CORRESPONDENCE

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The Author's Response:

Anti-Viral Therapy for Compensated Liver Cirrhosis Patients with Normal Alanine Aminotransferase

Junggyu Lee, Dong Hyun Sinn, and Seung Woon Paik

Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

We appreciate the valuable comment by Khosravi et al. on our recently published article (1). First, Khosravi et al., suggested analyzing the impact of body mass index (BMI) on the risk of hepatocellular carcinoma (HCC). As Khosravi et al., has suggested, serum alanine aminotransferase (ALT) levels are affected by body mass index (2). Obesity is also known to affect the risk of hepatocellular carcinoma (HCC) in chronic hepatitis B virus infected patients (3). Therefore, dynamic interaction between ALT, BMI and HCC risk in chronic hepatitis B patients warrants further validation, yet, our study could not do so due to the retrospective nature of the study. Second, they questioned whether anti-viral therapy (AVT) should be considered for patients with normal ALT levels, as they may have no liver damage for patients with normal ALT levels. Khosravi et al., also showed the data from Keshvari et al., whether they suggested chronic hepatitis B patients with elevated HBV DNA levels can be clinically managed as inactive carrier when they show persistently normal ALT levels (4). However, patients in Keshvari et al., are patients with no or mild liver fibrosis stage ≤ 2 on liver biopsy, who were not cirrhotic patients (4). Although liver biopsy was lacking, our study was comprised of patients with cirrhosis, defined by presence of one or more of the following clinical indicators of cirrhosis: thrombocytopenia (< 150,000/μL platelets), cirrhotic configuration of the liver (nodular liver surface or caudate lobe hypertrophy) and/or splenomegaly confirmed in imaging studies, or the presence of varices (abnormally enlarged veins, detected by upper endoscopy or cross-sectional images). As sensitive indicators of hepatocellular damage, serum ALT level is usually low in patients without hepatic inflammation, and high in patients with hepatocyte injury (5). The presence of significant fibrosis or liver injury is often reflected by an elevated ALT level (6). However, for cirrhotic patients with high HBV DNA levels, AVT is usually recommended regardless of ALT level (7-9). This recommendation is based on the well-documented observation that ALT levels can be normal in patients with cirrhosis (7,8). As we stated in the limitation part of the published article (1), randomized controlled trials are needed to provide higher level of evidence. Yet, nucleos(t)ide analogues (NUC) are generally safe and well-tolerated oral medications (10), and long-term NUC therapy has been shown to reverse cirrhosis (11), and reduce the incidence of HCC (12,13). Decision to treat is based on an assessment of the risks and benefits of the treatment. Although there are still some concerns over long-term safety of NUCs, given the potential harms and potential benefits of AVT, and data from our study (1), prompt initiation of AVT seems reasonable approach for cirrhotic patients with elevated HBV DNA levels, even for those with normal ALT levels. Lastly, quantitative hepatitis B surface antigen levels are not measured for our cohort. The role of quantitative hepatitis B surface antigen levels for cirrhotic patients with normal ALT levels requires further studies.

ORCID

Junggyu Lee http://orcid.org/0000-0002-7449-933X
Dong Hyun Sinn http://orcid.org/0000-0002-7126-5554
Seung Woon Paik http://orcid.org/0000-0002-6746-6652

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Seung Woon Paik, MD
Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul 06351, Korea
E-mail: sw.paik@samsung.com

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