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An intervention to prevent symptoms associated with hepatitis C: a pilot study

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Abstract The objectives of this study were to (a) pilot test instruments measuring fatigue and quality of life (QOL); (b) pilot test an exercise intervention; and (c) estimate the effect size of this intervention relative to completion of combination therapy, fatigue, QOL, and walking distance in 20 patients with chronic hepatitis C about to begin interferon alpha and ribavirin treatment. Alpha reliabilities for both the Schwartz Cancer Fatigue Scale and Hepatitis Quality of Life Questionnaire were moderately high. Power analyses of all outcome measures indicated a small effect size and sample size estimate of 30–40 per group to achieve power of >.80.

1. Introduction

The purpose of this article is to report on the results of a pilot study that examined the feasibility of a moderate home walking intervention for patients with hepatitis C virus (HCV) taking interferon alpha and ribavirin in combination. Outcomes of interest were completion of combination therapy, fatigue, quality of life (QOL), and walking distance. Progressive home walking was chosen as the intervention because it is an easy-to-do activity and because moderate activity has been seen as effective in the amelioration of symptoms and side effects in similar chronic illness populations.

2. Review of the literature

Armstrong et al. (2006) estimated that approximately 3.2 million U.S. citizens have evidence of chronic HCV infection. Although persons with HCV may not present with signs or symptoms for as long as 20 years, they experience much higher levels of morbidity and mortality as the disease progresses. Signs of chronic illness include persistent elevation of liver enzymes; persistent viremia; and rapid progression to cirrhosis, decompensation, hepatocellular carcinoma, and possibly even the need for liver transplantation (Seeff, 1999).

Fatigue was found to be a major symptom for patients with HCV (Clark, Mahoney, Clark & Erikson, 2002; Heitkemper, Jarrett, Kurashige, & Carithers, 2001) and as the most disabling symptom in patients with HCV 6 months before and 6 months after treatment with interferon (Cotler et. al., 2000). Goh, Coughlan, Quinn, O'Keane, and Crowe (1999) studied fatigue in women who are HCV positive. They found that the perceived functional impact of fatigue was not significantly different in those with autoimmune disorders or those treated with antiviral therapy compared with matched controls.

In patients who are HCV positive taking antiviral medication, varying "types" of fatigue may occur. Fatigue may result from a sleep disturbance or a perceived fatigue, such as the inability to focus or make sense of things. In addition, fatigue has been associated with anemia, dehydration, and depression. Unlike symptoms associated with other liver disorders, fatigue associated with hepatitis C diagnosis or its treatment may be variable and episodic, making coping with this symptom frustrating (Chopra, 2001).

There are no published studies of the impact of walking on fatigue associated with HCV, but the chronic illness literature illustrates the positive effects of structured walking

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interventions on other conditions with similar symptoms. A 16-week exercise program (progressive home walking was one of many options) showed that postexercise walking distance increased from baseline and 1 month in patients with melanoma taking interferon alpha and that exercise in combination with methylphenidate, as well as alone, appeared to reduce fatigue and have a positive effect on cognitive function (Schwartz, Thompson, & Masood, 2002). Mock et al. (1994) studied female breast cancer survivors receiving chemotherapy who participated in a walking program. Compared with matched controls, the exercisers reported having one half as much fatigue. In a similar study of patients with breast cancer receiving radiation therapy, Mock et al. (1997) found that the exercise group scored significantly higher than do the usual care group on physical functioning (p = .003) and symptom intensity, particularly fatigue, anxiety, and difficulty sleeping. Findings concluded that fatigue was the most frequent and intense subjective symptom reported.

Regardless of the chronic condition, a baseline for a home walking exercise prescription begins with reviewing the results of a purposeful exercise test (Gapinski & Zucker, 2005), and both a 12-minute walk test and a graded exercise stress test can be used for that purpose. Intensity of physical activity is defined by the American College of Sports Medicine (ACSM, 2007) and Centers for Disease Control (2007) in metabolic equivalent (MET) level or the ratio of exercise metabolic rate. One MET is equivalent to the energy expenditure for sitting quietly. Moderate activity is equal to between 3.0 and 6.0 METs (Hendelman, Miller, Baggett, Debold, & Freedson, 2000).

The most common form of moderate activity according to this definition is walking at a moderate or brisk pace of 3 to 4.5 mph on a level surface inside or outside. Using the ACSM calculations, it should take approximately 20 minutes to walk 1 mile expending a moderate activity level, and the ACSM (2007) recommends that physical activity is part of a healthy lifestyle. To date, research in this area has not focused on the effects of home walking exercise on the symptoms associated with HCV-related treatment.

The overall goal of this study was to examine the feasibility of offering a moderately intensive progressive home walking program to persons experiencing HCV-treatment-related symptoms.

