

Depression, anxiety, and delirium in the terminally ill patient

ROBERT L. FINE, MD

CME

ETHICS CME, Part 1 of 3

Target audience: All physicians

Learning objectives:

1. Identify depression, anxiety, and delirium near the end of life.
2. Describe management plans for depression, anxiety, and delirium near the end of life.

Faculty credentials/disclosure:

Robert L. Fine, MD, is director of the Office of Clinical Ethics for the Baylor Health Care System. He has no significant financial relationships to disclose. Dr. Fine does not address unapproved/off-label uses of any product.

Before beginning this activity, please read the instructions for CME on p. 214. This page also provides important information on the method of physician participation, estimated time to complete the educational activity, medium used for instruction, and date of release and expiration. The quiz, evaluation form, and certification appear on pp. 214–216.

In this article, I discuss depression, anxiety, and delirium in the context of terminal illness. These highly prevalent disorders are frequently underdiagnosed in this setting. The failure to diagnose and treat them may subsequently prevent “quality dying.” Death is not a good thing, to say the least, but sooner or later it comes to us all; when it comes to our patients, we need to do a better job of providing the highest quality of care.

Provision of a “good death” is one of the major goals of the Educating Physicians on End-of-Life Care (EPEC) curriculum and is perceived as more and more important by the public and the medical community. Although many physicians are comfortable dealing with depression and anxiety in a routine ambulatory setting, the context of a terminal illness requires different approaches to assessment and management of these disorders, as shown in the following summary of a patient encounter.

CASE STUDY

A 35-year-old man with AIDS met with his primary care physician. She shared with him the results of his blood tests, which revealed a high viral load. This didn't surprise the patient; he indicated that he had been both tired and anorexic (neither of which would be surprising in a patient with a serious illness like AIDS). His partner was present during the office visit and added that the patient had just been lying around in his pajamas, didn't seem to be interested in anything, and wasn't taking

his medications on schedule. “What's the point?” the patient asked. He said that he didn't care anymore, that he was going to die regardless of what he did. Through further questioning, the physician then determined that he had sadness, loss of energy, sleep disturbance, and recurrent thoughts about death. The patient said that although he had been thinking about death, he hadn't seriously contemplated suicide. On the basis of this discussion, the physician told the patient that it wasn't entirely the HIV making him feel this way, but clinical depression was also likely playing a major role. She encouraged him to take some antidepressant medications so that he could be back to his old self again—the person who wanted to fight the HIV disease. The patient agreed to give the medications a try.

Teasing apart the symptoms of depression from the symptoms of terminal disease can be difficult. This encounter could have been much less effective if the physician had not considered that many of the patient's physical symptoms—impaired sleep, lack of appetite, lack of energy—might be signs of depression. When those symptoms were combined with psychological symptoms such as lack of motivation, isolation, sadness, and suicidal ideation, depression became the most likely cause of the patient's decline. In this case, the patient's viral load was rising because he wasn't taking his medicine, and he wasn't taking his medicine because he was depressed. Treating the depression became an essential part of caring for this patient.

DEPRESSION

The medical literature suggests that the incidence of major depression in terminally ill patients ranges from 25% to 77%. Depression is both associated with intense suffering and a cause of intense suffering. Yet, it is not inevitable. It is treatable in many cases, and early treatment is more effective than late treatment. Early treatment is, of course, dependent on early recognition of the problem; all too often, physicians wait until the last weeks of a dying patient's life to decide to address the depression. By this point, it is generally too late.

From the Office of Clinical Ethics, Baylor Health Care System, and the Department of Internal Medicine, Baylor University Medical Center, Dallas, Texas.

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Corresponding author: Robert L. Fine, MD, 3434 Swiss Avenue, Suite 330, Dallas, Texas 75204 (e-mail: rl.fine@baylordallas.edu).

Looking for depression in terminally ill patients begins with a consideration of preexisting risk factors: a prior history of depression, prior suicide attempts, social stresses, a history of substance abuse, or a family history of depression. Sometimes those family histories are startling; the patient describes multiple members of each generation suffering from depression. From there, the physician can move on to specific factors associated with terminal illness.

Advanced disease increases the likelihood of depression. The more symptoms of dying the patients are experiencing—such as dyspnea, nausea, bowel problems, bladder problems, and skin problems—the more likely they will feel depressed. As the patients are less able to manipulate the outside world, they become less and less interested in that outside world. They often experience a constriction of interests as a result. In addition to progression of the underlying illness, certain medications, such as the benzodiazepines, are also associated with depression. Finally, specific illnesses, classically pancreatic cancer, have been linked with depression in a number of studies, with the depression even predating the diagnosis.

