EPEC-O

Education in **P**alliative and **E**nd-of-life **C**are - **O**ncology

Participant's Handbook

Module 3c:

Symptoms - Anxiety

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EPEC-O: Education in Palliative and End-of-life Care for Oncology.

ISBN: 0-9714180-9-8

The EPEC Project™ was created with the support of the American Medical Association and the Robert Wood Johnson Foundation. The EPEC-O curriculum is produced by The EPEC Project™ with major funding provided by the National Cancer Institute, with supplemental funding provided by the Lance Armstrong Foundation. The American Society of Clinical Oncology partners with the EPEC-O Project in dissemination of the EPEC-O Curriculum. Acknowledgment and appreciation are extended to Northwestern University's Feinberg School of Medicine, which houses The EPEC Project.

Special thanks to the EPEC-O Team, the EPEC-O Expert Panel, and all other contributors.

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Case*

B.C. is a 72-year-old married man with metastatic lung cancer who reports increasing worry about 'little things.' He is apprehensive about doing anything but lying in bed and he gets bouts of nausea, sweating, and shortness of breath, usually associated with going to see his oncologist. His wife reports that he is often restless and cannot get to sleep. His medications include ranitidine, dexamethasone, gabapentin, and albuterol. He uses opiate analgesics as needed for pain. Examination reveals non-specific neurological abnormalities. His vital signs show mild hypertension, tachycardia, and an elevated respiratory rate. CT scan confirms cerebral metastases. An initial Folstein Mini-Mental State Examination is normal.

* This case is not on an EPEC-O Curriculum trigger tape.

Introduction

Anxiety is *a state of feeling apprehension, uncertainty and fear*. High levels of concern and unremitting worry usually lead to some level of dysfunction.

A generalized anxiety disorder is *a state of excessive anxiety or worry lasting at least six months and impacting day-to-day activities*.[1]

Cancer patients and their families commonly experience anxiety over fears, therapies, their ability to live life as they have known it, and uncertainty about their future. Their distress may also be related to other physical, psychological, social, spiritual, practical, end of life, and loss issues that derive from the cancer, or it may be a component of other syndromes, eg, a primary anxiety disorder or an underlying panic disorder that is unmasked by advanced cancer.

A panic attack is *the sudden onset of intense terror, apprehension, fearfulness, terror, or a feeling of impending doom, usually occurring with symptoms such as shortness of breath, palpitations, chest discomfort, a sense of choking, and fear of "going crazy" or losing control*.[1] Panic attacks are discrete in nature and time-course, usually lasting 15 – 20 minutes.

Anxiety often co-occurs with adjustment disorders and/or depression. An adjustment disorder is *a psychological response to an identifiable stressor which results in the development of clinically significant emotional or behavioral symptoms*.[1] Common symptoms in depression, such as loss of appetite, decreased libido, and insomnia may also be part of anxiety states.[2]

Distress and anxiety in one person can spread to other people close to that person. Pro-active approaches to assist with adjustment and early detection and management of distress are essential.

Prevalence

Up to 21% of cancer patients may have persistent anxiety symptoms, although it appears that only a small percentage had any symptoms of anxiety prior to cancer diagnosis or treatment.[3] Because most patients have probably not seen a mental health provider prior to having cancer, consider a diagnosis of anxiety disorder if appropriate.[2,4]

A high proportion of cancer patients may develop hyperarousal and nightmares associated with their cancer diagnosis or treatments and meet the criteria for the diagnosis of Posttraumatic Stress Disorder,[5] ie, *they re-experience a traumatic event with symptoms of increased arousal and avoidance of reminders of the traumatic event*.[1]

Prognosis

Anxiety itself has no definite prognostic implications. Sequelae from anxiety, eg, anorexia, insomnia, harmful behaviors, can limit prognosis.

