Adding ribavirin to interferon α-2b for chronic hepatitis C infection increased virological response and nausea


Question
In patients with chronic hepatitis C virus (HCV) infection, is the addition of ribavirin to interferon α-2b effective and safe?

Design
48 week randomised, double blind, placebo controlled trial.

Setting
5 university hospitals in Sweden.

Patients
100 patients (mean age 40 y, 62% men) who had increased aminotransferase concentrations for ≥6 months, serum antibodies to HCV found by polymerase chain reaction (PCR), and a diagnosis of chronic hepatitis on a liver biopsy sample in the previous 12 months. Exclusion criteria included previous treatment with interferon α-2b or ribavirin, decompensated cirrhosis, autoimmune hepatitis, chronic hepatitis B infection, HIV infection, current intravenous drug use, liver disease related to drug use, or pregnancy.

Intervention
Patients were allocated to combination therapy (subcutaneous interferon α-2b, 3 MU three times/wk, plus ribavirin, 1000 mg daily in 2 divided doses) (n=50) or monotherapy (subcutaneous interferon α-2b plus a matching placebo) (n=50) for 24 weeks. Patients who weighed ≥75 kg received 1200 mg of ribavirin. 90% of patients completed 24 weeks of treatment.

Main outcome measures
Virological sustained response (absence of HCV RNA on PCR at weeks 24 and 48). Secondary outcomes were biochemical and histological responses and safety outcomes.

Commentary
Treatment with α interferon is widely recommended for chronic hepatitis C.1 However, the clinically relevant outcome of sustained response—that is, no HCV RNA in serum by PCR and normalisation of alanine aminotransferase (ALT) persisting after treatment for more than 6 months—is found in only about 15% of patients. Lower response rates are observed in patients with genotype 1, those with a high viral load, or cirrhosis at start of therapy.2 Ribavirin is an oral nucleoside analogue that lowers serum ALT in patients with genotype 1b.3 However, the number of patients in the study was too small to allow subgroup analysis with confidence.

The potential clinical impact of the Swedish findings is that combination therapy with interferon ribavirin will be regarded as the treatment of choice for patients with chronic hepatitis C and an indication for antiviral treatment. However, the greater number of side effects and the considerably higher cost of combination therapy compared with interferon monotherapy will mean that this treatment will probably not be universally applied. Interferon monotherapy will suffice for 10–20% of patients, and additional subgroup analysis is needed to identify those individuals. Furthermore, many patients do not respond to combination treatment, which should be suspended if HCV RNA is detected after 12 weeks. Such a cost effective strategy, coupled with the now appreciable chance to eradicate the virus as suggested by long term follow up studies,4 should widen the application of treatment in chronic hepatitis C.

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