Health-related quality of life and impact of antiviral treatment in Chinese patients with chronic hepatitis C in Taiwan

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Abstract

AIM: To evaluate health-related quality of life (HRQOL) in Chinese patients with chronic hepatitis C (CH-C), and the impact of antiviral treatment.

METHODS: Short Form 36 (SF-36) Health-related Quality of Life Questionnaires to interview CH-C patients, and age- and sex-matched control subjects at outpatient clinics of a medical center in Taiwan were used. Data were transformed to scores for comparisons of eight major SF-36 domains. We also enrolled consecutive CH-C patients who completed one course of antiviral treatment (interferon α with ribavirin), and measured the HRQOL before, at the 12th wk of treatment, at the end of treatment, and at mo 6, after stopping the treatment to evaluate the impact of antiviral treatment.

RESULTS: A total of 371 outpatients were enrolled, including 182 with CH-C and 189 age- and sex-matched subjects without CH-C. CH-C subjects had obviously lower educational status (P<0.01). Mean scores of domains in general health, physical functioning, role-physical, role-emotional, vitality, and mental health of the SF-36 were significantly lower in subjects with CH-C than those without CH-C (P<0.05). In an analysis of 47 CH-C patients who received and completed the whole course of antiviral treatment, mean scores of all domains were significantly lower at wk 12 of treatment compared to baseline. The scores returned to pretreatment values by the end of treatment, but were significantly increased at mo 6 after stopping the treatment. Among the 47 CH-C patients, 21 had sustained responses and 26 had non-sustained responses to antiviral treatment. Compared to pretreatment values, subjects with sustained responses had significantly lower social functioning scores at wk 12 of treatment, and scores for all SF-36 domains returned to pretreatment values, and increased significantly at mo 6 after stopping the treatment. For non-sustained virological responders, scores of all SF-36 domains significantly decreased at wk 12 of treatment, and did not increase significantly by the end of treatment, or at mo 6 after stopping the treatment when compared to the pretreatment values.

CONCLUSION: HRQOL in CH-C patients is significantly impaired in most SF-36 domains. Antiviral treatment impaired HRQOL of CH-C subjects during early treatment, mainly in non-sustained virological responders, and improved at mo 6 after stopping the treatment, mainly in sustained virological responders.

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INTRODUCTION

Hepatitis C virus infection (HCV), previously known as non-A, non-B hepatitis, has become an important health issue worldwide in the last 15 years. Its chronic sequelae, liver cirrhosis and hepatocellular carcinoma, have had a significant impact on the health of the population worldwide[1,2]. Antiviral treatments, including interferon with or without ribavirin, have been used in treating chronic hepatitis C (CH-C) patients to prevent the development of liver cirrhosis and hepatocellular carcinoma. In Taiwan, the prevalence of CH-C has been reported to be around 2-5% in urban populations. High HCV endemic villages with 20-60% positive rates of serum antibody to HCV have been found in central and southern parts of Taiwan[3,4]. Interferon α therapy with and without ribavirin for 6 mo has been used to treat CH-C patients since 1991 in Taiwan. The sustained virological response rate at the end of
the treatment ranged from 12% to 76%, but the sustained virological response rate at the 6th mo after stopping the treatment ranged only from 12% to 43%.

Health-related quality of life (HRQOL), which reflects what patients are concerned with and what they experience, has been widely researched in patients with CH-C in the West. Indeed, the impact on HRQOL and the adverse effects of antiviral treatment have been documented for Western populations. However, to our knowledge, such studies have not been done for HRQOL in Chinese patients with CH-C.

For evaluation of HRQOL in Chinese CH-C patients, the Short Form 36 (SF-36) Questionnaire is most commonly used. The aims of our study were to understand the characteristics of HRQOL in Chinese CH-C patients compared with age- and sex-matched subjects without CH-C, and to evaluate the impact of antiviral treatment on HRQOL in Chinese CH-C patients.