Pathophysiology

A biological understanding of anxiety is only just emerging. It can be characterized by a maladaptive or excessive response to stress primarily involving the neurotransmitters norepinephrine, serotonin, and gamma-aminobutyric acid (GABA). In contrast with depression, genetic factors play a modest role. Environment, particularly early in life, is thought to be more important. However, associated physical conditions such as hypoxia, sepsis, poorly controlled pain, and adverse medication reactions like akathisia or medication withdrawal syndromes may be associated with anxiety.[6]

Assessment

Anxiety states usually present with one or more symptoms or signs, including excessive worry, apprehension, dread, foreboding, tension, agitation, restlessness, hyperarousal, irritability, insomnia, sweating, tachycardia, hyperventilation, shortness of breath, gastrointestinal distress, and/or nausea.

Anxiety is very common and should be evaluated in every clinical encounter. Ask questions like:

- Do you find yourself worrying a lot?
- Are you often fearful?
- Do you feel anxious?

A detailed clinical interview is the preferred technique for a more comprehensive assessment. Ask direct questions about the aforementioned signs and symptoms. Input from family, friends, and other members of the interdisciplinary team may be invaluable. Tools such as the Hospital Anxiety and Depression Scale[7] or the Profile of Mood States[8]

may be helpful, particularly in the hands of specialists who are familiar with their strengths and weaknesses.

Look for:

- Insomnia (see EPEC-O Module 3l: Symptoms - Insomnia)
- Reversible causes of anxiety such as alcohol, caffeine, or adverse effects of medications (eg, beta-agonists and methylxanthines for the management of dyspnea; steroids, psychostimulants, thyroid medications, antipsychotics, or even anxiolytics).
- Medical states such as pulmonary emboli, uncontrolled pain, abnormal metabolic states, hormone producing tumors, withdrawal from alcohol, nicotine or opioids, and cardiac arrhythmias.

Attempt to differentiate between primary anxiety, depression, and delirium (see EPEC-O Module 3h: Symptoms - Depression and EPEC-O Module 3g: Symptoms - Delirium).[2]

Psychiatrists are well versed in the differential diagnosis of anxiety. If there is a question about the diagnosis, do not hesitate to ask for a consultation.

Management

Treat cancer patients experiencing anxiety with a combination of your own supportive care and psychotherapy, complementary or alternative therapies if they seem helpful, and pharmacotherapy. Treat any reversible causes. Ameliorate the active symptoms quickly. Lack of improvement within a couple of weeks may indicate a need for more aggressive therapy and consultation with a psychiatrist.

Counseling

The majority of patients and their families will be receptive to compassionate exploration of the specific issues that are causing or exacerbating their anxiety. Concerns about anti-cancer therapy, finances, family conflicts, future disability, dependency, existential questions, and dying will not resolve with medication. Instead, they will benefit from counseling and supportive therapy.

Weave in supportive counseling that uses aspects of brief supportive psychotherapy into routine interventions. Spend time educating the patient and family members about modifiable factors that contribute to anxiety and depression.

Supportive counseling has many goals. The interaction itself may be therapeutic. During the discussions, provide the patient with an improved understanding of his or her prognosis, potential treatments, and outcomes. These may help the patient put perceptions, expectations, needs, fears, and fantasies about his or her illness and death into a different perspective. Discuss short-term goals. Identify and reinforce the patient's previously demonstrated strengths and successful coping techniques. This will help the

patient and family to establish or reestablish their sense of self-worth and meaning (see EPEC-O Module 9: Negotiating Goals of Care).

It is important to understand issues of loss and grief when evaluating anxiety and psychological distress. They can occur at anytime during the course of the illness and bereavement for both patients and family members. They are discussed in more detail in EPEC-O Module 4: Loss, Grief, and Bereavement.

Time spent by the oncologist and other members of the cancer care team talking with patients about their feelings and reframing their ideas may be very helpful. In addition, formal and informal sessions with psychiatrists, psychologists, nurses, social workers, and chaplains may also be beneficial.

