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Exploring Hormonal Body Composition and Behavioral
Mechanisms

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13. ABSTRACT (Maximum 200 Words) Purpose: The purpose of this study is to prospectively and systematically observe the relative contribution of each viable mechanism such as nutritional intake, activity levels, body composition, hormonal function, thyroid function, coping mechanisms and fatigue scores during chemotherapy on weight gain in breast cancer patients. If changes in the above factors contribute to weight gain and thus alter prognosis, manipulation of these variables by timely intervention may improve prognosis and facilitate recovery from breast cancer. Progress: As planned and described in the Statement of Work, Task 1 of recruitment and data collection and Task 2 - abstraction of Medical record data during months 1-30, of which months 0-12 is currently reported, has been successful, thus far. Currently 63 subjects have been recruited, 30 completed, 26 active, 7 dropouts, five (5) of who did not wish to participate and 2 were eliminated, as the final treatment plan did not include adjuvant chemotherapy. All data were collected from the current sample, including blood sample for hormonal assays. In addition to the proposed study, a structured "Moffitt Weight Management Program", has been established for this group, post-treatment Data entry and analysis of preliminary data will be initiated in November 1999, and outcomes will be reported at that time.				
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FOREWORD

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Introduction:

Weight Gain in Breast Cancer Patients on Chemotherapy

It is estimated that over 181,600 new cases of female breast cancer will be diagnosed in the United States in 1997 and 44,190 will die of this disease.¹ Most of these patients will be diagnosed with stage I or II disease, and a significant proportion of these women will be treated with chemotherapy in addition to surgery and/or radiation therapy. Although the benefits of adjuvant chemotherapy and radiation therapy are well established, and although several side effects such as cancer cachexia challenge the health professionals, one of the most distressing side effect as reported by patients is weight gain.²⁻⁸ Weight gain in this population may prove to be a more serious side effect than others, since it can not only decrease quality of life but may potentially increase rate of recurrence and threaten long-term survival.^{7,9-11} The impact of weight gain may be even more profound, because it may predispose women to heart disease, diabetes, gall bladder disease, endometrial cancer and orthopedic disturbances. These chronic illnesses may pose a greater concern, since women with early stage breast cancer will be cured of the disease but may suffer long term negative consequences as a result of treatment.

Prevalence and Magnitude of Weight Gain in Breast Cancer Patients During

Chemotherapy: Weight gain, anywhere from 5-50lbs in breast cancer patients receiving adjuvant therapy has now been documented consistently for the past two decades.¹²⁻¹³

Significant weight gain occurred in 50-96% of all breast cancer patients receiving adjuvant chemotherapy³ irrespective of stage of disease, more so among premenopausal women compared to post menopausal women.⁹ In addition, significant gain in weight has been observed in patients receiving prednisone as a chemotherapeutic regimen¹⁴⁻¹⁵ or when multiple agents are used^{10, 12} compared to single agent therapies. Bonadonna et al found that longer duration of chemotherapy increased the total amount of weight gained¹⁶ and oral agents produce greater weight gains than infusion-based therapies.¹⁷

Consequences of Weight Gain: More recent findings suggest that obesity at time of diagnosis is an adverse prognostic indicator even after the administration of chemotherapy.¹⁸ We and other have observed that obesity in postmenopausal node positive patients was a negative prognostic indicator^{15, 19} and the risk for disease recurrence among obese patients was 1.33-1.5 times that of the non-obese population.^{9, 18} Camoriano, in addition reported 1.6 times greater risk of death in premenopausal women who gained weight.⁹

Possible Mechanisms: While the cause of weight gain in breast cancer patients remains unknown it, is most likely a result of several contributing factors. Some proposed explanations include psychological factors such as change in coping mechanisms leading to a change in eating behavior, change in activity level due to fatigue or disruption of normal lifestyle, hormonal changes, and the metabolic effects of chemotherapy or radiotherapy.

