Background: Relief of suffering is a central goal for palliative care. Achievement of this goal can be difficult, however, due to the complex nature of suffering.

Methods: A psychosocial perspective is used to understand suffering and to identify interventions to relieve suffering in patients with advanced disease.

Results: Clinical experience and research suggest that attending to the psychosocial aspects as well as the medical aspects of palliative care has the potential of further reducing the suffering experienced by patients with advanced disease.

Conclusions: Suffering is best viewed as a subjective phenomenon that can be influenced by biological, psychological and social processes. Interventions in each of these areas can help to relieve patient suffering.

Introduction

The relief of suffering is one of the central goals of palliative care efforts in oncology. Although this goal seems straightforward, its achievement can be difficult for several reasons. First, there is little agreement in the palliative care field on the definition of suffering.[1] Second, the mechanisms underlying suffering are quite complex. Suffering is frequently associated with the experience of aversive physical symptoms (eg, pain), however, many patients suffer even in the absence of such symptoms.[2-5] Third, suffering due to advanced disease does not appear to be limited to the affected patient. Family members also suffer,[6] which may, in turn, exacerbate the patient's suffering.[1,7] In an attempt to address these issues, several workers in the field of palliative care have adopted a psychosocial perspective.[1,8,9] According to this perspective, suffering is best viewed as a subjective phenomenon that can be influenced by biological, psychological, and social processes.

Sources of Suffering in Patients With Advanced Disease

Reviewing the various ways in which suffering has been characterized in palliative care, Chapman and Gavrin[4] note three features common to most descriptions. Suffering generally occurs in the context of a perceived threat to the integrity of the self, it is by definition an inherently unpleasant emotional experience, and it represents an enduring psychological state rather than a transient or fleeting experience. To this list, they add a fourth feature: suffering also reflects perceived helplessness in the face of threat. In addition to defining suffering, this description provides an understanding of how factors other than physical symptoms can contribute to suffering. Psychological symptoms (eg, depression) and existential distress (eg, concerns about death) also are sources of suffering since they, too, can be experienced as unpleasant, can occur on a frequent or chronic basis, and can be perceived as uncontrollable.[1,2,10]

In most instances, suffering in patients with advanced cancer is likely to have multiple origins (Table 1). Adequate control of physical symptoms is a central part of any effort to relieve suffering. However, the psychosocial model suggests that psychological and existential factors also should be examined as potential sources of suffering.

Psychological Issues

Most cancer patients develop psychological and psychiatric symptoms during the terminal phase of illness, either alone or in combination with physical symptoms.[11,12] Among the many possible psychological and psychiatric complications, the most common are anxiety disorders, depressive disorders, and cognitive disorders, which can be major sources of suffering for patients and can pose significant management problems both at home and in institutional settings.

Anxiety Disorders

The recognition of anxiety in the patient with advanced disease can be challenging. Individuals who are anxious may present with a variety of symptoms including subjective feelings of tension, apprehension, and worry, as well as overt signs of restlessness, autonomic hyperactivity, hypervigilance, insomnia, distractibility, shortness of breath, tingling, and numbness. Physical or somatic manifestations of anxiety often overshadow psychological or cognitive ones in patients with advanced disease and may be the initial presenting symptoms.[13]

Anxiety is a symptom that can have many etiologies. It may be encountered as a component of an adjustment disorder, panic disorder, generalized anxiety disorder, phobia, or agitated depression. It also can arise from medical complications of illness or treatment.[13-15] Hypoxia, sepsis, poorly controlled pain, adverse drug reactions such as akathisia, and withdrawal states can all present as anxiety. In the dying patient, anxiety also may reflect impending cardiac or respiratory arrest, pulmonary embolism, electrolyte imbalance, or dehydration.[16]

Anxiety in terminal illness commonly results from medical complications; however, psychological issues also may play a role.[13] The decision on whether to treat anxiety during the terminal phase of illness should be based primarily on the patient's subjective level of distress. Other considerations include the contribution of anxiety to noncompliance with medical care, family and staff reactions to the patient's distress, and the balance between the risks and benefits of treatment.[15] The management of anxiety in terminal illness typically involves the judicious use of psychotropic medications (Table 2).[13-15]

