Efficacy of lamivudine therapy in elderly patients with chronic hepatitis B infection

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Introduction

Chronic infection with hepatitis B virus (HBV) affects as many as 350 to 400 million people worldwide and 1.5 million people in Japan.\(^1\) Vaccination is mainly used in Japan to prevent HBV infection via mother-to-infant transmission and to reduce the number of HBV carriers. However, there are still many patients with HBV infection. Moreover, elderly patients with chronic hepatitis are on the increase, and the potential for development of cirrhosis or hepatocellular carcinoma in such patients is real. Hence, treatment of elderly patients with HBV is an important issue.

Lamivudine is an oral cytosine nucleoside analog that potently inhibits HBV replication by interfering with HBV reverse transcriptase activity.\(^2\) Several studies have reported the effectiveness of lamivudine in the suppression of HBV replication, improvement of transaminase levels and liver histology, and enhancement of the rate of loss of hepatitis B e antigen (HBeAg).\(^3\) In this regard, a major problem with the long-term use of lamivudine is the development of viral resistance, associated with increases in HBV-DNA and serum transaminase levels.\(^4\) Several studies have reported the effectiveness of lamivudine in the suppression of HBV replication, improvement of transaminase levels and liver histology, and enhancement of the rate of loss of hepatitis B e antigen (HBeAg).\(^5\) In this regard, a major problem with the long-term use of lamivudine is the development of viral resistance, associated with increases in HBV-DNA and serum transaminase levels.\(^6\) In this regard, a major problem with the long-term use of lamivudine is the development of viral resistance, associated with increases in HBV-DNA and serum transaminase levels.\(^7\) We already reported the efficacy of lamivudine therapy and factors associated with the emergence of resistance in chronic HBV infection in Japan.\(^8\) However, to our knowledge, there are no reports that describe the efficacy of lamivudine treatment in elderly patients (≥60 years) with chronic hepatitis B.

The aims of the present study were (1) to assess the benefits of lamivudine therapy for elderly patients (≥60 years) with chronic hepatitis B, and (2) to determine differences in the emergence rate of YMDD mutants and the appearance of breakthrough hepatitis between patients <60 years old and those ≥60 years old.

Background. The aim of this study was to evaluate the efficacy of lamivudine therapy in elderly patients with chronic HBV infection. Methods. Patients aged ≥60 years (n = 40) received lamivudine monotherapy between February 1995 and September 2005 at Toranomon Hospital. We compared the efficacy of lamivudine therapy in these patients and in 639 patients aged <60 years, including 80 patients aged <60 years matched for sex, hepatitis B e antigen (HBeAg) status, and hepatitis B virus (HBV) DNA level. Results. The rates of normalization of alanine aminotransferase (ALT) level in 40 patients aged ≥60 years and 639 patients aged <60 years were 85% versus 76%, and 86% versus 73% at 1 and 3 years, respectively. The respective rates of loss of HBV-DNA were 74% versus 74%, and 76% versus 68% at 1 and 3 years. The respective cumulative emergence rates of the YMDD mutant were 16% and 17% at 1 year, and 46% and 49% at 3 years. In 80 patients <60 years old matched for sex, HBeAg status, and HBV-DNA level, the rates of normalization of the ALT level and loss of HBV-DNA were similar to those in the 639 patients aged <60 years. The emergence rate of YMDD mutants in patients aged ≥60 years were similar to those in matched patients aged <60 years. Multivariate analyses identified low serum bilirubin (<1 mg/dl) as an independent factor associated with the emergence of the YMDD motif mutation in patients aged ≥60 years.

Conclusions. Our results suggest that treatment with lamivudine is both well tolerated and efficacious in elderly patients with chronic HBV infection.

Key words: HBV, elderly patients, lamivudine, YMDD mutant
Patients and methods

Patients

Between February 1995 and September 2005, 40 consecutive Japanese patients aged ≥60 years were enrolled in this study at Toranomon hospital, Tokyo. All patients fulfilled the following criteria: (1) presence of hepatitis B surface antigen (HBsAg) in serum (positive for HBsAg for >6 months); (2) HBV-DNA positivity by quantitative assay; (3) absence of hepatoma; (4) absence of coinfection with hepatitis C virus (HCV); and (5) no previous treatment with any nucleoside analog.

The baseline characteristics of the 40 patients included in the study are listed in Table 1. All patients were Japanese; 23 were men and 17 were women; 15 were HBeAg-positive and 25 were HBeAg-negative; 32 patients had genotype C, four had genotype B, and the genotype was unknown in four. To determine the efficacy of lamivudine therapy and emergence rate of YMDD mutants, we compared the 40 patients aged ≥60 years with another group of 639 patients aged <60 years with HBV-related chronic infection on lamivudine therapy in our hospital. The baseline characteristics of the 679 patients are also listed in Table 1.

Since sex and HBeAg status were significantly different between the two age groups, we selected 80 patients from the 679 patients aged <60 years with HBV-related chronic infection on lamivudine therapy in our hospital who were matched to the ≥60 age group with respect to sex, HBV-DNA level, and HBeAg status (Table 2). The median duration of lamivudine therapy in the 40 patients aged ≥60 years was 44 months (range, 6–69 months). All comparisons described in this study pertain to two age groups of patients matched for sex, HBeAg status, and HBV-DNA levels unless otherwise stated.