



Comparison of Laboratory Values of Prisoner and Civil Patients with Chronic Hepatitis B

Mahkum ve Sivil Kronik Hepatit B'li Hastaların Laboratuvar Değerlerinin Karşılaştırılması

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ABSTRACT

Objective: Since immune processes play a role in the pathogenesis of HBV infection, the immune system of the host is an important factor in the healing of the infection. The aim of the present study is to compare the laboratory findings related to hepatitis B in inmates with chronic hepatitis B, who live in a confined space and whose immune system is affected by various stress factors, and civilian chronic hepatitis B patients.

Materials and Methods: The approval of the Dicle University Medical School, Non-Invasive Clinical Studies Ethics Committee was obtained for the study. Inmates and civilians with hepatitis B who presented to the infectious diseases outpatient clinic between December 2010 and June 2013 were enrolled in the study. Both groups were statistically compared in terms of HBV DNA, ALT, AST and HBeAg.

Results: A total of 34 inmates and 34 civilian patients were evaluated. While no difference was observed in terms of the liver enzymes, HBeAg positivity was significantly higher among the inmates. Also, a HBV DNA > 104 copies/ml was more frequently observed in the group of inmates, although the difference was statistically insignificant.

Conclusion: Studies comparing chronic hepatitis B patients who are leading different lifestyles will help select the patients with priority for treatment. (Viral Hepatitis Journal 2014; 20(2): 57-60)

Key words: Prisoner, chronic hepatitis B, civil

ÖZET

Amaç: HBV enfeksiyonunun patogeneğinde immün kökenli süreçlerin rol oynadığı ve enfeksiyonun iyileşmesinde konağın immün sistemi önemlidir. Bu çalışmada amaç kapalı ortamda kalan ve çeşitli stres faktörleri ile immün sistemleri etkilenebilen mahkum kronik hepatit B hastaları ile sivil hepatit B hastalarının hepatit B ile ilgili laboratuvar sonuçlarının karşılaştırılmasıdır.

Gereç ve Yöntemler: Çalışma için Dicle Üniversitesi Tıp Fakültesi girişimsel olmayan klinik araştırmalar etik kurulundan onay alındı. Çalışma 2010 Aralık ve 2013 Haziran tarihleri arasında enfeksiyon hastalıkları polikliniğine başvuran mahkum hepatit B ve sivil hepatit B hastalarında yapıldı. Her iki hasta grubu da HBV DNA, ALT, AST ve HBeAg açısından istatistiksel olarak karşılaştırıldı.

Bulgular: Çalışmada toplam 34 mahkum ve 34 sivil hasta değerlendirildi. Hastaların karaciğer enzim değerleri açısından bir fark saptanmazken, HBeAg pozitifliği mahkum grubunda anlamlı bir şekilde yüksekti. HBV DNA'nın 104 kopya/ml< üzerinde olma sıklığı mahkum grubunda daha yüksek iken istatistiksel olarak anlamlı değildi.

Sonuç: Farklı yaşam tarzında yaşayan, kronik hepatit B tanılı hastaları karşılaştıran çalışmalar özellikle öncelikli olarak tedavi endikasyonu olabilecek hastaların belirlenmesinde yararlı olacaktır. (Viral Hepatit Dergisi 2014; 20(2): 57-60)

Anahtar Kelimeler: Mahkum, kronik hepatit B, sivil

Introduction

More than 2 billion people around the world are infected with the hepatitis B virus (HBV) (1). HBV infections are thought to claim 1 million lives every year and 33% of the deaths are reportedly caused by hepatocellular carcinoma (HCC). In our country, 3.5 million people are thought to be infected with HBV (2,3). It is known that 5% of adult patients with acute hepatitis due to HBV develop chronic disease and a major part of these cases advance to cirrhosis. Moreover, the risk of HCC is high among patients with cirrhosis (2).

The measurement of the HBV DNA levels is of utmost importance both for the diagnosis and treatment decision, and the follow-up of the patients. The assessment of the severity of the liver disease should include AST and ALT tests (4). Since the liver morphology may support the treatment decision, a liver biopsy to find out the degree of the necroinflammation and fibrosis is recommended in patients with ALT and/or HBV DNA levels >2000 IU/ml (4). When we look at the diagnostic criteria for chronic hepatitis B, these include positive hepatitis B virus surface antigen (HBsAg) test for longer than

>6 months, serum HBV DNA >20.000 IU/mL, constant or transient increases in ALT/AST levels, and evidence of moderate or advanced necroinflammation in the liver biopsies (5).

