Depression and Anxiety in Oncology: The Psychiatrist's Perspective

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Depression and anxiety are frequently undiagnosed and untreated in cancer patients, resulting in a significant negative impact on quality of life and disease outcome. Furthermore, although effective therapies for depression and anxiety are available, there have been few clinical trials of pharmacotherapy in cancer patients. This article explores how the diagnosis of depression and anxiety can be improved in cancer patients and reviews current treatment options in the oncology setting. The Hospital Anxiety and Depression Scale, a simple, patient-administered questionnaire, is effective in screening for psychiatric symptoms at an early stage of cancer treatment, particularly if vulnerable individuals can be identified and targeted. Selective serotonin reuptake inhibitors are currently first-choice therapy for depression, and many of the drugs in the class are effective in anxiety disorders. Further studies of these agents in the oncology setting are warranted.

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Depression and anxiety are highly treatable conditions, and failure to treat them in the cancer patient can have a serious negative impact. As well as compromising quality of life and social support for the cancer patient, depression and anxiety may prolong the duration of hospitalization, negatively influence compliance with treatment, and ultimately reduce chances of survival.[1,2]

Naturally, the corollary of the above applies: treatment of depression and anxiety can have a major positive impact on quality of life for the cancer patient, and there is also evidence that effective treatment can improve clinical outcomes, such as duration of hospitalization and survival rates.[3] Given the proportion of the population that will suffer from cancer at some stage in their lives, antidepressant therapy has been poorly utilized in relation to malignancy. Indeed, psycho-oncology has been recognized as a discipline only since the early 1980s, and little on the subject is taught in medical schools or postgraduate programs. Investigations of psychological vulnerability in oncology are now being carried out and reported in journals such as *Psycho-oncology* and *The Journal of Psychosocial Oncology*, but a significant gap remains to be filled in applying these findings to clinical practice.

For cancer patients to benefit from early intervention, it is essential that primary care physicians and oncologists be able to identify psychiatric symptoms in their cancer patients. This article considers diagnostic strategies and treatment options to relieve the burden of depressive and anxiety disorders in cancer patients.

PSYCHOLOGICAL ISSUES ASSOCIATED WITH MALIGNANCY

The field of oncology covers a wide range of illnesses with differing symptoms, medical problems, and prognoses. Irrespective of the type of cancer, however, depression and anxiety can result from the emotional impact of diagnosis, coping with treatment, anxiety regarding relapse, and facing the possibility of death. These issues may also be pertinent to other serious illnesses.

Other issues are relatively specific to the field of oncology. For example, cancer may be considered as inevitably terminal, particularly in the elderly. Also, it is sometimes cancer therapy, rather than the disease itself, that makes the patient feel worse. In this respect, treatments such as chemotherapy and radiotherapy may be particularly disabling for young people, who may have felt physically fit and healthy before starting treatment. The pattern of remission followed by relapse, frequently seen in cancer patients, may also contribute significantly to psychopathology. There is therefore a strong rationale for the detection and treatment of depression and anxiety in cancer patients.

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PREVALENCE OF DEPRESSION AND ANXIETY IN CANCER PATIENTS

A variety of surveys have been conducted to assess the prevalence of depression and anxiety in oncology patients. Estimates varied widely in early studies, owing to differences in methodology, reporting techniques, and patient populations.[4] The substantial overlap in symptomatology has also made it difficult to distinguish the somatic symptoms of disease or cancer therapy from the psychosomatic symptoms of depression. Thus, cancer patients frequently suffer from fatigue, lack of concentration, sleeplessness, and loss of appetite, all of which may be signs of depression or anxiety. More recently, structured interviews and self-reporting assessment scales have become more standardized, and best current estimates place the prevalence of depression at 15% to 20%.[5,6]

DIAGNOSIS OF DEPRESSION AND ANXIETY IN CANCER PATIENTS

Since depression and anxiety are highly treatable, it is essential that physicians recognize these conditions in the cancer patient so that appropriate, early intervention can be applied. Oncologists do not have time during a consultation to carry out the detailed assessments using structured interviews that psychiatrists would normally use in diagnosis. A more rapid, but accurate, method for screening those patients most likely to develop clinical depression or anxiety is required. A number of risk factors for psychological morbidity (Table 1) can be used to identify cancer patients appropriate for screening.

