Response to Various Treatments in the Patients With Chronic Hepatitis B; A Cross-Sectional Study

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Background: Hepatitis B is one of the most common chronic viral infections worldwide, especially in developing countries. The insufficient treatment of the disease increases the risk of cirrhosis and hepatocellular carcinoma, which impose heavy costs to the patient and the society. Different studies evaluated several protocols for the treatment of the disease.

Objectives: The aim of this study was to evaluate the response rate of the different treatments in patients with chronic hepatitis B (CHB).

Patients and Methods: In a cross-sectional study, 89 patients with CHB who were referred to Infectious Diseases Clinics during 2004 to 2009 were studied. Serological and biochemical outcomes to the different treatments were evaluated. The data were analyzed by SPSS 16.

Results: CHB was more frequent in men (74.2%) than women (25.8%). The mean age of the patients was 36 ± 1.36 years. Fifty-three patients (59.6%) had active CHB while 36 (40.4%) were asymptomatic carriers. Serologic and biochemical responses to the treatment were 50% and 69.44%, respectively. However, 50% of the patients with positive HBeAg showed serologic response to the treatment, 37.5% showed HBeAb as well as reduced amounts of HBeAg, and 12.5% just showed reduced amounts of HBeAg. Patients treated by lamivudine showed the highest serologic response rate (75%).

Conclusions: Serologic and biochemical response to the different treatments in the patients were better than other similar studies. Besides, it is recommended to begin antiviral therapy against CHB infection with lamivudine.

Keywords: Hepatitis B, Chronic; Lamivudine; Interferon-alpha

1. Background

Hepatitis B virus (HBV) infection is a major health problem worldwide. It is estimated that between 350 to 400 million people are HBV carriers and about one million of them die from HBV-related liver diseases each year (1, 2). The prevalence of HBV infection varies in different regions. There are areas with low prevalence rate such as the United States, Canada, western Europe, and Australia with an approximate 0.1% to 2% prevalence rate, areas with intermediate prevalence rate such as the Mediterranean countries, Japan, Central Asia, the Middle East, and South America with a prevalence rate between 3% to 5%, and areas with high prevalence rate such as Southern Asia, China, and Sub-Saharan Africa with a prevalence rate between 10% to 20% (1, 3). Iran is located in the region with intermediate prevalence rate. The first published study concerning the prevalence of HBV infection in Iran was referred to 1972 and later studies estimated the prevalence of HBV infection in Iran from 1% to 3.5% (4-7). In 1993, National Vaccination Program against HBV infection was started for neonates as a routine vaccination, which seemed to affect the prevalence rate of the infec-

tion in Iran (8, 9). A recent systemic review in 2008 estimated the HBV infection prevalence of 2.14% (95% CI, 1.92-2.35) in Iran, which was about 2.55% in men and 2.03% in women (10). In high prevalence areas, prenatal infection is the prominent transmission route (11). However, in intermediate prevalence areas horizontal transmission, especially in early childhood, is the cause of most chronic HBV infections while unprotected sexual intercourse and intravenous drug use in adults are the main transmission routes in low prevalence areas (12). Hepatitis B surface antigen (HBs Ag) is the hallmark of HBV infection that can be detected by both radioimmunoassay (RIA) or enzyme immunoassay (EIA) (13). HBs Ag seropositivity of more than six months implies the chronic infection with HBV. It is estimated that about 1% of patients who had acute hepatitis B progress to the chronic stage (14). Moreover, it is necessary to detect HBeAg that shows the replication of HBV to approve the chronic hepatitis B (CHB) stage. Falling levels of HBeAg and appearance of HBeAb or anti-HBe imply the recovery (15). There is no specific treatment for acute hepatitis B; however, treatment is recommended in

patients who develop chronic stage (16). The main purpose of treatment for CHB is preventing HBV replication prior to its irreversible liver damage, preventing the long term complications such as cirrhosis or liver cancer, preventing the spread of infection to the others, and increasing the survival of the patients (17, 18). There are several drugs to slow HBV replication such as lamivudine, adefovir, entecavir, telbivudine, tenofovir and alpha interferon (INF- ∝) (16, 19).

2. Objectives

The study was designed to evaluate and compare the efficacy of different anti HBV regimens in the treatment of CHB patients who were referred to Infectious Diseases Clinics (Farshchian Hospital and Emam Khomeini Clinic) in Hamadan, west of Iran.