Complementary therapies

Complementary or alternative medical approaches may help some patients. Progressive muscle relaxation, massage therapy, guided imagery, hypnosis, meditation or aromatherapy can be particularly useful tools to decrease anxiety.[2] Patients should be advised to minimize or avoid caffeine and alcohol and sleep habits should be evaluated as necessary.

Pharmacological management

Acute anxiety

Benzodiazepines are usually the medications of choice for the short-term management of acute anxiety reactions when immediate relief is desired. They have four major actions as anxiolytics/hypnotics, amnestics, skeletal muscle relaxants and antiepileptics. Choose a benzodiazepine based on the desired half-life.

Longer half-life benzodiazepines, eg clonazepam ($t_{½}$ = 30–40 hr), have a more sustained effect, although some, eg, diazepam ($t_{½}$ = 0.83–2.25 days), may accumulate. Common starting doses are:

- Clonazepam, 0.5–2 mg PO daily to bid PRN

Shorter half-life benzodiazepines, eg lorazepam ($t_{½}$ = 12 hr), can be dosed more frequently. Lorazepam may also reduce anticipatory nausea and vomiting associated with chemotherapy[9,10] and produce amnesia for procedures or chemotherapy.[11] Common starting doses are:

- Lorazepam, 0.25–2 mg PO, SL q 6 h PRN

Very short half-life benzodiazepines, eg, oxazepam ($t_{½}$ = 2.8–8.6 hr), triazolam ($t_{½}$ = 1.5–5.5 hr), are not indicated for the treatment of anxiety because the half-life is too short and the risk of rebound anxiety too great. Some, eg, alprazolam ($t_{½}$ = 11.2 hr), have a greater risk of withdrawal and rebound anxiety.

Midazolam, with its very short half-life ($t_{½}$ = 1.8–6.4 hr), may be an ideal anxiolytic/amnestic for procedures, particularly when given SC or IV. Common starting doses are:

- Midazolam, 1–5 mg SC, IV, IM q 1 h PRN
- Midazolam, 0.5–5.0 mg/hr SC continuous infusion

Whichever medication is chosen, start with low doses and titrate to effect and tolerability.

Benzodiazepines and anticholinergics, eg, hydroxyzine and diphenhydramine, may worsen memory or induce delirium, particularly in the elderly. They can cause confusion in patients with preexisting cognitive impairment, or increase gait instability.

Do not use more than one benzodiazepine at a time. When discontinuing benzodiazepines, taper them slowly, ie, reduce the dose by 25-50% each day.

When benzodiazepines are contraindicated, eg, among geriatric patients who are susceptible to their amnestic action, and/or when a primary hypnotic effect is desired, gabapentin or trazodone may be better choices.[12] Common starting doses are:

- Gabapentin, 300 mg PO at bedtime. If ineffective, increase the dose every 3-5 days: first to 300 mg PO q 12 h, then to 300 mg PO q 8 h, then by 100 mg q 8 h. The maximum dose is 3,600 mg daily.
- Trazodone, 12.5 mg PO q 2 h PRN for anxiety or agitation
- Trazodone, 25–100 mg PO at bedtime for insomnia

Chronic anxiety

Selective serotonin reuptake inhibitors (SSRIs) are the medication of choice to manage chronic anxiety. Paroxetine is often chosen because it tends to be more sedating and can provide a calming effect. Usually, higher selective serotonin reuptake inhibitor doses are needed to manage chronic anxiety. Common starting doses are:

- Paroxetine, 10-20 mg PO daily. Target is 20-40 mg PO daily. Maximum dose is 50 mg/day. To reduce the risk of adverse effects, consider an extended-release formulation, eg, Paroxetine CR.
- Citalopram, 10−20 mg PO daily. Increase weekly by 10−20 mg PO daily. Usual target is 40 mg PO daily. Maximum dose is 60 mg/day.
- Escitalopram, 5−10 mg PO daily. Maintenance and maximum dose is 10−20 mg PO daily.