Purpose:

The purpose of this study is to prospectively and systematically observe the relative contribution of each viable mechanism such as nutritional intake, activity levels, body composition, hormonal function, thyroid function, coping mechanisms and fatigue scores on weight gain in breast cancer patients on chemotherapy.

Objectives

Specific Aim 1: To characterize the severity and course of weight gain among women undergoing adjuvant chemotherapy.

Specific Aim 2: To examine the impact of chemotherapy-induced change in activity levels on weight gain among women undergoing adjuvant chemotherapy.

Specific Aim 3: To examine the effect of chemotherapy-induced hyperphagia on weight gain among women undergoing adjuvant chemotherapy.

Specific Aim 4: To examine the effect of chemotherapy-induced sex-hormone level changes on weight gain among women undergoing adjuvant chemotherapy.

Specific Aim 5: To examine the effect of chemotherapy-induced change in thyroid function on weight gain among women undergoing adjuvant chemotherapy.

Specific Aim 6: To systematically investigate the relative contribution of thyroid function, sex-hormonal levels, physical activity, body composition, psychological state and nutritional intake on changes in body weight in a group of pre-menopausal and post-menopausal stage I-III breast cancer patients, receiving adjuvant chemotherapy.

Key Research Accomplishments:

As planned and described in the Statement of Work, Task 1 of recruitment and data collection and Task 2 - abstraction of Medical record data during months 1-30, of which months 0-12 is currently reported, has been successful, thus far.. The first two months of the study was spent organizing (a) Instruments and procedures to be used in the study, (b) Consent form and procedures, (c) establishing procedures for recruitment from various medical oncology clinics at the cancer Center, (d) timely, safe blood draws thus preventing duplication of draws, (d) preventing any additional patient visit to the center, (e) collaboration with lab to plan for safe, accurate and timely handling of blood and transport.

Task 1: Subject Recruitment: The patient sample selected for the study is to include a total of 200 consecutive pre-menopausal and post-menopausal patients recruited over a 27 month period, with primary, operable, Stage I to IIIB, axillary lymph node positive and negative breast cancer patients who have consented to be treated using one of two adjuvant or systemic chemotherapy protocols at the H. Lee Moffitt Cancer Center & Research Institute during the study period. Women, of all races and ethnicity, between ages 25 and 75, and breast cancer patients who will receive at least 75% Cytoxan, Methotextrate, 5FU (CMF), Cytoxan, Cytoxan, Adriamycin and 5FU(CAF) or Cytoxan and Adriamycin (CA) chemotherapy regimens with or without radiation therapy at first screening contact will be admitted to the study. Currently 63 subjects have been recruited, of whom 30 have completed the 6 month treatment/observation phase of the study, and an additional 26 subjects are currently active in this protocol. As predicted we had seven(7) dropouts in the study, five(5) of whom did not wish to participate and 2 were eliminated from the study as the final treatment plan did not include adjuvant chemotherapy. We have thus successfully recruited 32% of the sample planned for the study, in a period of 10 months.

Data Collection: Upon recruitment, and upon receiving consent from subjects, the following data were collected, as planned:

1. Confirmation of the accuracy of eligibility information, including the using an initial screening form.

2. Demographic information, personal and medical history, hormonal and reproductive history, exercise, smoking and alcohol use history will be obtained by an RD using the Epidemiological Questionnaire.
3. Anthropometric measurements such as subject's height, weight, skinfolds and circumference measurements.
4. Twenty (20) ml of blood will be drawn into heparinized tubes in a non-fasting state at the same time of day, between 7:00 AM and 12:00 noon, for each individual to obtain 10 ml of serum for analysis of total and free estradiol, sex-hormone binding globulin, T4 and thyroid binding globulin assessment for T3 uptake.
5. Subjects will be asked to complete a self-administered version of the Stanford-five city Project Questionnaire to monitor Activity Levels.
6. Standard 4-day diet record(FDFR).
7. Menstrual histories will be obtained from all peri- and pre-menopausal subjects. This information will be recorded on the FDFR.
8. The Profile of Mood States Fatigue Subscale (POMS-F), a scale to measure fatigue (Appendix 6) will be used to quantify fatigue in these subjects.³⁷
9. The Ways of Coping Checklist (WOCC) consists of 66 items that describe a broad range of cognitive and behavioral strategies people use to manage internal and/or external demands in specific stressful encounters defined here as breast cancer treatment, will be used.³⁸

