The analysis of the correlations between HBsAg quantitation level, virological markers and histopathological findings in patients with chronic hepatitis B

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Abstract

In recent years, several studies suggested that HBsAg titers in blood samples obtained during Hepatitis B treatment could be used to estimate the treatment outcomes. The present study aims to discuss the correlation between HBsAg quantification levels and the virological, serological and histopathological findings in chronic hepatitis B patients.The study included chronic hepatitis B patients who underwent liver biopsy between 2011 and 2013 at Dicle University, Faculty of Medicine, Infectious Diseases and Clinical Microbiology Clinic.. The patient demographics were recorded (age, gender). Patient AST tests were conducted with the spectrophotometric method. After the DNAs were isolated with AmplipPrep Total Nucleic Acid Isolation Kit, DNA level was determined with the COBAS® Amplip / Cobas® Taqman® HBV test V2.0 for HBV. The patient HBV DNA levels were recorded as IU / ml. HBsAg quantitation was studied with the Access device and the Elisa method.The study was conducted with 53 patients. The mean patient age was 28,73 ± 8.15. Out of the 53 patients, 35 (66%) were male and 18 (34%) were female. The mean patient HBsAg quantitation was 631,42 ± 406.55, fibrosis score was 1,35 ± 0.87, ALT index score was 67,07 ± 53.37, and HAI index score was 4,54 ± 1.55. In the statistical analysis, it was determined that there were negative correlations between the HBsAg DNA level (R: -0,273, P: 0.048) and HBSAG quantitation (R: -0,273, P: 0.048), fibrosis score , ALT (R: -0,477, P: 0.001), and HAI index scores (R: -034, P: 0,013), while there was a positive correlation with the HBeAg positivity (R: 0.477, p: 0.001). There were negative correlations between the HBsAg quantitation level and virological (HBV DNA level), histopathological (fibrosis score, HAI index) findings and a positive correlation with serological (HBeAg positivity) findings. As HBsAg quantitation level increased, fibrosis score and HBV DNA level decreased.

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Background: Although quantitative HBsAg measurement was described 20 years ago, it has been only recently employed in routine due to the development in reliable quantitative ELISA methods. In recent years, several studies suggested that HBsAg titers in blood samples obtained during Hepatitis B treatment could be used to estimate the treatment outcomes. The present study aims to discuss the correlation between

HBsAg quantification levels and the virological, serological and histopathological findings in chronic hepatitis B patients.

Material and Method : The study included chronic hepatitis B patients who underwent liver biopsy between 2011 and 2013 at Dicle University, Faculty of Medicine, Infectious Diseases and Clinical Microbiology Clinic. The patient serums were obtained and stored at -80^{0}C. The patient demographics were recorded (age, gender). Patient AST tests were conducted with the spectrophotometric method. After the DNAs were isolated with AmplipPrep Total Nucleic Acid Isolation Kit, DNA level was determined with the COBAS® Amplip / Cobas® Taqman® HBV test V2.0 for HBV. The patient HBV DNA levels were recorded as IU / ml. HBsAg quantitation was studied with the Access device and the Elisa method.

Results : The study was conducted with 53 patients. The mean patient age was 28,73 ± 8.15. Out of the 53 patients, 35 (66%) were male and 18 (34%) were female. The mean patient HBsAg quantitation was 631,42 ± 406.55, fibrosis score was 1,35 ± 0.87, ALT index score was 67,07 ± 53.37, and HAI index score was 4,54 ± 1.55. In the statistical analysis, it was determined that there were negative correlations between the HBsAg DNA level (R: -0,273, P: 0.048) and HBSAG quantitation (R: -0,273, P: 0.048), fibrosis score (R: -0,618, p <0.001), ALT (R: -0,477, P: 0.001), and HAI index scores (R: -034, P: 0,013), while there was a positive correlation with the HBeAg positivity (R: 0.477, p: 0.001).

Conclusion : There were negative correlations between the HBsAg quantitation level and virological (HBV DNA level), histopathological (fibrosis score, HAI index) findings and a positive correlation with serological (HBeAg positivity) findings. As HBsAg quantitation level increased, fibrosis score and HBV DNA level decreased.

What is already known about this topic?

There is a lot of different information on this subject. Some studies found a relationship between HBsAg level and HBV DNA, while in others it was not. We evaluated the difference of our study with the fibrosis score. That's why this study is important.

What does this article add?

In addition, the number of studies on this subject is limited. Therefore, it increases the importance of our work.

