centers of the SHCS did not undergo any vaccine intervention and were used as control. In all these centers, HBV vaccination was prescribed by the physician in charge of the patient. The nurse intervention consisted of (1) documenting HBV serostatus in all patients with previously missing information, (2) providing vaccination (3 doses with a minimal interval of 1 and 6 months) to all nonimmune patients, (3) measuring vaccination effectiveness 1–12 months after the third dose, and (4) providing a second course of vaccination (according to the physician in charge) to nonresponders (anti-HBs <10 IU/L). Clinical and demographic data were extracted from the SHCS database. Because vaccination history is not recorded in the SHCS database, it was obtained from medical records at the intervention center only.

HBV vaccine is available as a single-antigen formulation and in fixed combination. Two single-antigen formulations are available in Switzerland: Engerix-B (GlaxoSmithKline Biologicals, Rixensart, Belgium) and HBVAXPRO (Merck Research Laboratories, West Point, PA). One combination vaccine is available for adults: Twinrix (GlaxoSmithKline Biologicals, Rixensart, Belgium). Engerix and Twinrix formulations contain 20 μg and HBVAXPRO 10–40 μg/mL of HBsAg protein.

Group comparison was done using T test for continuous variable or χ² test for categorical variable. Statistical level for significance was assigned for P value lower than 0.05. Logistic regression was used for univariate and multivariate calculation of odds ratios. Variables with a significant P value on univariate analysis were used as covariate in the multivariate model. Statistical analyses were performed using Stata software (StataCorp, College Station, TX, version 11.1).

RESULTS
Among 6098 study patients, 3148 had a previous HBV infection (anti-HBc or HBs antigen positive). Among the 2950 uninfected patients, only 956 (32%) were immune against HBV, although 1782 (60%) were not immune and 212 (7%) had unknown immunity (Fig. 1). Lack of HBV immunity was associated with older age (P < 0.001) and low CD4 T-cell counts (P = 0.006; see Table, Supplemental Digital Content 1, http://links.lww.com/QAI/A225). Infection by homosexual contact or IV drug use demonstrated reduced odds for lack of immunity (P < 0.001 and P = 0.01, respectively) compared with infection by heterosexual contact. Furthermore, at baseline in January 2007, there was an important center effect (increased risk in centers 1, 3, 4, 5, 6 compared with center 0, all P < 0.001). In the intervention center, among the 124 nonimmune patients before the vaccination program, 58 (47%) were not vaccinated, 58 other (47%) were vaccine nonresponders after at least 3 vaccine doses, whereas the remaining 8 patients had an incomplete or undocumented vaccination.

During the study period, the number of immune patients increased from 76 (32%) to 180 (76%) in the intervention center, but only from 880 (33%) to 1057 (39%) in the control centers (ie, 137% increase versus 20% increase, P < 0.001). The number of patients with undocumented serostatus decreased from 38 (16%) to 0 (0%) in the intervention center, but only from 174 (6%) to 131 (5%) in the control centers (ie, 100% versus 25% decrease, P < 0.001, Fig. 1).

Two patients (0.8%) in the intervention center and 19 (0.7%) in the control centers (P = 0.9) developed new HBV infections, all of which resolved spontaneously. In the intervention center, 1 of the 2 infections occurred at the beginning of 2007 (ie, before vaccination was proposed) and the other occurred in a vaccine nonresponder. We do not have details on the vaccination history of the 9 patients followed up in the control centers. After the vaccination program, 56 patients remained not immune in the intervention center. The reasons for persisting lack of immunity after the intervention were vaccine nonresponse (36 patients, 64%) and vaccine refusal (11 patients, 20%). Nine patients (16%) were in the course of vaccination at the time of analysis. No factor was significantly associated with nonresponse to vaccination in the intervention center, but the number of vaccine responders (n = 60) and nonresponders (n = 54) were small. However patients with HCV coinfection and absence of combination antiretroviral therapy had a worse vaccine response (both P = 0.08) (see Table, Supplemental Digital Content 2, http://links.lww.com/QAI/A226). The majority of patients (68%) received Engerix vaccine...
formulation. The use of a specific type of vaccine did not influence vaccine response (see Table, Supplemental Digital Content 2, http://links.lww.com/QAI/A226).

**DISCUSSION**

Overall, this study shows that HBV immunity is insufficient in HIV-positive patients in Switzerland and can be significantly improved by a nurse vaccination program. It demonstrated that nonresponse to vaccination has only a minor impact on HBV immunity among HIV-positive patients.

Previously, intervention studies to improve the rate of HBV vaccination consisted mainly of free vaccine delivery to high-risk populations. We identified only 3 studies in which the rate of vaccine coverage was reported before and after such an intervention. In a study conducted in different medicalized or nonmedicalized locations, such as sexually transmitted disease clinics, sites of methadone outlet, gay bars, homeless shelter, brothels or zones of street prostitution, free immunization compared with simple flyers distribution improved full vaccine coverage from 4% to 13%. In another study performed in an urban sexually transmitted disease clinic, proposing an HBV fact sheet with free immunization compared with no specific intervention resulted in an improvement of full-vaccine coverage from 54% to 68%. A nurse-managed program consisting of informative sessions plus targeted hepatitis education and tracking among homeless population versus standard targeted hepatitis education resulted in an improvement of full vaccine coverage from 54% to 68%. Overall, previous interventions yielded only a modest improvement in HBV coverage compared with the marked improvement observed in our HIV clinic, where all patient charts were systematically reviewed.

Factors associated with lack of immunity in our study were older age and low CD4 T-cell count, which is concordant with previous studies (reviewed in 3). Infection through homosexual contact and intravenous drug use demonstrated reduced odds for lack of immunity, which is in opposition to other studies that observed lower seroconversion rates in homosexual compared to heterosexual patients. The discordance with our results could be related the difference in vaccination rate rather than the availability to respond to vaccine. Indeed, these data suggest that homosexual and intravenous drug users have a higher vaccine coverage. We also found a strong center effect, which is concordant with another study. The physicians are responsible for vaccination in every SHCS center, but the local habits and individual management may differ.

Overall, this study highlights the weak immunity against HBV among HIV-positive individuals in Switzerland and the significant impact of nurse intervention to improve the rate of immunization in this population.

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**REFERENCES**