

Medical Writers' Circle

July • 2003

a series of articles
written by medical
professionals about
the management
and treatment of
hepatitis C

David Bernstein, MD

North Shore University
Hospital, Manhasset, NY

Health Related Quality of Life and Hepatitis C

The perception of chronic hepatitis C infection is that it is an asymptomatic disease, with less than 20% of patients experiencing the non-specific symptoms associated with the disease¹, including fatigue, musculoskeletal pain, pruritus, jaundice and headache. Despite this widely held perception, several studies have documented impaired health-related quality of life (HRQL) associated with chronic hepatitis C infection.²⁻⁴

Perhaps the greater question is, "Why all this sudden interest in hepatitis C related quality of life? The simple answer is that quality of life has moved to the forefront of patient concern. Aside from efficacy, patients care most about their quality of life. Nobody wants to feel miserable and unhappy. Examples of quality of life considerations include the ability to maintain a job, the ability to maintain personal relationships with friends, spouses and children, the ability to continue to feel viable, and the ability to enjoy situations or events that previously gave pleasure. Since current therapies are not yet good enough to eradicate the hepatitis C virus in all treated patients,

factors regarding the impact of therapy on quality of life must be entertained and discussed with the patient, prior to embarking on a course of treatment.

The assessment of quality of life in the clinical setting is difficult. Because of this challenge, self-administered tools have been developed to help the health care professional estimate the effect of hepatitis C on a patient's quality of life. Examples of tools used to measure quality of life include the following: SF-12, SF-36, hepatitis quality of life questionnaire, sickness impact profile, gastrointestinal quality of life index, chronic liver disease questionnaire, the liver disease quality of life instrument and the fatigue severity scale.⁵⁻¹⁰ The most common tool used to date in patients with chronic hepatitis C is the Short Form 36 or SF-36. The SF-36 is a tool composed of 36 questions which is used to measure generic health status. The 36 questions measure 8 domain scales; physical function, role limitations—physical, vitality, general health perceptions, pain, social function, role limitations—emotional, and mental health.⁶ Domain scale scores are linearly transformed onto a scale from 0 (worst

health) to 100 (best health). Subscores assessing mental and physical health summary (MCS and PCS respectively) scores are also generated. The SF-36 has demonstrated good reliability and validity in primary care and chronic disease populations including chronic hepatitis C infection.⁶

The effects of hepatitis C virus infection on quality of life are emerging as important parameters in the evaluation of patients. Physicians have the perception that patients with hepatitis C are largely asymptomatic and that the disease seldom has an impact on patients' lives. However, studies with large numbers of patients show that hepatitis C has a negative impact on quality of life, which may help justify therapy in patients with less advanced histological disease.^{3, 4, 11, 12} Quality of life has also been shown to decrease in patients recently made aware of their hepatitis C status. The reason for this decline in quality of life seen after diagnosis, in the absence of treatment, may be in part secondary to a labeling phenomenon.¹³

A study of 642 patients confirmed that patients with hepatitis C report lower quality of life scores than healthy

control patients.⁴ Furthermore, this study demonstrated that patients who achieved a sustained viral response with interferon monotherapy experienced significant improvements in perceived wellness and functional status, translating to significant improvements in

make patient adherence to long-term therapy difficult to achieve. Poor adherence to therapy results in inferior sustained virological response rates. Examples of common side effects which negatively affect quality of life include fatigue, flu-like illness, anxiety,

but once therapy is completed. At this point, treatment may have a positive effect on quality of life. It has been previously shown that patients who have a sustained viral response to interferon alfa-2b in combination with ribavirin report an improved quality of life and

Poor virologic response rates, high side-effect profiles, and poor quality of life on conventional interferon and ribavirin therapies have led to the use of complimentary medicine in approximately 60% of patients infected with HCV. Many patients who take alternative therapies either delay or do not seek the use of conventional therapies. Despite the widespread use of these modalities, few, if any, well-designed clinical trials have been published to evaluate the efficacy of complimentary medicine in patients infected with the hepatitis C virus.¹⁹⁻²² Physicians must keep an open mind and familiarize themselves with the purported efficacy and potential toxicities of alternative medications in order to provide effective counsel to their patients. Patients must inform their physicians of all their medications, alternative or conventional.