Associated with the problem of depression is that of spiritual pain experienced by many terminally or irreversibly ill patients. About 96% of persons nationwide say they believe in a deity and some sort of afterlife. When confronted by a terminal illness, these people may be thinking, “Why me?” This question, not always directly articulated, asks not for a scientific answer but often for a spiritual answer. Of course, to know that the patient is having these thoughts, the clinician may need to ask specifically about spiritual or religious concerns.

In my role as an ethics consultant, I find myself spending much time talking to patients and families about their spirituality, their religious beliefs, and what they think is going to happen to them when they die. Many are convinced they are going to heaven, and they often are able to accept the end of their life on this earth with some equanimity. Studies have shown that individuals who are intrinsically religious—who do not participate in religion or prayer for any sort of secondary gain—have an easier time letting go and making end-of-life decisions than those who are extrinsically religious (i.e., persons who participate in religious activity because they believe they will gain some sort of reward). Alternatively, a number of individuals I’ve talked to over the years were experiencing difficulty letting go since they were convinced they were going to go to hell. Still other patients are simply uncertain. Involving the pastoral care staff in working with terminally ill patients and their families can be beneficial in any of these circumstances.

Moving beyond these historical factors, how else might a clinician recognize depression? Psychological and cognitive symptoms associated with depression include sadness, flat affect, anxiousness, irritability, a sense of worthlessness, hopelessness, helplessness, guilt and despair, anhedonia, and loss of self-esteem. While depression also leads to somatic symptoms, it can be hard to know whether the symptoms seen in an individual patient are related to the depression or the underlying illness.

Another sign of depression in the terminally ill patient is pain that is not responding to treatment as expected. People cannot deal with all of the psychological and spiritual issues of dying when they’re in pain. However, the principal cause of continu-

ing pain is an inadequate dose of pain medication. Physicians may want to consider both increasing the pain medication dosage and adding an antidepressant. I have had good results using amitriptyline as both an adjuvant pain therapy and antidepressant for patients with severe pain in the setting of terminal illness.

Suicide

Clinicians should assess for the risk of suicide in all patients who are depressed. This is especially important in older men with a terminal disease, since this population is the most likely to commit suicide. Another problem is murder-suicide, seen in some geriatric practices; typically, men kill their wives and then kill themselves after one or both of them become terminally ill. Often the couples that wind up in this circumstance lack necessary social support.

Discussion about thoughts of suicide may reduce the risk. How to approach this topic with a patient is an individual decision and depends on the relationship with the patient. The physician may ask a question such as, “Have you had thoughts about giving up?” or, more bluntly, “Are you having suicidal thoughts?” If the patient has had such thoughts, the physician should find out how far they have progressed and how frequently they occur. By discussing suicidal thoughts, the physician can normalize them for the patient and make it easier for the patient to bring up the subject in the future so that the issue can be dealt with early on. If a patient has tangible, specific plans—a time, place, and method—for suicide, intervention is more difficult.

Management of depression

Depression is managed with psychotherapeutic intervention, cognitive approaches, and behavioral interventions. Some mistakenly believe that either psychotherapy alone or drugs alone are appropriate. We ought to be doing both together, especially for terminally ill patients. I would suggest that physicians who care for dying patients strongly consider bringing in psychiatrists for consultation; physicians do not do this nearly enough. I feel this can be quite beneficial to patients if they are willing; I also believe that psychiatrists will let other members of the treatment team know if psychiatric services are not really needed in a particular case.

Pharmacologic management. Physicians may choose from psychostimulants, selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants, or other agents based on the time to effect needed for a particular patient as well as side effect profiles. If a response is needed in days, a psychostimulant is a good choice. If a response is needed in weeks to months, SSRIs, tricyclics, or atypical antidepressants are often chosen. Generally, physicians should start with a low dose and titrate slowly.

Psychostimulants, such as methylphenidate, have a rapid onset, can be continued indefinitely, and can be titrated to effect. A good starting dose is 5 mg taken once in the morning and again around noon. These drugs are used frequently to “perk up” elderly patients who are becoming lethargic “prematurely.” Psychostimulants have several good qualities, such as counteracting opioid sedation and not suppressing the appetite, but they may exacerbate anxiety, tremulousness, anorexia, and insomnia.

SSRIs (e.g., fluoxetine, sertraline, and citalopram, to name only a few) are said to be highly effective, with about 70% of

patients showing a response. The latency period for SSRIs is 2 to 4 weeks, they tend to be well tolerated, and they require only once-daily dosing. Low doses may be effective in advanced illness. This principle is also true of many other drugs in the setting of advanced illness.

