Depression, anemia and health-related quality of life in chronic hepatitis C[☆]

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Background/Aims: Hepatitis C (HCV) infected patients have significant health-related quality of life (HRQL) impairment which worsens during anti-viral therapy. Our aim was to examine the association of HRQL with treatment-induced depression and anemia.

Methods: Two hundred and seventy-one HCV patients who received pegylated interferon alfa 2b and ribavirin were included. Data on HRQL, depressive symptoms, laboratory values and socio-demographic characteristics were collected.

Results: Mean age was 47.1 ± 6.5, 69% were male, and 73% were White. HCV patients' HRQL declined during anti-viral therapy but returned to or exceeded baseline levels within 24 weeks of completion. Anemia and depression were both associated with HRQL impairment. The effects of depression on HRQL were strong; once depression scores were included other factors were no longer significant. Patients' depressive symptoms tended to increase during the initial half of treatment regimen. Those with higher body mass index (BMI), cirrhosis, and women reported more HRQL impairments. HRQL scales were generally not associated with alcohol abuse, age, race, ALT and HCV RNA levels.

Conclusions: Anti-viral therapy for HCV is associated with diminished HRQL. Although anemia and depression were associated with this impairment, depression was the most consistent predictor. Future studies are needed to see whether proactive management of these side effects can improve patients' HRQL and the efficacy of antiviral therapy for hepatitis C.

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1. Introduction

Hepatitis C virus (HCV) affects approximately four million people in the United States, three-quarters of whom have chronic infection [1]. Annual health care costs associated with HCV have been estimated to be one billion dollars [1]. Given the number of HCV infected patients, the

serious health problems commonly resulting from the disease such as cirrhosis and its complications, and significant economic costs, clinicians and researchers have become increasingly interested in understanding HCV's impact on patients' well-being.

HCV patients commonly experience fatigue, anxiety, and depression. These symptoms negatively affect patients' functional health, ability to work, self-perceived health, HRQL and well-being. Psychosocial issues and reduced HRQL are frequently experienced by HCV patients [2–4]. HCV patients have more HRQL impairment than the general population [2,3,5–7]. There is some evidence that HCV patients who experience greater fatigue, greater psychiatric symptoms, and poorer HRQL are more likely

to discontinue treatment prematurely with its negative impact on virologic response [8,9]. In addition to well-known side effects of interferon, one important determinant of HRQL during anti-viral therapy for HCV is development of ribavirin-induced anemia [10–13]. Treatment of anemia improves HRQL, potentially impacting adherence to antiviral regimen and improving virologic response [10]. These issues emphasize the importance of investigating the physical and psychosocial experiences and HRQL of HCV patients.

In this in-depth study, the association of HRQL with depressive symptoms and anemia were assessed. Clinical and socio-demographic predictors of depression and HRQL were also examined.

2. Methods

Two hundred and seventy-one patients with CH–C who received a regimen of pegylated interferon alfa 2b and ribavirin were included in this study. Survey data were prospectively collected in a standardized manner before antiviral therapy began; weeks 4, 12, 24, 36 and 48 during treatment; and 4, 12 and 24 weeks after the treatment regimen was completed. At the beginning of these office visits, patients completed questionnaires assessing HRQL, depressive symptoms, and demographics. Hemoglobin levels and other relevant clinical data were also recorded. Our Institutional Review Board approved the protocol.

2.1. Measures

2.1.1. HRQL
The short-form 36 (SF-36) health survey and chronic liver disease questionnaire (CLDQ) were used to evaluate HRQL.

The SF-36 [14] consists of 36 items measuring general health in eight domains: physical function, role limitations-physical, bodily pain, general health perceptions, vitality, social functioning, role limitations-emotional and mental health. Each scale has scores ranging from 0 to 100. SF-36 has good validity and reliability in chronic disease samples, including hepatitis C [2,3,15]. SF-36 is also divided into summary scores for mental and physical components. The mental health summary component ranges from 10–74 to 8–73 for the physical component. Higher scores on each scale reflect better HRQL.

The CLDQ is a liver disease-specific HRQL instrument comprised of 29 items reflecting four domains: activity, emotional function, systemic symptoms, and worry. Each item has responses ranging from 'all of the time' [1] to 'none of the time' [7]. An overall CLDQ score is also calculated. Scores on each scale range from 1 to 7. This instrument is valid and has good test–retest reliability [5,16,17]. Higher scores indicate better HRQL.

2.1.2. Depressive symptoms
The 20-item Center for Epidemiologic Studies Depression Scale (CES-D) [18] was administered to patients. This is a valid and reliable measure for screening depressive symptoms in HCV populations [19]. Summary scores range from 0 to 30.

2.1.3. Clinical, demographic, and psychosocial data
Baseline clinical and demographic data were collected. The following variables were assessed as potential predictors of HRQL and depression: age, gender, race (Non-latino White, Black or other race), BMI, ALT level, HCV RNA level using polymerase chain reaction (PCR), cirrhosis, history of depression, history of alcoholism, and whether the patient was taking an anti-depressant/anti-anxiety medication. Cirrhosis was determined histologically by a liver biopsy prior to the initiation of antiviral therapy. Additionally, alcohol consumption was estimated by the quantity and

frequency of alcohol intake. In addition to considering predictors of depressive symptoms, baseline CES-D scores were included as a predictor of HRQL. While actual depression scores were utilized when depression was an outcome, when used as a predictor, baseline CES-D scores were divided into three levels: low (CES-D scores ≤ 16), moderate (>16 and <23), and high (≥ 23) [18].

3. Analytic strategy

Analysis was divided into four sections. First, descriptive statistics for the sample were summarized. Second, clinical and demographic predictors of baseline HRQL and depressive symptoms were assessed using ordinary least squares (OLS) regression. Third, paired t-tests were utilized to examine changes in HRQL and depressive symptoms between baseline and each post-baseline assessment. The fourth section focuses on the HRQL of patients who became anemic during therapy. To assess factors affecting HRQL at time of anemia, OLS regression analyses were undertaken. Additionally, predictors of change in HRQL among those with anemia were examined using repeated measures ANOVA. $P<0.05$ was designated as statistically significant for all analyses. Analysis was performed using SPSS Version 12.0.

4. Results

Demographic characteristics and clinical data are summarized in Table 1.

4.1. Cross-sectional analysis

4.1.1. Predictors of depressive symptoms
Age, race, gender, ALT level, BMI, HCV RNA level, and alcohol abuse history were not statistically significantly associated with depressive symptoms at baseline ($P>0.05$). Patients with a history of depression, those receiving anti-anxiety/anti-depression medication at baseline, and those

Table 1
Baseline descriptive statistics

Characteristics	
Female % (N)	31.1 (82)
Race % (N)	
White	72.9 (191)
African–American	13.4 (35)
Other race	13.7 (36)
Age (years)	47.1 (6.5)
Body mass index $>30\%$ (N)	34.8 (86)
HCVRNA $\geq 850,000$ IU/mL % (N)	59.0 (154)
ALT ≥ 40 U/L (N)	91.6 (241)
Cirrhosis % (N)	31.6 (83)
History depression % (N)	25.4 (47)
History of alcoholism % (N)	35.1 (26)
Taking anti-depressant or anti-anxiety medication % (N)	32.4 (24)
CES-D baseline	9.7 (7.6)