Introduction

Chronic hepatitis C virus (HCV) infection affects approximately 300 million people worldwide and currently is the most frequent cause for liver transplantation in the United States and Europe ***(Lauer and Walker, 2001)***. Natural history studies suggest that up to 20% of chronic HCV patients develop liver cirrhosis after 20 years of infection. Moreover, the incidence of chronic liver failure is expected to increase over the next 10 years as a result of the "silent epidemic" of HCV infection ***(Seeff, 2002)***.

The World Health Organization (WHO) has declared hepatitis C a global health problem, with approximately 3% of the world's population (roughly 170-200 million people) infected with HCV.

In Egypt, the situation is quite worse. The national prevalence rate of HCV antibody positivity has been estimated to be between 10-13% (1). Since 30-40% of individuals clear the infection shortly after exposure based on national studies and village studies in Egypt, the estimated adjusted national prevalence rate of chronic hepatitis C infection is 7.8% or 5.3 million people in 2004 ***(American Journal of Gastroenterology 2006)***.

Only one third of these individuals (1.75 million) were estimated to have chronic liver disease (elevated ALT) and, furthermore, among these one third (577,000 people) were suffering from advanced liver disease. Chronic HCV is the main cause of liver cirrhosis and liver cancer in Egypt and, indeed, one of the top five leading causes of death. Interestingly, genotype 4 represents over 90% of cases in Egypt ***(Mohamed MK 2004)***

Introduction

The main aim of treating patients with chronic hepatitis C virus infection is to prevent progressive hepatic fibrosis by eradicating viral RNA. Sustained virological clearance is defined as the absence of hepatitis C virus RNA as judged by a sensitive polymerase chain reaction (PCR) assay 24 weeks after the end of treatment. The potential long term benefits of sustained virological clearance include normalization of serum aminotransferase levels, improvement in hepatic necroinflammation and fibrosis, improvement in health related quality of life measures, survival benefits, and reduction in risk of developing hepatocellular carcinoma ***(Patel K et al 2006).***

Although all patients should be considered for treatment, balancing the risks of progressive disease with potential side effects of current therapy remains a major challenge for healthcare providers. Thus patients with mild disease activity should be given the option of deferring therapy ***(Patel K et al 2006).***

The current standard of care for treating previously untreated patients with chronic hepatitis C virus infection is combination pegylated interferon alpha by subcutaneous injection once weekly and oral ribavirin daily .Combination of pegylated interferon alfa and ribavirin therapy can achieve a sustained virological response in 54%-56% of patients, including 42%-46% of patients with genotype 1 infection and about 80% of those with genotype 2 or 3 infection ***(Patel K et al 2006).***

Several factors are predictive of favorable virological responses to standard antiviral therapy, a combination of pegylated interferon and ribavirin. Viral genotype and baseline hepatitis C virus RNA levels seem to be the most important predictors of response ***(Patel K et al 2006)***.

Introduction

The recommended treatment for patients with HCV genotypes 1 and 4 is pegylated interferon plus ribavirin for 48 weeks ***(Freid et al., 2002)***. Such treatment has yielded overall sustained viral response (SVR) rates of 54-63% in randomized controlled phase III clinical trials ***(Hadziyannis et al., 2004 and Zeuzem et al., 2005)***. However, treatment responses are not uniform across all populations, and are dependent on various viral and host factors ***(Dienstag and McHutchison, 2006)***.

Treatment of patients with chronic hepatitis C virus (HCV) infection remains suboptimal, with the current pegylated interferon (PEG-IFN) and ribavirin combination therapy providing sustained viral response (SVR) rates of 54 - 63%. The aim of this study is to identify clinical, laboratory and histological findings that can predict non-response to this treatment ***(Nachnani et al., 2007)***.

The aim of treatment in chronic hepatitis C is to achieve a sustained virologic response (SVR) defined as undetectable HCV RNA with a sensitive PCR assay (<50 IU/ml) 24 weeks after the end of antiviral therapy. In patients who achieved an SVR following standard interferon (IFN)-based antiviral therapy, virological relapse after 5 years of follow-up was observed in 2– 4% only, and no relapse was reported after 5–10 years ***(Veldt et al., 2004)***. Moreover, the 5-year durability of an SVR was in excess of 99% in patients treated with pegylated (PEG) IFN. A number of host and viral factors have been identified that influence treatment outcomes ***(Swain et al., 2007 and Lindsay et al., 2008)***.

Introduction

Treatment predictors are important tools for the management of therapy in patients with C virus (HCV) infection. For the current standard treatment with pegylated interferon alfa and ribavirin in patients with chronic hepatitis C, infection with HCV genotypes 2 and 3, baseline viral load below 400,000–800,000 IU/ml, Asian and Caucasian ethnicity, younger age, low GGT levels, absence of advanced fibrosis/cirrhosis, and absence of steatosis in the liver have been identified as independent pretreatment predictors of a sustained virologic response. After initiation of treatment, initial viral decline with undetectable HCV-RNA at week 4 of therapy (RVR) is the best predictor of sustained virologic response independent of HCV genotype ***(Kau et al., 2008)***.