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TITLE: The Use of a Cognitive Protectant to Help Maintain Quality of Life and Cognition
in Premenopausal Women with Breast Cancer Undergoing Adjuvant Chemotherapy

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14. ABSTRACT Significant reductions in quality of life and cognitive function are experienced by women with breast cancer receiving adjuvant chemotherapy. These decrements can be identified in some women even several years following treatment. The majority of relevant research has been based on retrospective data in women with breast cancer. Moreover, current estimates suggest that 25% of breast cancers will be diagnosed in women under age 50, and very little data are available regarding younger women's cognitive function and quality of life during chemotherapy. The goal of the proposed study is to examine change in cognitive function and quality of life in 30 premenopausal women with breast cancer receiving chemotherapy. To determine if accelerated menopause is associated with change in cognition and quality of life, serum hormone levels, measures of cognitive function, quality of life variables, and symptoms of depression will be assessed. Measures will be collected at baseline before the initiation of chemotherapy, prior to the third cycle of chemotherapy, and following completion of chemotherapy, but prior to any additional treatment. A better understanding of the association between chemotherapy and quality of life is essential to provide appropriate preventive approaches and interventions aimed at maximizing the quality of life and health of young women diagnosed with breast cancer.					
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Introduction:

Breast cancer affects more than 200,000 women each year in the United States (1), and most women diagnosed at an early stage have potentially curable disease. The 5-year survival rate for those diagnosed with localized breast cancer has increased from 80% in the 1950's to 98% in 2000 (2). Between 1990 and 2000, the mortality rate from breast cancer decreased by 2.3% annually. Decreases were most impressive in women under age 50, for whom mortality rates decreased by 3.7%.

Owing to the improved survival associated with administration of adjuvant chemotherapy and/or radiation therapy, the majority of women diagnosed with breast cancer will receive some type of adjuvant treatment (3). Impairment in neurocognitive function can accompany chemotherapy with deficits including memory loss, difficulty with concentration, difficulty learning new material, reading comprehension, distractibility, difficulty in performing multiple tasks (multi-tasking), altered visual/spatial orientation, verbal fluency, and the ability to work with numbers (4). Adult cancer survivors also report persistent changes in cognitive function following chemotherapy (5). The President's Cancer Panel (1999) identified cognitive deficits associated with cancer treatment as having a dramatic negative impact on quality of life; the Panel cited cognitive deficits and quality of life as problems that should be addressed both clinically and in the research arena.

Research on the impact of chemotherapy on cognitive function can be traced to the early 1980's. This research produced mixed results regarding the impact of therapy on the development of cognitive deficits (6-9). More recently, studies have revealed relationships among cognitive deficits, chemotherapy receipt, and diminished quality of life. However, questions remain regarding the neurotoxic impact of chemotherapy: Are the problems acute or chronic? Does the type and duration of therapy make a difference? How does chemotherapy affect the central nervous system? Does undergoing an accelerated menopause and change in the hormonal milieu associated with chemotherapy relate to cognitive change? Do other psychological factors influence the extent of cognitive decline? Does the stage of disease influence the severity or duration of symptoms? The proposed research will attempt to address some of these unanswered questions, specifically focusing on evaluating change in cognitive function and quality of life associated with cancer treatment in a sample of young breast cancer patients receiving a relatively uniform treatment regimen.

Body:

This is a hypothesis generating pilot study to explore multiple variables including cognitive function and quality of life in response to receiving adjuvant or neoadjuvant chemotherapy every two or three weeks for the treatment of breast cancer. Approximately sixty pre and peri-menopausal women with breast cancer receiving adjuvant or neoadjuvant chemotherapy every 2 to 3 weeks will be recruited to participate in this pilot study. Women will undergo a battery of psychosocial tools and have serum estradiol, FHS levels and hemoglobin values assessed. The battery of psychosocial tools and serum values will be collected at baseline, prior to the third cycle of chemotherapy, and approximately three to four weeks following completion of chemotherapy but prior to any antihormonal or radiation therapy. The battery of psychosocial tools will include measurements of cognition by the Cognitive Difficulties Scale and High Sensitivity Cognitive Screen; quality of life measured by the MOS-SF-36 and the BCPT Symptom Checklist; fatigue will be measured by the FACT-An and the Brief Fatigue Inventory; Depression and Coping will be measured by the Beck Depression Index and the Brief COPE; and Hope, Optimism and Pessimism will be measured by the Hope scale, the LOT-R, and the PANAS.

