Treatment Update of Chronic Hepatitis B

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ABSTRACT

Hepatitis B virus (HBV) infection is a global health problem and causes a wide spectrum of clinical manifestations, ranging from acute or fulminant hepatitis to various forms of chronic liver disease, including inactive carrier state, chronic hepatitis, cirrhosis and hepatocellular carcinoma (HCC). Early seroconversion from HBeAg to the corresponding antibody (anti-HBe) generally indicates a favorable outcome, because it is usually associated with the cessation of virus replication and non-progressive liver disease. On the contrary, late or no HBeAg seroconversion after multiple hepatitis flares may accelerate the progression of chronic hepatitis to cirrhosis, and therefore, has a poor clinical outcome. Other factors associated with increased risk of liver disease progression include male gender, older age, presence of cirrhosis, persistence of ALT elevations, co-infection with HCV or HDV, family history of HCC and viral factors such as persistently high HBV DNA level, genotype C infection, basal core promoter mutation and pre-S deletion.

Hepatitis B is not only a preventable but also now a treatable disease, 5 anti-viral agents have been approved for the treatment of chronic hepatitis B: standard interferon (IFN) alfa, lamivudine, adefovir dipivoxil, pegylated interferon (peginterferon) alfa-2a and entecavir. Standard IFN monotherapy has a narrow range of efficacy, should be administered subcutaneously and is commonly associated with adverse effects. Lamivudine is cheaper and well tolerated, but the virologic response may not be durable and prolonged lamivudine treatment is commonly associated with the emergence of drug-resistant mutants. Adefovir dipivoxil is potent but with nephrotoxicity at higher doses. Entecavir is active against both lamivudine- and adefovir dipivoxil-

resistant HBV, however, its long-term efficacy remains to be evaluated. Peginterferon alfa-2a is shown to be superior to conventional IFN and lamivudine in the treatment of both HBeAg-positive and -negative chronic hepatitis B. However, peginterferon alfa-2a in combination with lamivudine does not improve the results at the end of follow-up.

Ideally, a treatment algorithm for chronic hepatitis B tailored to host (immune status and genetic polymorphisms), virus (HBV DNA level, HBeAg status, genotype, and precore/basal core promoter mutants) and liver disease (hepatitis activity and fibrosis stage) is eagerly awaited. These safe, easy to administer, and affordable ideal treatments may hopefully be available and widely distributed in the next one to two decades. Along with universal hepatitis B vaccination, the global eradication of HBV infection is therefore possible by the first half of 21st century.