RESEARCH NOTE

COMPLIANCE WITH HEPATITIS B AND HEPATITIS C VIRUS INFECTION SCREENING AMONG HIV-1 INFECTED PATIENTS IN A RESOURCE-LIMITED SETTING

Somnuek Sungkanuparph[1], Pawinee Wongprasit[1], Weerawat Manosuthi[1,3]
and Kalayanee Atamasirikul[2]

[1]Department of Medicine, [2]Department of Pathology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok; [3]Bamrasnaradura Infectious Diseases Institute, Ministry of Public Health, Nonthaburi, Thailand

Abstract. Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are important risk factors for mortality among HIV-infected patients. We assessed compliance with screening for HBV and HCV infection prior to initiation of ART in a resource-limited setting. Six hundred thirty-eight patients with a mean age of 38.4 years (53% males) were studied. Prior to initiation of antiretroviral therapy (ART) 371 patients (58%) were screened for HBV and 273 (43%) were screened for HCV infection. Of those screened, 9.7% had HBV infection and 8.8% had HCV infection. Given the relatively high prevalence of HBV and HCV infection among HIV-infected patients, screening for HBV and HCV infections prior to ART initiation should not be omitted in the resource-limited setting.

INTRODUCTION

The accessibility of combined antiretroviral therapy (ART) has been associated with dramatic declines in the morbidity and mortality from opportunistic infections in many countries including those in resource-limited settings (Weidle *et al*, 2002; Manosuthi *et al*, 2006; Jongwutiwes *et al*, 2007). Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections have become major risk factors for mortality in patients receiving ART (Ockenga *et al*, 1997; Bonacini *et al*, 2004). Coinfection with HBV and HIV-1 or HCV and HIV-1 are common because these viruses have the same routes of transmission. In western Europe and the United States, chronic HBV infection has been found in 7-10% of HIV-1 infected patients (Puoti *et al*, 2000; Levy and Grant, 2006) whereas the prevalence of this co-infection is higher in the Asia Pacific region (Chung *et al*, 1989; Sungkanuparph *et al*, 2004; Zhou *et al*, 2007). HCV infection among HIV-1 infected patients has been observed worldwide in 9% to 60%, with a significantly higher prevalence among intravenous drug users (Sungkanuparph *et al*, 2004; Alter 2006; Roy *et al*, 2007; Zhou *et al*, 2007). Although screening for HBV and HCV infection in HIV-1 infected patients is recommended in many HIV-1 treatment guidelines (Gazzard *et al*, 2006; Rockstroh *et al*, 2008; US DHHS, 2008), this screening has not been performed regularly in resource-limited settings. Therefore, the aim of our study was to assess the compliance of laboratory screening for HBV and HCV

Correspondence: Dr Somnuek Sungkanuparph, Division of Infectious Diseases, Department of Medicine, Ramathibodi Hospital, 270 Rama VI Road, Bangkok, 10400, Thailand.
Tel: +66 (0) 2201-1581; Fax: +66 (0) 2201-2232
E-mail: rasuy@mahidol.ac.th

infection prior to initiation of ART in a resource-limited setting.

MATERIALS AND METHODS

This observational study was conducted by including HIV-1 infected patients who initiated ART at a tertiary-care HIV clinic in Bangkok, Thailand, between January 2004 and October 2007. Inclusion criteria were as follows: (1) HIV-1 infected patients >15 years of age, (2) who were naïve to antiretroviral agents prior to the study period, and (3) initiated ART during the study period. Patients were excluded if they were participants of clinical trials. The medical records were reviewed for: demographic data, baseline CD4 count, HIV-1 RNA, ART regimen, and date and test results of hepatitis B surface antigen (HBsAg, Architect i2000 SR, ELISA, Abbott Laboratories, IL) and anti-HCV antibody (Architect i2000 SR, ELISA, Abbott Laboratories, IL). Patients were categorized into two groups on the basis of their screeening for HBV and HCV infection. A Student's t-test and the Mann-Whitney U test were used to compare the mean and median values of continuous variables between the two groups. The Fisher's exact test was used to compare categorical variables. Logistic regression analysis was used to determine the factors associated with screening for HBV and HCV infection. Statistical calculations were performed using SPSS program version 13.0 (SPSS Inc, Chicago, IL). A two-sided p-value of less than 0.05 was considered statistically significant. The study was approved by the institutional review board.