MATERIALS AND METHODS

We used questionnaires to conduct interviews of CH-C patients at the Outpatient Clinics of Taipei Veterans General Hospital, a medical center in Taipei City, Taiwan. CH-C patients were defined as those who had sustained elevation of serum transaminase and positive tests for serum antibody to HCV for more than 6 mo, and/or pathological changes consistent with the diagnosis of CH-C on liver biopsies. CH-C patients who showed decompensated cirrhosis or hepatocellular carcinoma were excluded from the study. Age- and sex-matched subjects without CH-C were interviewed at the same places and at the same times as CH-C patients. The enrolled outpatients were randomly selected and interviewed from January 1, 2002 to December 31, 2002. Demographic data, including subjective difficulty in completing the questionnaire, acute illness within the last 2 wk, combined chronic systemic diseases such as hypertension, coronary artery disease, chronic obstructive pulmonary disease, diabetes mellitus and osteoarthritis, were obtained for each subject. We trained senior-grade medical students and nurses to interview the subjects and to assist them in filling out the questionnaire.

We used the SF-36 HRQOL questionnaire, Taiwan version, as a tool for our study. The SF-36, developed by John E. Ware Jr. in late 1980s, has been widely used in different fields for health evaluations all over the world. Translated into several languages, the SF-36 has shown similar reliability and validity in studies conducted in different countries. For the SF-36 Taiwan version, the norms and internal consistency have been validated by local researchers. It measures eight main domains: (a) general health (GH); (b) physical functioning (PF); (c) limitation of roles due to physical problems, known as role-physical (RP); (d) limitation of roles due to emotional problems, known as role-emotional (RE); (e) social functioning (SF); (f) bodily pain (BP); (g) vitality (VT); and (h) mental health (MH). We recorded demographic data, summarized the original scores of each SF-36 domain, and translated them into final scores from 0 to 100 linearly via the formulas of the SF-36. A score of “0” indicates the least favorable health status; a score of “100”, the most favorable health status.

We also enrolled and collected data from 47 consecutive CH-C patients who had completed one course of antiviral treatment. This included: (a) 24 patients who received pegylated interferon α-2a subcutaneously at a dose of 180 μg per week plus oral ribavirin (1 000 mg/d if body weight <75 kg, and 1 200 mg/d if body weight ≥75 kg) for 6 mo; and (b) 23 patients receiving interferon α-2b subcutaneously 3 million units thrice a week plus oral ribavirin (1 000 mg/d if body weight <75 kg, and 1 200 mg/d if body weight ≥75 kg) for 6 mo. We interviewed the subjects and recorded their SF-36 scores before the initiation of treatment, at the 12th wk of treatment, at the end of treatment, and at the 6th mo after the stopping treatment. The sustained virological responders were defined as those whose serum HCV RNA was detected to be negative by branched chain signal amplification assay (VERSANT HCV RNA 3.0 Quantitative Assay, Chiron Corporation, Tarrytown, NJ, USA) with a sensitivity of 3 200 copies/mL and reverse transcription-nested polymerase chain reaction with a sensitivity of 100 copies/mL at the 6th mo after stopping the treatment.

The data in the text and tables are expressed as mean ±SD. Mann-Whitney U tests, χ2 tests, Fisher’s exact tests, and paired t-tests were done appropriately depending on the type of data analyzed by using SPSS software (SPSS version 11.0, SPSS Inc., Chicago, IL, USA). Cronbach’s α expressed both internal consistency of each domain and overall consistency of the SF-36. A two-tailed P<0.05 was considered statistically significant.

RESULTS

Three hundred and seventy-one subjects, including 182 CH-C patients and 189 age- and sex-matched control subjects without CH-C, received interviews and filled out questionnaires during the period of study. The internal consistency of each domain of the SF-36 shown by Cronbach’s α was greater than 0.6 (GH: 0.75, PF: 0.87, RP: 0.90, RE: 0.88, SF: 0.69, BP: 0.81, VT: 0.83, MH: 0.67), and the
overall consistency of the SF-36 (Cronbach's α) was 0.91. The demographic data for the 371 study subjects are listed in Table 1. Subjects with CH-C showed lower educational status than those without CH-C (P<0.01). The subjects with subjective difficulty in completing the questionnaire, with acute illness within the previous 2 wk, or combined chronic diseases showed no significant differences than the subjects without these characteristics.

The original scores of the SF-36 in 371 study subjects were translated to linear scores from 0 to 100, which are listed in Table 2. Subjects with CH-C had significantly lower scores in GH, PF, RP, RE, VT, and MH domains than those without CH-C (P<0.05). The domains of SF and BP showed no significant differences between subjects with or without CH-C.