Benzodiazepines are among the mainstays of the pharmacologic treatment of anxiety in the terminally ill patient. The shorter-acting benzodiazepines, such as lorazepam,
Among the various medications, alprazolam, and oxazepam pose the least risk of toxic accumulation due to impaired metabolism.[17] The disadvantage of using short-acting benzodiazepines is that patients often experience breakthrough anxiety or end-of-dose failure usually related to long dosage intervals. This potential problem can be treated by increasing the dosage frequency or by switching to longer acting benzodiazepines such as diazepam or clonazepam. Dying patients also can be given diazepam rectally (when no other route is available) to control anxiety, restlessness, and agitation.[18] Fears of respiratory depression should not prevent the clinician from using adequate dosages of benzodiazepines to control anxiety. The likelihood of respiratory depression is minimized when one uses shorter-acting drugs, increases the dosages in small increments, and ultimately switches to longer acting drugs.

High-potency neuroleptics (eg, haloperidol) are useful in the treatment of anxiety, particularly when benzodiazepines are insufficient for symptom control.[15] Neuroleptics also are indicated when an organic etiology is suspected or when psychotic symptoms, such as delusions or hallucinations, accompany anxiety. Neuroleptics may be the safest class of anxiolytics when respiratory depression or compromise is a concern. With this class of drugs in general, one must be aware of extrapyramidal side effects (particularly when patients are taking additional neuroleptics for antiemetic purposes) and the remote possibility of neuroleptic malignant syndrome. Tardive dyskinesia is rarely a concern given the generally short term usage and low dosages of these medications in this population.[19] Low-potency neuroleptics (eg, thioridazine and chlorpromazine) are used less often because patients may experience akathisia and hypotension as side effects.

Tricyclic and heterocyclic antidepressants are the most effective treatment for anxiety that may accompany depression and for panic disorder.[20,21] The usefulness of tricyclic and heterocyclic antidepressants with dying patients often is limited by their anticholinergic and sedative side effects as well as their delayed onset of action.

Opioid medications such as the narcotic analgesics are primarily indicated for the control of pain. However, these medications also are effective in the relief of dyspnea and anxiety that may be associated with this symptom.[22] When respiratory distress is not a major problem, opioids may be preferred solely for their analgesic purposes and for adding more specific anxiolytics (such as the benzodiazepines) to control concomitant anxiety.

Nonpharmacologic interventions for anxiety include supportive psychotherapy and cognitive-behavioral psychotherapy. In the patient with advanced disease, these interventions are used typically in combination with pharmacotherapy. Supportive psychotherapy with the anxious patient is intended to reduce perceived isolation and provide an outlet for the expression of fears and worries. By identifying the sources of worrying, acknowledging realistic concerns, and challenging unrealistic concerns, the therapist can help the patient to achieve some measure of control over psychological sources of suffering. Cognitive-behavioral interventions for anxiety include relaxation training, guided imagery, and hypnosis.[23] These techniques involve the use of suggestion to induce physical and mental relaxation and to direct attention away from anxiety-arousing cognitions. Following brief instructions by a therapist, many patients are able to self-administer these cognitive-behavioral techniques when needed. However, the presence of a confusional state can interfere with the patient’s ability to focus attention and, thus, may limit the usefulness of these techniques.[23]

