



PIC QUESTION OF THE WEEK: 11/17/08

Q: What is the importance of genotype in relation to the management of hepatitis C?

A: The hepatitis C virus (HCV) was discovered in 1989 and is one of the most significant causes of acute and chronic liver disease. This single-stranded RNA virus replicates extensively in the liver and infects almost 180 million people worldwide and approximately 4 million Americans. It is the most common cause of chronic liver disease, cirrhosis, and liver neoplasms in the Western world. Although it can be transferred through sexual contact or from mother to unborn child, the most common mode of transmission is by needle-sharing during intravenous drug use. The disease is often silent, and only a portion of infected patients experience symptoms of fatigue, dark urine, loss of appetite, abdominal pain, nausea, etc. Jaundice may appear in only about one third of those with acute infection. There are two types of hepatitis C infection: acute (resolves spontaneously) and chronic (defined as lasting for more than 6 months and not resolving without intervention). Approximately 55-85% of patients develop chronic infection and become candidates for drug therapy. Disease progression and the response to treatment are dependent on the particular HCV genotype possessed by the patient. There are six genotypes of HCV with each differing in nucleotide sequence by 30-50%. In the United States, the HCV type 1 genotype accounts for approximately 75% of cases. Genotypes 2 and 3 are causative for 15% and 7% of the cases, respectively. African Americans are more commonly affected by genotype 1 and their response to treatment is generally poorer than that of other populations. Factors other than genotype are, however, considered responsible for their decreased response to therapy. Pegylated versions (alpha-2a; Pegasys and alpha-2b; Peg-Intron) of interferon increase its half-life and permit once weekly administration. In most clinical trials, response rates to standard and pegylated interferon regimens appear to be greater in patients with genotypes 2 or 3 than those with genotype 1. Another study concluded that patients with HCV genotypes 2 or 3 could also be successfully treated with *lower doses* of ribavirin (800 mg vs 1 g to 1.2 g daily) than those with genotype 1. Patients with genotypes 4, 5, and 6 generally receive the same course of therapy as patients with genotype 1. Today, patients with genotype 1 should receive ribavirin 1 g (body weight \leq 75 kg) or 1.2 g (body weight $>$ 75 kg) daily combined with interferon alpha-2a (180 μ g) or alpha-2b (1.5 μ g/kg) weekly for 48 weeks. Patients with genotype 2 or 3 can receive a 24-week course of therapy using the same regimen of interferon, but reduce the dose of ribavirin to 800 mg daily. In conclusion, the specific genotype of the hepatitis C virus plays an important role in patient response to therapy as well as selection of the appropriate dosage regimen.

References:

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