3. Methods

The objectives of this study were (a) to pilot test instruments measuring fatigue and QOL; (b) to pilot test an exercise intervention; and (c) to estimate the effect size of this intervention relative to completion of combination therapy, fatigue, QOL, and walking distance. This study used two Massachusetts sites to recruit 20 participants, one private gastroenterology practice, and one university-affiliated liver clinic. Both practices see approximately 30 to 50 chronic hepatitis C participants per month. We excluded persons under the age of 18 and those unable to speak or understand English. Men and women with chronic HCV, about to begin interferon alpha and ribavirin therapy in combination, and who had no physical disabilities preventing them from walking were included in this study. Physicians and nurse practitioners from each site discussed the study with each eligible patient and got verbal consent. The patient was then contacted by the principal investigator, and an appointment was made for further information and to secure informed consent. This study was granted University of Massachusetts Human Subjects' approval and institutional review board's approval from the two Massachusetts gastroenterology/hepatology practices.

The study employed a two-group pretest–posttest design. Once informed consent was obtained, the investigators randomly assigned participants to exercise (EX) or control (CT) groups using a standard table of random numbers. Prior to group assignment, all participants completed questionnaires and a 12-minute walk test (Cooper, 2008). Those assigned to the EX began a self-paced home walking program 3 weeks prior to beginning combination therapy and ended at the completion of therapy (24 or 48 weeks or discontinuation of therapy). Both groups had regular telephone contact with nurses to answer questions and offer support. Exercisers kept a weekly journal of their walking distance and duration using a pedometer, appraised their walking effort using a Borg scale, and kept track of their pulse immediately after walking. Incremental increases in walking duration and or distance were recommended during weekly telephone counseling. All pretest measures were collected again within 1 week of cessation of treatment of all participants.

3.1. Measures

A general demographic instrument collected identification and contact information for all participants, baseline laboratory results including genotype, treatment dose, and other medications. Other measures, not elaborated here, were before and after the 12-minute walk test and perceived exertion. Pretests and posttests of fatigue using the Schwartz

Table 1
Sample characteristics

	Control group, n = 10	Experimental group, n = 10
Gender	80% male	80% male
Mean age, years	48	46
Mean weight, lb	174	189
Diagnosis	90% naive, 10% nonresponder	80% naive, 20% nonresponder
Genotype, %		
1a	50	50
1b	10	10
2b	20	20
3a	20	10
4		10
Completed therapy, %	70	60

Table 2
Reliability statistics—Schwartz Cancer Fatigue Scale

Cronbach's α	Cronbach's α based on standardized Items	*n* of items
.862	.844	6

Note. SPSS Version 12 for Windows (Chicago, IL).

Cancer Fatigue Scale (SCFS) (Schwartz, 1998a) and QOL using the Hepatitis Quality of Life Questionnaire (HQLQ; Ware, Bayliss, Mannocchia, & Davis, 1999) were measured on all participants.

The SCFS is a 6-item multidimensional scale developed for patients with breast cancer taking chemotherapy. The total scale's internal consistency reliability has been reported as >.90 (Schwartz, 1998b). Physical and perceptual scales were similarly excellent at .88 and .81, respectively. The HQLQ Version 1998 is a 17-question 56-item questionnaire composed of the eight subscales of the 36-item Short Form-36 version 1 and has been previously validated (Ware et al., 1999). The remaining four subscales are the hepatitis subscales. Internal consistency for all subscales ranged from .82 to .93 (Bayliss et al., 1998). Scores are summed, and means are transformed to a 0–100 scale, with 100 as the best possible score (e.g., best physical function and best mental health).

4. Findings

Most participants were treatment-naive genotype 1 men with an average age of 47 years and 182 lb. Most participants required 48 weeks of treatment (see Table 1).

Study Objective a was to measure alpha reliabilities for the SCFS computed on the pretest data for both groups. The overall alpha for this study with patients with HCV was .844 (see Table 2).

The SCFS is scored by summing the items across a 5-point Likert scale. Scores range from 5, representing low fatigue, to a high score of 30. In this study, the pretest mean score for the CT group was 11.9 and that in the EX group was 10.3. A few patients stated that they did not know what *listless* meant. Apart from the item measuring "helpless," there were strong interitem correlations for most of all the other items (see Table 3).

Table 3
Alpha reliabilities—SCFS—interitem correlation matrix

	Tired	Difficulty thinking	Overcome	Listless	Worn out	Helpless
Tired	1.00	.636	.444	.655	.823	.140
Difficulty thinking	.636	1.000	.722	.349	.810	.140
Overcome	.444	.722	1.000	.362	.689	.140
Listless	.655	.349	.362	1.000	.610	.195
Worn out	.823	.810	.689	.610	1.000	.401
Helpless	.140	.140	.140	.195	.401	1.000

Note. SPSS Version 12 for Windows.

Table 4
Subscale alpha reliabilities[a]—HQLQ

Physical function = .941	Role emotional = .896
Physical role = .853	Mental health = .885
Bodily pain = .706	Health distress = .948
General health = .831	Positive well-being = .780
Vitality = .879	Hepatitis limitations = .960
Social function = .572	Hepatitis distress = .963

[a] SPSS Version 12 for Windows.