Of the 47 CH-C patients who received antiviral treatment and completed the whole course of therapy, all had significantly lower mean HRQOL scores in all SF-36 domains at the 12th wk of treatment as compared with pretreatment values, but mean scores returned to pretreatment values by the end of treatment and significantly increased at the 6th mo after stopping the treatment (Figure 1). Among the 47 CH-C patients who received antiviral treatment, 21 were sustained virological responders and 26 were non-sustained virological responders. Sustained virological responders and non-sustained virological responders showed no significant difference for mean age, gender, and treatment modality. Mean scores for the SF-36 in all domains before antiviral treatment showed no significant difference between the two groups except that mean scores for MH was significantly higher in sustained virological responders than in non-sustained virological responders (Table 3).

Mean SF-36 scores at different time points of antiviral treatment in both sustained virological responders and non-sustained virological responders are listed in Tables 4 and 5, respectively. Compared to pretreatment values, subjects with sustained virological response showed significantly lower SF scores at the 12th wk of treatment. Mean scores of all SF-36 domains returned to pretreatment values by the end of treatment, and increased significantly by the 6th mo after stopping the treatment (P<0.05). For non-sustained virological responders, mean scores for all domains of the SF-36 significantly decreased at the 12th wk of treatment compared to pretreatment values, and did not increase significantly at the end of treatment and at the 6th mo after stopping the treatment.

**DISCUSSION**

Chronic HCV infection has become an important health issue in Taiwan and worldwide. Moreover, the chronic sequelae of liver cirrhosis and hepatocellular carcinoma have led to considerable morbidity and mortality in CH-C patients, and a negative impact on HRQOL in CH-C patients has been well documented for Western populations.[22,23] In Asia, impaired HRQOL in Korean patients with chronic viral hepatitis has been reported.[24] Till now, however, there have been no reports on HRQOL in Chinese patients with CH-C.

To the best of our knowledge, our study is the first study investigating HRQOL and the impact of antiviral treatment in Chinese CH-C patients. Our results showed...
that HRQOL in Chinese CH-C patients in outpatient clinics was significantly impaired compared to non-CH-C subjects. This finding may reflect the fact that chronic viral hepatitis is more commonly seen in Chinese nationals than in Caucasians and the chronic sequelae of chronic viral hepatitis, such as cirrhosis and hepatocellular carcinoma, may have greatly affected the health of Chinese patients. We propose that Chinese patients with CH-C should be paid more attention regarding their HRQOL, health education and disease management.

Interferon was introduced for the antiviral treatment of CH-C in the late 1980s[26,27]. Due to the poorer sustained response rate using interferon therapy alone, combined treatment of interferon and ribavirin has been widely used in treating CH-C patients, which recently had 40-60% sustained virological response rate. However, the side effects of interferon with or without ribavirin, such as fatigue, malaise, flu-like symptoms, anemia, itching, skin rash or eruption, arthralgia, myalgia, depression, impaired sleeping quality, and loss of concentration, have been notable and have bothered CH-C patients during antiviral treatment[27]. Previous reports from Western countries had focused on comparison of HRQOL before and after antiviral therapy in CH-C patients, and they revealed that the HRQOL of CH-C patients could be improved through aggressive antiviral therapy, and sustained virological responders showed greater improvement[28,29]. Our results for Chinese CH-C patients were consistent with reports from Western countries that sustained virological responders to antiviral treatment have improved HRQOL.

Our results also revealed that all regimens of antiviral therapy improved HRQOL of the subjects at early therapeutic stages, and especially bothered non-sustained virological responders. Initially therapeutic discomfort would impair patients’ compliance and willingness to continue antiviral therapy. We suggest that active explanations of possible side effects and discomforts to patients before antiviral therapy are needed. If patients have insights into and are aware of possible adverse side effects, the compliance and continuity of antiviral therapy should be improved.

The limitations of our research are the different regimens of antiviral treatment. Therefore, we did not perform comparisons of the therapeutic effects and impact on HRQOL among different kinds of antiviral regimens. Further evaluations and comparisons of the impact of different therapeutic regimens on HRQOL in CH-C patients are now indicated.

In conclusion, our study suggests that CH-C patients have a lower HRQOL than those without CH-C in Chinese populations visiting outpatient clinics. Antiviral treatment reduced HRQOL of CH-C patients at the early phase of treatment, mainly in non-sustained virological responders. The HRQOL may return to pretreatment values at the end of treatment and improve significantly at the 6th mo after stopping the treatment, mainly in sustained virological responders.