Depressive Disorders

Many clinicians rely on the presence of cognitive symptoms (eg, feelings of worthlessness and hopelessness, excessive guilt, and suicidal ideation) to make a diagnosis of major depression.[24-26] but this strategy can present problems. How is the clinician to interpret feelings of hopelessness in the dying patient when there is no hope for cure or recovery? For many patients, hope is contingent on the ability to find continued meaning in their day-to-day existence. Hopelessness that is pervasive and accompanied by a sense of despair or despondency is more likely to represent a symptom of a depressive disorder.[24] Likewise, suicidal ideation, even in mild forms, is likely to be associated with significant degrees of depression in terminally ill cancer patients.[27,28] In addition to psychological causes, organic factors can produce a depressed mood in patients with advanced disease. Possible organic causes of depression include: administration of corticosteroids,[29] chemotherapeutic agents (eg, vincristine, vinblastine, asparaginase, intrathecal methotrexate, interferon, and interleukin)[30-32] amphetamine,[33] whole brain radiation,[34] endocrine complications, [35] and paraneoplastic syndromes.[36]

Approximately 25% of patients with advanced disease experience clinically significant depression.[37,38] Although psychotherapy can be effective in reducing mild to moderate depressive symptomatology in cancer patients, pharmacotherapy is the mainstay for treating major depression in the terminally ill (Table 2).[24,39] Factors such as the prognosis and the time-frame for treatment may play an important role in determining the type of medication used to treat depression. A depressed patient with several months of life expectancy may be able to wait the two to four weeks it can take to respond to a tricyclic antidepressant. A depressed dying patient with less than three weeks to live may do best with a rapid-acting psychostimulant.[39,40] A patient who is within hours to days of death and is in distress is likely to benefit most from the use of sedatives or narcotic analgesic infusions.

Tricyclic antidepressants (TCAs) have been the cornerstones for treating depression in the general cancer setting since the early 1960s. Their use with the terminally ill, however, requires a careful analysis of the risk-benefit ratio. Although nearly 70% of patients treated with TCAs for nonpsychotic depression can anticipate a positive response, these medications are associated with a side-effect profile that can be particularly troublesome for terminally ill patients.[30] Side effects of TCAs include constipation, dry mouth, urinary retention, postural hypotension, and dizziness. To avoid exacerbating symptoms associated with genitourinary outlet obstruction, decreased gastric motility or stomatitis, relatively nonanticholinergic TCAs (eg, desipramine or nortriptyline) may be a reasonable choice.

Selective serotonin reuptake inhibitors (SSRIs) add a recent and important new class of agents to the list of available antidepressant medications. SSRIs have been found to be effective in the treatment of anxiety and panic disorder.[41] and have a number of features that may be advantageous in the terminally ill. The SSRIs have a low affinity for adrenergic, cholinergic and histamine receptors, resulting in negligible orthostatic hypotension, urinary retention, memory impairment, and sedation.[42] They do not cause clinically significant alterations in cardiac conduction and generally are well tolerated. Moreover, they have a wider margin of safety than TCAs in the event of an overdose. Most of the side effects of SSRIs (eg, increased intestinal motility, nausea, vomiting, insomnia, headaches, and sexual dysfunction) result from their selective central and peripheral serotonin reuptake. Some patients also may experience anxiety, tremor, restlessness, and akathisia. This last side effect occurs in up to 15% of patients treated with fluoxetine.[43] SSRIs currently being marketed in the United States include sertraline, fluoxetine, paroxetine, and fluvoxamine.

The psychostimulants (dextroamphetamine, methylphenidate, and pemoline) offer an alternative and effective pharmacologic approach to the treatment of depression in terminally ill patients.[39,44,45] These drugs have a more rapid onset of action than TCAs and are most helpful in the treatment of depression that is accompanied by severe psychomotor slowing and/or mild cognitive impairment. At relatively low doses, psychostimulants also can stimulate appetite, promote a sense of well being, and provide an outlet for the expression of fears and worries. By identifying the sources of worrying, acknowledging realistic concerns, and challenging unrealistic concerns, the patient and ultimately switches to longer acting drugs.