Physicians need to focus more on the impact of chronic hepatitis C therapy on the quality of life of their patients to help maintain adherence to the therapeutic regimen, especially in the initial twelve to twenty-four weeks of treatment and in order to better understand the true impact of this disease on a patient and his/her family and environs. Failure to remain on treatment will compromise the clinical benefits of therapy, such as virological response. Failure to maintain an adequate quality of life while on therapy can lead to difficulties with interpersonal relations at home and work, depression and decreased feelings of self-value and utility. Chronic hepatitis C therapies, such as peginterferon plus ribavirin,

Perhaps the greatest challenge facing clinicians who treat patients with chronic hepatitis C virus is maintaining full-dose therapy for the appropriate

duration of time. ■



quality of life. The hepatitis quality of life questionnaire was used to evaluate patients who relapsed following interferon monotherapy and subsequently underwent treatment with interferon in combination with ribavirin. Sustained virological response was associated with improvements in vitality, social functioning, and health distress.

Hepatitis C infection has also been associated with increased fatigue, and a decreased ability to function at work, at home and in school. People with hepatitis C report less confidence in their current health and more concern about their health in the future.¹⁴

Implications of Side Effects on Response and Quality of Life

Perhaps the greatest challenge facing clinicians who treat patients with chronic hepatitis C virus is maintaining full-dose therapy for the appropriate duration of time. Pegylated interferon and ribavirin have significant side effect profiles that reduce quality of life and

depression, irritability, insomnia, mood swings, loss of libido, loss of concentration, anemia, rash, pruritus, joint pains, muscle aches and fever. All studies which have measured the impact of interferon alone or interferon plus ribavirin therapy on quality of life show a decline in quality of life during therapy. Recently, studies have shown that both therapy with pegylated interferon alfa-2a alone and pegylated interferon alfa 2a in combination with ribavirin have less of a deleterious effect on quality of life while on therapy than standard Rebetron™ therapy.^{11,15} In patients who develop anemia on anti-viral therapy, the addition of the growth factor, erythropoetin, has been shown to improve patients' quality of life on therapy, especially fatigue.¹⁶

Anti-viral therapies are associated with a decline in quality of life, which returns to baseline when therapy is terminated. Therefore, the effect of therapy on quality of life is best assessed not during therapy

have significant improvements in work functioning and productivity.¹⁴ Perillo et al. showed that pegylated interferon alfa-2a was associated with superior health related quality of life and superior work productivity during the first four weeks of therapy when compared to standard interferon alfa-2b plus ribavirin.¹⁷ For employers, this can be translated into cost savings. When patients are treated with pegylated interferon alfa-2a versus standard interferon alfa-2a, quality of life parameters such as fatigue severity scales and SF-36 scores, are statistically better.¹⁸ Sustained viral response rates correlate positively with improvements in quality of life.⁴ These improvements are seen whether the patient, on liver biopsy, has minimal disease or cirrhosis. Unfortunately, non-responders to combination interferon and ribavirin therapy are not as lucky. This group does not see any significant improvements in quality of life at the end of therapy, regardless of the therapy received.^{4,11,14}

which have fewer side effects and less impairment in health related quality of life, also have greater sustained virological response rates as compared to unmodified interferon with and without ribavirin.⁸ In addition, physicians and patients need to consider the impact of treatment on quality of life when making decisions about alternative therapies for hepatitis C treatment. ■