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REFERENCES

1 Hwang SJ. Hepatitis C virus infection: an overview. J Microbiol Immunol Infect 2001; 34: 227-234
2 Seeff LB. The natural history of chronic hepatitis C virus infection. Clin Liver Dis 1997: 1: 587-602
3 Lu SN, Chue PY, Chen IL, Wang JH, Huang JF, Peng CF, Shih CH, Chang WY. Incidence of hepatitis C infection in a hepatitis C endemic township in southern Taiwan. Kaohsiung J Med Sci 1997; 13: 605-608
4 Lin CC, Hwang SJ, Chioou ST, Kuan CL, Chen LW, Lee TC, Lee MB, Lee HH, Hsu PS, Tsai ST. The prevalence and risk factors analysis of serum antibody to hepatitis C virus in the elders in northeastern Taiwan. J Chin Med Assoc 2003; 66: 103-108
5 Hwang SJ, Lee SD, Chan CY, Lu RH, Chang Fy. A random-
ized, double blind, controlled trial of consensus interferon in the treatment of Chinese patients with chronic hepatitis C. Am J Gastroenterol 1999; 94: 2496-2500.

6. Hwang S, Lee S, Chu C, Lu R, Chang F. An open-label trial of consensus interferon 15 μg in the treatment of Chinese patients with chronic hepatitis C. Hepatol Res 2001; 19:284-293.

7. Hwang SJ, Chan CY, Lu RH, Wu JC, Lee SD. Randomized controlled trial of recombinant interferon-alpha 2b in the treatment of Chinese patients with chronic hepatitis C. J Interferon Cytokine Res 1995; 15: 611-616.

8. Lai MY, Kao JH, Yang PM, Wang JT, Chen PJ, Chan KW, Chu JS, Chen DS. Long-term efficacy of ribavirin plus interferon alfa in the treatment of chronic hepatitis C. Gastroenterology 1996; 111: 1307-1312.

9. Ware JE. John E. Ware Jr. on health status and quality of life assessment and the next generation of outcomes measurement. Interview by Marcia Stevic and Katie Berry. J Health Qual 1999; 21: 12-17.

10. Keller SD, Ware JE, Bentler PM, Aaronson NK, Alonso J, Apolone G, Björner JB, Brazier J, Bullinger M, Kaasa S, Leplege A, Sullivan M, Gandek B. Use of structural equation modeling to test the construct validity of the SF-36 Health Survey in ten countries: results from the IQOLA Project. International Quality of Life Assessment. J Clin Epidemiol 1998; 51: 1179-1188.

11. Ware JE, Gandek B, Kosinski M, Aaronson NK, Apolone G, Brazier J, Bullinger M, Kaasa S, Leplege A, Prieto L, Sullivan M, Thunstedborg K. The equivalence of SF-36 summary health scores estimated using standard and country-specific algorithms in 10 countries: results from the IQOLA Project. International Quality of Life Assessment. J Clin Epidemiol 1998; 51: 1167-1170.

12. Ware JE, Kosinski M, Gandek B, Aaronson NK, Apolone G, Bech P, Brazier J, Bullinger M, Kaasa S, Leplege A, Prieto L, Sullivan M. The factor structure of the SF-36 Health Survey in 10 countries: results from the IQOLA Project. International Quality of Life Assessment. J Clin Epidemiol 1998; 51: 1159-1165.

13. Gandek B, Ware JE, Aaronson NK, Alonso J, Apolone G, Björner JB, Brazier J, Bullinger M, Fukuhara S, Kaasa S, Leplege A, Sullivan M. Tests of data quality, scaling assumptions, and reliability of the SF-36 in eleven countries: results from the IQOLA Project. International Quality of Life Assessment. J Clin Epidemiol 1998; 51: 925-932.

14. Wagner AK, Gandek B, Aaronson NK, Acquaro C, Alonso J, Apolone G, Bullinger M, Björner JB, Fukuhara S, Kaasa S, Leplege A, Sullivan M, Wood-Dauphinee S, Ware JE. Cross-cultural comparisons of the content of SF-36 translations across 10 countries: results from the IQOLA Project. International Quality of Life Assessment. J Clin Epidemiol 1998; 51: 925-932.

15. Ware JE Jr, Gandek B. Overview of the SF-36 Health Survey and the International Quality of Life Assessment (IQOLA) Project. J Clin Epidemiol 1998; 51: 903-912.

16. Lu JFR, Tseng HM, Tsai YJ. Assessment of health-related quality of life in Taiwan (I): development and psychometric testing of SF-36 Taiwan version. Taiw J Public Health 2003; 22:501-511.

