CLINICAL UPDATE

Early treatment of acute hepatitis C infection may lead to cure

Jaeckel E, Cornberg M, Wedemeyer H, Santantonio T, Mayer J, Zankel M, et al. Treatment of acute hepatitis C with interferon alfa-2b. *N Engl J Med 2001* (early release). Available: content.nejm.org/cgi/reprint/NEJMoa011232v1.pdf (accessed 2001 Oct 26).

Background: Infection with hepatitis C virus (HCV) is common, affecting about 1% of the Canadian population[1] and an estimated 170 million people worldwide.[2] Infection occurs through the transmission of body fluids, usually because of injection drug use, needle-stick injuries, other medical misadventures or, rarely, sexual contact. About 70% of those infected develop chronic infection and 20% of them will develop cirrhosis.[2] Hepatitis C is a serious infection and is the single most common reason for liver transplantation.[1]

Although peginterferon alfa-2b (an interferon with attached polyethylene glycol moiety and extended half-life) in combination with ribavirin appears to be an effective treatment for chronic HCV infection, only about 50% of patients appear to benefit.[3] These researchers wondered whether therapy would be more effective if treatment was begun in the early course of illness as opposed to later when the infection became chronic.

Question: Does administration of interferon alfa-2b in the acute phase of HCV infection prevent progression to chronic infection?

Design: In a study conducted throughout Germany, investigators identified 44 patients who tested positive for HCV RNA (by polymerase-chain-reaction assay), had elevated serum alanine aminotransferase levels and had been diagnosed with acute HCV infection (i.e., if 1 or more of the following criteria was met: known or suspected exposure to HCV within the preceding 4 months, documented seroconversion with a known previous negative HCV test, or a serum alanine aminotransferase level of more than 350 U/L, with a documented normal level during the year before infection). There were numerous exclusion criteria, including other causes of hepatitis, HIV infection or contraindications to interferon therapy, such as a history of severe depression, neutropenia or thrombocytopenia, decompensated liver disease, seizures, decompensated thyroid disease and other autoimmune diseases. Study subjects were treated subcutaneously with 5 million U of interferon alfa-2b (a recombinant version of human interferon alpha-2b) daily for 4 weeks, and then 3 times per week for another 20 weeks. Biochemical and hematologic testing was performed regularly during treatment, at the completion of treatment and 24 weeks after treatment ceased. There was no control group.

Results: Twenty-five women and 19 men with an average age of 36 were identified and treated. Sources of HCV infection were: needle-stick injuries (14), other medical procedures (7), sexual contact (10), intravenous drug use (9) and uncertain (4). The average time from presumed infection to the signs or symptoms of the disease was 54 days (range, 15–105 d), and the average time from infection until the start of therapy was 89 days (range 30–112 d).

All 44 patients experienced rapid decreases in alanine aminotransferase levels (normalizing in 80% of patients after 24 weeks of therapy, and in the rest by the end of follow-up), and serum levels of HCV RNA became undetectable for all patients (mean time before levels were undetectable, 3.2 wk). One patient stopped treatment after 12 weeks because of hair loss and influenza-like symptoms and was lost to follow-up. After 24 weeks of follow-up, the remaining 43 patients still had undetectable levels of HCV RNA.

All patients experienced known side effects of interferon alfa-2b therapy, including thrombocytopenia (with platelet count dropping at week 4 to an average of 161×10^9/L) and leukopenia (with average count at week 4 of 3.9×10^9/L), which both reversed after therapy was completed. Except for the single patient, side effects were not severe and no dosage adjustments were needed.

Commentary: This is a carefully conducted study. Although there is no control group, the 100% success rate of treatment might now preclude, ethically, a randomized placebo-controlled clinical trial. Spontaneous remission of HCV infection appears to occur in about 30% of patients, so some of the benefit or cure attributed to interferon alfa-2b in this study would have occurred without therapy. The authors knew this and looked at their data for predictors of early response to treatment but were unable to identify any.

Practice implications: This study strongly suggests a beneficial effect from intensive therapy with interferon alfa-2b administered early in the course of HCV infection. Side effects appear minimal. Follow-up was not reported beyond the end of active therapy, but patients appeared to have levels of HCV RNA that are undetectable by current methods; presumably, they had been cured. These cure rates are substantially better than those reported for the current treatment of chronic HCV infection, which eliminates the virus in about 50% of patients.[2]

Anyone with recent-onset acute HCV infection should be informed of the potential value of therapy with interferon alfa-2b. The authors point out that more studies are needed to determine if less intensive therapy will be equally effective, and longer follow-up of treated patients is needed to ascertain cure rates. — *John Hoey, Eric Wooltorton*, CMAJ

References

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