Biomarkers, Fatigue, Sleep, and Depressive Symptoms in Women With Breast Cancer: A Pilot Study

Judith K. Payne, PhD, RN, AOCN®, Barbara F. Piper, DNSc, RN, AOCN®, FAAN, Ian Rabinowitz, MD, and M. Bridget Zimmerman, PhD

Purpose/Objectives: To evaluate the changes in reports of fatigue, sleep disturbances, and depressive symptoms and serum cortisol, melatonin, serotonin, and bilirubin during adjuvant chemotherapy in women with breast cancer and to determine whether any correlations exist between the symptom parameters and biomarkers.

Design: Prospective longitudinal, correlational, repeated-measures pilot study.

Setting: Large southwestern, university-based, National Cancer Institute–designated cancer center.

Sample: 22 subjects (11 women with stage II breast cancer receiving adjuvant chemotherapy and 11 cancer-free women who were matched by age, ethnicity, and menopausal status).

Methods: Questionnaires (fatigue, sleep, depressive symptoms), wrist sleep actigraphy, and laboratory analysis of serum samples. All subjects (i.e., women with breast cancer receiving chemotherapy and a comparison group of cancer-free women who were matched by age, ethnicity, and menopausal status) were admitted to a general clinical research center for two nights during cycles 1 and 4 for data collection.

Main Research Variables: Biomarkers (serum cortisol, melatonin, serotonin, and bilirubin), fatigue, sleep, and depressive symptoms.

Findings: Mean fatigue scores of the subjects with cancer were significantly higher than the healthy comparison group. Subjects with cancer had a significantly lower mean actual sleep time compared to the comparison group at cycle 1. No significant difference was found between the groups at cycle 4. Depression scores also differed significantly between the cancer group and comparison group. Select biomarkers changed over time and were associated with subjective parameters of fatigue, sleep, and depressive symptoms.

Conclusions: Findings suggest that fatigue, sleep, and depressive symptoms are more prevalent in women with cancer than a cancer-free comparison group. Biomarkers changed over time and provide a possible explanatory mechanism for the three related symptoms.

Implications for Nursing: Data help to explain a mechanism that may underlie fatigue, sleep, and depressive symptoms and provide a theoretical framework from which to establish evidence-based interventions for symptom management.

Key Points . . .

- Fatigue, sleep disturbances, and depressive symptoms are significantly higher in women with stage II breast cancer receiving adjuvant chemotherapy compared to disease-free women.
- Select hypothalamic-pituitary-adrenal biomarkers may be related to fatigue, sleep disturbances, and depressive symptoms.
- Healthcare providers need to be aware of a possible underlying mechanism of related symptoms in an effort to establish evidence-based practice for tailored symptom management interventions.

Breast cancer frequently requires adjuvant chemotherapy to treat micrometatastic disease following surgery. Although clinical trials have demonstrated long disease-free intervals with curative intent, the treatment frequently involves significant short- and long-term side effects, including fatigue, sleep disturbances, and depressive symptoms. Fatigue continues to be described as the most common and distressing symptom associated with chemotherapy (Irvine, Vincent, Graydon, Bubela, & Thompson, 1994; Jacobsen et al., 1999; Mock, 2004; Payne, 2002; Piper, Lindsey, & Dodd, 1987; Winningham et al., 1994), but little is known about the underlying etiology of fatigue and its closely interrelated association with sleep disturbances and depressive symptoms or its association with select biomarkers (i.e., serum cortisol, melatonin, serotonin, and bilirubin). The frequency and prevalence of this symptom cluster and related sequelae identify it as a significant problem for patients with cancer receiving treatment.

The neuroendocrine system, specifically the hypothalamic-pituitary-adrenal (HPA) axis, provides regulatory functions; the changes in the production of biochemical levels produced in the axis likely exert complex interactions and influences that researchers are only beginning to understand (Cleeland et al., 2003; Payne, 2004; Vgontzas & Chrousos, 2002).

Judith K. Payne, PhD, RN, AOCN®, is an assistant professor in the oncology program in the School of Nursing at Duke University in Durham, NC; Barbara F. Piper, DNSc, RN, AOCN®, FAAN, is an associate professor in the College of Nursing at the University of Nebraska Medical Center in Omaha; Ian Rabinowitz, MD, is an associate professor in the Department of Internal Medicine at the University of New Mexico in Albuquerque; and M. Bridget Zimmerman, PhD, is an associate professor and director of the Biostatistics Consulting Center in the Department of Biostatistics at the University of Iowa in Iowa City. *This study was funded by the National Institutes of Health General Clinical Research Center 5M01 RR 0997, Sigma Theta Tau (Gamma Sigma), and Ortho Biotech. (Submitted June 2005. Accepted for publication October 17, 2005.)*

Digital Object Identifier: 10.1188/06.ONF.775-783