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Management of Depression and Anxiety in Advanced Illness

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Disclosure Slide

E. Alessandra Strada, PhD, MSCP, FT, has no financial arrangements or affiliations with any commercial entities whose products, research, or services may be discussed in these materials. Any discussion of investigational or unlabeled uses of a product will be identified.

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Objectives

- Review the prevalence and clinical presentation of depression and anxiety in the palliative care setting
- Discuss diagnosis and differential diagnosis of depression and anxiety in advanced illness
- Present evidence-based and integrated treatment approaches

Burden of Depression in Advanced Illness

- Depressive syndromes are common in advanced illness, but under recognized and undertreated
- Associated with increased morbidity, reduced quality of life, reduced autonomy
- Increased risk for suicide and desire for hastened death

Irwin et al., 2008; Misono et al., 2008

Prevalence of Depression in Advanced Illness

- Patients with advanced cancer: 3% to 58% depending on assessment methodology used – different thresholds
 - Pancreatic cancer: 40% to 50% – suicide risk 11 times higher than in general population
 - Children with cancer: 10% to 14%
- Noncancer population
 - End-stage renal disease: up to 27%
 - Parkinson's disease: 20% to 40%
 - Multiple sclerosis: 35%
 - Advanced heart failure: 22% to 46%
 - End-stage AIDS: 23% to 52%

Turaga et al., 2011; Rosestein, 2011

Barriers to Diagnosis and Treatment

- Belief that depression in advanced illness is “normal”
- Challenge of differentiating expected emotional distress from major depression as psychiatric disorder
- Overlap of neurovegetative symptoms in depression and advanced illness
- Medications and medical conditions can mimic depression
- Fear of overpathologizing end-of-life
- Concern about use of psychotropic medications

Risk Factors for Depression

- Prior history of depression
- Poorly controlled pain and other symptoms
- Treatment and illness-related factors
- Existential and spiritual suffering

Seow et al., 2011; Meyer et al., 2003

Risk Factors for Depression

- Metabolic abnormalities
 - Hypercalcemia
 - Sodium, potassium imbalance
 - Anemia
 - Deficient vitamin B12 or folate
- Endocrinologic abnormalities
 - Hyper- or Hypothyroidism
 - Adrenal insufficiency

Risk Factors for Depression

- Medications
 - Steroids
 - Clonidine, Propanolol
 - Barbiturates
 - Reserpine
 - Interferon and Interleukin-2
 - Methyldopa
 - Chemotherapy agents
 - Procarbazine
 - Vincristine
 - Vinblastine

Patten et al.2004; Denicoff et al., 1987

Assessment Methods

- Diagnostic classification systems
 - Diagnostic and Statistical Manual (DSM-5)
 - Endicott Substitution Criteria
- Screening instruments – self-report
 - Center for epidemiologic Studies-Depression (CES-D) Boston Short Form – 10 items
 - Hospital Anxiety and Depression Scale (HADS)
 - Geriatric depression Scale (Short Form) – 15 items

Clinical Features of Major Depression

—DSM-5

Depressed mood or loss of interest – most of the time for two weeks

- Behavior that is agitated or slowed down
- Fatigue or diminished energy
- Worthlessness or extreme guilt
- Decreased ability to concentrate and make decisions
- Significant weight loss or gain
- Frequent thoughts of death or attempts
- Insomnia or hypersomnia

Endicott's Criteria

Endicott, 1984

Somatic Symptoms → Psychological Symptoms

Weight loss/gain	Depressed appearance
Insomnia or hypersomnia	Social withdrawal or decreased talkativeness
Fatigue/loss of energy	Brooding, self-pity, pessimism
Diminished ability to concentrate	Lack of reactivity, cannot be cheered up

Differential Diagnosis

- Hypoactive delirium
 - Psychomotor retardation, lethargy, **reduced awareness of surroundings**
- Grief reactions
 - Mood fluctuates
 - Self-esteem generally not affected
 - Retains some ability to experience some degree of wellbeing

General Treatment Considerations

- Manage uncontrolled symptoms
 - pain in diseases not usually considered painful – e.g., heart disease
- Patients with excessive guilt, hopelessness, anhedonia, ruminative thinking, and impairment in quality of life may benefit from medication **even if MDD criteria not fully met**
- Successful treatment can decrease desire for hastened death

