Duration and Dose of Antiviral Treatment for Chronic Hepatitis C

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The full report is titled "Peginterferon-α2a and Ribavirin Combination Therapy in Chronic Hepatitis C. A Randomized Study of Treatment Duration and Ribavirin Dose." It is in the 2 March 2004 issue of *Annals of Internal Medicine* (volume 140, pages 346-355). The authors are S.J. Hadziyannis, H. Sette Jr., T.R. Morgan, V. Balan, M. Diago, P. Marcellin, G. Ramadori, H. Bodenheimer Jr., D. Bernstein, M. Rizzetto, S. Zeuzem, P.J. Pockros, A. Lin, and A.M. Ackrill, for the PEGASYS International Study Group.

What is the problem and what is known about it so far?

Hepatitis C is inflammation of the liver caused by hepatitis C virus (HCV). Hepatitis C virus has at least 6 distinct genetic makeups (genotypes). The type is important because it affects the way that the virus reacts to drug treatments. Genotype 1 is the most common and the most resistant. Hepatitis C virus is transmitted primarily by blood-to-blood contact; sexual transmission appears to be uncommon. Risk factors include body piercing, intravenous drug use, needlestick accidents, and blood transfusions (before hepatitis screening in 1992). Most people cannot get rid of HCV on their own. More than 80% keep the virus in their blood for longer than 6 months and get chronic hepatitis C.

Chronic hepatitis C progresses slowly over 10 to 30 years. It causes inflammation and scarring of the liver and, if untreated, can lead to liver failure and liver cancer. Treatment clears HCV from the blood and prevents further liver damage. Doctors treat chronic hepatitis C with powerful antiviral drugs that have many side effects. Recently, they found that combining a long-acting immunity-boosting protein (pegylated interferon) with another antiviral drug (ribavirin) was very effective in ridding the body of HCV. However, they did not determine the optimal duration or dose of this therapy.

Why did the researchers do this particular study?

To compare short- with long-term pegylated interferon therapy combined with either low or standard doses of ribavirin in patients with chronic hepatitis C.

Who was studied?

1311 patients with chronic hepatitis C from 99 international centers.

How was the study done?

Researchers randomly assigned patients to 1 of 4 groups. The groups received either pegylated interferon-α2a for 6 months or 1 year plus either low-dose (800 mg) or standard-dose (1000 to 1200 mg) ribavirin. Pegylated interferon-α2a was injected under the skin weekly. Ribavirin tablets were taken by mouth daily. The researchers and the patients did not know who got which dose of ribavirin. The researchers measured levels of HCV in the blood regularly during treatment and at 3 to 6 months after treatment. They routinely did blood tests, physical examinations, and interviews to check for side effects. They then assessed which treatment regimen got rid of the virus most often (undetectable levels of HCV at the end of treatment and during follow-up) and whether HCV genotype affected treatment response.

What did the researchers find?

In patients with HCV genotype 1, long-term treatment for 1 year with pegylated interferon-α2a plus standard doses of ribavirin more often rid the body of HCV than did short-term treatment or low-dose ribavirin. Longer treatment duration and higher ribavirin dose were not necessary to rid the body of virus in patients with genotypes 2 or 3. Severe side effects and stopping treatment early were more common with patients receiving 1-year treatment than in those receiving 6-month treatment.

What were the limitations of the study?

Study participants had abnormal liver enzyme levels and no other serious illnesses. We do not know whether patients with normal liver enzyme levels or other coexisting conditions, such as HIV infection, will respond similarly.

What are the implications of the study?

Patients with chronic hepatitis and HCV genotype 1 require higher ribavirin doses and longer-term combination treatment than do those with genotypes 2 or 3.