Chronic hepatitis B (CHB) manifests itself in the hepatitis B e antigen (HBeAg)-positive and HBeAg-negative forms. HBeAg-positive CHB results from the "natural type" of HBV and is typically observed in the early phase of HBV infection. HBeAg-negative CHB is caused by the replication of the naturally occurring HBV variants resulting from the nucleotide mutations in the precore and/or main core promoter regions and represents a later phase of chronic HBV infection. The prevalence of the HBeAg-negative form of the disease has been increasing within the last ten years parallel to the aging of the HBV-infected population and these cases constitute the majority of the patients in various regions including Europe (6-8). The viral load of HBV is claimed to be closely associated with HCC and cirrhosis. In patients with a viral load over 105 copy/ml, the risk of HCC increases six times compared to undetectable HBV DNA levels (9,10). It is already known that immune-related processes play a role in the pathogenesis of prHBV infection and the immune system of the host is of central importance in the recovery (11). The main mechanism of immunity is the lysis of infected hepatocytes by the cytotoxic T-cells (12). The aim of the present study was to compare the hepatitis B-related laboratory results of the inmates with chronic hepatitis B, who live in an enclosed space and whose immune system are affected by various stress factors, with those of civilian hepatitis B patients.

Material and Method

The study was conducted at Dicle University Medical School, Department of Infectious Diseases and Microbiology outpatient clinic between December 2010 and June 2013. From 3000 hepatitis B patients followed up at the clinic, 34 untreated inmates with CHB were enrolled in the study. The control group consisted of 34 untreated civilian hepatitis B patients. The approval of the Dicle University Medical School, Non-Interventional Clinical Trials Ethics Committee was obtained before the study. The HBeAg, antiHBe, HBV DNA, anti-delta, and AST and ALT values of the inmates and civilians with hepatitis B were recorded. The HBsAg, HBeAg, and AntiHBe were tested using the enzyme-linked immunosorbent assay (ELISA) method (Cobas e 601 device, Roche, Germany). The anti-delta tests were performed with the help of the Triturus fully automated Dia Prodiagnostic device (Bioprobes, Italy). In all patients, complete blood count (CBC), biochemical parameters, viral hepatitis markers, aspartate aminotransferase (AST), alanine aminotransferase (ALT), HBV DNA, and hepatitis D (delta) virus (HDV) RNA levels were evaluated. ALT and AST tests were conducted through the spectrophotometric method (Architect CT16000 Abbott, USA). DNA levels were tested using the COBAS®AmpliPrep Total Nucleic Acid Isolation Kit (Roche Molecular Systems Inc., Branchburg, NJ, USA), and after the DNA was isolated, HBV DNA levels were evaluated with the COBAS®AmpliPrep/COBAS®Taqman® HBV Test v2.0 (Roche Molecular Systems Inc., Branchburg, NJ, USA). The HBV DNA levels of the patients were recorded in IU/ml.

Statistical Analyses

The obtained data were entered to the SPSS 15.0 statistics software. Categorical data were analysed using the chi-square test.

The normality of the distribution of the numeric data was tested through the Kolmogorov-Smirnov test. The normal data were analysed with the help of the student's t-test, while those outside the normal distribution were analysed using the Mann-Whitney U test. Statistical significance was based on a value of $p < 0.05$.

Results

Thirty-four untreated inmates and 34 untreated civilian patients diagnosed with CHB were enrolled in the study. No statistically significant difference was observed between the group of inmates and the group of civilians. The mean AST value in the group of inmates was 26.97 ± 9.12 , while the mean AST in the civilian patient group was 23.8 ± 6.5 . The mean ALT value in the group of inmates was 40.91 ± 25.56 , while it was 34.5 ± 16.27 in the group of civilians. No statistically significant difference was observed regarding the ALT and AST values between the groups (Table 1). In terms of HBeAg positivity, 8 among the 34 inmates were positive, while only 2 patients were positive in the group of civilians. This ratio was statistically significant (Table 1). Two patients in the group of civilians, who were tested positive for HBeAg, were also positive for HBV DNA. Among 8 patients in the group of inmates, who were positive for HBeAg, only three were tested positive for HBV DNA. No significant difference was observed between the groups in terms of anti-delta positivity. Although the number of patients with HBV DNA values $\geq 10^4$ copy/ml was greater in the group of inmates in comparison to the group of civilians, this difference was statistically insignificant (Table 1). Demographic characteristics of the civilian and inmate patients).

Discussion

Incarceration in a closed and crowded space, such as a correctional facility, leads to an increased risk of HCV, HBV and HIV infections and sexually transmitted diseases (13). The lifestyle of the inmates before they arrive at the prison reportedly involves drug use, unprotected sex, and tattooing. The ratio of the inmates committing new criminal offenses has been reported to be over 67%. Among these, 50% return to jail within three years (14). Since inmates are in the risk group for sexually transmitted and blood-borne diseases, the high rate of returning patients to the correctional facility increases the risk of transmission between the inmates. These inmates are also a great public health risk, since a study from the USA has pointed out the ratio of unprotected sex within the first 12 hours after the release from prison as 51%, while the ratio of intravenous drug use was found to be 11% (15).

