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Opinion

Vitamin D in Patients with Chronic Hepatitis C Virus Infection Receiving the Direct Antiviral Agents

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Recent studies have investigated the relationship between the vitamin D status of patients with chronic hepatitis C (CHC) [1]. Some researchers found no insufficient vitamin D in noncirrhotic viral liver disease [2]. However, the majority insisted that the hepatitis C virus (HCV)-positive subjects have deficient vitamin D levels [3-5]. Similarly, in our CHC cohort [6], up to 38% of the HCV infected patients had vitamin D deficiency (< 20 ng/mL).

Some in vitro studies have uncovered the synergic effect of vitamin D and interferon-based treatment in inhibiting HCV RNA replication [7-9]. Consistent with these findings, some researchers reported a positive correlation between 25-hydroxyvitamin D_3 levels and the success rate of achieving the sustained virological response (SVR) [10-12], but others failed to establish any

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consistency in results [13-16]. However, in the era of direct antiviral agents (DAA), pre-treatment vitamin D level does not impact treatment response [17, 18].

It has been known that $1,25(OH)_2D_3$ treatment could be able to slow the fibrotic progression of hepatic stellate cells, via the transduction of vitamin D—vitamin-D-receptor signaling. This signaling pathway inhibits the expression of pro-fibrogenic genes and reduces liver fibrosis induced by thioacetamide in vitro and in vivo, respectively [18]. These findings suggest a role of vitamin D deficiency in liver fibrosis. However, patients' clinical data remain scarce and inconclusive.

Another issue is concerning the kinetic changes in vitamin D after achieving SVR, but even in this case, the data are inadequate. Only Lange et al. investigated serum vitamin D status before and after antiviral therapy in 50 HCV patients with SVR. They discovered a trend toward a lower incidence of severe vitamin D deficiency after HCV eradication. An improved hepatic function resulted from the eradication of HCV may also positively contribute to the production of vitamin D. However, it should also be clarified that whether hypovitaminosis D regresses or worsens after SVR.

In summary, despite vitamin D deficiency is common in CHC, vitamin D level has no synergic effect with DAA therapy in HCV-infected patients. However, among patients who achieved an SVR for HCV, some patients (48%) did not regress after SVR, and some (6%) even worsened, with an increased risk for hepatocellular carcinoma [19]. Therefore, further clinical studies are required to evaluate the role of vitamin D in hepatic fibrogenesis and possible therapeutic use of supplementation of vitamin D in patients after the SVR.

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Author Contributions

HW.C. and JC.L. drafted the article. HW.C., HH.L., YL.S., TY.H., and JC.L. recruited the patients, analyzed and interpreted the data. TY.H. gave a critical advice. JC.L. edited the article and approved the final version to be published. All authors read and approved the final manuscript.

Competing Interests

There is no conflict of interest to disclose.

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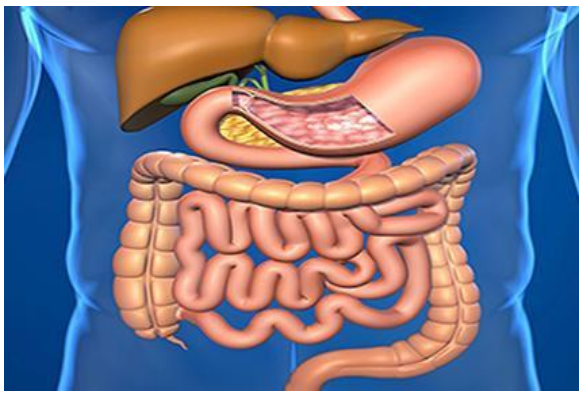

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