3. Patients and Methods

A cross-sectional study was conducted to evaluate the patients with CHB who had been referred to Infectious Diseases Clinics (Farshchian Hospital and Emam Khomeini Clinic) in Hamadan during a five-year period from 2004 to 2009. All the patients with the diagnosis of chronic hepatitis B who were referred to the clinics during the study period were assessed, and the patients with at least six months history of hepatitis B infection were included in the study. The patients who underwent drug therapy for at least three months were considered as under treatment. Overall, 89 patients with CHB were enrolled to this study. Data were gathered using census counting employing a predesigned checklist and reviewing each patient's medical file. The gathered data included basic characteristic data (age and sex) as well as treatment strategy and drugs (including lamivudine, adefovir, and INF-α), and the biochemical as well as serologic response to the treatment. The biochemical response to the treatment was defined as normal values of serum aminotransferase levels in the patients who had previous high values of serum aminotransferase levels; moreover, the serologic response to the treatment was defined as a negative HBeAg serologic test result or presence of HBeAb in the serum in the absence of HBeAg. The duration of the treatment was between 12 to 52 months with various regimens according to the seroconversion in the patients. The data were analyzed using SPSS V.16 (SPSS Inc, Chicago, Illinois, USA). Frequency and mean values were calculated for the demographic parameters as well as for the therapeutic parameters. Comparative analysis were performed using Chi-squared test. P value bellow 0.05 was regarded as statistically significant.

4. Results

Of 89 patients with chronic Hepatitis B, 23 (25.8%) patients were female and 66 (74.2%) were male. The youngest patient was 11 years old and the eldest one was 76 years
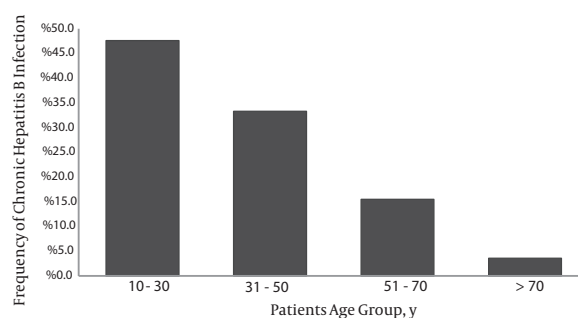

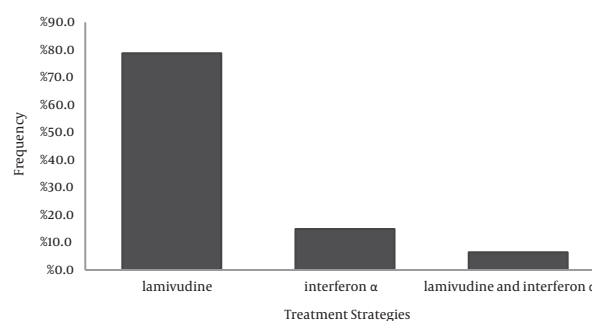**Figure 1.** Frequency of Chronic Hepatitis B Infection Among the Different Age Groups of the Patients

Figure 2. Frequency of Different Treatment Strategies Among the Patients With Chronic Hepatitis B
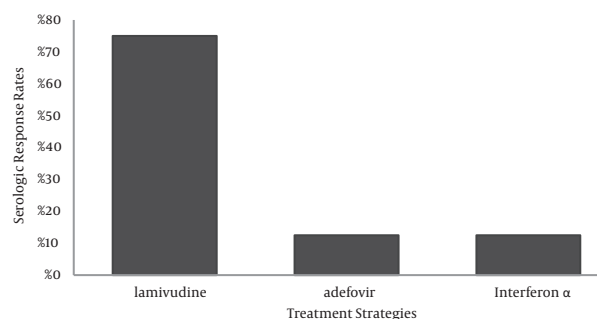

Figure 3. Serologic Response Rates for the Different Treatment Strategies Among the Patients With Chronic Hepatitis B

old. The mean age of the patients was 36 ± 1.36 years. The patients who were in the age group of 10-30 years of age had the highest frequency of CHB (Figure 1). Fifty-three (59.6%) patients had active CHB while 36 (40.4%) were asymptomatic carriers. A higher frequency of asymptomatic carriers was observed in women than in men. Moreover, 54.5% of female patients had active CHB while 45.5% were asymptomatic carriers. Among male patients, 61.5% had active chronic HBV infection while 38.5% were asymptomatic carriers. Although the proportion of healthy carriers was higher among women, there was no significant association between the frequency of healthy carriers and patients' gender (P = 0.5). Out of 53 patients with

Table 1. Frequency of Treatment Strategy Changes Among Patients With Chronic Hepatitis B [a]

First Regimen	Second Regimen	Reason for Change	Frequency, %
Lamivudine	Lamivudine + adevofir	Irresponsive to the treatment	50
Lamivudine	Lamivudine + INF-α	Irresponsive to the treatment	28.57
Lamivudine	INF-α	Irresponsive to the treatment	7.14
INF-α	Lamivudine	Drug induced complications	7.14
Lamivudine	INF-α	Unknown	7.14

[a] INF-α: alpha-interferon

active chronic HBV, 47 (88.67%) were under treatment, 37 (78.72%) patients were treated by lamivudine, 7 (14.89%) cases by interferon α, and 3 (6.38%) cases by the combination of lamivudine and INF-α (Figure 2).

The interval between the disease diagnosis and treatment ranged from zero to ten months with the mean interval of 2.4 ± 2.7 months. The treatment strategy was changed in 14 (29.78%) patients as follows: 12 (85.71%) patients because of insufficient therapeutic response, 1 (7.14%) patient because of drug-induced complications, and 1 (7.14%) patient due to unknown reason. The time interval between treatment and drug change ranged from one to 50 months with the mean interval of 18.57 ± 15.73 months. The treatment strategy was changed from INF-α to lamivudine in 7.14% of the patients, lamivudine to INF-α in 14.28% of the patients, lamivudine to the combination of lamivudine and INF-α in 28.57% of the patients, and lamivudine to the combination of adefovir and lamivudine in 50% of the patients (Table 1).

