Stress, Depression May Speed Breast Ca Progression

Combination may dysregulate the hypothalamic-pituitary-adrenal axis and lead to more stress.

BY DAMIAN McNAMARA
Miami Bureau

SAN JUAN, P.R. — Women who experience stressful life events, especially trauma, together with depression have a shorter time to breast cancer progression than women with no such history, Dr. David Spiegel said at the annual meeting of the American College of Psychiatrists.

Based on this study, which is under review, screening women with breast cancer for depression and stressful and/or traumatic life events might be worthwhile, said Dr. Spiegel, Willson Professor at Stanford (Calif.) University.

In a second study he conducted with Janine Giese-Davis, Ph.D., antidepressant treatment improved survival in this population. Improving depression might improve breast cancer prognosis independent of other risk factors that affect survival, such as metastatic spread of disease, he said.

So what is the connection? The combination of trauma and depression may dysregulate the hypothalamic-pituitary-adrenal (HPA) axis and lead to more stress among women with breast cancer. "Our breast cancer patients look more like depressed patients than healthy people, which means they may share some aspect of HPA dysregulation," Dr. Spiegel said.

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DR. SPIEGEL

Stressful life events can diminish a person's ability to handle subsequent challenges, including cancer. Diminished physical capability, changes in social environment and family roles, difficult treatments, fear, pain, and facing mortality can all cause stress in women with breast cancer.

"Cancer is a chronic and severe stressor with constant reminders because of its effects on the body," said Dr. Spiegel, who is also a member of the university's comprehensive cancer center.

Chronic stress causes changes to brain structures and the endocrine system, according to neuroimaging and other studies in humans and animals. Specifically, researchers have found that stress alters the size and/or activation of the hippocampus and amygdala.

"A smaller amygdala and hippocampus do not buffer a patient from the effects of stressful life situations as well," he said.

Other researchers determined that serious life events increase risk of cancer (Am. J. Epidemiol. 2003;157:415-23).

This prospective study included 10,808 women in Finland surveyed in 1981 about adverse life events. A total of 180 incident cases of breast cancer occurred between 1982 and 1996. Participants who reported any single event had a slightly elevated risk of breast cancer compared with controls (hazard ratio, 1.07). The risk increased with a major event (1.35), death of close relative or friend (1.36), death of husband (2.00), and divorce or separation (2.26). "The findings suggest a role for life events in breast cancer etiology through hormonal or other mechanisms," the researchers wrote.

"We looked at our own data, and those with an early stress, especially early trauma, have a shorter time to progression of breast cancer from diagnosis compared to women with no such history," Dr. Spiegel said.

Stress is not the only culprit. "A shorter disease-free interval has also been shown with depression," and the study he conducted with Dr. Giese-Davis showed that "if you treat depression, you can improve survival," he said.

Stress can also adversely affect the endocrine system. People with posttraumatic stress disorder or depression tend to have constant levels of cortisol throughout the day. Normally, cortisol levels increase and decrease according to a circadian rhythm. "Waking up is stressful—think of getting up this morning," Dr. Spiegel said, "and in healthy individuals, cortisol levels are five times higher in the morning compared to at bedtime."

He and another group of investigators have published data showing that these abnormal cortisol patterns predict shorter survival with breast cancer (J. Natl. Cancer Inst. 2000;92:994-1000).

When a person attending the meeting asked about changes in catecholamine levels, Dr. Spiegel said, "We did not measure that—cortisol is easier to measure."

Dr. Spiegel said that patients with relatively flat cortisol slopes have fewer natural killer cells. As breast cancer progresses, natural killer cell levels tend to decrease "so it's a salient finding, because this component of the immune system is linked to cancer progression.

"We are trying to construct a model that links a history of stress or trauma to progression of cancer," he said. ■

Optimism Tied To Lower CVD Mortality in White Men

Older white men who have an optimistic nature have about half the risk of dying from cardiovascular causes as their less optimistic peers, according to Dr. Erik J. Giltay of the Institute of Mental Health, Delft, the Netherlands, and his associates.