The patient with advanced disease who is depressed and suicidal is likely to require additional treatment beyond pharmacotherapy. The early involvement of a psychiatric consultant is critical to adequately assess the meaning of suicidal thoughts, the degree of intent, and the quality of internal and external controls against self-
Factors that increase the risk of suicide among patients with advanced disease include depression, pain, delirium, substance/alcohol abuse, family history of suicide, and the lack of social supports.[28] These factors should be reviewed as part of the evaluation and management of the suicidal patient. Neuroleptic, antidepressant, and analgesic medications should be used when appropriate to treat agitation, psychosis, major depression or pain that is contributing to suicide risk. Attempts should be made to involve family members or close friends to comfort the patient, provide information, and assist in treatment planning. The goal of these efforts is to prevent suicidal behavior that is driven by desperation over physical or psychological symptoms that have not been adequately managed.

Cognitive Disorders

The American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)[49] divides cognitive disorders into the subcategories of (1) delirium, dementia, amnesia, and other cognitive disorders, (2) mental disorders due to a general medical condition (including mood disorder, anxiety disorder, and personality change due to a general medical condition), and (3) substance-related disorders. Although all of these mental syndromes may be seen in the patient with advanced disease, delirium has received the most attention.

Delirium has been defined as etiologically nonspecific, global, cerebral dysfunction manifested by concurrent disturbances of level of consciousness, attention, thinking, perception, memory, psychomotor behavior, emotion, and the sleep-wake cycle. Disorientation, fluctuation, or waxing and waning of these symptoms, as well as acute or abrupt onset of such disturbances, are other critical features of delirium. Reversibility of the process of delirium often is possible even in the patient with advanced illness; however, it may not be reversible in the last 24 to 48 hours of life. This is most likely due to the fact that irreversible processes such as multiple organ failure are occurring in the final hours of life. Delirium occurring in these last days of life often is referred to as terminal restlessness or terminal agitation in the palliative care literature.

Delirium and dementia share common clinical features such as impaired memory, thinking, and judgment, and disorientation. Dementia generally appears in relatively alert individuals and is accompanied by little or no clouding of consciousness. The temporal onset of symptoms in dementia is more subacute or chronically progressive, and the sleep-wake cycle seems less impaired in the earlier stages. Most prominent in dementia are short-term and long-term memory impairment, impaired judgment and abstract thinking, and disturbances in higher cortical functions (eg, aphasia and apraxia). Occasionally, delirium may be superimposed on an underlying dementia such as in the case of an elderly cancer patient with preexisting dementia.

Delirium is common among terminally ill patients. Survey data suggest that 25% to 85% of cancer patients experience delirium prior to death.[50] Delirium can arise as a direct result of central nervous system (CNS) disease (eg, primary brain tumor, brain metastasis) or as a result of other forms of disease that affects the CNS (eg, metabolic encephalopathy due to organ failure). Early symptoms of delirium can be misdiagnosed as anxiety, anger, depression, or psychosis. A diagnosis of delirium should be considered in any patient showing acute onset of agitation, impaired cognitive function, altered attention span, or a fluctuating level of consciousness.[51] A common error among medical and nursing staff is to conclude that a new psychological symptom is functional without ruling out all possible organic etiologies. Given the large numbers of medications that many terminally ill patients receive and the fragile state of their physiologic functioning, even routinely ordered hypnotics may promote delirium in some patients. Other medications that can induce delirium include opioid analgesics (eg, levorphanol, morphine sulphate), antineoplastic agents (eg, methotrexaate, fluorouracil, cisplatin, procarbazine) and corticosteroids (eg, dexamethasone).

A standard approach to managing delirium includes a search for the underlying causes, correction of those factors, and management of the symptoms of delirium. The treatment of delirium in the dying patient is unique, however, because (1) the etiology of terminal delirium is often multifactorial or may not be found, (2) when a distinct cause is found, it is often irreversible (eg, hepatic failure or brain metastases), (3) workup may be limited by the setting (eg, home or hospice), and (4) diagnostic procedures that are unpleasant or painful (eg, computed tomography scan, lumbar puncture) may be avoided since the focus of care usually is on patient comfort.

When confronted with a delirium in the terminal illness or dying cancer patient, a differential diagnosis should be formulated; however, studies should be pursued only when a suspected factor can be identified easily and treated effectively. Bruera[52] reported that an etiology was discovered in less than 50% of terminally ill patients with cognitive failure.

