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PRINCIPAL INVESTIGATOR: Anna L. Schwartz

CONTRACTING ORGANIZATION: University of Utah
Salt Lake City, UT 84102

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Anna L. Schwartz

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University of Utah
Salt Lake City, UT 84102

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Seventy-eight women with breast cancer have been entered in the study. All subjects received instruction to follow an eight-week, home-based exercise program. Two preliminary analyses have been conducted. The first examined the relationship of exercise to fatigue and quality of life in 31 subjects. This analysis demonstrated that the effect of exercise was strongly mediated by fatigue and that fatigue accounted for 71% of the variance in quality of life. The second analysis examined the pattern of fatigue over the first three cycles of chemotherapy in 68 subjects. Results indicated a curvilinear relationship between fatigue and duration of exercise; as the number of minutes of exercise increased fatigue declined. Findings from both analyses support exercise as an intervention for fatigue in women with breast cancer receiving chemotherapy. The results indicate that while there appears to be a dose response relationship of exercise to fatigue, fatigue appears to be the mechanism through which exercise affects quality of life. This research indicates that exercise is important to help maintain functional ability, reduce fatigue and improve quality of life during breast cancer treatment.

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FOREWORD

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Introduction

This is the annual report for Year 02 of the project titled 'The Relationship of Exercise to Fatigue and Quality of Life in Women with Breast Cancer". The purpose of this Year 02 report is to describe the scope of work accomplished in the past 12 months and over the first 24 months of the project. The primary purpose of this study is to test the direct and indirect relationships of exercise to fatigue and quality of life in newly diagnosed women with breast cancer who were receiving chemotherapy. The following information will review the work accomplished to date and future work plans as related to the Statement of Work, the results of preliminary analyses and conclusions.

Body

Review of Statement of Work:

The Statement of Work for months 1-12 (Task 1) of the project was accomplished on schedule in year 01 of the study. The Tasks proposed for months 13-24, completion of coursework, and continued data collection were also completed in the proposed timeframe. Presentations, abstracts, manuscripts and awards that have resulted from this award are listed in the appendix.

To date, 78 women with breast cancer were recruited into the study before they began chemotherapy, when they were drug naive. Although there have been no adverse effects of the study, eight women dropped-out of the study or were lost to follow-up. All subjects received instruction on the 8-week home-based low intensity exercise program and use of the Caltrac accelerometer and exercise logs. At baseline all subjects completed a 12-minute walk, and measures of fatigue (Profile of Mood States fatigue and vigor subscales, and visual analog scale of fatigue), and quality of life (Positive Affect Negative Affect Scale, and Quality of Life Index for patients with cancer). All of these measures were re-administered during weekly follow-up calls, except the 12-minute walk and Quality of Life Index. The weekly calls also served as a reminder for subjects to return their exercise and fatigue logs, and a time to answer questions about exercise. At posttest the measures were all re-administered.

Data collection on the last study subject ended in June, 1998. Data entry has been ongoing throughout the study period, and is projected to continue over the next 4 months. The work described above represents completion of the goals in Task 2 of the Statement of Work.

A change to the work plan was the decision to accept a position at University Washington. This change was effective July 1, 1998 and involved the process of grant transfer. New application for Human Subjects approval was made and approved. The move was projected to have a minimal effect on the project since all the data has been collected. For this reason, no changes to the proposed work for months 25-36 (Task 3) of the Statement of Work were necessary. Tasks 3 for the final year of the project include: completion of data entry, data analysis and manuscript preparation.

Preliminary Findings

Two preliminary analyses have been conducted to examine the mediating effect of fatigue and pattern of fatigue in women with breast cancer. The next two sections describe the findings of each of these analyses.

Analysis 1: Testing the mediating effect of fatigue (Schwartz, in review).

The purpose of this preliminary analysis was to examine the relationship of exercise to fatigue and quality of life. Using the pretest-post test one group design, 31 women with breast cancer were enrolled prior to beginning chemotherapy and 27 completed the study. All baseline measures were obtained before the first chemotherapy treatment. All subjects were instructed on a home-based exercise program. Women were asked to exercise 3 to 4 days per week for 15 to 30 minutes. Measures included daily and weekly measures of fatigue, and baseline and posttest measures of functional ability (12-minute walk) and quality of life. Results indicated that the women who

adopted the exercise program (60%) showed significant increases in functional ability at posttest. Standard procedures for testing the mediation hypothesis were conducted (Barron & Kenny, 1986.). Three multiple regression analyses were computed. The final analyses demonstrated that the effect of exercise was strongly mediated by fatigue and that fatigue accounted for 71% of the variance in quality of life (Table 1).

Table 1. Regression analysis of mediational hypothesis.

	R^2		p	β	Partial	Signif
	Combined	Individual			R^2	t
Fatigue on Exercise	0.732		.001			
Exercise intensity		.379		.365	.344	.039
Functional ability		.353		-.645	-.535	.003
Quality of life on Fatigue	.709		.018			
POMS[1]-vigor		.433		.433	.384	.006
SCFS[2] total		.593		-.503	-.363	.009
Quality of life on Exercise	.558		.018			
Exercise intensity		.206		-.491	-.564	.044
Functional ability		.352		.407	.493	.018
Exercise and Fatigue on Quality of Life[3]	.714		.026			
SCFS total		.575		-.444	-.537	.039
POMS-vigor		.140		.488	.573	.026

[1] Profile of Mood States vigor subscale; [2] Schwartz Cancer Fatigue Scale; [3] Level of exercise did not enter equation, accounting for 0 variance.

Analysis 2: Examining the pattern of fatigue (Schwartz et al, in review).

