Prevalence of Occult Hepatitis B Virus Infection in Hemodialysis Patients

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Background/Aims: The prevalence of occult HBV infection depends on the prevalence of HBV infection in the general population. Hemodialysis patients are at increased risk for HBV infection. The aim of this study was to determine the prevalence of occult HBV infection in hemodialysis patients.

Methods: Total of 98 patients undergoing hemodialysis in CHA Bundang Medical Center (Seongnam, Korea) were included. Liver function tests and analysis of HBsAg, anti-HBs, anti-HBc and anti-HCV were performed. HBV DNA testing was conducted by using two specific quantitative methods.

Results: HBsAg was detected in 4 of 98 patients (4.1%), and they were excluded. Among 94 patients with HBsAg negative and anti-HCV negative, one (1.1%) patient with the TaqMan PCR test and 3 (3.2%) patients with the COBAS Amplicor HBV test were positive for HBV DNA. One patient was positive in both methods. Two patients were positive for both anti-HBs and anti-HBc and one patient was negative for both anti-HBs and anti-HBc.

Conclusions: The present study showed the prevalence of occult HBV infection in HBsAg negative and anti-HCV negative patients on hemodialysis at our center was 3.2%. Because there is possibility of HBV transmission in HBsAg negative patients on hemodialysis, more attention should be given to prevent HBV transmission. (Korean J Gastroenterol 2013;61:209-214)

Key Words: Hepatitis B virus; DNA; Hepatitis B surface antigens; Hemodialysis

INTRODUCTION

Chronic HBV infection is characterized by persistent detection of HBsAg and HBV DNA for 6 or more months after acute infection. It is known that the clearance of HBsAg in patients with HBV infection is associated with the disappearance of HBV DNA and active viral replication. However, several studies revealed that low levels of HBV DNA still remain detectable in the serum or liver tissue of some patients whose HBsAg disappeared spontaneously or by successful anti-viral treatment. The presence of HBV DNA in the liver tissue (with detectable or undetectable HBV DNA in the serum) of HBsAg negative individuals is defined as occult HBV infection.

Although the mechanism and clinical implications of occult HBV infection have not identified clearly, occult HBV infection has the risk of disease transmission through transfusion, hemodialysis, and organ transplantation. Occult HBV infection may contribute to the development and acute exacerbation of HBV associated diseases such as cryptogenic...
liver disease, fulminant hepatitis, liver cirrhosis (LC), and hepatocellular carcinoma (HCC). It may also affect disease progression and treatment response of chronic HCV infection.\(^3\)\(^5\)

The prevalence of occult HBV infection is related to the overall prevalence of HBV infection in the general population.\(^6\) South Korea is still an endemic area for HBV infection and chronic renal failure (CRF) patients on hemodialysis are at risk for HBV infection. The prevalence of occult HBV infection in HBsAg negative patients on hemodialysis ranges between 0% and 58% in published reports.\(^7\)\(^-\)\(^12\) There has been limited data about the prevalence of occult HBV infection among CRF patients in South Korea. The aim of this study was to investigate the prevalence of occult HBV infection in patients receiving hemodialysis at a single center in South Korea.

**MATERIALS AND METHODS**

1. Patients

Among CRF patients undergoing hemodialysis in CHA Bundang Medical Center (Seongnam, Korea) between May and June 2007, a total of 98 patients were included in the study. Four patients were HBsAg positive and they were excluded. Patients with history of other liver disease including LC, HCC, autoimmune hepatitis, or alcoholic hepatitis, history of alcohol drinking over 20 g/day for recent 6 months, and other risk factors such as human immunodeficiency virus (HIV) and intravenous drug abuse were not included. All patients have no family history of HBV infection and they were anti-HCV negative. The study was approved by the Institutional Review Board at the CHA Bundang Medical Center of CHA University and informed consent was obtained from the subjects.

2. Blood samples

Blood samples were obtained from patients when they visited the hospital for hemodialysis and centrifuged at 2,500 rpm for 5 min. Separated serum samples were used serological tests and the rest of serum samples were stored at \(-70^\circ\text{C}\) for PCR assay. Blood was tested for complete blood count, AST, ALT, total bilirubin, and hepatitis B and C viral markers (HBsAg, anti-hepatitis B surface antigen [anti-HBs], anti-hepatitis B core antigen [anti-HBc] and anti-HCV antibody).

3. Detection of HBV DNA

HBV DNA testing was performed using two different PCR methods. COBAS Amplicor HBV monitor test (Roche Molecular Diagnostics, Basel, Switzerland) is widely used automated PCR assay for the quantitation of HBV DNA in serum. This test is based on the four major processes: specimen preparation, PCR amplification of target DNA with biotinylated primers, hybridization of the amplicon to oligonucleotide probes specific for the target, detection of the am- plicon-probe complex by colorimetric determination.\(^13\) The biotinylated HBV-104UB primer and the nonbiotinylated HBV-104D primer were used to define a sequence of 104 nucleotides within the highly conserved precore-core region of the HBV genome. TaqMan real-time PCR test was performed with an Applied Biosystems 7300 real-time PCR system (Applied Biosystems, Foster City, CA, USA). This is based on the 5'-3’ exonuclease activity of the Taq DNA polymerase, which results in cleavage of fluorescent dye-labeled probes during PCR. Two PCR primers (forward primer 5’-CTCCCG- GTCTGTGCTTCTCTAC-3’ [HBVRT1F; K=G or T]; reverse primer 5’-GGCGTTCAGGGTTCCATGC-3’ [HBVRT1R]) and TaqMan probe 5' FAM-CCGTGTGCACTTCGCTTCACCTCTGC- TAMRA 3’ (HBV1TAQ) were created against a region of the HBV genome overlapping the genes encoding the X-protein and DNA polymerase. Quantitation of HBV DNA by the COBAS Amplicor HBV monitor test and Taqman PCT test was performed according to the protocol previously described.\(^13\)\(^14\) Linear dynamic range of detection in the COBAS Amplicor HBV monitor test and TaqMan PCR test was found to be 300-2×10\(^5\) copies/mL and 120-1.2×10\(^{10}\) copies/mL, respectively.

4. Statistical analysis

IBM SPSS Statistics 19.0 (IBM Co., Armonk, NY, USA) was used for the statistical analysis. All data are expressed as means±standard deviation or median and range in continuous variables and percentage in categorized variables. Mann-Whitney test and Fisher’s exact test were used for comparing variables between HBV DNA positive patients and negative patients. All p-values less than 0.05 were considered statistically significant.