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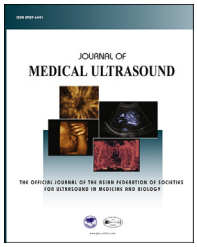

ORIGINAL ARTICLE

Long-term Nucleos(t)ides Analogues for Chronic Hepatitis B Improve Liver and Spleen Size: A Noninvasive Sonographic Study

Ruei-Hsin Chang [1], Tsolmon Nyamsuren [1,2], Sarvesh Gyawali [1,3], Szu-Chieh Fu [1], Yi-Wen Huang [1,4,5,6*], Rui-Ting Hu [1,7], Sien-Sing Yang [1,7*]

[1] *Liver Center, Cathay General Hospital Medical Center, Taipei, Taiwan,* [2] *Chingeltei District Health Unit, Ulaanbaatar, Mongolia,* [3] *Bhaktapur Cancer Hospital, Bhaktapur, Nepal,* [4] *School of Medicine, Taipei Medical University College of Medicine, Taipei,* [5] *School of Medicine, China Medical University, Taichung,* [6] *Division of Gastroenterology, Department of Internal Medicine, National Taiwan University College of Medicine, Taipei, and* [7] *School of Medicine, Fu-Jen Catholic University College of Medicine, New Taipei, Taiwan*

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KEYWORDS
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Abstract *Background:* Histological improvement and regression of liver fibrosis after long-term use of nucleos(t)ides analogues (NUCs) have been documented. The aim of the present investigation was to evaluate the usefulness of traditional sonography to detect hepatic and splenic changes during NUC therapy in chronic hepatitis B (CHB) patients.
Methods: A total of 181 CHB patients receiving NUC treatment were enrolled in this study. The study population was divided into three groups: 72 cirrhotic, 58 noncirrhotic CHB, and 51 non-replicative hepatitis B virus carriers. All patients had blood chemistries taken and sonography at baseline and during the NUC treatment period. The changes in liver size, liver edge, spleen size, platelet count, and platelet count/spleen diameter (PC/SD) ratio were compared among the three groups of patients.

Abbreviations: AFP, α-fetoprotein; ALT, alanine transaminase; AST, aspartate transaminase; CHB, chronic hepatitis B; Hb, hemoglobin; HBV, hepatitis B virus; INR, international normalized ratio; NUCs, nucleos(t)ides analogues; PC/SD, platelet count/spleen diameter; WBC, white blood cells.

Conflicts of interest: All authors do not have an association that might pose a conflict of interest.

* Correspondence to: Dr Sien-Sing Yang or Dr Yi-Wen Huang, Liver Center, Cathay General Hospital Medical Center, Number 280, Section 4, Jen-Ai Road, Taipei 10630, Taiwan.
E-mail addresses: ywhuang@cgh.org.tw (Y.-W. Huang), jaab@cgh.org.tw (S.-S. Yang).

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Results: CHB Patients with and without cirrhosis have improved clinical features during NUC therapy with lower aspartate aminotransferase, alanine aminotransferase, international normalized ratio, hepatitis B virus DNA, and spleen size and higher platelet, liver edge, liver size, and PC/SD ratio compared with the baseline data ($p < 0.05$). The differences in liver edge, liver size, spleen size, and PC/SD ratio are higher in the cirrhosis group than in the noncirrhotic group ($p < 0.001$). A decrease in spleen size exhibited a linear relationship with treatment duration ($R^2 = 0.905$).
Conclusions: Traditional sonography is helpful to monitor changes in liver fibrosis of CHB patients under NUC therapy.

Introduction

Chronic hepatitis B (CHB) is one of the major causes of liver cirrhosis and hepatocellular carcinoma [1,2]. Antiviral nucleos(t)ides analogue (NUC) therapy is effective in achieving viral suppression, and their long-term use leads to histological improvement and regression of liver fibrosis [3,4]. Liver biopsy is the gold standard of histological diagnosis; however, it has the disadvantage of being invasive [5–9].

Ultrasonography is easily accessible and convenient in daily clinical practice to evaluate liver disease severity. Ultrasonography is routinely performed in clinical follow-up of patients with chronic liver disease for cirrhosis and hepatocellular carcinoma surveillance according to clinical practice guidelines [10,11]. Several studies demonstrated platelet count and splenic size ratio as a reliable predictor of esophageal varices [12,13]. An early study depicted that spleen size was significantly larger in cirrhotics than in noncirrhotics [14]. Recent studies showed spleen diameter and platelet count as a more reliable noninvasive method to detect clinically significant portal hypertension in patients with compensated cirrhosis [15,16].

The aim of the present investigation is to evaluate the usefulness of ultrasonography to detect alterations in disease severity during NUC therapy in CHB patients.

Patients and methods

Ethics statement

The present study was approved by the Institutional Review Board of the Cathay General Hospital (CGH-P102068) under the ethical guidelines of Helsinki Declaration. Informed consent was waived as the data were analyzed anonymously.

Study population

We conducted a retrospective study of 181 consecutive hepatitis B virus (HBV) carriers in Cathay General Hospital Medical Center, which consisted of 72 cirrhotic and 58 noncirrhotic CHB patients undergoing regular NUC therapy to compare with 51 nonreplicative HBV carriers who did not require NUC therapy. All patients were followed up for more than 12 months. All patients with hepatitis other than HBV, malignancy, or other major systemic diseases were excluded. Thirty-five cirrhotic patients had liver histology to confirm the clinical diagnosis of cirrhosis, and the remaining 37 patients had upper endoscopies to confirm the presentation of esophageal varices. All 58 noncirrhotic patients were confirmed by liver histology.

We defined cirrhosis CHB patients as those with ultrasonographic findings of coarse echotexture, uneven hepatic surface, tortuous narrowed hepatic veins, and splenomegaly or with esophageal varices on upper gastrointestinal panendoscopy. Noncirrhotic CHB patients were defined as those with no sign of cirrhosis on ultrasonography with episode(s) of abnormal transaminases ($\geq$1.5$\times$ upper normal limit). Nonreplicative HBV carriers was defined as undetectable HBV DNA ($<$17 IU/mL) and no episode of elevated transaminases ($<$1.5 upper normal limit).

Methods

All patients were examined for their age, sex, blood chemistries, and ultrasonography at baseline and during the NUC treatment period. The blood chemistries were collected every 3 months for serum level of aspartate transaminase (AST), alanine transaminase (ALT), total bilirubin, hemoglobin (Hb), white blood cells (WBCs), platelet count, prothrombin time [PT; international normalized ratio (INR)], and α-fetoprotein (AFP). The sonography (iU22; Philips Ultrasound, Bothell, WA, USA) was assessed under overnight fasting status every 6 months by the one physician (SSY) to avoid interobserver variations. We use a C5-1 broadband curved array transducer with a median frequency of mainly 3.5 MHz (range, 3–5 MHz) to examine the liver and spleen. For each measurement, at least three reproducible spectral patterns were made to calculate the spleen diameter, liver edge, and liver size.

The maximal spleen size is measured as longitudinal coronal plan encompassing the splenic hilum [17] (Figure 1). The liver size is measured as the craniocaudal diameter at the midsternal line [18] (Figure 2). Liver edge is measured at the midsternal line and is presented as degree of angle [19,20] (Figure 3).

Statistical analysis

The comparison of demographics and clinical characteristics between cirrhotic, noncirrhotic, and nonreplicative

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