

Treatment of hepatitis B and C

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Summary – Hepatitis B

Hepatitis B is caused by a hepadnavirus, which can cause acute and chronic hepatitis. The majority of patients are able to spontaneously clear infection but less than 10% are unable to eliminate the virus. Worldwide 2 billion people are infected, with 350 million suffering from chronic HBV infection. Transmission risk factors are blood-blood contacts (transfusions, needle sharing), sexual contacts or mother to child transmission. Newer data has clearly demonstrated a correlation between progression to cirrhosis or hepatocellular carcinoma (HCC) in hepatitis B-infected persons and the level of circulating virus. Indeed the risk for cirrhosis increases significantly with increasing HBV-DNA levels and is independent of hepatitis B e-antigen status and serum alanine transaminases level. Therefore, the long-term goals of therapy for chronic hepatitis B are to reduce serum HBV DNA to low or undetectable levels and ultimately reduce or prevent the development of cirrhosis and HCC. Currently seven drugs are available for the treatment of chronic hepatitis B: adefovir, entecavir, lamivudine, peginterferon alfa-2a, peginterferon alfa-2b, telbivudine, and tenofovir. Treatment with peginterferon remains an option particularly in genotype A patients with low HBV DNA levels and elevated liver enzymes where it still is regarded as the best therapy to achieve HBsAg clearance. When using an oral agent, a major focus of management is the selection of a drug with high potency and low rate of resistance, and active on-treatment management to optimize therapy. Preventing the sequelae of antiviral drug resistance and appropriate management when resistance is initially detected is also a major focus of current management. The addition of an antiviral agent that is not cross-resistant is critical to restore suppression of viral replication. Newer agents and modified treatment strategies, especially using combination therapy, holds promise to optimize the management of patient with chronic hepatitis B by achieving the high potency and the lowest rate of resistance.

Summary – Hepatitis C

While approximately 85% of patients with asymptomatic acute HCV develop a chronic course of disease, in patients with symptomatic acute HCV spontaneous elimination of the virus has been described in up to 50%. Chronic hepatitis C is affecting an estimated 170 million people worldwide. Chronic HCV is clearly linked to the development of cirrhosis, HCC, and end-stage liver disease requiring liver transplantation. The consequences of HCV infection constitute a significant disease burden and demonstrate the need for effective medical care. Treatment of chronic HCV is aimed at slowing disease progression, preventing complications of cirrhosis, reducing the risk of HCC, and treating extrahepatic complications of the virus. As part of a comprehensive approach to HCV management, antiviral therapy with peginterferon combined with ribavirin is the current standard of care. Antiviral therapy should be provided to those individuals who meet criteria for treatment (positive HCV RNA, >F1 fibrosis and elevated liver enzymes) and who are at greatest risk for progressive liver disease. Current international guidelines state that 48 or 24 weeks of treatment should be recommended in accordance with HCV genotype; i.e. 48 weeks for genotypes 1 and 4, and 24 weeks for 2 and 3. Cure of HCV infection defined as sustained virological response (SVR: negative HCV PCR in an ultrasensitive assay 6 months after stopping PEG-IFN/ribavirin therapy) can overall be achieved in almost 60% of treated patients. Important predictive response factors are HCV genotype, level of HCV viremia and time to HCV undetectability. More recently, individualized treatment schedules have been introduced allowing shorter treatment schedules in patients achieving fast and persistent viral clearance. Current antiviral regimens however, are associated with significant adverse effects that can lead to noncompliance, dose reduction, and treatment discontinuation. To overcome these barriers and to address

these issues, it has become crucial to facilitate the setup of a multidisciplinary team who can respond to and provide HCV-specific care and treatment.

Recommended reading

Buster EH, Flink HJ, Cakaloglu Y et al. Sustained HBeAg and HBsAg Loss After Long-term Follow-up of HBeAg-Positive Patients Treated With Peginterferon alpha-2b. *Gastroenterology*. 2008 May 15. [Epub ahead of print]

Cornberg M, Protzer U, Dollinger MM et al. Prophylaxis, diagnosis and therapy of hepatitis B virus (HBV) infection: the German guidelines for the management of HBV infection. *Z Gastroenterol*. 2007 Dec;45:1281-328.

Strader DB, Wright T, Thomas DL, Seeff LB; American Association for the Study of Liver Diseases. Diagnosis, management, and treatment of hepatitis C. *Hepatology*. 2004 Apr;39(4):1147-71.

Ferenci P, Laferl H, Scherzer TM et al. Peginterferon Alfa-2a and Ribavirin for 24 Weeks in Hepatitis C Type 1 and 4 Patients With Rapid Virological Response *Gastroenterology*. 2008 May 27. [Epub ahead of print]

Useful website

The American Association for the Study of Liver Diseases (www.aasld.org)