The HQLQ is composed of 12 subscales. Certain challenges were presented by 3 subscales. The bodily function subscale had questions with two different Likert scales (range = 1–5 and 1–6). The pain subscale questions asked the respondent to report severity of pain on a 6-point scale and the amount of interference with normal work. These questions did not apply to all respondents as many did not have pain, and a few participants were unemployed. The social function scale measures how much time and to what extent one's emotional and physical problems have interfered with normal social activities with family and friends and to what extent one is limited in those activities. Analysis of the interitem correlations for this subscale described negative correlations between Questions 10 and 13. Question 10 asked, "how much of the time have your physical and emotional problems interfered with social activities?" and Question 13 asked, "compared to others your age, were your social activities more or less limited due to your physical and emotional problems?" Roughly 60% of the sample responded that they had good social functioning. Analyses of the positive well-being subscale eliminated one item due to no variability. The remaining 8 HQLQ subscales had excellent reliabilities (see Table 4).

Study Objective b was to pilot test the walking intervention. Dropout rates were 30% and 40% in the CT and EX groups, respectively. Reasons for dropout included medical termination of therapy for severe interferon-related symptoms, relapse to pretreatment behaviors, and being lost to follow-up.

Study Objective c sought to determine the effect size of the intervention relative to the outcome variables completion of therapy, distance walked, and fatigue. Posttest scores were used for these analyses using Solo Power (BMDP, Los Angeles, CA) analysis. To achieve a power of .80 or greater, the sample in a future study must have at least 30 or more participants per group (see Table 5).

Table 5
Prediction of sample size based on the effect size for the completion of therapy, distance walked, and fatigue

	Predicted *n*	Power[a]
Outcome a: completion of therapy	30	.83
Outcome b: distance walked, 12-minute walk test	30	1.0
Outcome c: SCFS	30	.86

[a] α = .05, SOLO Power analysis (effect size < .30).

Table 6
Effect size—HQLQ subscales

	Predicted *n*	Power[a]
Physical function	20	.88
Physical role	30	.87
Bodily pain	50	.76
General health	40	.85
Vitality	30	.87
Social function	10	1.0
Emotional role	20	.92
Mental health	30	.87
Well-being	40	.80
Health distress	20	1.0
Hepatitis distress	20	.99
Hepatitis limitations	20	.88

[a] $\alpha = .05$, SOLO Power (effect size < .20).

Effect size for the intervention relative to the HQLQ was calculated for each of the transformed subscales. Predicted sample sizes ranged from 10 to 40 participants. Small effect sizes ranging from .20 or less were reported (Table 6).

5. Discussion of findings

Our aims were (a) to pilot test instruments measuring fatigue and QOL; (b) to pilot test an exercise intervention; and (c) to estimate the effect size of this intervention relative to the completion of combination therapy, fatigue, QOL, and walking distance. The first study objective was to pilot test the SCFS. There were weak interitem correlations for the term *helpless* (perceptual scale), and some participants reported difficulty interpreting the term *listless*. Overall reliability was strong at .86, which is consistent with reported reliabilities for this instrument tested in other chronic illness populations.

The HQLQ was easy to administer, although some participants had to be reminded that the form was multipage, with questions on the front and back sides of the pages. There were 17 questions requiring 56 answers. The alpha reliability for the HQLQ was moderately high. Selected subscales had weak interitem correlations. The social function, bodily pain, and positive well-being subscales had weak interitem correlations.

The second objective was to pilot test the walking intervention. Hepatitis C treatment and its side effects challenged participants' motivation and ability to engage in home walking. However, with regular nursing coaching, exercisers who completed the program felt well and found moderate walking a reasonable routine to add to their day.

The third objective was to estimate the effect size of the walking intervention relative to outcome measures of completion, fatigue, QOL, and walking distance. Power analyses of all outcome measures indicated a small effect size, as well as sample size estimates of 30–40 per group, to achieve power $\geq .80$.

6. Summary

Nursing care of patients undergoing treatment of chronic hepatitis C requires close attention and follow-up. More research is needed to support the assumption that there is a relationship between adherence to therapy, good outcomes of treatment, and minimization of side effects of treatment (Gish, 2006). In this study, fatigue was a prominent side effect of treatment for most participants. Nursing coaching during moderate walking exercise was seen as a necessary component of exercisers' success. Results of this study reinforce the importance of attending to the symptoms associated with treatment. We found that a home walking intervention was feasible and low cost, and dropout rates were consistent with national data.

Walking activity has been seen as a helpful adjunct to staying healthy in select chronic illness populations. Before a larger scale study is proposed, further exploratory work using surveys and focus groups might be helpful to elicit descriptions of QOL and tailor leisure activity for patients with hepatitis C who are treatment naive and have relapsed or not responded to treatment.

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