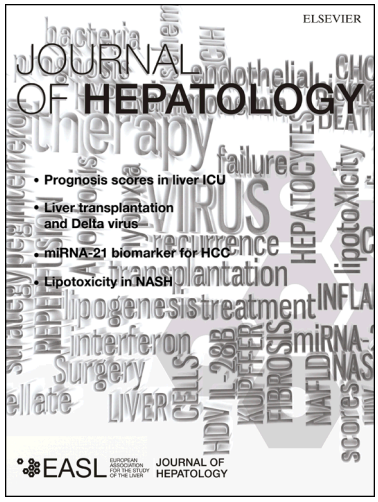

Letter to the Editor

Evidence supporting a beneficial role of vitamin D in chronic hepatitis C

Qing Pang, Kai Qu, Jing-Yao Zhang, Chang Liu

PII: S0168-8278(15)00292-5
DOI: http://dx.doi.org/10.1016/j.jhep.2015.03.037
Reference: JHEPAT 5647

To appear in: *Journal of Hepatology*

Received Date: 14 March 2015
Accepted Date: 18 March 2015

Please cite this article as: Pang, Q., Qu, K., Zhang, J-Y., Liu, C., Evidence supporting a beneficial role of vitamin D in chronic hepatitis C, *Journal of Hepatology* (2015), doi: http://dx.doi.org/10.1016/j.jhep.2015.03.037

Evidence supporting a beneficial role of vitamin D in chronic hepatitis C

Qing Pang, Kai Qu, Jing-Yao Zhang, Chang Liu*

Department of Hepatobiliary Surgery, The First Affiliated Hospital of Xi'an Jiaotong University College of Medicine, Xi'an, China

***Correspondence:** Chang Liu, MD, PhD, Professor, Department of Hepatobiliary Surgery, First Affiliated Hospital, School of Medicine, Xi'an Jiaotong University, No.277 West Yan-ta Road, Xi'an 710061, Shaanxi Province, China. Email: liuchangdoctor@163.com

To the Editor:

We read with interest the recent meta-analysis by Kitson *et al.* [1]. The authors demonstrate that baseline vitamin D level is not associated with sustained virologic response (SVR) to pegylated interferon (PEG-IFN) plus ribavirin therapy in patients with chronic hepatitis C (CHC). Based on this finding, they question [1] the non-skeletal benefits of supplementation with vitamin D, an essential determinant in regulating bone metabolism in chronic liver disease [2], on CHC. However, as vitamin D deficiency has been identified as a main risk factor for CHC development, we believe that the non-skeletal benefits of this kind of vitamin on patients with CHC can not be negligible and the conclusions of this meta-analysis [1] need to be further discussed and researched.

First, the studies included in the meta-analysis by Kitson *et al.* [1] were performed in America, Europe, Australian, or Israel, all of which are predominantly white in skin color. A community-based cross-sectional study showed that, compared with whites, blacks had lower levels of vitamin D and vitamin D-binding protein [3]. In addition, potential differences of the influence of vitamin D status in the degree of hepatic fibrosis in CHC patients between whites and blacks were also observed [4]. As a consequence, levels and benefits of vitamin D might vary in individuals with different ethnicity, leading to question whether the irrelevance between vitamin D and SVR, and the ineffectivity of vitamin D in CHC, can also apply to other races.

Second, this meta-analysis only summarized eleven studies, seven of which with 1,951 patients were published articles and the other four were conference abstracts with less convincing evidence. Among the eleven studies, the sole outlier identified by funnel and forest plots just belonged to conference abstract. Another contemporaneous meta-analysis with eleven full-text studies demonstrated that a lower level of vitamin D was significantly associated with a lower probability of SVR in CHC patients receiving PEG-IFNα/ribavirin therapy, especially when a cutoff value of 20 ng/mL for vitamin D deficiency was adopted [5]. Furthermore, low vitamin D status was also found to be associated with a higher risk of advanced liver fibrosis in these patients [5]. Numerous clinical evidence also suggested that vitamin D supplementation might protect against disease progression and elevate the SVR rate following treatment for CHC [6,7]. Recurrence of hepatitis C after liver transplantation is universal worldwide [8]. In addition to its association with primary CHC, vitamin D insufficiency could also result in a low SVR in patients with recurrent hepatitis C following antiviral therapy while vitamin D supplementation significantly improves the probability of achieving a SVR [8].

