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Relationship Between Viral Load of HDV RNA and Serum Level of HBsAg in Patients with Chronic Hepatitis B with Delta Agent

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Abstract This article identifies the relationship of quantitative HBsAg with the viral load of HDV to monitor disease dynamics. Thirty patients with mixed HBV and HDV infection were examined. HDV RNA viral load was associated with serum HBsAg levels. The results of the study suggest that the level of HBsAg in the blood can be used to dynamically monitor the disease and assess the progression of the disease in patients with chronic hepatitis B + D with an undetectable DNA level. The viral load of HDV RNA is associated with serum HBsAg levels. Quantification of HBsAg in the blood can have important diagnostic and prognostic value.

Keywords Quantitative indicators of qHBsAg, Polymerase chain reaction, Chronic hepatitis B with delta agent, Viral load, Cirrhosis of the liver

1. Introduction

Hepatitis B virus (HBV) is a major public health problem. About 400 million people worldwide were chronically infected with HBV [1]. Some people infected with hepatitis B virus develop a chronic liver disease that can lead to liver cirrhosis (LC) or hepatocellular carcinoma (HCC) [2]. Hepatitis B serum surface antigen (HBsAg) is a reliable biomarker of viral hepatitis B. HBsAg can be detected in the patient's blood serum within one week after infection with hepatitis B. Therefore, HBsAg can serve as a serological marker for HBV infection [3]. Relevant studies have shown that serum HBV DNA loading positively correlates with HBsAg levels, and serum HBsAg can reflect the degree of viral activity, as well as virus replication and the degree of disease progression [4]. An innovation in the definition of HBV markers was development in the early 2000s. Abbott Laboratories (USA) standardized chemiluminescent test that measures the amount of HBsAg in international units. A little later, a similar test was developed by the Swiss company Roche Diagnostics [5]. Over the past few years, several studies have been published on the diagnostic value of determining levels of HBsAg in the blood - a simple and inexpensive technique, and therefore a number of works have appeared on the relationship between the level of HBV viremia and the concentration of HBsAg in the blood. It was initially shown that the quantitative serum HBsAg content is significantly higher in patients with HBeAg (+) HBV compared with anti-HBe-positive chronic carriers of HBV infection [5]. Differences in the content of HBsAg in acute and chronic HBV infection [6]. Part of the studies on the determination of HBsAg in the blood showed a positive correlation between the level of HBV viremia and the concentration of HBsAg [7,8]. However, a study by M.C. Kuhns et al. showed a weak correlation ($r = 0.33$) [9]. A recent association has been found between serum HBsAg concentrations and HBV DNA levels in patients with hepatitis B. Serum HBsAg concentrations have been linked to HBV. Other authors believe that it is not possible to use HBsAg concentrations to monitor HBV replication [10]. Study Results Zhu H.Y. and Zhang X.S. showed that serum HBsAg levels gradually increase with an increase in HBV DNA load in patients with HBV with statistical significance ($P<0.05$), which indicates that serum HBsAg levels are associated with HBV DNA load. Other authors came to the same conclusion, suggesting that serum levels of HBsAg might reflect viral activity [11]. Studies in various countries have shown a wide range of quantitative characteristics of HBsAg in patients with chronic HBV infection during natural development. At present, the role of quantitative determination of HBsAg in the prognosis of viral hepatitis B diseases with a delta agent has not been studied.

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In the present study, a correlation was made between the load of HBV DNA and serum HBsAg levels in an attempt to improve the diagnosis and prognosis of the disease.

Objective: To determine the association of quantitative HBsAg with the viral load of HDV for monitoring and prognosis of the disease.

2. Materials and Methods

Serum samples of 30 patients with mixed HBV and HDV infection were examined and taken at the Virology Research Institute of the Ministry of Health of the Republic of Uzbekistan, of which there were 15 patients with chronic hepatitis B + D, with an age range of 26 to 45 years (average age - 35.0 ± 1.5 years) with cirrhosis of the liver HDV etiology of 15 patients aged 28 to 60 years (mean age - 38.2 ± 1.8 years). There were 13 men (43.3%), 17 women (56.7%). All patients met the diagnostic criteria for chronic hepatitis and LC. In the present study, no patients received antiviral therapy.

An etiological diagnosis was made based on the results of an enzyme-linked immunosorbent assay (ELISA). The diagnostic kits DS Nizhny Novgorod were used as test systems to detect antibodies to viral hepatitis B, C, D in blood serum.

Quantitative determination of serum HBsAg was carried out by enzyme-linked immunosorbent assay using test systems "VECTOR-BEST" (Novosibirsk).

Molecular genetic studies included blood PCR to detect HBV DNA and AmpliSens HDV RNA AmpliSens HBV-FL and HDV-FL (Russia).