Breitbart et al., 2010

Pharmacological Management

- General lack of high-quality evidence
- Randomized trials and meta-analyses indicate effectiveness of antidepressants
- Systematic review – 25 placebo-controlled randomized trials: benefit of treatment over placebo within four to five weeks

Rayner et al., 2010; Fish, 2004; Ly et al., 2002

Antidepressant Medications

SSRIs

(mg, PO)

- Fluoxetine 10-40
- Sertraline 25-100
- Paroxetine 10-40
- Citalopram 10-40
- Escitalopram 5-20

SNRIs

- Venlafaxine 37.5-225
- Duloxetine 10-60

Kennedy & Marcus, 2005

Antidepressant Medications

Tricyclics

		(mg, PO)
• Desipramine	10	25-150
• Nortripyline	10	10-100

Atypical antidepressants

• Bupropion		75-300
• Trazodone	12.5	25-100
• Mirtazapine	7.5	15-60

Kennedy & Marcus, 2005

Psychostimulants

- | | | |
|---------------------|--------|----------|
| • Dextroamphetamine | | 5-15 bid |
| • Methylphenidate | 2.5 | 5-10 bid |
| • Modafinil | 50-100 | 50-200 |

Kennedy & Marcus, 2005

Pharmacological Management

- Clinical Practice Guidelines 2008 from American College of Physicians: depression in primary care
 - Initiate SSRI, SNRI, or atypical
 - SSRIs more favorable side-effect profile
 - TCAs may be more effective for severely depressed patients
- Psychostimulants
 - Prognosis of weeks
 - Improvement in mood and energy possible in 24 to 48 hours
 - As initial agents when longer prognosis but depression is severe
 - SSRI introduced and titrated while psychostimulants decreased

Qasees et al., 2008; Pereira & Bruera, 2001

Selecting an Antidepressant

- Side-effect profile
- Available time frame for treatment
- Patient's past treatment responses
- Target symptoms and use of adverse effects
- Coexisting medical problems
- Pharmacologic properties (e.g., half-life, potential for drug-drug interaction, availability of liquid formulation)

Psychological and Integrative Interventions

- Supportive psychotherapy
- Cognitive Therapies
- Meaning-Centered Psychotherapy – (Breitbart et al., 2012)
- Dignity therapy - (Chochinov et al., 2011)
- Creative arts therapies

Case 1

Mr.C.B. is a 63-year-old diagnosed with non-small-cell lung cancer (NSCLC) 1 year ago. He is followed by the palliative care services for treatment of progressive symptoms. He has been unable to work, and he is very anxious about finances. He spends most of the day on his recliner. His cough interferes with his sleep; he has lost about 10 pounds in the last 3 months; he has difficulty reading, which he used to enjoy. He moves slowly and feels very fatigued. He states he feels like a burden, and he is very upset that he cannot help his wife financially. For the past month, he has been more tearful and withdrawn. He speaks in short sentences, and his speech is often interrupted by coughing. He admits thinking about dying and wishing that he could just “not wake up”, but he denied he would kill himself. Ten years ago, he was treated with an antidepressant and therapy for clinical depression after the sudden death of his brother in a car accident. He was in the car and suffered a traumatic brain injury with early post-traumatic seizures.

Case example

- Clinical interview and exploration of passive suicidality
- Sertraline 25 mg titrated to 150 mg
- Biweekly psychotherapy focused on positive life-review and problem solving
- Symptom management

Anxiety in Advanced Illness

- Symptoms of anxiety are normal in advanced illness
- Difference between anxiety and anxiety disorder
- Prevalence of anxiety disorders is about 10% in palliative care patients
- Persistent, nonadaptive, interferes with function, persists more than seven days requires aggressive intervention

Payne et al., 2009; Alici and Levin, 2010; Spencer et al., 2010

Burden of Untreated Anxiety

- Increased interest in a hastened death
- Decreased ability to understand clinical information
- Decreased trust in their physicians
- Decreased expectation of adequate symptom control at the end of life
- Belief that they will be offered futile therapies

