Kaohsiung Journal of Medical Sciences (2015) 31, 102–107

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.kjms-online.com

ORIGINAL ARTICLE

Changing serum levels of quantitative hepatitis B surface antigen and hepatitis B virus DNA in hepatitis B virus surface antigen carriers: A follow-up study of an elderly cohort

Yuan-Hung Kuo [a], Kuo-Ching Chang [a], Jing-Houng Wang [a], Pei-Shan Tsai [b], Shu-Feng Hung [a], Chao-Hung Hung [a], Sheng-Nan Lu [a,*]

[a] *Division of Hepato-Gastroenterology, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan*
[b] *Health Center of Zihguan Township, Kaohsiung, Taiwan*

Received 21 May 2014; accepted 29 August 2014
Available online 4 December 2014

KEYWORDS
Community screen;
Hepatitis B virus;
Hepatitis B virus surface antigen;
Viremia

Abstract This study was to elucidate longitudinally quantitative changes of hepatitis B virus (HBV) surface antigen (HBsAg) and HBV DNA in elder HBsAg carriers in a community. Among 1002 residents screened for HBsAg in 2005, 405 responded to this follow-up study in 2010. Fifty-nine (14.6%) were HBsAg carriers in 2005; HBsAg quantification and HBV DNA were measured. HBsAg quantification (cutoff 1600 IU/mL) and HBV DNA (cutoff 2000 IU/mL) were combined to stratify the participants between two screens. A total of 30 men and 29 women with a mean age of 63.9 ± 7.9 years were enrolled. Quantitative levels of HBsAg and HBV DNA were significantly correlated in 2005 ($r = 0.509$, $p < 0.001$) and 2010 ($r = 0.777$, $p < 0.001$). Concentrations of HBsAg (IU/mL) significantly decreased from 2.2 ± 1.0 log in 2005 to 1.7 ± 1.5 log in 2010 ($p < 0.001$). The level of HBsAg was decreased in 48 (81.4%) individuals and HBsAg was undetectable in eight (13.6%). The annual incidence of HBsAg clearance was 2.7%. These 59 HBsAg carriers in 2005 were divided into four groups: low HBsAg low HBV DNA ($n = 32$), high HBsAg low HBV DNA ($n = 5$), low HBsAg high HBV DNA ($n = 12$) and high HBsAg high HBV DNA ($n = 10$). All 32 individuals in the low HBsAg low HBV DNA group were still in that group in 2010, whereas only two of the high HBsAg high HBV DNA group became inactive. As with a younger cohort in hospital, HBsAg quantification was still well correlated with HBV DNA in elderly HBsAg

Conflicts of interest: All authors declare no conflicts of interest.

* Corresponding author. Division of Hepato-Gastroenterology, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, 123 Ta-Pei Rd, Niao-Sung, Kaohsiung County, Taiwan.
E-mail address: juten@ms17.hinet.net (S.-N. Lu).

http://dx.doi.org/10.1016/j.kjms.2014.11.002

carriers in the community. Lower levels of both HBsAg and HBV DNA might represent an inactive HBV infection.

Introduction

Chronic hepatitis B virus (HBV) infection affects 350—400 million people worldwide and is associated with 1 million mortalities every year [1]. The purpose of treatment for patients with chronic HBV infection is to decrease the progression of liver disease to cirrhosis and hepatocellular carcinoma in order to improve the rate of survival. Currently, anti-HBV therapies can include long-term treatment with nucleos(t)ide analogs to maintain constant inhibition of viral replication and a limited treatment period where interferon can be used to induce a sustained immune response [2,3]. Quantification of HBV DNA is widely used as the indicator of viral replication to assess the type of treatment that is appropriate [4—6]. However, the high expense of this assay has limited its utility clinically. The serum concentration of HBV surface antigen (HBsAg) is proposed to reflect the amount of covalently closed circular DNA (cccDNA) in the liver, where it acts as template for the transcription of viral genes [7]. Recently, several studies have reported that serum HBsAg levels may be a good indicator in predicting a patient's response to interferon-based therapy, and was shown to have good association with serum HBV DNA levels [8—11].

The nature history of chronic HBV infection has been well illustrated with four phases: immune tolerant phase, immune clearance phase, residual inactive phase, and reactive immune clearance phase [12]. Most studies were conducted with younger HBV carriers to evaluate the association of HBV infection and treatment. By contrast, older HBV carriers have been studied less, especially in hospitals. However, the association between virus infection and host might be varied in different aged cohorts [13].

In the past decade, some immunoassays have been developed to measure the HBsAg titer quantitatively [14,15]. In addition, these tests are inexpensive and the detection process is much more convenient. The HBsAg quantification test has been applied in chronic hepatitis B patients in the hospital to evaluate the severity of liver disease and clinical outcome [16—19]; however, the test has never been used for studying older HBV carriers in community screening. Therefore, we have conducted this follow-up community-based study to elucidate the longitudinally quantitative changes in HBsAg and HBV DNA levels in elder HBsAg carriers.

Materials and methods

Study participants

Tzukuan township is located in southern Taiwan with a total population of about 40,000, and has been reported to be an HBV-endemic area, with an estimated HBsAg-positive prevalence of 12.6% [20]. In 1997, 2909 residents (30.6% of the total population within the age group of 45 years and older), were screened for HBsAg [21]. In 2005, a follow-up study was conducted; however, only 1002 participants responded [22—24]. In 2010, a follow-up community screening was again performed with the cohort from 2005. Using invitation methods such as phone calls and mail, 405 (40.4%) residents were enrolled, 59 of whom were HBsAg carriers in 2005. Serum quantitative HBsAg level and HBV DNA levels were further measured and analyzed using the carriers' stored sera (collected both in 2005 and 2010). To distinguish active HBV infection from inactive reaction, cutoff values of 1600 IU/mL and 2000 IU/mL were set for HBsAg and HBV DNA, respectively [3,22]. These two cutoff points were also used as grouping indices. According to the data collected in 2005, the 59 HBsAg carriers were divided into four groups: low HBsAg low HBV DNA (LsLD group), high HBsAg low HBV DNA (HsLD), low HBsAg high HBV DNA (LsHD), and high HBsAg high HBV DNA (HsHD). This study was approved by the Institutional Review Board of Chang Gung Memorial Hospital, Kaohsiung, Taiwan.

Quantitative HBsAg assay

The quantification of HBsAg was performed with Architect qHBsAg (Abbott Diagnostic, Wiesbaden, Germany), following the manufacturer's instructions [25]. The sensitivity of the Architect assay was 0.05—250 IU/mL. Samples with HBsAg titer >250 IU/mL were diluted from 1:500 to 1:1000 to bring the reading within the range of the calibration curve.

HBV DNA assay

The levels of HBV DNA were quantified using the COBAS AmpliPrep-COBAS TaqMan HBV test (CAP-CTM; Roche Molecular Systems Inc., Branchburg, NJ, USA), with a lower detection limit of 12 IU/mL (70 copies/mL). Dilution was performed if the HBV DNA levels was $>10^6$ copies/L.

Statistical analysis

The continuous variables in this study were expressed as mean ± standard deviation. The paired *t* test was used to determine the significances of the continuous dependent variables. The Chi-square test was used to verify the differences between the categorical factors. Linear regression analysis was used to assess the linear associations between serum HBsAg and HBV DNA levels (HBsAg and HBsAg levels as well as HBV DNA and HBV DNA levels were analyzed in