Although some physicians do not recommend tricyclics (amitriptyline, nortriptyline, etc.) as first-line therapy, others have had good results choosing these drugs first for terminally ill patients with chronic pain and depression. Tricyclic agents often cause sedation and, thus, when dosed at night, are also helpful in treating sleep disturbances. Because they also tend to slow down bladder and bowel function, they may sometimes be useful for patients with irritable bladders or loose bowels. On the other hand, for a patient on the verge of urinary retention or constipation, they may be detrimental. I have found this class of drugs to be useful, with relatively few side effects when used in low dosages in terminally and irreversibly ill patients. I like to use them in this setting because drugs like amitriptyline can potentiate other analgesics and are themselves often useful in treating neuropathic pain. Onset of action occurs in 3 to 6 weeks.

Some patients will develop an agitated depression. Drugs available to treat such agitated depression include haloperidol, risperidone, and olanzapine. Haloperidol (0.5 to 1 mg by mouth, intravenously, or subcutaneously given every hour until calm and then every 12 hours) is, of course, time honored and traditional for treating significant agitation, but it does not have much of an antidepressant effect. Risperidone (0.5 to 1 mg every 12 hours) is a good choice because of its combination of sedation and good antipsychotic effects. In addition, newer agents like venlafaxine hydrochloride work on 2 or 3 different receptor types, and more and more psychiatrists are beginning to use multiple therapy with 2 or 3 different agents because the synergistic effect can be dramatic. In patients with severe symptoms, psychiatrists may often use very high doses of drugs and even high doses of several drugs in combination. The only problem that may result from the high doses is sedation, and dosages can always be decreased. Thus, consultation with a psychiatrist in this setting can be very helpful.

Counseling. Counseling should be woven into routine interventions whenever possible. The primary treating physician of a terminally ill patient need not be the only counselor to the patient, and others besides psychiatrists and psychologists can have good results in counseling. This includes trusted family members or friends, personal clergy, social workers, and pastoral care staff members. It goes without saying that hospice professionals are particularly well trained and suited to counsel terminally ill patients and their families. In the hospital, the pastoral care staff can be particularly effective, since many end-of-life decisions involve spiritual as well as physical matters.

Counseling a patient in these circumstances may have several goals. One goal of counseling is to improve patient understanding of the disease and its expected course. As a general rule, withholding information does not help patients, although there are right and wrong times as well as better and worse techniques for delivering bad news. Another counseling goal is to identify strengths and coping strategies. Most patients—at least most adult patients—will have had experience coping with major stresses. I find it useful to take them back to that time and ask

them how they found the strength to cope. This method takes the attention off of the current crisis. It encourages patients and reminds them of their previous successes. At other times, however, patients may need help developing new coping strategies.

ANXIETY

If I were told that I had a terminal illness, I would be anxious, too—despite the fact that my career has involved much talking about, teaching about, and dealing with death. Anxiety about the end of life is normal. I would worry about those who were not fearful, uncertain, or anxious when told they had 3 months, 6 months, or 2 years to live.

Anxiety has physical, psychological, social, spiritual, and practical aspects. It can present as agitation, insomnia, restlessness, sweating, tachycardia, hyperventilation, panic disorder, worry, or tension. As with depression, separating some physical symptoms of extreme anxiety from symptoms of the underlying disease is difficult at times. Anxiety should be differentiated from delirium, depression, bipolar disorder, medication side effects, insomnia, and substance abuse.

Management of anxiety consists of counseling and supportive therapy. Benzodiazepines are the drugs of choice. They work quickly—generally within an hour. However, in very elderly patients, they can result in a paradoxical agitation.

A common source of anxiety in seriously ill patients—or at least of patient agitation and disorientation—is sleep deprivation. Patients are awakened several times every night for blood pressure checks, blood draws, change of intravenous lines, and other medical interventions. Since it is not usually possible to place a hold on these activities during the night, the use of sedative drugs can be beneficial. For example, the Transplant Service at Baylor often sedates patients with zolpidem tartrate to put them asleep and diazepam to keep them asleep. This has been called the “Klintmalm cocktail.” The Transplant Service has found that patients who sleep better at night feel better and are more lucid in the daytime.

DELIRIUM

Delirium is common in the final stages of a terminal illness. I consider delirium in the setting of a terminal illness a reasonable marker of when to tell the family that the patient's life is near its end. Delirium is characterized by the acute onset of a global change in cognition and awareness. It usually presents as a fluctuating level of consciousness and cognitive impairment and must be distinguished from dementia, depression, and anxiety. For example, dementia in its terminal stages manifests itself in day-night reversal, agitation, restlessness, and moaning and groaning. Acute delirium is often misdiagnosed as chronic dementia and vice versa. This misdiagnosis is not surprising, since the two are closely related: delirium is particularly common in patients who have dementia, whether that dementia has been previously recognized or not. Thus, it is important to know if your patient has dementia.

