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Course of depression, mental health service utilization and treatment preferences in women receiving chemotherapy for breast cancer☆,☆☆

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ABSTRACT

Objective: This prospective study aimed to estimate the prevalence and course of depression during chemotherapy in women with Stage I–III breast cancer, identify potential risk factors for depression and determine which treatments for depression were being used and which were most preferred.
Method: Thirty-two women were followed over consecutive chemotherapy infusions, with 289 assessments conducted altogether (mean, 9.0 assessments/subject). Current depression, anxiety, physical symptoms and mental health service use were recorded during each assessment. A linear mixed effects model was used to identify factors associated with depression. Patients also ranked depression treatment preferences. We referred patients with more severe depression for treatment.
Results: Clinically significant depression was identified in 37.5% of patients. Depression severity tended to peak at 12–14 weeks and 32 or more weeks of chemotherapy. Depression severity was associated with anxiety severity, physical symptom burden, non-White race, receiving one's first chemotherapy regimen, Adriamycin-Cytoxan chemotherapy and chemotherapy duration. Most (65.5%) patients preferred evidence-based treatments for depression, and 66.7% of depressed patients were using such treatments.
Conclusions: Depression is common in women receiving chemotherapy for breast cancer. Most patients prefer evidence-based depression treatments. We recommend regular screening for depression during chemotherapy to ensure adequate detection and patient-centered treatment.

1. Introduction

Prevalence estimates of depression in breast cancer patients range from 5 to 40%, with most falling between 10 and 25% [1,2]. The variability of these findings is likely due to the range of populations observed, screening methods used and timing of assessments. In addition, most studies include a mixture of patients at different stages of treatment. According to several large studies, breast cancer ranks third among the types of cancers most likely to be associated with depression, following oropharyngeal and pancreatic cancers [3,4].

Depression arises most frequently during the first year after diagnosis of breast cancer [5,6]. However, few studies have longitudinally examined the clinical course of depression during chemotherapy. Our understanding of depression prevalence and severity in this population is further hampered by the fact that most studies are either cross-sectional or have a small number of assessments at widely spaced intervals. Such study designs may fail to identify or document the course of depression during chemotherapy.

Breast cancer patients undergoing chemotherapy may experience higher rates of depression than patients in other treatment stages [7,8]. Chemotherapy-related pain, sleep disruption, fatigue and menopause symptoms are likely contributors [9,10]. The symptom cluster of pain, depression and fatigue observed in this population may be associated with the high levels of proinflammatory cytokines released from tissue damage during chemotherapy or radiation therapy. Rapid declines in estrogen during chemotherapy may also contribute to depression since estrogen normally increases the brain's sensitivity to serotonin.

Depression hinders acclimation to symptoms associated with cancer and its treatment, amplifies the perception and effects of these symptoms and may impact survival [11,12]. The persistence of depression diminishes health and quality of life through its adverse influence on cognition, family functioning, treatment adherence and

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other patient health behaviors like diet, exercise, alcohol use and smoking cessation [13,14]. Such consequences of depression may exacerbate the already stressful process of chemotherapy. Although chemotherapy side effects have been shown to impact daily functioning in women with breast cancer, it is not clear whether an association exists between chemotherapy-related symptom burden and depression [15,16]. Anxiety is often comorbid with depression after a diagnosis of breast cancer and may be heightened during chemotherapy [8,17].

Many studies have revealed underdetection of depression, especially major depressive disorder (MDD), despite the growing availability of effective, evidence-based treatments [18]. Little is known about which treatments for depression are most commonly used by breast cancer patients or which treatments are most preferred [19]. Such knowledge would assist clinicians and researchers in assessing health service needs and targeting appropriate treatments to this patient population.

The aims of this study were (a) to describe the prevalence and course of depression in women with Stage I–III breast cancer who are undergoing chemotherapy and to identify factors associated with depression; (b) to determine which treatments for depression are being used by this population; and (c) to determine which treatments for depression are considered most preferred and acceptable by this population.

2. Methods

2.1. Sample

Participants were recruited at the Seattle Cancer Care Alliance (SCCA), a cancer care consortium for the Fred Hutchinson Cancer Research Center, University of Washington Medical Center and Children's Hospital and Regional Medical Center in Seattle, WA. Eligible subjects met the following criteria: female, at least 18 years old, able to communicate in English, diagnosed with Stage I–III breast cancer and currently receiving neoadjuvant or adjuvant chemotherapy during the study period.

