

Occult Hepatitis C Infection Should Be More Noticed With New Treatment Strategies

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1. Hepatitis C Virus Infection, a Global Concern

Hepatitis C Virus (HCV), as the only member of genus Hepacivirus within the family of Flaviviridae, is the major worldwide health concern. Diagnosis of HCV infection is based on finding antibodies against the virus (HCV-antibodies) or HCV-RNA in the serum (1). It is known that some of the recently infected patients can recover from the acute infection. A meta-analysis of almost 700 patients with acute HCV-infection showed that the range of spontaneous viral clearance is about 26% (95% confidence interval 22% - 29%) (2). However, the remaining patients can develop Chronic Hepatitis C (CHC) infection that affects about 3% of world population, related to more than 170 million people all over the world. Chronic hepatitis C can lead to liver fibrosis and cirrhosis and finally Hepatocellular Carcinoma (HCC) in about 20% of cases. It is estimated that about 500000 deaths per year is related to CHC (3). On the other hand, in the acute phase of HCV infection, some patients stay unrecognized. These individuals can make transmission of HCV to other people by some high-risk behaviors like IV drug abuse, organ donation and blood transfusion (4). Now think about a condition that CHC cannot be diagnosed with the mentioned routine diagnostic tests and imagine about dimensions of this condition on the health status of society.

2. Occult Hepatitis C Virus Infection and Its Clinical Significance

About eleven years ago a new type of CHC infection, Occult Hepatitis C Infection (OCI), was introduced. It means finding of HCV-RNA in the hepatocytes in the absence of serum HCV-RNA that is checked by aforementioned usual tests (5). The most precise method for diagnosis of OCI is checking the presence of HCV-RNA in the liver cells by liver biopsy. Occult hepatitis C infection seems to be milder

than CHC. However, the literature has some evidences that show it can lead to liver cirrhosis and ultimately HCC (6). On the other hand, OCI has been reported in some high-risk population groups like hemodialysis and kidney transplanted patients, cryptogenic liver disease, and immunodeficient patients. Furthermore, some data suggest existence of OCI among healthy subject without liver disease and even spouse and family members of OCI infected patients. Hence, using of an alternative diagnostic method, instead of invasive procedure of liver biopsy seems to be reasonable. These suggested alternative methods are checking HCV-RNA in ultracentrifuged serum and in peripheral blood mononuclear cells (PBMCs) that can lead to diagnosis of about 57% and 61% of OCI infected patients, respectively. Also, it is said that using of both methods can help to find about 91% of these patients (7, 8). Studies showed that HCV genotypes 1 through 4 are involved in the OCI. This may indicate that OCI is a probable worldwide issue. More prevalence studies are still needed to investigate this topic (1, 9).

3. New Treatment Regimens and Occult Hepatitis C Infection

Recently, recommended treatment regimens for HCV infection have been led to a revolution in its treatment. Among them introducing Sofosbuvir, a nucleotide analogue inhibitor, opened new horizons for HCV treatment. (10) Adding Sofosbuvir to the peg-interferon pulls ribavirin regimen has showed an effective and safe result for HCV treatment (11). In addition, it is reported that combination of sofosbuvir with ledipasvir can result in high rate of Sustained Virological Response (SVR) among both treatment-naïve and treatment-experienced patients infected with genotype 1-HCV (12, 13). This suggests a successful noninterferon-based therapy for HCV.

Because of OCI related complications, its treatment

seems necessary. On the other hand, some data showed that eradication of OCI cannot be achieved in all patients. However, data regarding OCI treatment are still very limited (14). To the best of our knowledge, there are two studies about this important issue and both of them recommended that interferon-based antiviral therapy can be useful in OCI treatment (15, 16).

4. Conclusions

We address important issues here and they should be considered in future studies. The first point is related to the effect of new treatment regimens on the patients with OCI and the second point is related to remaining the HCV infection as OCI after therapy with new regimens. Some data reported that spontaneous relapse due to OCI should be considered even after existence of 24 weeks of SVR (17). Perhaps new treatment regimens kill this 11 year-old kid of HCV infection forever but HCV-RNA can persist in immune cells and liver tissue (14) and therefore as a reason for relapse, we recommend that some original studies be performed to evaluate the effect of recently suggested treatment on the OCI. On the other hand, we probably need some studies that investigate the existence of HCV-RNA in BMCs and in liver cells, after successful treatment of HCV-infected patients with new regimens.

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