The researchers used data from a large, prospective study of cardiovascular disease (CVD) in healthy, middle-aged Dutch men to examine a possible link with dispositional optimism. Their study differed from previous research in that it adjusted for classic CVD risk factors, socioeconomic characteristics, and depression.

Dispositional optimism was defined as having "generalized positive expectancies for one's future." It was measured using a four-item questionnaire in which subjects rated their agreement with the following statements: "I still expect much from life," "I do not look forward to what lies ahead for me in the years to come," "My days seem to be passing by slowly," and "I am still full of plans."

A total of 545 healthy men aged 64-84 years in 1985 began the study and were followed up at 5-year intervals until 2000. During that time, 373 (68.4%) died, including 187 (50.1%) who died of cardiovascular causes.

"Compared with men in the lowest tertile of dispositional optimism, those in the top tertile had a 55% lower multivariate-adjusted hazard ratio of cardiovascular mortality," the investigators said (Arch. Intern. Med. 2006;166:431-6).

Optimism was not related to CVD risk factors such as body mass index, hypertension, diabetes, or HDL cholesterol levels. It also proved to be a relatively constant personality trait through the years.

"Our results demonstrate a strong and consistent association between dispositional optimism and an about 50% lower risk of cardiovascular mortality in elderly men during 15 years of follow-up," Dr. Giltay and his associates said.

"A low subjectively perceived level of optimism should be added to the list of independent risk markers for cardiovascular mortality in elderly men," they said. The study findings may not be generalizable to women or to other ethnic groups, as all of the subjects were white men, the researchers noted.

—Mary Ann Moon

Herbal, Nutritional Therapies Can Play Supportive Role in Practice

BY PATRICE WENDLING
Chicago Bureau

TUCSON, ARIZ. — Complementary herbal and nutritional therapies can play an important role in an integrated psychiatric practice, Dr. Iris R. Bell said at a psychopharmacology conference sponsored by the University of Arizona.

Disputes remain about the lack of randomized trials supporting the use of complementary and alternative medicine (CAM). But evidence continues to mount about the benefits of CAM therapy that is individualized to a patient's specific needs and preferences.

Ginkgo biloba has produced mixed results and should be used with caution in those patients on concomitant warfarin or other anticoagulants.

The use of broad-based nutritional supplements has been reported to ameliorate psychiatric symptoms such as mood swings, depression, and aggression in a variety of patients, including young criminal offenders. The mechanisms by which these changes occur are not established. But the supplements may provide the nutritional support needed to improve brain chemistry and promote better use of traditional medications, said Dr. Bell, a professor at the university and director of research for its integrative medicine program.

Activated forms of pyridoxine, niacin, iron, and tetrahydrobiopterin are cofactors for the enzymes tyrosine hydroxylase and tryptophan 5-hydroxylase, which participate in brain biosynthesis of catecholamines and serotonin. It has been shown that patients with the melancholic form of depression have low levels of folate and respond poorly to fluoxetine, in part because they don't have adequate neurotransmitters to use it, she said.

Studies of high-dose antioxidant supplements by themselves, such as vitamin E alone in Parkinson's disease, may have failed because the vitamin needs other components of its biochemical network, such as vitamin C and other nutrients, to regenerate antioxidant forms from prooxidant forms of the vitamin, Dr. Bell said. Folate, B_{12}, and B_6 vitamin supplements are now being used together as a low-risk strategy to lower homocysteine levels in Alzheimer's patients. Studies suggest that elevated homocysteine is an independent risk factor for Alzheimer's disease and a variety of vascular diseases. "We may have a more preventive role to play than we thought," she said.

Ginkgo biloba has produced mixed results in patients with dementia and should be used with caution in those patients on concomitant warfarin or other anticoagulant agents, Dr. Bell said.

Small controlled studies have shown that kava kava can reduce anxiety over a 4-week period, but Dr. Bell said she is uncomfortable recommending its because of the potential for serious liver damage from the forms available in Western countries.

The folk remedy passion flower has been helpful in generalized anxiety and when used in combination with clonidine to reduce mental symptoms in opiate addicts. "It might provide an added benefit to get them through acute withdrawal, but it's not a long-term solution," Dr. Bell said. ■