

Treatment of Chronic Hepatitis C

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As hepatitis C virus (HCV) infection is a major cause of liver cirrhosis (LC) and hepatocellular carcinoma (HCC), eradication of HCV in patients with chronic hepatitis C contributes to decrease incidence of LC/HCC and death rates from LC/HCC. Thus, the goal of treatment of chronic hepatitis C is suppression of LC/HCC development. There are two ways of treatment of chronic hepatitis C. One is antiviral treatment and the other is anti-inflammatory treatment. Antiviral treatment is most desirable.

Antiviral Treatment:

In treatment of chronic hepatitis C, interferon (IFN) α , natural and recombinant, and IFN β have been introduced since 1990. When first approved, IFNs were administered for 6 months but achieved a sustained virologic response (SVR) was below 10% in patients with genotype 1 and high HCV RNA load infection and 30% in patients with non-genotype 1 and low HCV RNA load infection. Combination therapy in addition to the IFN of daily ribavirin (an oral guanosine nucleotide) increased SVR rate up to 40%. Ribavirin enhances the efficacy of IFN by reducing the virologic relapse after stopping IFN therapy.

Recently for the treatment of chronic hepatitis C, pegylated IFN α s (PEG-IFN α) are used instead of standard IFNs. PEG-IFN α is a long-acting IFN bound to polyethylene glycol (PEG), and has elimination times up to sevenfold longer than standard IFNs. Once a week PEG-IFN monotherapy is twice effective when compared with standard IFN monotherapy. However, recent clinical trials showed that the combination therapy of PEG-IFN and ribavirin is more effective. In Japanese comparative trial for PEG-IFN α 2b plus ribavirin (48 weeks) and standard IFN α 2b plus ribavirin (48 weeks) for chronic hepatitis C patients with HCV genotype 1 and high HCV RNA load, SVR was 47.6% (121/254) and 44.8% (113/252), respectively. Now, the standard treatment of chronic hepatitis C is PEG-IFN α combined with ribavirin worldwide. This combination therapy is applied for patients with normal ALT level.

Antiviral treatment for chronic hepatitis C started in 1992 in Japan. Standard IFN monotherapy using natural alpha interferon, beta interferon, recombinant interferon alpha 2a and 2b has been performed by 2001. Several researchers reported that during this period SVR was about 30% though different SVR rate by genotypes and viral load. In addition, they reported that HCC occurrence rate was 2% in SVR patients and 10% in non-SVR patients and 17% in non-treated patients. This indicated that the reduction of incidence of HCC was more convincingly shown in patients with SVR as compared with no responders and no treated patients. Between 1992 and 2001, approximately 300,000 patients with chronic hepatitis C had received interferon monotherapy.

Thus, it was estimated that about 100,000 patients escaped from occurrence of HCC. This fact will be reflected in the reduction of the numbers of deaths and the death rate of HCC in future. In fact, according to the vital statistics of Japan, the death rate showed decreasing tendency from 2003. The combination therapy of interferon and ribavirin and combination therapy of PEG-IFN and ribavirin has been introduced since 2001 and 2004, respectively. These treatments showed higher SVR rate closed to 60% or more in all patients with chronic hepatitis C. This indicated that further improvement in prognosis should be expected and occurrence of HCC should be decreased.

Anti-inflammatory treatment

There are many treatments in anti-inflammatory treatment of chronic hepatitis C such as glycyrrhizin and ursodeoxycholic acid. Recently, phlebotomy and low iron diet have been introduced for patients with chronic hepatitis C who showed resistant for antiviral treatment. These treatments indicated biochemical and histological improvement by release from of oxidative stress against hepatocytes.

In conclusion, antiviral therapy by interferon and rivabirin clearly suppress HCC.