To recruit a consecutive sample of patients, we arranged for infusion clinic pharmacists to notify us of all patients who were receiving chemotherapy (either initial or ongoing) for Stage I–III breast cancer as the information became available during the first 12 weeks of the study period. Forty-four patients met eligibility criteria for the study. Of these, 3 were not approached because their infusion nurses reported that they were too distressed, and 3 were not approached because of scheduling difficulties. Of the 38 patients approached, 3 refused, citing time constraints, and 35 consented to participate. Due to the variability in chemotherapy infusions schedules prescribed by each patient's oncologist, we were able to interview 23 patients every week, 9 patients every other week, 2 patients every 3 weeks and 1 patient every 4 weeks. In order to minimize the heterogeneity of infusion frequencies in our sample, data from the 3 patients interviewed every 3 or 4 weeks were excluded from the final analysis, leaving 32 patients in the final sample.

2.2. Procedures

This study took place between June and November 2007. All procedures were approved by the Fred Hutchinson Cancer Research Center Institutional Review Board. Potential study participants identified by breast clinic pharmacists were approached by research assistants in the infusion suite prior to their chemotherapy infusions. After obtaining informed consent, medical records were reviewed for demographic variables, menopausal status, cancer-related variables and time since initiation of chemotherapy (if not initiated during the study period). Surveys were administered during consecutive chemotherapy infusions and assessed for depression, anxiety, physical symptoms, past and current mental health treatments and preferences for depression treatments. .

Follow-up assessments were administered during as many chemotherapy infusions as possible. Thirty (9.4%) of the 319 possible assessments were missed, with 9 missed because patients were experiencing severe side effects that precluded their ability to be interviewed and 21 missed due to scheduling difficulties. The total number of assessments was 289, and the mean number of assessments per patient was 9.0 [standard deviation (S.D.) 4.6].

In the event that a subject's responses to our survey revealed suicidal ideation [Patient Health Questionnaire-9 (PHQ-9) depression scale item 9 >0] or depression that was at least moderately severe (PHQ-9 sum score ≥15), the research assistant immediately notified the patient's medical team of her responses. Patients were encouraged to notify their infusion nurse or primary team of any chemotherapy-related side effects not already reported.

2.3. Measures

Depression was evaluated using the PHQ-9 depression scale [20]. The PHQ-9 consists of the nine diagnostic symptom criteria for MDD, as defined by the Diagnostic and Statistical Manual for Mental Disorders (DSM-IV) [21]. This scale has shown excellent validity and reliability [22], has clinically validated cutoffs for depression severity [23] and is sensitive to change due to treatment effects [26]. In addition, the PHQ-9 scale has been validated and used with cancer patients and other medical populations [24,25,43]. MDD can be diagnosed by applying DSM-IV criteria to PHQ-9 responses [i.e., the patient endorses at least five of nine symptoms, including at least one of the cardinal symptoms (depressed mood or anhedonia), more than half the days in the last 2 weeks]. The PHQ-9 sum score ranges from 0 to 27, and the validated cutoffs are as follows: 5–9 for mild depression, 10–14 for moderate depression, 15–19 for moderately severe depression and ≥20 for severe depression. For this study, the PHQ-9 cutoff of 10 or above was applied to identify patients with clinically significant depression.

Anxiety was assessed using the Generalized Anxiety Disorder-7 (GAD-7) scale [26]. Like the PHQ-9, the GAD-7 scale is based on DSM-IV criteria and was developed and tested with medical populations. A study of primary care populations has shown the GAD-7 scale to be a reliable and valid tool for identifying and rating the severity of clinically significant anxiety [27]. GAD-7 sum scores range from 0 to 21, and the validated cutoffs are 5–9 for mild anxiety, 10–14 for moderate anxiety and ≥15 for severe anxiety. We used a cutoff of 10 or above to identify those with clinically significant anxiety.

Side effects of chemotherapy and other physical symptoms were recorded in an open-ended manner by asking patients during each assessment, “What side effects are you currently experiencing from chemotherapy?” We then categorized symptoms according to the M.D. Anderson Symptom Inventory, a validated tool that assesses 19 symptoms commonly experienced with cancer and its treatment [28].

Current use of psychosocial services was assessed using the Cornell Services Index (CSI) [29]. The CSI is a standardized tool for documenting mental health service use during the past 90 days, including the type of treatment, type of provider, site of service and frequency of visits. We liberally defined evidence-based treatments as a therapeutic dose of antidepressant medication or psychotherapy from a psychiatrist or psychologist.

To determine patient preferences for treatments of depression, study participants were educated about the common symptoms and course of depression and then asked to rank their top three choices of depression treatments (assuming no cost to the patient). Choice of treatment modalities included (a) antidepressant medications; (b)