RESULTS

A total of 638 patients were included into this study. The mean (SD) age of the patients was 38.4 (8.4) years, 53% were males. Five hundred twenty-seven (83%) patients acquired HIV infection from heterosexual contact; 13 (2%) patients had a history of intravenous drug use. The risks for HIV infection in the others are unknown. The median (IQR) baseline CD4 cell count and HIV-1 RNA were 246 (77-459) cells/mm^3 and 143,000 (45,825-445,000) copies/ml, respectively. Prior to initiation of ART, HBV infection was screened for 371 (58%) patients. There were no differences in demographics or characteristics between patients who had been screened for and those who had not been screened for HBV infection prior to initiation of ART (p > 0.05). Logistic regression analysis revealed no factors associated with screening for HBV infection. Of the 371 patients screened for HBV infection, 36 (9.7%) had HBV infection.

Two hundred seventy-three of 638 patients (43%) had been screened for HCV. On univariate analysis, patients who had been screened for HCV infection were more likely to be males (p=0.016), younger (p=0.043) and have prior screening for HBV infection (p<0.001). On logistic regression analysis, only male gender [odds ratio (OR) 1.7; 95% confidence interval (CI) 1.1-2.5; p=0.014] and prior screening for HBV infection (OR 35.8; 95% CI 20.5-62.4; p<0.001) were significant factors associated with screening for HCV infection. Of the 273 patients who were screened, HCV infection was found in 24 (8.8%). Infection with both HBV and HCV was observed in one patient (0.4%).

On initiation of ART, 542 of 638 patients (85%) received non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimens. There were no differences in ART regimens between patients who were screened for and those who were not screened for HBV and HCV infection (p>0.05).

DISCUSSION

The results of the present study demonstrate that about half of HIV-1 infected patients who were on ART had never been checked for HBV or HCV infections. Screening for HBV

infection was not associated with any factors, including age, gender, risk of HIV-1 infection, CD4 cell count, HIV-1 RNA level, ART regimen, or use of lamivudine in the regimen. HCV infection was more likely to be screened for in males and patients with previous HBV screening; some patients with risk for intravenous drug use had never been tested. This reiterates the need for intervention to improve the compliance with screening for HBV and HCV infection.

A previous study in Thailand reported prevalences of HBV and HCV infection in HIV-1 infected Thai patients as 8.7% and 7.8%, respectively (Sungkanuparph *et al*, 2004). This prevalence is relatively high but may not convince health care providers to routinely screen for coinfection. Many factors may explain this lack of screening for HBV and HCV infections. First, the impact of HBV and HCV infection in HIV-1 infected patients may not be well recognized. ART in Thailand became widely accessible after the year 2002 (Cohen, 2003) and the long-term effects of HBV and HCV infections, such as cirrhosis and hepatocellular carcinoma, have not been seen yet. Second, the options for the first-line ART are very limited in this resource-limited setting. The majority of patients rely on a regimen of a generic fixed-dose combination of stavudine, lamivudine, and nevirapine (Tin *et al*, 2005; Manosuthi *et al*, 2007). Tenofovir was not available in Thailand until December 2006. Thus, health care providers may not see the benefit of screening in choosing an ART regimen. Third, the limited resources for HIV care in a resource-limited setting may prohibit health care providers from screening for HBV and HCV infections. All these problems need to be solved before screening for HBV and HCV infections can be routinely performed among HIV-1 infected patients in resource-limited settings. Lastly, the lower rate of screening for HCV infection compared to HBV infection may be explained by the fact that treatment for HCV

infection is less affordable than treatment for HBV infection in resource-limited settings.

The prevalences of HBV and HCV infections among HIV-1 infected patients in this study were 9.7% and 8.8%, respectively. These prevalences were slightly higher than that of the year 2003 (Sungkanuparph *et al*, 2004). These findings emphasize the magnitude of these coinfections among HIV-1 infected Thai patients. It may be necessary to integrate HIV and HBV/HCV care into the national AIDS program and commence interventions such as education of health care providers, provide for laboratory screening for HBV and HCV infection, and establish treatment guidlines for patients with HIV-1 and HBV or HCV coinfection in a resource-limited setting.

In conclusion, approximately half of HIV-1 infected patients were screened for HBV and HCV infection prior to initiation of ART in a resource-limited setting. Lack of screening for HBV infection prior to ART initiation was seen in HIV-infected patients, and screening for HCV infection was performed less frequently than HBV infection. Given the relatively high prevalence of HBV and HCV infections, screening for HBV and HCV prior to ART initiation should not be omitted in resource-limited settings.