Statistical processing of the results was carried out by the method of V.I. Oyvina (1960) and V.G. Genes (1964). To assess the statistical significance of differences between comparable average values, the correctness or inaccuracy of the answer was determined by the Student criterion (t). The significance level of this response (P) was determined by the student distribution table (P-confidence coefficient). Differences were considered significant at $P < 0.05$. A correlation analysis of the relationship between the quantitative indicators of HBsAg and the level of HDV RNA was performed by the Pearson method.

3. Results of the Study

In this study, HDV and serum HBsAg RNA levels were determined in patients with chronic HBV + HDV infection to analyze the correlation between different HBV DNA scores, HDV viral load, and HBsAg levels.

The data obtained show that in chronic HBV+HDV infection with an undetectable level of HBV DNA in the blood, quantitative HBsAg values averaged 1.9 ± 0.56 IU / ml. With HBV DNA positive chronic viral hepatitis B with a delta agent, the quantitative indicators of HBsAg were 4.3 ± 0.62 IU / ml ($P < 0.05$).

No significant changes were found in the quantitative indicators of HBsAg with HBV DNA positive and HBV DNA with negative HDV LC ($P > 0.05$). These data clearly demonstrate that in chronic hepatitis B with a delta agent, quantitative serum HBsAg values were directly dependent on the level of HBV DNA and did not differ in patients with LC ($P > 0.05$).

In patients with chronic hepatitis B+D and cirrhosis of the liver, the indicators of quantitative determination of HBsAg were studied at different viral loads of HDV RNA. Indicators of RNA HDV were conventionally divided into low, medium and high. Low viral load included 10^2–10^3 copies of HDV RNA / ml, medium — 10^4–10^5 copies of HDV RNA / ml, high — 10^6–10^7 copies of HDV RNA / ml.

Table 1. Quantitative indicators of HBsAg with different viral load HDV RNA

HDV RNA (copies/ml)	HBsAg Level	
	Chronic hepatitis B with delta agent (n=15)	Cirrhosis of the liver HDV etiology (n=15)
Low	1,37	-
Average	2,79	2,54
High	3,68	3,30

From the data in table 1, it is seen that the quantitative indicators of HBsAg increased with increasing viral load. At low viral load, the amount of HBsAg was 1.37 IU / ml, medium - 2.79 IU / ml and high - 3.68 IU / ml. Thus, evaluating all of the above, it can be concluded that there is a relationship between the viral load of HDV RNA and the amount of serum HBsAg.

The correlation between the viral load and the level of serum HBsAg was determined. At low and medium levels of HDV RNA in patients with chronic hepatitis B+D, a direct average correlation was observed ($r = 0.59$, respectively, $r = 0.39$), with a high viral load of HDV RNA, an inverse correlation was observed ($r = -0.64$) viral load with quantitative indicators of HBsAg. In liver cirrhosis of HDV etiology, the average viral load indices had a direct weak correlation with serum HBsAg indices. At high viral load, an inverse weak correlation was observed.

4. Discussion

Hepatitis B DNA is the most commonly used marker of therapeutic efficacy when monitoring patients chronically infected with hepatitis B. Serum HBsAg levels in patients with HBV can significantly monitor HBV DNA [12,13]. The availability of commercial quantitative assays has rekindled interest in quantitative serum HBsAg as a biomarker for predicting [14] and treating HBV and has stratified the risk of disease progression by predicting treatment responses, mainly in patients receiving PEGIFN therapy [15]. However, objective indicators are still not available for dynamic disease monitoring of patients with undetectable levels of HBV DNA. Currently, the quantification of serum HBsAg

levels in patients with chronic hepatitis B has been widely reported [16]. In the present study, a correlation analysis was performed between HBV DNA loading and serum HBsAg levels in an attempt to improve the assessment of progression of HBV. The results of our study show that there is a relationship between the viral load of HDV RNA and quantitative indicators of HBsAg. To monitor the dynamics of the disease, you can use the level of serum HBsAg, instead of quantitative indicators of HBV DNA.

The results of our study show that there is a relationship between the viral load of HDV RNA and quantitative indicators of HBsAg. To monitor the dynamics of the disease, you can use the level of serum HBsAg, instead of quantitative indicators of HBV DNA. Quantification of HBsAg is much cheaper than the determination of DNA and RNA by PCR. A combination of HBV load assessment, process activity, and serum HBsAg levels can determine the state of infection.

5. Conclusions

Blood HBsAg levels can be used to dynamically monitor the disease and assess disease progression in patients with chronic hepatitis B+D with an undetectable DNA level.

The viral load of HDV RNA is associated with serum HBsAg levels.

Quantification of HBsAg in the blood can have important diagnostic and prognostic value.

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