Potential mechanisms that link vitamin D and CHC are complex and manifold. Treatment with vitamin D reduces the extra- and intracellular levels of hepatitis C virus (HCV) core antigen in a dose-dependent manner [9] and produces calcitriol which could remarkably inhibit HCV productions [10], suggesting that vitamin D plays a natural antiviral role. In addition, the anti-inflammatory effects by reducing several proinflammatory factors like TNF-α, IFN-γ, and IL-17, as well as the anti-fibrotic role of vitamin D [7], might also partly explain the benefits of this vitamin supplementation in CHC.

As the global high prevalence of hypovitaminosis D among CHC patients, it is crucial to determine the association between vitamin D status/vitamin D supplementation and outcomes of CHC. Larger random clinical trails are still required to confirm the important non-skeletal effects of vitamin D in patients with CHC.

Conflicts of interest

The authors declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

Qing Pang

Kai Qu

Jing-Yao Zhang

Chang Liu*

Department of Hepatobiliary Surgery, The First Affiliated Hospital of Xi'an Jiaotong, University College of Medicine, Xi'an, China

*Corresponding author.

E-mail address: liuchangdoctor@163.com

References

[1] Kitson MT, Sarrazin C, Toniutto P, Eslick GD, Roberts SK. Vitamin D level and sustained virologic response to interferon-based antiviral therapy in chronic hepatitis C: a systematic review and meta-analysis. J Hepatol 2014;61:1247-1252.

[2] Yurci A, Kalkan AO, Ozbakir O, Karaman A, Torun E, Kula M, et al. Efficacy of different therapeutic regimens on hepatic osteodystrophy in chronic viral liver disease. Eur J Gastroenterol Hepatol 2011;23:1206-1212.

[3] Powe CE, Evans MK, Wenger J, Zonderman AB, Berg AH, Nalls M, et al. Vitamin D-binding protein and vitamin D status of black Americans and white Americans. N Engl J Med 2013;369:1991-2000.

[4] White DL, Tavakoli-Tabasi S, Kanwal F, Ramsey DJ, Hashmi A, Kuzniarek J, et al. The association between serological and dietary vitamin D levels and hepatitis C-related liver disease risk differs in African American and white males. Aliment Pharmacol Ther 2013;38:28-37.

[5] Garcia-Alvarez M, Pineda-Tenor D, Jimenez-Sousa MA, Fernandez-Rodriguez A, Guzman-Fulgencio M, Resino S. Relationship of vitamin D status with advanced liver fibrosis and response to hepatitis C virus therapy: a meta-analysis. Hepatology 2014;60:1541-1550.

[6] Villar LM, Del Campo JA, Ranchal I, Lampe E, Romero-Gomez M. Association between vitamin D and hepatitis C virus infection: a meta-analysis. World J

Gastroenterol 2013;19:5917-5924.

[7] Rahman AH, Branch AD. Vitamin D for your patients with chronic hepatitis C? J Hepatol 2013;58:184-189.

[8] Bitetto D, Fabris C, Fornasiere E, Pipan C, Fumolo E, Cussigh A, et al. Vitamin D supplementation improves response to antiviral treatment for recurrent hepatitis C. Transpl Int 2011;24:43-50.

[9] Matsumura T, Kato T, Sugiyama N, Tasaka-Fujita M, Murayama A, Masaki T, et al. 25-Hydroxyvitamin D3 suppresses hepatitis C virus production. Hepatology 2012;56:1231-1239.

[10] Gal-Tanamy M, Bachmetov L, Ravid A, Koren R, Erman A, Tur-Kaspa R, et al. Vitamin D: an innate antiviral agent suppressing hepatitis C virus in human hepatocytes. Hepatology 2011;54:1570-1579.