Table 1. The demographic characteristics and laboratory results of the inmate and civilian hepatitis B patients

	Group of Civilians n=34 (%)	Group of Inmates n=34 (%)	p
Mean age	34.61±11.46	34.82±8.81	0.934
AST	23.8±6.5	26.97±9.12	0.114
ALT	34.5±16.27	40.91±25.56	0.222
HBeAg positivity	2 (5.9)	8 (23.5)	0.040
HBV DNA>10 ⁴ copy/ml	10 (29.4)	13 (38.2)	0.442
Anti-Delta positivity	1 (2.9)	2 (5.9)	1.000
Anti-HBe positivity	32 (94.1)	26 (76.5)	0.100

Serum HBV DNA values of patients followed up with the diagnosis of CHB are a specific and efficient marker of HBV replication in various clinical conditions (16). Regular follow up of HBV DNA levels is more important than any other test in estimating the need for treatment (5). Besides, quantitative measurement of HBV DNA levels helps us observe if the treatment scheme is effective, determine the dose and duration of the therapy, and modify the treatment modality when necessary (17). In a study by Bayram et al. focussing on the HBV DNA levels in hepatitis B patients, a total of 703 patients were evaluated and 37% of the patients were found to have HBV DNA levels over 104 copy/ml (18). In a study by Ozbilge et al. where they accepted HBV DNA values over 1000 copy/ml as positive, the ratio of positive cases was 41% (19). In our study, the ratio of the patients with HBV DNA results over 104 copy/ml was 38.2% and this ratio was in compliance with their study. Although a lower ratio like 29.4% was observed in the group of civilian patients, the difference was statistically insignificant. In another study, Dagtekin et al. have tested HBV DNA levels in patients who were coincidentally found to be HBsAg-positive (20). In this study, 153 out of the 267 patients (57.6%) were observed to have HBV DNA levels below 2000 IU/ml, while 42.6% tested below 2000 IU/ml. In the same study, HBeAg positivity was found to be 7.9%, while we observed HBV DNA ratios of 23.5% in the group of inmates and 5.9% in the group of civilians. In our study, the rate of HBeAg positivity in the group of inmates was higher than both the group of civilians, and the previous studies. The cause of this high rate of HBeAg positivity in our study can be associated with the higher risk of HBV transmission among inmates and points to a recent contact with the virus. This phase - also called the immunotolerant phase - is the stage where, although the organism has come into contact with HBV, the immune system is not stimulated and the immune response cannot be observed yet. During this phase, HBeAg is positive, ALT is normal and the HBV DNA value is high (21). In another study conducted on 31 chronic patients followed up with the diagnosis of hepatitis B, 10 patients (32.2%) were observed to be positive for HBeAg (22). When we look at the HBV DNA results, 21 patients (67%) were found to be HBV DNA-positive, while the rate of patients with values over 105 copy/ml was 11.36%. In the literature, there are studies pointing out varying serum HBV DNA levels between HBeAg-positive and -negative patients (23-25). In our study, among the HBeAg-negative patients in the group of civilians, 23.5% of those with positive serum HBV DNA levels had HBV DNA levels over 105 copy/ml. In the group of inmates, 25% of the HBeAg-negative patients had HBV DNA levels over 105 copy/ml. Among the 8 HBeAg-positive patients, 2 patients (25%) had HBV DNA levels over 105 copy/ml. In a study where the serum HBV DNA levels of HBeAg-positive CHB patients were evaluated, 9 out of 11 patients with levels over 105 copy/ml were tested positive for HBeAg (22). According to the study results, the serum HBV DNA levels of the HBeAg-positive patient group were statistically significantly higher. In a study by Kose et al., HBV DNA levels over 107copy/ml were observed in 84.4% of HBeAg-positive patients (25). The presence of the HBeAg is considered to be an indication of the presence of viral particles, DNA polymerase and HBV DNA in the serum, and of active replication and infectiousness. However, especially in recent

years, uncertainties have arisen about the idea that the HBeAg/anti-HBeAg system is a reliable marker of replication (26). The fact that the majority of infectious patients in a study conducted on patients followed up for CHB consisted of HBeAg-negative/AntiHBe-positive patients also supports this view. These patients were positive for HBV DNA (26). In our study, 37 (63.7%) among the 58 HBeAg-negative patients in both groups were positive for HBV DNA. In 5 out of the 10 HBeAg-positive patients (50%), HBV DNA was observed to be positive. These results are in compliance with the study by Kose et al. (17).

In conclusion, studies comparing CHB patients living under different conditions with a general CHB patient population shall be helpful in selecting the patients with treatment priority. In addition, patients such as inmates, who live in closed and crowded spaces and are in the higher risk group for sexually transmitted and blood borne diseases, should be scanned and the necessary precautions should be taken.

Conflict of interest: None declared.

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