References

1. National Institutes of Health Consensus Development Panel Statement. Management of hepatitis C. *Hepatology* 1997;26(3Suppl 1): 2S-10S.
2. Davis GL, Balart MD, Schiff ER, Lindsay K, Bodenheimer HC, Perrillo RP, Carey W, Jacobson IM, Payne J, Dienstag JL et al. Assessing health-related quality of life in chronic hepatitis C using the sickness impact profile. *Clin Ther* 1994;16:334-343.
3. Ware JE, Bayliss MS, Mannocchia M, Davis GL, the International Hepatitis Interventional Therapy Group. Health-related quality of life in chronic hepatitis C: Impact of disease and treatment response. *Hepatology* 1999;30:550-555.
4. Bonkovsky HL, Woolley JM, the Consensus Interferon Study Group. Reduction of health-related quality of life in HCV and improvement with interferon therapy. *Hepatology* 1999;264-270.
5. Davis GL, Balart LA, Schiff ER, et al. Assessing health-related quality of life in chronic hepatitis C using the sickness impact profile. *Clin Ther.* 1994;16:334-343
6. Ware JE, Kosinski M, Keller S. *SF-36 Physical and Mental Health Summary Scores: A User's Manual*. Boston: The Health Institute, New England Medical Center, 1994
7. Younossi ZM, Boparai N, McCormick M et al. Assessment of utilities and health related quality of life in patients with chronic liver disease. *Amer J of Gastro* 2001; 96:579-583.
8. Krupp LB, LaRocca NG, Muir-Nash J et al. The fatigue severity scale. *Arch Neurol* 1989; 46:1121-1123.
9. Gralnek IM, Hays RD, Kilbourne A et al. Development and evaluation of the liver disease quality of life instrument in persons with advanced, chronic liver disease-the LDQOL 1.0. *Amer J Gastro* 2000;95:3552-3565.
10. Yacavone RF, Locke GR, Provenzale DT et al. Quality of life measurement in gastroenterology: what is available? *Amer J Gastro* 2001; 96:285-297.
11. Bernstein DE, Kleinman L, Barker CM, et al. Relationship of health related quality of life to treatment adherence and sustained response in chronic hepatitis C patients. *Hepatology.* 2002;35:704-708.
12. Foster GR, Goldin RD, Thomas HC. Chronic hepatitis C infection causes a significant reduction in quality of life in the absence of cirrhosis. *Hepatology* 1998; 27:209-212.
13. Rodger AJ, Jolley D, Thompson SC et al. the impact of hepatitis C virus on quality of life. *Hepatology* 1999;30:1299-1301.
14. McHutchison JG, Ware JE, Bayliss MS et al. The effects of interferon alfa-2b in combination with ribavirin on health related quality of life and work productivity. *J. of Hepatology* 2001; 34:1400-147.
15. Hassanein T et al. Treatment with 40KDA peginterferon alfa-2a (Pegasys) in combination with ribavirin significantly enhances quality of life compared with interferon alfa-2b plus ribavirin. *EASL* 2002. Abstract 622.
16. Afdhal N, Dieterich D, Pockros P et al. Epoetin alfa treatment of anemic hepatitis C infected patients allows for maintenance of ribavirin dose, increases hemoglobin levels and improves quality of life versus placebo: a randomized, double-blind, multicenter trial. *Hepatology* 2003;124:A714.
17. Perillo RP, Thuluvath PJ, Rothstein K et al. Improved work productivity, safety, and quality of life with pegylated interferon (40kD) alfa-2a therapy in the treatment of chronic hepatitis C. *Hepatology* 2000
18. Raseneck J, Zeuzum S, Feinman SV et al. Peginterferon alfa 2a improves HR-QOL outcomes compared with unmodified interferon alfa 2a in patients with chronic hepatitis C. *Pharmacoeconomics* 2003; 21:341-349.
19. Eisenberg DM, Davis RB, Ettner SL, et al. Trends in alternative medicine use in the United States, 1990-1997:results of a follow-up national survey. *JAMA.* 1998;280:1569-1575.
20. Flora K, Hahn M, Rosen H, et al. Milk thistle for the therapy of liver disease. *Am J Gastro.*1998;93:139-143.
21. Angulo P, Patel T, Jorgensen RA, et al. Silymarin in the treatment of patients with primary biliary cirrhosis with a suboptimal response to ursodeoxycholic acid. *Hepatology.* 2000;32:897-900.
22. Ernst E. Harmless herbs? A review of recent literature. *Am J Med.* 1998;104:170-178

A publication of the
Hepatitis C Support Project

MWC
Medical Writers' Circle

The Mission of the Hepatitis C Support Project is to offer support to those who are affected by the hepatitis C Virus (HCV) and HIV/HCV coinfection.

Support is provided broadly, through information and education, as well as access to support groups. The (Project) seeks to serve the HCV community as well as the general public.

Visit our web site at
www.hcvadvocate.org



Executive Director
Editor-in-Chief,
HCSF Publications
Alan Franciscus

Editor
Liz Highleyman

Webmaster
C.D. Mazoff, PhD

Design and Production
Paula Fener