The purpose of this analysis was to examine the pattern of cancer-related fatigue over the first three cycles of chemotherapy in women receiving cyclophosphamide, methotrexate and fluorouracil (CMF) or Adriamycin and cyclophosphamide (AC) for breast cancer. Sixty-eight newly diagnosed women with breast cancer were instructed in an 8-week home-based low-intensity exercise program. Measures of functional ability, energy expenditure, fatigue and side effect severity were obtained at baseline and posttest. Subjects maintained daily records (visual analog scales) of 4 types of fatigue (worst, least, average, and fatigue right now) and exercise duration, intensity (Caltrac recording of calories expended) and type. Unbalanced repeated measures using the SAS 6.11 program were used in the analysis (Jennrich, & Schuchter, 1986; SAS, 1996). Results indicate that exercise demonstrated a strong effect on reducing fatigue intensity. A linear relationship between fatigue and the square root of the number of minutes exercised indicated that as the number of minutes of exercise increased CRF declined. The model predicted a steeper decline in fatigue in the first hour of exercise and a linear decline between 1-2 hours of exercise. Baseline fatigue was neither associated with number of days of exercise nor amount of exercise, suggesting that fatigue level does not predict exercise. Side effect severity was associated with both exercise frequency and duration. Tables 2 and 3 show the least squares means and standard errors for four types of fatigue by exercise/no-exercise day (frequency) and by number of minutes of exercise (duration).

Table 2. Least squares means and standard errors for four measures of fatigue on no-exercise and exercise days.

	Worst fatigue	Least fatigue	Fatigue now	Average fatigue
Non-exercise day	50.98 (1.26)	22.81 (0.94)	47.11 (2.50)	36.90 (1.06)
Exercise day	46.01 (1.36)	18.14 (1.03)	40.66 (2.67)	31.65 (1.15)
p value	<.0001	<.0001	<.0001	<.0001

Table 3. Least squares means and standard errors for four measures of fatigue by number of minutes of exercise.

	Worst fatigue	Least fatigue	Fatigue now	Average fatigue
0 minute	50.99 (1.24)	22.85 (0.94)	47.11 (2.50)	36.89 (1.05)
1-30 minutes	47.87 (1.49)	18.69 (1.14)	42.30 (2.86)	33.55 (1.25)
31-60 minutes	43.43 (1.83)	17.29 (1.43)	36.16 (3.39)	28.47 (1.53)
>60 minutes	39.79 (3.01)	14.76 (2.44)	40.33 (5.33)	26.89 (2.56)
p value	<.0001	<.0001	.0005	<.0001

Conclusions

The findings of both analyses support exercise as an intervention for fatigue in women with breast cancer who are receiving chemotherapy. Conclusions from analysis 1 suggest that the low intensity, home-based exercise program was feasible for women with breast cancer receiving chemotherapy, and resulted in improved functional ability and quality of life in subjects who exercised. The results indicate that while there appears to be a dose-response relationship of exercise to fatigue, fatigue appears to be the mechanism through which exercise affects quality of life. This research indicates that exercise is important to help maintain functional ability, reduce fatigue and improve quality of life during cancer treatment.

Findings from analysis 2 demonstrate that the impact of exercise on CRF was strong. These findings reflect the effectiveness of low-intensity regular exercise in maintaining functional ability and reducing fatigue in patients with breast cancer. The implications of these findings support the need for regular daily, low intensity exercise to reduce CRF in women with breast cancer receiving chemotherapy.

In conclusion, the project is progressing as planned in the Statement of Work. No adverse events have been observed, and preliminary results are promising. Work completed in the final year (Year 03) of the study will test the hypothesis that fatigue mediates the effects of exercise on quality of life with a larger sample of women with breast cancer.

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Schwartz, A.L. Mori, T., Gau, R., Nail, L.M., King, M.E., Madsen, S. (in review). Exercise dose and fatigue: Day-to-day variation. Journal of Clinical Oncology.

Appendix

Presentations resulting from this support:

"Relationship of exercise to fatigue and quality of life in women with breast cancer." Podium and poster presentation Department of Defense Era of Hope Breast Cancer Meeting, Washington, DC, November 1997.

"Effect of exercise on the pattern of daily fatigue in women with breast cancer." Moderated poster, Oncology Nursing Society annual meeting, San Francisco, CA, May, 1998.

"Energy expenditure and exercise adherence in women with breast cancer receiving chemotherapy." American College of Sports Medicine annual meeting, Orlando, Fl, June 1998.

Peer reviewed publications resulting from this support:

Schwartz, A.L. (in review). Fatigue mediates the effect of exercise on quality of life in women with breast cancer. Journal of Clinical Oncology.

Schwartz, A.L. Mori, T., Gau, R., Nail, L.M., King, M.E., Madsen, S. (in review). Exercise dose and fatigue: Day-to-day variation. Journal of Clinical Oncology.

Published abstracts resulting from this support:

Schwartz, A.L. (1998). Effect of exercise on side effects, affect, and weight changes experienced by breast cancer patients receiving chemotherapy. Proceedings of the American Society of Clinical Oncology meeting, Los Angeles, CA.

Schwartz, A.L. (1998). Energy expenditure and exercise adherence in women with breast cancer receiving chemotherapy. Medicine & Science in Sports & Exercise, 30, S902.

Schwartz, A.L. (1998). Effect of exercise on the pattern of daily fatigue in women with breast cancer. Oncology Nursing Forum, 25, 310.

Schwartz, A.L. (1997). Effect of exercise on fatigue and quality of life in women with breast cancer. Proceedings of the Department of Defense: Era of Hope Breast Cancer Conference, Washington, D.C., November.

Awards resulting from this support:

1998 Outstanding Doctoral Dissertation Award, University of Utah, College of Nursing.