

Recognizing and Treating Depression

Although the reported incidence of depression in cancer patients varies widely, it is certainly common and often missed, since patients are reluctant to add another “symptom” to their list of medical complaints. It is important to disentangle symptoms of depression from other medical and psychological factors in this population and to adequately treat them.

Bruce E. Compas, PhD, Professor of Psychology and Human Development at Vanderbilt University and Director of Psycho-Oncology at the Vanderbilt-Ingram Cancer Center, Nashville, noted there are three general levels of depression: depressed mood, symptoms of depression (subthreshold depression), and major depressive disorder or dysthymic disorder, based on Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria. They are measured with self-report surveys or questionnaires about symptoms and by diagnostic interviews, which are required to diagnose major depressive disorder.

“Complications can arise from confusing these three ways we talk about depression,” he stated. To be diagnosed with major depressive disorder, patients must report a sad, unhappy or depressed mood, or anhedonia (loss of pleasure) lasting at least 2 weeks, plus three additional symptoms from a list that includes excessive guilt, impaired concentration, psychomotor retardation, weight loss or gain, hypersomnia or hyposomnia, loss of sexual drive, and suicidal ideation or attempt.

“You have to disentangle these from the effects of the cancer or its treatment,” Dr. Compas said, pointing out that symptoms can be a consequence of cytokine activity, fatigue, and changes in sleep and appetite as a result of disease or its treatments. He predicted that the future approach to depression will use powerful statistical methods to “pry apart these factors.”

In Dr. Compas’ own studies of breast cancer patients (*Luecken LJ et al. J Psychosom Res 2004;56:13–15*), 27% of subjects reported depression at some point in their lives; about 4% of patients reported current depression, and 8% reported depression within the previous 12 months. When generalized anxiety was included in the survey, about 18% of patients reported having either anxiety or depression and 54% reported a lifetime history of one or both of these conditions. “Anxiety disorders and mood dis-

Patients need to be reassured that symptom management—including treatment for depression—will not ‘thin the menu’ of other cancer therapies they consider important.

—Michael J. Fisch, MD, MPH

orders affect half the population of breast cancer patients,” he concluded.

Interestingly, his study also found that subthreshold symptoms of anxiety and depression were better predictors of impaired quality of life than a DSM-IV diagnosis of the same. Therefore, clinicians should be vigilant of and attentive to all levels of depression. They should also be aware that some patients are at higher risk for depression than are others. For instance, female gender conveys double the risk for depression versus male gender. The second most important risk factor is a family history of depression, apparently the result of genes related to serotonin and dopamine. Stressful life

events naturally can trigger depression in susceptible individuals.

The combination of stress and genetic vulnerability most likely leads to depression, he said. “Hearing the three words ‘You have cancer’ triggers ‘kindling,’ and once the initial episode occurs, the patient is more vulnerable to the potential for stress to trigger a recurrence. The embers are there and it does not take much to start a fire,” Dr. Compas added.

Pharmacologic Treatment Options

Interestingly, screening instruments may not detect depression, because it is the one symptom that many patients are reluctant to reveal, said Michael J. Fisch, MD, MPH, Medical Director, Community Clinical Oncology Program at the University of Texas M. D. Anderson Cancer Center, Houston. Recognition of depression is also confounded by overlapping weight loss, sleep disturbance, and loss of libido, which can be caused by factors other than depression.

“If patients do not show you their ‘hand,’ to use a poker analogy, you may not recognize the problem or treat it aggressively enough. Patients need to be reassured that symptom management—including treatment for depression—will not ‘thin the menu’ of other cancer therapies they consider important,” he said. In addition, clinicians should be aware that patients may be particularly hesitant to report depression based on cultural influences. He provided examples that include Chinese, Central Americans, Koreans, Arabs, and African Americans.

Antidepressants are prescribed in about half of patients identified with depression, and about half of moderate-to-severe episodes improve with antidepressant treatment, he noted. Although few trials of antidepressants used specifically in cancer patients have been performed, available data suggest these response patterns are similar to those in patients without cancer. Minor or sub-syndromal depression (depressed mood

or anhedonia of < 2 weeks' duration or fewer than five symptoms) is not as likely to respond to antidepressant treatment, Dr. Fisch stated.

In cases of mild-to-moderate depression, psychotherapy is equally effective as antidepressants. When both modalities are combined, the outcomes are superior to either alone, at least in the general population. In cancer patients, data are scarce, but several large reviews suggest that about 20%–25% of patients respond to psychotherapy alone, he said. The nearly two dozen antidepressants on the market work by at least seven distinct mechanisms. In the emerging cytokine hypothesis of depression, tissue injury or immune activation releases cytokines in the periphery; cytokine transduction to the central nervous system results in the release of numerous other factors, such as serotonin, dopamine, and norepinephrine. Antidepressants can modu-

late these cytokine-induced changes, he said.

In addition to their effects on depressive symptoms, antidepressants may also influence the ability of patients to complete important cancer therapy. An interesting study (*Musselman DL et al. N Engl J Med 2001;344:961–966*) found that patients with high-risk malignant melanoma taking the antidepressant paroxetine were significantly more likely to remain on interferon-alpha treatment and to have less depression and better quality of life than those receiving a placebo.

Regarding specific agents, Dr. Fisch noted that the common selective serotonin reuptake inhibitors are backed by a substantial body of efficacy data; however, they can cause some degree of nausea and sexual side effects. Venlafaxine and duloxetine (Cymbalta) are dual-acting agents, with both serotonin and norepinephrine reuptake inhibition, and also may be useful in treating some types of

neuropathic pain. These agents tend to cause constipation, and this side effect may need specific management in some cancer patients receiving other constipating therapy, such as opioids.

Mirtazapine, a new mixed-action agent that can have ancillary benefits beyond treating the mood disorder, is sedating at low doses (whereas fluoxetine, venlafaxine, and bupropion are activating) and is also an appetite stimulant. Therefore, mirtazapine is sometimes prescribed to patients with insomnia and loss of appetite, with the mood-stabilizing effects considered an added benefit.

As a psychostimulant, methylphenidate is also an activating drug, and in addition to its effects in counteracting sedation, it can bring an antidepressant response within a few days. Use of methylphenidate as a rapidly acting antidepressant may be particularly beneficial to patients during the last weeks of life, Dr. Fisch concluded.