17. Tseng HM, Lu JFR, Tsai YJ. Assessment of health-related quality of life in Taiwan (II): norms and validation of SF-36 Taiwan version. Taiw J Public Health 2003; 22: 512-518.

18. Lu RH, Hwang SJ, Chan CY, Chang FY, Lee SD. Quantitative measurement of serum HCV RNA in patients with chronic hepatitis C: comparison between AmpliCor HCV monitor system and branched DNA signal amplification assay. J Clin Lab Anal 1998; 12: 121-125.

19. Elbeik T, Surhadi J, Destree M, Gorlin J, Holodniy M, Jortani SA, Kuramoto K, Ng V, Valdes R, Valsamakis A, Terrault NA. Multicenter evaluation of the performance characteristics of the bayer VERSANT HCV RNA 3.0 assay (bDNA). J Clin Microbiol 2004; 42: 563-569.

20. Hwang SJ, Lee SD, Chan CY, Lu RH, Lo KJ. A randomized controlled trial of recombinant interferon alpha-2b in the treatment of Chinese patients with acute post-transfusion hepatitis C. J Hepatol 1994; 21: 831-836.

21. Kao JH, Chen PJ, Lai MY, Yang PM, Sheu JC, Wang TH, Chen DS. Mixed infections of hepatitis C virus as a factor in acute exacerbations of chronic type C hepatitis. J Infect Dis 1994; 170: 1128-1133.

22. Ware JE Jr, Bayliss MS, Mannocchia M, Davis GL. Health-related quality of life in chronic hepatitis C: impact of disease and treatment response. The Interventional Therapy Group. Hepatology 1999; 30: 550-555.

23. Foster GR, Goldin RD, Thomas HC. Chronic hepatitis C virus infection causes a significant reduction in quality of life in the absence of cirrhosis. Hepatology 1998; 27: 209-212.

24. Park CK, Park SY, Kim ES, Park JH, Hyun DW, Yun YM, Jo CM, Tak WY, Kweon YO, Kim SK, Choi YH, Park SG. [Assessment of quality of life and associated factors in patients with chronic viral liver disease] Taehan Kan Hakhoe Chi 2003; 9: 212-221.

25. Davis GL, Balart LA, Schiff ER, Lindsay K, Bodenheimer HC, Perrillo RP, Carey W, Jacobson IM, Payne J, Dienstag JL. Treatment of chronic hepatitis C with recombinant interferon alfa. A multicenter randomized, controlled trial. Hepatitis Interventional Therapy Group. N Engl J Med 1989; 321: 1501-1506.

26. Di Bisceglie AM, Martin P, Kassianides C, Lisker-Melman M, Murray L, Waggoner J, Goodman Z, Banks SM, Hoofnagle JH. Recombinant interferon alfa therapy for chronic hepatitis C: A randomized, double-blind, placebo-controlled trial. N Engl J Med 1989; 321: 1506-1510.

27. Bonkovsky HL, Woolley JM. Reduction of health-related quality of life in chronic hepatitis C and improvement with interferon therapy. The Consensus Interferon Study Group. Hepatology 1999; 29: 264-270.

28. Kuehne FC, Bethe U, Freedberg K, Goldie SJ. Treatment for hepatitis C virus in human immunodeficiency virus-infected patients: clinical benefits and cost-effectiveness. Arch Intern Med 2002; 162: 2545-2556.

29. Michielsen P, Brenard R, Reynaert H. Treatment of hepatitis C: impact on the virus, quality of life and the natural history. Acta Gastroenterol Belg 2002; 65: 90-94.

30. Bernstein D, Kleinman L, Barker CM, Revicki DA, Green J. Relationship of health-related quality of life to treatment adherence and sustained response in chronic hepatitis C patients. Hepatology 2002; 35: 704-708.

31. Teuber G, Berg T, Naumann U, Raedle J, Brinkmann S, Hofp U, Zeuzem S. Randomized, placebo-controlled, double-blind trial with interferon-alpha 2b without and without amantadine sulphate in primary interferon-alpha nonresponders with chronic hepatitis C. J Viral Hepat 2001; 8: 276-283.

32. McHutchison JG, Ware JE, Bayliss MS, Pianko S, Albrecht JK, Cort S, Yang I, Neary MP. The effects of interferon-alpha-2b in combination with ribavirin on health related quality of life and work productivity. J Hepatol 2001; 34: 140-147.