Alici and Levin, 2010

Clinical Manifestations of Anxiety

- Emotional
 - Edgy, impending doom, terror
- Cognitive
 - Dread, fear, obsessions, confusion, uncertainty, constant worry, catastrophizing, unable to take in information
- Behavioral
 - Avoidance, compulsions, psychomotor agitation, suspicious
- Autonomic
 - Diaphoresis, diarrhea, nausea, dizziness, tachycardia, or tachypnea
- Worries, fears, and concerns
 - Events leading up to death, scary fantasies about moment of death

Irwin et al., 2012; Wilson et al., 2007

Medical Causes of Anxiety

- Associated with specific cancers
- Anticipatory nausea and vomiting
- Corticosteroids
- Drug intoxication
- Metabolic disturbances
- Encephalopathy with systemic infection

Medical Causes of Anxiety

- Uncontrolled pain
- Endocrine disorders
- Withdrawal syndromes
- Delirium
- Psychotic disorders
- Cognitive impairment
- Depression
- Existential, spiritual distress

Assessment of Anxiety

- Patients may not recognize, acknowledge, or verbalize anxiety
- Listen for key words that can signal anxiety and explore own countertransference reactions
 - Concerned, scared, nervous, worried
- Patient Health Questionnaire for Anxiety and Depression (PHQ-4): anxiety and depression

Differential Diagnosis

- Depression
 - Suicidal ideation, brooding, early morning awakenings
- Delirium
 - Psychotic behaviors, delusions, altered cognition
- Dementia
 - Cognitive decline; hiding deficits

Anxiety Disorders

- Adjustment disorder with anxious features
- Generalized anxiety disorder
- Panic disorder
- Post-traumatic stress disorder

Psychosocial Treatment Modalities

- Cognitive-behavioral therapies
- Complementary therapies
 - Hypnotherapy
 - Music therapy, art therapy
 - Relaxation training
 - Acupuncture
 - Massage, reiki

Strada & Portenoy, 2011

Pharmacological Treatment

- Benzodiazepines
 - Acute anxiety reactions
 - Chosen based on desired half-life
 - Longer half-life → accumulation, side effects, toxicity
 - Shorter acting → nausea, panic attacks
 - Compromised hepatic function better with lorazepam or temezepam
 - Slow taper
 - Sedation
 - Memory loss
 - Delirium
 - Confusion

Pharmacological Treatment

- Benzodiazepine

Long-acting

Diazepam	5 – 10 BID
Clonazepam	0.25 – 1.0 BID

Short-acting

Alprazolam	0.25 – 5.0 TID
Lorazepam	0.5 – 2.0 TID
Triazolam	0.125 – 0.25 HS

Pharmacologic Treatment

- SSRIs
 - Chronic anxiety
 - Mixed depression and anxiety
- Gabapentin
- Trazodone; mirtazapine
- Initiate both benzodiazepine and SSRI in severe anxiety

Case 2

Mrs. L.L. is a 50-year-old woman who has been living with metastatic breast cancer for three years and is now receiving palliative radiation therapy for bone metastases. Past treatment has included lumpectomy, chemotherapy, and radiation. Mobility is affected by moderate to severe hip pain, and she ambulates with a walker. She was recently started on hydromorphone. As her mobility has decreased, she has been feeling more anxious and worried about being alone. Over the past 3 weeks, she has been waking up at night with intense fear, palpitations, sweating, and SOB. She cannot identify a trigger for the anxiety but thinks it is related to anxiety about the future. These episodes last about 20 to 30 minutes, but she is usually unable to go back to sleep and watches television for another couple of hours. Mrs. L.L. denies low mood and depression. She enjoys connecting with her family.

Case example

- Escitalopram 10 mg titrated to 20 mg daily
- Lorazepam 0.5 mg daily as needed
- Relaxation and breathing techniques “box breathing”
- Psycho-education about panic attacks
- “Life Alert” installed

Conclusion

- Depression and anxiety in advanced illness should be actively and adequately assessed and treated
- Physiological/medical causes of depression and anxiety should always be identified and addressed first
- Combined approaches – medication and psychological interventions – may effectively improve symptoms and quality of life

Management of Depression and Anxiety in Advanced Illness

Q/A