Symptomatic and supportive therapies also are important[51] and, in the dying patient, may be the only steps taken. Fluid and electrolyte balance, nutrition, and vitamins may be helpful. Measures to help reduce anxiety and disorientation (eg, structure and familiarity) include a quiet, well-lit room with familiar objects, a visible clock or calendar, and the presence of family. One-on-one nursing observation and, on rare occasions, judicious use of physical restraints to prevent harm to oneself or others may be necessary. Often, these supportive techniques alone are not effective, and symptomatic treatment with neuroleptic or sedative medications is necessary (Table 2).

Haloperidol, a neuroleptic agent that is a potent dopamine blocker, is the drug of choice in the treatment of delirium in the medically ill.[51,53-55] The majority of delirious patients can be managed with oral haloperidol, although delivery by the subcutaneous route also is used by many palliative care practitioners.[56,57] Methylthionephrine and midazolam often are used to control confusion and agitation in terminal delirium.[58-60] The goal of treatment with midazolam, and to some extent with methylthionephrine, is quiet sedation only. In contrast to neuroleptic drugs like haloperidol, midazolam does not clear a delirious patient’s sensorium or improve cognition. Although neuroleptic drugs such as haloperidol can diminish agitation, clear the sensorium, and improve cognition, this is not always possible in the last days of life since the processes causing delirium may be ongoing and irreversible. Two reports[61,62] indicate that 10% to 20% of terminally ill patients experience delirium that can be controlled only by sedation to significantly decreased levels of consciousness.

The use of neuroleptics to manage delirium in the dying patient remains controversial. Delirium is viewed by some as a natural part of the dying process that should not be altered. Another rationale is that these patients are so close to death that aggressive treatment is unnecessary. Parenteral neuroleptics or sedatives may be mistakenly avoided because of exaggerated fears that they might hasten death through hypotension or respiratory depression. Many clinicians are unnecessarily pessimistic about the possible results of neuroleptic treatment for delirium and believe that since the underlying pathophysiologic process often continues unabated (such as hepatic or renal failure), no improvement can be expected in the patient’s mental status. In addition, there is concern that neuroleptics or sedatives may worsen a delirium by making the patient more confused or sedated; however, clinical experience in managing delirium in dying cancer patients suggests that the use of neuroleptics in the management of agitation, paranoia, hallucinations, and altered sensorium is safe and effective. Management of delirium on a case-by-case basis is wisest. The dying patient who is agitated and confused should probably be given neuroleptics to help restore calm. Conversely, the dying patient who is lethargic and somnolent may benefit from a “wait and see” approach to the use of neuroleptics.

Existential Issues

Existential distress is probably the least understood source of suffering in patients with advanced disease.[10] Although the phenomenon has been well described in clinical reports,[3] little quantitative research is available on this topic. Consequently, there are no generally accepted methods for defining, categorizing, or assessing common forms of existential distress.
Cherny and colleagues[1] recently proposed one of the first taxonomies for existential distress among patients with advanced disease. According to this schema, existential distress can be classified in terms of whether patients are focused on past, present, or future concerns. With regard to past concerns, distress can occur if patients focus on unfulfilled aspirations or previous actions they regret.[1,3,10,63] With regard to present concerns, distress can occur if patients focus on the loss of personal integrity or the loss of important occupational, social, and familial role functions. In addition, patients may become distressed if they perceive that their continued existence represents a burden and source of distress for family members.[8,64] With regard to future concerns, distress can occur if patients focus on their impending death and separation from loved ones.[63] These future concerns appear to be particularly common. Surveys indicate that 50% to 80% of terminally ill patients experience troubling thoughts or concerns about death.[1]

This taxonomy also can be used to formulate interventions to relieve existential distress. Past concerns contributing to existential distress can be addressed using life review techniques. One such technique, known as the psychodynamic life narrative, involves a review of the patient's life in order to place the current illness in a personal context.[65] Working with a therapist, the patient can evaluate his or her past successes and failures, and the therapist validates the patient's current feelings of distress, restores hope, relieves despair, and diminishes isolation.