The Hospital Anxiety and Depression Scale (HADS),[7] a simple, self-administered patient questionnaire, provides a useful screening tool for depression and anxiety at the time of cancer diagnosis. The HADS questionnaire includes separate subscales for depression and anxiety; it is short and easily completed, and thus has a high rate of patient acceptance. The validity of the HADS in diagnosing depression and anxiety in cancer patients has been confirmed by detailed investigation in subgroups of patients.[8,9] Moreover, the HADS is reported to be highly effective in monitoring patient responses to antidepressant treatment.[10]

PHARMACOTHERAPY FOR DEPRESSION IN CANCER PATIENTS

Although a variety of agents have proved efficacious in the treatment of depression in psychiatric patients, there is a distinct lack of clinical trials of antidepressant treatment in the oncology setting. A small number of studies[11–14] have investigated the efficacy of antidepressants in cancer patients suffering from depression. These studies have mostly utilized tricyclic antidepressants and have reported favorable responses. In particular, clinical studies conducted in female cancer patients have reported significant improvement in depressive symptoms with mianserin compared with placebo.[13–15] However, problems due to adverse events and toxicity have led to high rates of poor compliance and withdrawals from studies.[16,17] Toxicity and safety are particularly important considerations for antidepressant therapy in cancer patients, since many will be receiving treatment, such as chemotherapy, that leaves them in a weakened and vulnerable state. The unfavorable safety profile of tricyclic antidepressants may preclude their use, to a significant degree, in cancer patients.

Table 1. Risk Factors for Psychiatric Morbidity in Cancer

Family history of psychiatric disorder
Personal history of psychiatric disorder
Poor socioeconomic status
Advanced disease
Recent stressors (eg, bereavement, divorce)
Pain

Selective serotonin reuptake inhibitors (SSRIs) have proved at least equally effective to tricyclic antidepressants in the treatment of depression,[18,19] and SSRIs are associated with significantly fewer, and less severe, adverse events.[20,21] There have, however, been few clinical trials of SSRIs in the treatment of depression in cancer patients. In a 5-week placebo-controlled trial, fluoxetine was no more effective than placebo in reducing depressive symptoms in 91 cancer patients.[22] However, fluoxetine was reported to be equally as effective as desipramine in 40 depressed women with advanced cancer.[23] More recently, a larger study of 175 patients has shown paroxetine to be equally effective as amitriptyline in patients with breast cancer.[24]

Selective serotonin reuptake inhibitors therefore show promise in treating psychiatric morbidity in cancer patients, but there is a need for further placebo-controlled, multicenter trials that enable representative samples of the target population to be tested. Although the efficacy of SSRIs in the treatment of depression is well established, cancer patients comprise a population markedly different from the psychiatric patients in the basic placebo-controlled trials of antidepressants. Depression or anxiety is the same in cancer patients as in anyone else, but it is important that the control population be drawn from cancer patients, particularly since monitoring of response to antidepressant therapy will suffer from the difficulties alluded to earlier regarding symptom overlap between cancer and depression. Repeated HADS assessment during therapy offers the best method for monitoring response.

The safety profile of SSRIs is significantly superior to that of tricyclic antidepressants; however, the most common adverse event reported in studies of SSRIs is nausea. Under most circumstances, this nausea is not too severe and will resolve with continued treatment. However, patients receiving radiotherapy or chemotherapy may already

suffer from nausea and vomiting, and so the use of SSRIs during this phase of cancer therapy may be less appropriate than at other times. Outside the active treatment period, however, SSRIs have good potential as a well-tolerated, effective treatment for depression in cancer patients.

The role of psychotherapeutic intervention has also been explored in a number of studies of cancer patients with depression, reviewed by Sellick and Crooks.[25] Significant improvements in depressive symptoms have been obtained with structured cognitive-behavioral therapy[26,27] and individually tailored counseling.[28] The most effective approach to alleviate depression in cancer patients may be to combine psychotherapeutic approaches with pharmacologic interventions. Clinical trial data are needed to evaluate this type of combination therapy.