Twenty-nine (54.2%) patients in active chronic HBV group had a history of positive HBeAg. However, 50% of the patients with positive HBeAg showed serologic response to the treatment, 37.5% showed HBeAb as well as reduced amounts of HBeAg, and 12.5% just showed reduced amounts of HBeAg. Patients treated by lamivudine showed the highest serologic response rate (75%). No significant association was observed between treatment strategy and seroconversion (P > 0.05) (Figure 3).

The time interval between treatment and HBeAg seroconversion ranged from six to 48 months; moreover, 40 (44.95%) patients had high serum aminotransferase levels from which 36 cases had active CHB and were under treatment. Among 25 (69.44%) patients with CHB, serum aminotransferase levels became normal within six to 24 months after initiation of the treatment. However, serum aminotransferase levels remained high even after the treatment in 11 (30.55%) patients with CHB.

5. Discussion

Hepatitis B virus infection is a major global public health problem. It is estimated that over 350 million people worldwide are infected by this virus and about one million of them die from HBV-related diseases annually (1). CHB infection might result in cirrhosis and hepatocellular carcinoma (HCC). Treatment strategies for CHB infection are various and many new treatments are under evaluation. In the present study, 89 patients were evaluated from which 74.2% were male and 25.8% were female. According to our results, HBV infection was more frequent in men than in women. Ahmad et al. conducted a study during 2001 to 2007 in Bangladesh to evaluate the prevalence of CHB infection on 2617 patients with HBV infection, which 87.7% of them were males (20). In addition, Alavian et al. conducted another study in 2002 in Tehran, the capital city of Iran, to evaluate the efficacy of lamivudine in the treatment of CHB infection. From 72 patients evaluated in the study, 63 (87.5%) were male (21). Panahi et al. also evaluated the therapeutic efficacy of lamivudine and INF-α on CHB infection in 2003 in Mashhad, a major eastern city of Iran; from 22 patients with chronic HBV infection, 12 (54.5%) were males (22).

The high prevalence of infection among men could be due to the high frequency of risky behaviors such as intravenous drug use and unprotected sexual intercourse, known as important HBV transmission routes among men. Alavian et al. reported the mean age of patients as 40.2 ± 13.4 years (21). In addition, in Ahmad et al. study, most of the patients were 13-47 years old (20). The mean age of Mashhad patients was 30 years (22). In this study, the mean age of the patients was 36.4 ± 1.36 years and most of the patients belonged to the 10-30 and 30-50 years old age groups . According to the results of the present study and other similar studies, HBV infection is more prevalent in younger ages. This might be due to the higher frequency of risky behaviors as risk factors for HBV infection among the youth. The most prominent drug used to treat CHB infection in this study was lamivudine (78.72%) which was the same as Yoon et al. in South Korea (23), Souto et al. in Brazil (24), and Alavian et al. in Iran (21). However, Chan et al. in China (25), Sarin et al. in India (26), and Panahi et al. in Iran (22) also used the combination of lamivudine and INF-α for the treatment of CHB infection. The serologic response to lamivudine was 50% in the present study while it was only 14% in a study conducted in China (25). The serologic response to lamivudine was 24.7% in South Korea (23), 37.8% in India (26), 37.8% in Brazil (24), and 66% in Tehran, Iran (21). The serologic response to the combination of lamivudine and INF-α was 23% in Turkey (27), 39.5% in India (26), 33% in China (25), and 59% in Mashhad, Iran (22). The serologic response to lamivudine in this study was better in comparison to the results from studies in Turkey (27), China (25), and South Korea (23) while the results in Tehran (21), Iran showed a better serologic response.

The higher seroconversion rate in Iran compared with other Asian countries could pertain to the lower rate of drug resistance in Iran. The biochemical response to lamivudine in this study was reported in 69.4% of the patients that was the highest response rate among similar studies. The biochemical response to lamivudine was 48.14% in Turkey (27), 57% in Brazil (24), and 40.5% in India (26). The biochemical response to the combination of lamivudine and INF-α was 47.7% in India (26). The same as serologic response, the biochemical response to lamivudine was better in the present study in comparison to the similar studies in other countries that might be due to the lower rate of drug resistance in Iran, especially the city of Hamadan. The results of the study showed better serological and biochemical outcomes to lamivudine in Hamadan. Thus, it is recommended to begin antiviral therapy against CHB infection with lamivudine alone as a first-line therapy and recommend adefovir for the patients with lamivudine-resistant HBV. However, additional studies on other treatment strategies are required to obtain a clear strategy for the treatment of CHB infection in different stages.

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Authors' Contribution

Mamani, Majzoobi, Eini and Keramat were involved in the study concept and design, the study supervision, analysis and interpretation of data and drafting of the manuscript. All authors provided comments and approved the final manuscript.

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