Present concerns regarding physical integrity can be addressed in several ways. One method is to enhance the patient's appearance by attention to grooming, alteration of clothing for appropriate fit, and use of cosmetic prostheses.[1] Physical integrity can be preserved with auxiliary or orthotic devices that allow the patient to maintain social functioning and decrease dependency on others.[1] Addressing the perceived meaninglessness of life has been described as a central goal in the existential care of the incurably ill.[66] A psychological approach to this issue involves helping the patient to identify short-term goals whose fulfillment could preserve a sense of self-efficacy.[23,66,67] A spiritual approach involves meeting with a chaplain or pastoral counselor to explore and reaffirm religious beliefs.[63]

Present concerns related to family suffering require additional intervention strategies. The first step in addressing this issue is to identify the sources of family suffering. Potential sources include lack of information or understanding about the patient's illness, physical and emotional burdens associated with caregiving, family dysfunction, and anticipatory grief. Improving communication among family members and between health care providers and family members is a key component of efforts to reduce family distress. This can be accomplished by scheduling family conferences with the patient, family members, and health care providers.[1,11,68] Instructing palliative care professionals in effective communication and counseling skills may also be useful.[69,70]

For many family members of patients with advanced disease, the physical and emotional burdens of providing care at home are a major source of suffering.[6] The many reasons that caregiving can cause suffering may require different intervention strategies.[11,66,68] For example, if family members are distressed because the patient's symptoms are poorly controlled, then intervention efforts should focus on symptom relief. If their distress is due to the physical requirements of caregiving, then additional help in the home may be required. If their distress is related to the emotional aspects of caregiving, then supportive psychotherapeutic interventions may be required. Coyle et al.[64] described a supportive home care program that can be used to identify and ameliorate these sources of caregiver distress. Through telephone calls, home visits, and occasional clinic visits, the supportive care team continually monitors the well-being of the patient as well as the family. This information is used to coordinate the delivery of medical and psychosocial care by hospital-based professionals, community agencies, and/or private practitioners. By assuming responsibility for the welfare of both patient and family, the supportive care team insures that potential familial sources of suffering will be addressed adequately.

Future concerns that contribute to existential distress frequently involve fears of death and separation from others. Such concerns can be a potent source of suffering and should be addressed as part of palliative care efforts.[10] The first step in attempting to deal with these concerns is to create an atmosphere in which patients are willing to discuss their fears. Health care providers and family members convey either implicitly or explicitly that they are uncomfortable discussing such issues.[10,71] Spiegel and Gafkides[72] observed that when patients with advanced disease openly discuss issues of death and dying, their fears usually diminish, and they generally realize that the process of dying more than death itself. As a consequence, the focus of their attention tends to shift to issues over which they can exercise some control (eg, pain management, participation in medical decision-making).[71] For some patients, however, the resolution of concerns about death requires an examination of religious and spiritual issues. According to Doyle,[10] religious issues refer to the practices of a particular faith that usually can be addressed by respecting and facilitating the patient's wishes to practice their religious beliefs. Spiritual issues, on the other hand, refer to universal questions about the meaning of life and death that may or may not be related to belief in a particular faith.[10] Consultation with a chaplain experienced in working with the terminally ill may be useful in deciding how to address issues that transcend specific religious faiths.[63,73]

Conclusions

Relief of suffering is a fundamental goal of palliative care, but the identification of these sources of suffering among patients with advanced disease is complex. The potential sources of suffering for this population can extend beyond physical symptoms to include psychological and psychiatric complications (eg, anxiety, depression, and cognitive disorders) and existential distress emanating from past, present, and future concerns. These psychosocial factors often are overlooked as potential sources of suffering in patients with advanced disease. Relief of these sources of suffering can be achieved through a multidisciplinary approach to patient care in which experts in mental health and pastoral care contribute to the treatment effort. Addressing the psychosocial aspects as well as the medical aspects of palliative care can further reduce the suffering experienced by patients with advanced disease.

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