REFERENCES

Alter MJ. Epidemiology of viral hepatitis and HIV co-infection. *J Hepatol* 2006; 44 (1 suppl): S6-9.

Bonacini M, Louie S, Bzowej N, Wohl AR. Survival in patients with HIV infection and viral hepatitis B or C: a cohort study. *AIDS* 2004; 18: 2039-45.

Cohen J. Thailand's do-it-yourself therapy. *Science* 2003;301:1662.

Chung DC, Ko YC, Chen CJ, Chen ER, Wu CC, Wu PS. Seroepidemiology of hepatitis B virus, hepatitis D virus, and human immunodeficiency virus infections among parenteral drug abusers in southern Taiwan. *J Med Virol* 1989; 28: 215-8.

Gazzard B, Bernard AJ, Boffito M, *et al*. British HIV Association (BHIVA) guidelines for the treatment of HIV-infected adults with antiretroviral therapy (2006). *HIV Med* 2006; 7: 487-503.

Jongwutiwes U, Kiertiburanakul S, Sungkanuparph S. Impact of antiretroviral therapy on the relapse of cryptococcosis and survival of HIV-infected patients with cryptococcal infection. *Curr HIV Res* 2007; 5: 355-60.

Levy V, Grant RM. Antiretroviral therapy for hepatitis B virus–HIV-coinfected patients: promises and pitfalls. *Clin Infect Dis* 2006; 43: 904-10.

Manosuthi W, Chottanapand S, Thongyen S, Chaovavanich A, Sungkanuparph S. Survival rate and risk factors of mortality among HIV/tuberculosis-coinfected patients with and without antiretroviral therapy. *J Acquir Immune Defic Syndr* 2006; 43: 42-6.

Manosuthi W, Kiertiburanakul S, Chaovavanich A, Sungkanuparph S. Plasma nevirapine levels and 24-week efficacy of a fixed-dose combination of stavudine, lamivudine and nevirapine (GPO-VIR) among Thai HIV-infected patients. *J Med Assoc Thai* 2007; 90: 244-50.

Ockenga J, Tillmann HL, Trautwein C, Stoll M, Manns MP, Schmidt RE. Hepatitis B and C in HIV-infected patients: prevalence and prognostic value. *J Hepatol* 1997; 27: 18-24.

Puoti M, Spinetti A, Ghezzi A, *et al*. Mortality for liver disease in patients with HIV infection: a cohort study. *J Acquir Immune Defic Syndr* 2000; 24: 211-7.

Rockstroh JK, Bhagani S, Benhamou Y, *et al*. European AIDS Clinical Society (EACS) guidelines for the clinical management and treatment of chronic hepatitis B and C coinfection in HIV-infected adults. *HIV Med* 2008; 9: 82-8.

Roy E, Alary M, Morissette C, *et al*. High hepatitis C virus prevalence and incidence among Canadian intravenous drug users. *Int J STD AIDS* 2007; 18: 23-7.

Sungkanuparph S, Vibhagool A, Manosuthi W, *et al*. Prevalence of hepatitis B and hepatitis C virus co-infection with human immunodeficiency virus in Thai patients: a tertiary-care-based study. *J Med Assoc Thai* 2004; 87: 1349-54.

Tin EE, Bowonwatanuwong C, Desakorn V, Wilairatana P, Krudsood S, Pitisuttithum P. The efficacy and adverse effects of GPO-VIR (stavudine+lamivudine+nevirapine) in treatment-naïve adult HIV patients. *Southeast Asian J Trop Med Public Health* 2005; 36: 362-9.

US Department of Health and Human Services (USDHHS) Panel on Antiretroviral Guidelines for Adults and Adolescents - A Working Group of the Office of AIDS Research Advisory Council (OARAC). Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. [Cited 2008 Jan 29]. Available from: URL: http://AIDSinfo.nih.gov

Weidle PJ, Malamba S, Mwebaze R, *et al*. Assessment of a pilot antiretroviral drug therapy programme in Uganda: patients' response, survival, and drug resistance. *Lancet* 2002; 360: 34-40.

Zhou J, Dore GJ, Zhang F, Lim PL, Chen YM. TREAT Asia HIV Observational Database. Hepatitis B and C virus coinfection in The TREAT Asia HIV Observational Database. *J Gastroenterol Hepatol* 2007; 22: 1510-8.