I would suggest on epidemiological grounds that we should never be surprised when an elderly patient has dementia. Most studies suggest that about 5% of the 65-year-old *ambulatory* (non-nursing home bound) elderly population has dementia. In 85-year-old ambulatory adults, depending on the study you look at,

that incidence ranges from 30% to 50%. Many of these elderly people are able to hide the dementia from their families. These families (and often physicians, too) are then startled when the elderly patient becomes delirious. As with other diagnostic challenges in medical practice, the history is important.

When I assess patients for dementia, I often do a functional history with the family. I ask questions like, How were they doing paying the bills? How were they doing balancing the checkbook? How were they doing using the telephone? How were they cooking? It is not unusual for a daughter to admit that Mom called her every 5 minutes all day long and couldn't seem to call anybody else or that Dad has really been making mistakes in the checkbook. Health care professionals should recognize this as a possible symptom of dementia, while the family may see the same symptom as "just what happens when people get old." One family described to me how their mother used to be a great cook but "got tired of cooking" the past few years. The patient had declined in her culinary creations over several years, going from 4-course gourmet meals to microwave dinners. It was not until she started having trouble following the typical 3 steps it takes to heat up a microwave dinner that the family became concerned. Even then, the family did not suspect dementia; they just thought Mom was "too old to cook."

After obtaining the history, screening for dementia involves assessing patients' abilities to complete a series of tasks (as in cooking) in a logical way. A number of useful tools are available that take only about 5 minutes to perform. I like to use the Folstein Mini-Mental Status exam. Sometimes only part of the exam is needed to determine if a patient meets certain minimal standards of mental capacity. For example, most physicians and nurses will ask simple orientation questions and then ask the patient to squeeze their fingers. If the patient is oriented and follows a simple command, they will then assume that the patient has decision-making capacity. When I'm assessing the mental status of seriously ill patients for decision-making capacity in my role as an ethics consultant, I like to move well beyond orientation or simple one-step commands and better assess patient understanding of what is being said. One way to do this is to give 3-step commands. My 3-step command might be something like, "Pick up your right hand, bring it over and touch your left hand, and point one finger up in the air." I also like to ask "nonsense questions" such as if we are on the planet Mars. It is only when the patient passes these tests of cognitive ability that I proceed to more complex decision assessment. Remember that no single test differentiates delirium from dementia, but the factors I have just mentioned are important as part of the comprehensive assessment of almost any adult patient sick enough to be in the hospital and almost all terminally ill patients.

When the patient is delirious, what possible contributing factors should be considered? I would suggest at least the following: drug reaction, infection, progression of the underlying illness, hypoxemia, metabolic disorders, vitamin deficiencies, fecal impaction, urinary retention, renal failure, or hepatic failure. Recognizing the cause of delirium does not mean that the underlying cause (as opposed to the symptoms) must always be treated in a dying patient. For example, physicians have turned what used to be the terminal stages of Alzheimer's disease—pneumonia—into a medical crisis, with interventions consisting of intravenous antibiotics, pressor drugs, and mechanical ventilation. For some patients with advanced dementia, we should remember Osler's adage, "Pneumonia is a friend of the aged." That is, in some patients with advanced dementia who develop pneumonia with sepsis and delirium, the most appropriate treatment might be haloperidol, morphine, acetaminophen, and oxygen, allowing nature to run its course.

To manage delirium, neuroleptic drugs such as haloperidol and chlorpromazine are the treatment of choice. Other drugs are available, such as risperidone and, of course, benzodiazepines for acute agitation, but I generally consult with a psychiatrist for the extreme cases. If the patient has only a negligible or partial response to the treatment, the physician should reevaluate the diagnosis and consider the possibility of underlying processes that need to be addressed and adjustment of drug dosages.

SUMMARY

Depression, anxiety, and delirium are common phenomena associated with terminal and irreversible illness. They tend to be underdiagnosed and undertreated in patients with terminal disease. Through careful history taking, physical examination, and laboratory assessment, they can be appropriately diagnosed, even in difficult circumstances. Psychiatric consultation is often very appropriate in working with these patients. Once we recognize these problems, we can employ a number of effective treatments. These therapies, when judiciously applied, can definitely improve the quality of life for dying patients, who, after all, although dying, are still alive!

Suggested reading

- Breitbart W, Chochinov HM, Passik S. Psychiatric aspects of palliative care. In Doyle D, Hanks GWC, MacDonald N, eds. *Oxford Textbook of Palliative Medicine*, 2nd ed. Oxford, England: Oxford University Press, 1998:933–954.
- Storey P, Knight CE. *UNIPAC Two: Alleviating Psychological and Spiritual Pain in the Terminally Ill. Hospice/Palliative Care Training for Physicians: A Self-study Program*. Gainesville, Fla: American Academy of Hospice and Palliative Medicine, 1997.