- **Hypothesis:**

We predict that young women with breast cancer receiving chemotherapy will experience decrements in cognitive function and quality of life, and increases in menopausal symptoms and fatigue over the course of treatment. We also predict that deficits in cognitive function, and an increase in treatment-related symptoms and fatigue, may be associated with accelerated menopause (i.e., decline in estradiol).

- **Proposed Study Aims:**

1. Evaluate whether or not premenopausal women with breast cancer who are receiving chemotherapy will experience changes in cognitive function.
2. Explore the relationship between cognitive function and quality of life variables associated with receiving chemotherapy for breast cancer including: change in serum hormone levels (estradiol and FSH), self-reported symptoms collected on the Breast Cancer Prevention Trial Symptom Scales (Stanton et al., 2005), depressive symptoms, and anxiety.
3. Examine the relationship between fatigue, serum hemoglobin level, and cognitive function in premenopausal women with breast cancer receiving chemotherapy.
4. Suggest questions to be explored in future research in a similar population of women receiving chemotherapy for breast cancer.

To analyze these data we will use repeated measures analysis of variance, with Time as a three-level factor, to examine pre-mid-post changes in cognitive function using the Cognitive Difficulties Scale and the HSCS scales. Repeated measures analysis also will be used to assess changes in serum estradiol levels, serum hemoglobin levels, fatigue, menopausal symptoms, depressive symptoms, and quality of life measures. Follow-up paired *t*-tests will be conducted to determine the locus of significant effects (i.e., Time 1 to Time 2, Time 2 to Time 3, Time 1 to Time 3).

We also will evaluate the relationship between change in cognitive function (i.e., HSCS, Cognitive Difficulties Scale) and change in the following individual variables: serum estradiol levels, symptoms of fatigue, serum hemoglobin level, depressive symptoms, menopausal symptoms, and measures of quality of life. We will examine correlations of change scores (e.g., change in estradiol from Time 1 to Time 2 correlated with change in a cognitive function variable from Time 1 to Time 2), although it can be difficult to specify the source of variability accounting for the obtained relationship in correlated change scores. We also will examine partial correlations (e.g., Time 3 cognitive function correlated with Time 2 estradiol, partialling out Time 2 cognitive function). If multiple variables are found to predict change in cognitive function, we will conduct exploratory multiple regression analyses (e.g., cognitive function at Time 3 regressed on Time 2 cognitive function, estradiol, and fatigue). In these analyses, we will pay greater attention to proportion of variance accounted for by each predictor than to significance level, in light of the small sample size.

Key Accomplishments:

- Revised protocol was accepted by the Human Subjects Committee in April 2005.
- Attended and presented a poster at the DOD's Vision's of Hope Conference in Philadelphia, PA, in June 2005.
- Ongoing study recruitment of subjects
 - 7/9 recruited have participated
 - 7/30 subjects have been recruited
 - Data collection (psychosocial assessments and serum) have been 100% successful for all three time-points for subjects who are currently on study or who have completed the study.
- Anticipate completion of subject recruitment Spring 2006.
- Anticipate completion of data analysis Summer 2006.
- Anticipate submitting an abstract to the San Antonio Breast Cancer Symposium in July 2006.

Conclusions:

Young women with breast cancer are concerned about their quality of life and cognition during and following chemotherapy. The results of this study will facilitate our understanding of the impact of chemotherapy on a young and growing population of breast cancer patients. Potential deficits in cognitive functioning and quality of life are important aspects to consider in making decisions regarding breast cancer treatments. Data from the proposed study will provide a foundation for continued research on the impact of chemotherapy in a population of women that is not well understood.

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