New globally faces of hepatitis B and C in the world

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Introduction

Worldwide, infections with hepatitis B virus (HBV) and hepatitis C virus (HCV) have become a major cause of chronic hepatitis, cirrhosis and hepatocellular carcinoma (HCC) and the major global problems for public health in the world and Iran (1-3). HBV infection is the main cause of chronic liver disease in Iran (4) and the seroprevalence of HBV infection in Iran has been decreased during the last two decades (5). The main risk factor for HBV transmission was related to maternal-to-infantile transmission and the infantile vaccination with high coverage is the main cause for changes in epidemiology of HBV infection. But today, we have more risk factors for transmission in adulthood. The community contacts more in adolescence and the health policy makers should attend more for control of HBV infection. People awareness, risk factors modifications, harm reduction programmes in young addicted persons, vaccination against HBV in adults should be consider for control of HBV infection in future. We have less new cases, but we will have more cirrhotic cases and we need to consider the best therapy for prevention of HBV infection to end-stage phases.

Therapy of HBV infection in which phase and which drugs are the debate. The goal of therapy in chronic hepatitis B (CHB) patients is sustained suppression of HBV viremia and decrease progression of liver disease to cirrhosis and HCC with the ultimate goal of improving survival. This can be pursued by maintaining constant inhibition of viral replication through a long term treatment with nucleos(t)ide analogs or by inducing, through the combined antiviral and immunomodulatory effects of interferon, a sustained immune response (6). Standard interferon is the oldest approved drug in therapy of HBV infection, but it has a limited response rate. Recently new published data have shown the better response with pegylated interferon in therapy of chronic HBV infection (7, 8). PEG-IFNα-2a has been licensed for the treatment of both HBeAg-positive and HBeAg-negative chronic HBV as a 48-week course, given by subcutaneous injection once weekly in a dosage of 180 mg.

The main side effects of therapy with nucleos(t)ide analogs such as lamivudine, adefovir and entecavir, is emergence of resistance (9, 10). These events will decrease benefit of therapy with anti-viral agents.

HBs Ag level in prediction of therapy response

The main question was and is regarding how and when we can conclude the therapy in HBV
infection is effective and we should continue or it is ineffective and we should discontinue it. During recent years serum HBsAg is hypothesized to be a marker for immunological response to therapy, independent of virological response as measured using HBV DNA levels, because of its correlation with intrahepatic HBV covalently closed circular (ccc) DNA, the main replicative template of HBV (11). HBsAg levels appear to differentiate patients in the inactive carrier state from those with active disease or from inactive carriers with a high probability of subsequent relapse. Furthermore, recent studies have shown that on-treatment HBsAg levels are predictive of a durable off-treatment response to peginterferon (PEG-IFN), and can accurately identify non-responders early during therapy, both in HBeAg-positive, and HBeAg-negative patients. Among those who underwent HBsAg loss within 6 years of follow-up, serum HBsAg levels were a better predictor than HBV DNA levels. Low serum levels of HBsAg, alone or in combination with HBV DNA levels, 1 year after HBeAg seroconversion can predict HBsAg loss in patients with HBV infection (12). Currently, multiple diagnostic assays are available for quantification of HBsAg. That we should use the validate method for diagnosis.

HCV Infection and the epidemiological and treatments views

HCV can spread parenterally through transfusion or contact with infected blood and its products. The hemophilia, thalassemia and hemodialysis patients, intravenous drug abusers and health care workers are at higher risk for HCV infection (12). Fortunately after screening the blood for HCV infection in 1990 in the world and in 1996 in Iran, the burden of infection has changed significantly (13, 14). But it is expected to increase in mortality over next decade and for the need of liver transplantation in the future and the occurrence of end-stage liver disease caused by HCV is estimated to peak around 2020 (15, 16). Pegylated Interferon and ribavirin combination therapy has been accepted as the standard treatment regimen for hepatitis C patients; however, but less than 50% of patients infected with HCV genotype 1 achieve a sustained virological response (SVR) (17, 18). The rates of SVR among patients infected with HCV genotype 1 range from 25% to 42% in different studies and different ethnicities (19,20). Despite these findings, the development of new regimens is required to increase the efficacy and safety of treatment options for HCV-infected patients, especially those infected with genotype 1, which is recognized as an HCV strain against which it is difficult to elicit a sustained response. Boceprevir and Telaprevir have recently been approved by FDA, and this appears to have opened up a new treatment options for patients infected with HCV genotype 1. The main problems are cost and chance of resistant of HCV to new drugs that limit the routine using of these new drugs in general practice. Response-guided therapy is a model for treating chronic hepatitis C infection in which treatment decisions are based on how rapidly HCV infection responds to therapy. With response-guided therapy, patients who rapidly clear virus from their bloodstream (after 4 weeks of therapy) are eligible to receive a shorter duration of therapy, while slower responders or partial responders receive extended durations of therapy. Today we have more resistant and non-responders case in HCV infection. The discovery of new drugs should be more rapid for solving this conflict.

Recently IL28B is recognized as a predictor of treatment response in hepatitis C patients and is associated with improved early viral kinetics and a greater likelihood of RVR; a genetic polymorphism rs12979860 is highly associated with SVR among naïve subjects as well (21, 22). It seems that in future the role of genetics factors in guidelines of HCV management will be more
emphasized. Among patients with HCV genotype 1 infection, those with genotype C/C infection have a greater chance of SVR than patients with genotype C/T and T/T. However, patients with C/T and T/T genotypes benefit more from a regimen that includes Boceprevir and Telaprevir, and the rate of SVR is significantly higher than in the case of a regimen them.

There is only limited publications regarding the long-term outcome of HCV infected patients with sustained virologic response (SVR) after therapy. There are few long-term studies about evaluation of outcomes of chronic hepatitis C patients who were treated with peg-interferon alfa-2a plus ribavirin in (23, 24). Giannini et.al, in 2010, conducted a large cohort study that evaluate SVR to pegylated IFN combination with ribavirin in chronic hepatitis C and demonstrated SVR prolonged in 99% of patients (23). Our experiences showed similar results in Iran (in press). Cirrhosis can develop among cirrhotic patients who have had a SVR (25) and we should integrate the surveillance system for finding HCC in this high risk group.

IFN-α not only has antiviral activities with clearance or suppression of HBV and HCV, but also possesses anti-tumor properties including antiproliferative, antiangiogenic, and immunomodulatory effects and in SVR cases the risk of HCC decreases significantly but it can occur in some patients and needs to follow up (17).

Comments

It is important to identify and address risk factors for acquiring HBV and HCV the new facilities for diagnosis and therapy of patients should be available and the insurance companies should cover the costs. These include the assessment of genetic factors when treating HCV.

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