Interestingly, antidepressant therapy may also have a positive impact on the cancer patient in areas other than depression. The analgesic properties of the older tricyclic antidepressants have been recognized for some time,[29,30] and evidence is now emerging to suggest that SSRIs may also have adjuvant pain-relieving properties.[31] Roth and Scher[32] have also demonstrated a marked effect of an SSRI, sertraline, on reduction of hot flushes in men requiring hormone replacement therapy in prostatic cancer.

ANXIETY IN CANCER PATIENTS

Cancer provokes a significant degree of situational anxiety, and frequently depression and anxiety may coexist in the cancer patient. Diagnosis, investigation, and treatment are all stressful for the patient. Furthermore, reintegration into society for patients in remission can be a time of exceptional stress, as they are expected to resume their normal function, often with little support or understanding. Short-term pharmacotherapy in these patients can help them to get through the most difficult periods. Although benzodiazepines are, rightly, generally discouraged for prolonged treatment of anxiety owing to concern about potential abuse, judicious short-term use, to help the cancer patient through particularly traumatic periods, can certainly be justified. For longer-term anxiety, particularly comorbid with depression, antidepressants such as SSRIs, which also have recognized anxiolytic properties and are much better tolerated over long periods, may be more appropriate.

MANAGEMENT OF DEPRESSION AND ANXIETY IN CANCER PATIENTS

Depression and anxiety in the oncology setting can be effectively treated, leading to a better quality of life and, possibly, improved disease outcome. Clinical trial data for antidepressant therapy in cancer remain relatively scarce. Not all of the trials that have been performed take into account the different stages of the cancer process.

In the absence of sufficient formal trial data in cancer patients, clinical decisions should be influenced by experience in the general population, trial data from studies involving other forms of physical illness, case reports, and naturalistic studies appearing in the cancer literature.

Situational anxiety and distress precipitated by events such as investigatory procedures (for example, bone marrow aspiration) are sometimes best treated using a benzodiazepine, such as sublingual lorazepam, and adequate analgesia. Patients suffering from chronic stress, generalized anxiety, phobic anxiety with or without panic disorder, and/or depression (major depression, organic mood disorder, and adjustment disorder) should be prescribed antidepressants, notably SSRIs; recent literature indicates that SSRIs are well tolerated and effective in this group of patients. In considering treatment, the clinician needs to adopt a proactive approach, tailoring therapy to the needs of individual patients on the basis of clinical experience and available data. What is common to all cancer patients, however, irrespective of the type of cancer or stage of disease, is the need for appropriate management of their psychological distress.

CONCLUSIONS

Depression and anxiety in cancer patients result in reduced quality of life, poor compliance with treatment regimens, prolonged hospital stays, and greater overall disability. Perhaps as a result, cancer patients suffering from depression and anxiety may have poorer survival rates. In this context, the benefit of early intervention for depression and anxiety in oncology is readily apparent.

There are 3 main obstacles to the effective treatment of depression and anxiety in the cancer patient. The first obstacle is the difficulty in diagnosis due to overlap in symptomatology with cancer or its treatment. The second is constraints on physicians' time. The third is the lack of clinical trial data on treatment strategies for depression and anxiety in oncology patients. While a number of pharmacologic agents, notably the SSRIs, are effective and well-tolerated treatment for depression and concomitant anxiety, the particular characteristics and requirements of cancer patients mean that data gathered on depressed psychiatric patients are not necessarily transferable to an oncology setting.

It is clear that depression and anxiety can be treated in oncology patients and that treatment will have substantial benefits. The use of a short screening tool, such as the HADS, can identify depression and anxiety at an early stage in primary care or the oncology clinic. Implementation of the HADS in these settings should greatly improve the rate of diagnosis of depression and anxiety. Further studies are now needed to confirm the potential of treatment with SSRIs in oncology. Since different types of cancer, stages of cancer, and patient groups may respond in different ways, a range of studies is needed.

Drug names: amitriptyline (Elavil and others), desipramine (Norpramin and others), fluoxetine (Prozac), lorazepam (Ativan and others), paroxetine (Paxil), sertraline (Zoloft).

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