We have observed that several patients have had difficulty completing the 4-day food records during the 3 to 4 chemotherapy treatments. During those situations, the research team has been able to obtain a 24-hour recall or a 2-day record of intake from the patient or a family member. Apart from this instrument, we have had excellent compliance to completion of serial information from our breast cancer patients.

Task 2: Abstraction of Medical Record Data:

Upon completion of the study, data regarding patient's disease related prognostic indicators is currently being extracted from their medical chart. Quality control procedures for data collection and abstraction have been ongoing. We are currently continuing to obtain information on tumor size, ER/PR positivity, DNA ploidy status and proliferative indices such as Ki-67, which are routinely available for this population.

Nutritional Intervention in Patients post completion of the study period:

Upon completion of the study, we have felt the need for and have had several requests from medical oncologists and patients for continued follow-up of patients who have gained weight during chemotherapy. We have established a structured "Moffitt Weight Management Program", which is currently offered as a pilot program, specifically for this post-treatment Breast Cancer Patient group to enable them to successfully manage weight, post-treatment. The program includes 8-1 hour sessions and incorporates body composition and nutritional analysis, Behavior Management, Assessing fitness and incorporating physical activity and improving food choices towards long-term weight management.

Data Entry & Analysis:

We plan to initiate data entry within the month of November 1999. Quality control procedures for data entry will be applied., as planned.

Reportable Outcomes:

As data entry nor analysis has not been initiated, there is no reportable outcomes at this time.

Conclusions:

Definitive prospective studies that systematically observes the relative contribution of each viable mechanism such as nutritional intake, activity levels, body composition, hormonal function, thyroid function, coping mechanisms and fatigue scores during chemotherapy on weight gain are needed. While it is important to initiate action to prevent the problem of weight gain in breast cancer patients, an essential first step to intervention or rehabilitation is to identify the mechanisms by which weight gain occurs which may hasten the development of effective intervention strategies for weight management for specific regimens. In our current longitudinal research study, we are exploring the impact of adjuvant chemotherapy for breast cancer treatment on these clinical and psychological outcomes and identify systematically the mechanisms and offer opportunities for delivering effective care to prevent and facilitate recovery from breast cancer. If changes in body weight, body composition, hormonal levels, psychological health, dietary and other lifestyle factors alter prognosis, manipulation of these variables by intervention and counseling may improve prognosis, facilitate recovery from breast cancer and the credibility of such interventions will be enhanced.

Based on the relevant literature and the results of our pilot study, we hypothesize that weight gain will occur in a significant number of breast cancer patients on adjuvant chemotherapy and in addition that this weight gain will be a result of hyperphagia, significant lowering of activity level, decrease in free and total estradiol levels, similar to the hormonal milieu of menopause which is known to alter body composition and appetite and lowering of thyroid function resulting in decreased activity levels, all contributing to weight gain in this population. The purpose of the current study is to explore the impact of adjuvant chemotherapy for breast cancer treatment on these clinical and psychological outcomes and identify systematically the mechanisms and offer opportunities for delivering effective care to prevent and facilitate recovery from breast cancer, which will further the programmatic goals of the BCRP of the Department of Defense. Our research may in addition lead to the elucidation of hormonal markers that predict the probability of disease recurrence. This may also establish the mechanisms by which weight gain has an impact on the neoplastic process. If changes in body weight, body composition, hormonal levels, psychological health, dietary and other lifestyle factors alter prognosis, manipulation of these variables by intervention and counseling may improve prognosis, facilitate recovery from breast cancer and the credibility of such interventions will be enhanced.

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