Introduction

In the clinical prognosis in Chronic hepatitis B (KHB) patients, the follow-up of HBsAg, HBeAg seroconversion, HBV DNA and aminotransferase (lower) levels in the region guide the physicians (1). Early diagnosis of serious liver disease may improve the status of the disease even in patients who develop decompensation with treatment (2). However, noninvasive tests are insufficient to determine the liver disease to a certain level (3). Thus, new diagnostic methods are required to diagnose liver fibrosis in the early period. Among these methods, there is a rising interest in the clinizal determination of serum HBsAg quantification in recent years due to the standardization with automatic systems (4, 5). A correlation was reported between the HBsAg serum level and liver cccDNA (Covalently Closed Circular DNA) (6). As the understanding about the molecular virology of HBsAg has improved, it was suggested that serum HBsAg concentration reflected the cccDNA content, which serves as the transcription pattern for the integrated viral genes in liver hepatocytes. It was reported that the measurement of the HBsAg concentration could be a beneficial marker in addition to HBV DNA level and HBeAg in HBV patients under Peginterferon or Nucleotide analogue treatment (7, 8). Thus, it was argued that it allows the prediction of the viral replication levels of circulation HBsAg concentrations to determine disease activity and response to antiviral treatment (9). In recent studies, it was reported that serum HBsAg levels may be a good indicator in the evaluation of patient disease activity and response to interferon-based treatment in CHB, and there was a strong correlation between serum HBsAg and HBV DNA levels (10,11,12) In a study conducted by Tuaillon et al., it was observed that there was a weak correlation between HBSAG and HBV DNA levels (13).

The present study aimed to analyze the correlations between HBsAg level and virological properties in CHB patients.

Material and Method

The study was conducted on Dicle University Faculty of Medicine, Infectious Diseases and Clinical Microbiology Clinic Between 2011-2013. The patient serums were obtained and stored at -80^{0}C. The patient demographics were recorded (age, gender). Patient AST tests were conducted with the spectrophotometric method. After the DNAs were isolated with AmplipPrep Total Nucleic Acid Isolation Kit, DNA level was determined with the COBAS® Amplip / Cobas® Taqman® HBV test V2.0 for HBV. The patient HBV DNA levels were recorded as IU / ml. HBsAg quantitation was studied with the Access device and the Elisa method.

Findings

The study was conducted with 53 patients. The mean patient age was 28,73 ± 8.15. Out of the 53 patients, 35 (66%) were male and 18 (34%) were female. The mean patient HBsAg quantitation was 631,42 ± 406.55, fibrosis score was 1,35 ± 0.87, ALT index score was 67,07 ± 53.37, and HAI index score was 4,54 ± 1.55. In the statistical analysis, it was determined that there were negative correlations between the HBsAg DNA level (R: -0,273, P: 0.048) and HBSAG quantitation (R: -0,273, P: 0.048), fibrosis score (R: -0,618, p <0.001), ALT (R: -0,477, P: 0.001), and HAI index scores (R: -034, P: 0,013), while there was a positive correlation with the HBeAg positivity (R: 0.477, p: 0.001).

Discussion

The qualitative determination of HBsAg is employed in the diagnosis of HBV infection (14). Serum HBV DNA level is the most significant indicator of virus replication. In patients with CHB infection, it is an important indicator of disease activity and hepatocellular carcinoma risk. Quantitative HBsAg was shown as an important viral factor in the initiation of antiviral treatment and response to treatment (15). HBsAg levels were recently used to monitor the prognosis or treatment in CHB infection (16). However, molecular tests are more important in monitoring the HBV DNA positive patients with no identifiable HBsAg levels (14). In a previous study, it was observed that the HBsAg level was effective in the evaluation of different CHB phases. It was reported that it could help the differentiation of immune tolerance and immune scavenging in HBeAg positive patients. In HBeAg negative patients, it was reported that spontaneous serum HBsAg scavenging and inactive disease could be estimated (10). In the present study, it was determined that there was a statistically significant correlation between HBsAg and HBV DNA in CHB patients (10). In a study repeated on monitored CHB carriers after five years, it was reported that there was a statistically significant correlation between quantitative HBsAg and HBV DNA levels (7). The studies conducted in Turkey revealed that there was a correlation between HBsAg and HBV DNA levels (17-19). In one of these studies, it was shown that the HBsAg level could be used to differentiate inactive and active hepatitis B patients (19). In the present study, a negative correlation was determined between HBsAg and HBV DNA levels. As HBsAg level increased, HBV DNA level decreased. The change was statistically significant. In a study conducted with patients with high ALT levels, it was determined that HBV DNA and HBsAg levels were high as well (20). However, in inactive carriers, no correlation was determined in a study where the correlation between the HBsAg and HBV DNA levels was investigated, while there was a moderate correlation between HBsAg and HBV DNA levels in CHB patients. In the current study, only the HBsAg levels were investigated in CHB patients. Furthermore, it was determined that quantitative HBsAg levels in HBeAg positive patients were significantly higher when compared to the HBeAg negative patients in the present study (20). There was a significant positive correlation between HBeAg positivity and HBsAg level in our study as well. In another study, there was a significant and positive correlation between HBsAg and HBV DNA levels in the HBeAg positive CHB patient group (21). It was reported that the differences between HBsAg and HBV DNA levels were due to the mutations induced by the high spontaneous error rate transcriptase enzyme of the virus and viral variants that develop due to the selective pressure caused by the antiviral treatment and endogenous host immunity (22,23). No correlation was determined between the fibrosis score and the HBsAg level in a

study conducted with HBeAg negative patients (24). In our study, there was a negative correlation between the HBsAg level and the fibrosis score. As the HBsAg level increased, the fibrosis score decreased. There are certain studies where a stronger correlation was reported between HBsAg level and fibrosis stage in HBeAg positive and CHB patients (25, 26).

In conclusion, studies reported different results about the correlations between HBsAg level and virological markers and histopathological findings. Larger-scale studies are required to standardize these findings.

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