Antidepressants can also help to ameliorate mixed states of anxiety and depression.

For severe anxiety, consider starting both a benzodiazepine and a selective serotonin reuptake inhibitor together. Once the selective serotonin reuptake inhibitor becomes effective in 4 to 6 weeks, the benzodiazepine can be stopped.

If there is a question about the appropriate treatment or if initial treatments are not working in a timely manner, ie days to 1−2 weeks, consult a psychiatrist. For complicated benzodiazepine discontinuation or when alcohol withdrawal is involved, also consider consulting a psychiatrist.

Summary

Anxiety is common among cancer patients and their families. It is often overlooked and/or not treated aggressively. Careful, proactive attention to anxiety will improve cancer management, psychosocial and family stress, quality of life, and, ultimately, quality of dying. Counseling, complementary or alternative therapies, and psychopharmacology all have a role to play in the management of anxiety. Therapies can be tailored to an individual patient's and family's needs and preferences. Do not hesitate to consult with mental health professionals, including psychiatrists, psychologists, nurses, social workers, and chaplains as appropriate if there is a question about anxiety or if simple interventions do not yield improvement in a timely manner.

Key take-home points

1. Anxiety causes dysfunction in patients and those near them and undermines quality of life and quality of care.
2. Proactively manage anxiety with supportive care.
3. Early detection and management is essential.

Pearls

1. Assess openness to counseling as a personal management approach for the patient.
2. Consider caffeine and alcohol use and sleep habits.
3. Choose a benzodiazepine for short-term pharmacological treatment needs; choose a selective serotonin reuptake inhibitor for chronic anxiety.

Pitfalls

1. Overlooking the need for expectant management.
2. Missing early diagnosis.

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Of two hundred fifteen randomly accessed cancer patients, 47% of the patients received a DSM-III diagnosis, with 44% being diagnosed as manifesting a clinical syndrome and 3% with personality disorders. Approximately 68% of the psychiatric diagnoses consisted of adjustment disorders, with 13% representing major affective disorders (depression). The remaining diagnoses were split among organic mental disorders (8%), personality disorders (7%), and anxiety disorders (4%). Approximately 85% of those patients with a positive psychiatric condition were experiencing a disorder with depression or anxiety as the central symptom.

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This study measured the rate and determinants of posttraumatic stress disorder (PTSD) in a group of cancer survivors (N = 27). Cancer patients have a higher rate of PTSD than found in the community. Symptoms closely resemble those of individuals who have experienced other traumatic events.

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The General Health Questionnaire 28 (GHQ 28), Hospital Anxiety and Depression Scale (HADS), and Rotterdam Symptom Checklist (RSCL) seemed promising in their ability to detect anxiety and depression in cancer patients. To compare their screening performance, 513 patients with cancer were recruited. The HADS and RSCL performed well comparably. The HADS did best in those free of disease and when the disease was judged to be stable. Only the RSCL performed well in those with progressive disease. Both the HADS and RSCL were effective in those on treatment. The GHQ was superior to the RSCL in those off treatment.

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An 11-item short form of the Profile of Mood States' 58-item Total Mood Disturbance Score (TMDS) is described. The Brief TMDS was derived from a sample of 619 adults with mixed cancer diagnoses, and replicated on a second sample of 295 lung cancer patients. Given the difficulty many medically ill people have with lengthy self-report scales, and the increasing importance of measuring distress as an adjunct to patient care, this measure shows promise as a rapid, reliable tool.

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Many clinicians have found benzodiazepines to be useful adjuncts to a cancer chemotherapy regimen because of their anxiolytic, sedative, and amnesic properties and also because of their suspected antiemetic properties when these medications are used in conjunction with known antiemetic agents. The ability of lorazepam to induce antegrade amnesia has proved particularly useful in alleviating anticipatory nausea and vomiting connected with repeated courses of cytotoxic chemotherapy..

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