Management Considerations for Anxiety, Agitation & Delirium in Hospice Care

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Program Learning Objectives

• Describe the clinical presentation and the symptomatology of anxiety, agitation and delirium.

• Differentiate between the experiences of agitation, anxiety and delirium.

• Discuss and recommend current pharmacotherapeutic treatment options for the management of anxiety, agitation and delirium.
Epidemiology

• The elderly population is growing rapidly. The number of persons over the age of 65 is expected to double over the next 30 years in the US.

• It is estimated that 40% of ER patients over 70 years of age present with altered mental status, approximately 25% of them with delirium.

Definitions

• Anxiety – An abnormal/overwhelming sense of apprehension and fear often marked by physiological signs

• Agitation – A psychotic state characterized by restlessness, hyperactivity, anxiety, and despair but not accompanied by gross disorganization or deterioration

• Delirium – An organic mental syndrome defined by a global disturbance in consciousness and cognition, which develops abruptly and may fluctuate throughout the day.

Etiology of Anxiety

• Situational
  – Stress of impending death

• Psychiatric
  – Pre-existing mental illness

• Organic
  – Complication of illness or treatment

• Existential
  – Pre-existing or reactivation of anxiety disorder
**Symptoms of Anxiety**

- Apprehension
- Diarrhea
- Autonomic hyperactivity
- Diaphoresis
- Dyspnea
- Fear
- Insomnia
- Nervousness
- Tremulousness
- Palpitation
- Uncontrolled worry
- Vigilance

**Anxiety disorders**

- Obsessive Compulsive Disorder (OCD)
- Phobias
- Panic attacks
- Post-traumatic Stress Disorder (PTSD)
- Generalized Anxiety Disorder (GAD)

*Panic attacks and Generalized Anxiety Disorder are the most common in Hospice population.*

**Anxiety disorders**

- **Panic Attacks**
  - Unexpected and unprovoked periods of the following symptoms
    - Dyspnea
    - Chest pain
    - Palpitations
    - Sweating
    - Trembling
    - Shaking
    - Dizziness/lightheadedness
    - Fear of dying
Anxiety disorders

- **Generalized Anxiety Disorder (GAD):**
  - Excessive anxiety or worry not caused by another psychiatric illness or panic attack
  - Apprehensive expectation
  - Difficult to control worry
  - Long term disease process (lasting several months)

Agitation

**Etiology of Agitation**

- Physical discomfort/pain
- Isolation/change in environment
- Over-stimulation
- Underlying mental illness or dementia
- Anxiety
- Depression
- Sleep disturbances
- Medications
- Decreased sense of hope
- Constipation/urinary retention
Etiology in Elderly Population

• Agitation should be presumed to be a manifestation of delirium in the elderly patient until proven otherwise

Symptoms of Agitation

• Irritability
• Pacing, wandering
• Arguing, screaming
• Moaning, crying
• Hallucinations
• Suspiciousness
• Extreme arousal

• Physical aggression
• Verbal aggression
• Kicking
• Scratching others
• Self injury
• Throwing objects

Delirium
**Etiology of Delirium**

Delirium can be precipitated by medical illness, substance intoxication/withdrawal or medication effect.

- Decreased sleep
- Metabolic/Electrolyte imbalances
- Decreased blood supply to the brain
- Inability to cope with surroundings/situation
- Impending death
- Infection

**Etiology of Delirium – cont.**

- Age
- Medications
  - Anticholinergics, Steroids, Phenytoin, Narcotics, Sedatives
- Alcohol/drug withdrawal
Etiology of Delirium: Medications

- Acute change in MS
  - Antiparkinsonian drugs
  - Corticosteroids
  - Urinary incontinence drugs
  - Theophylline
  - Emptying drugs
  - Insomnia drugs
  - Narcotics
- CV drugs
- H2 blockers
- Antimicrobials
- NSAIDS
- Geropsychiatric drugs
- ENT drugs
- Muscle relaxants
- Seizure drugs

Etiology of Delirium: Alcohol dependence/withdrawal

- Alcohol dependence seen in 28% patients in oncology/palliative care setting
- Can complicate symptom management
- Assessing risk
  - Look for S&S in first 12 hours to 5 days after cessation
    - Tremors, anxiety, insomnia, autonomic dysfunction
  - S&S can last for 6-12 months after cessation
- Overlapping signs/symptoms
- CAGE questionnaire; Michigan Alcohol Screening test (MAST)
- Pharmacologic therapy
  - Benzodiazepines, phenobarbital, neuroleptics, gabapentin, dexamethasone

Dementia vs. Delirium

- **Dementia**
  - Gradual, insidious
  - No diurnal variation
  - Continuous duration
  - Clear and normal alertness in the beginning
  - Memory impaired recent to remote
  - Fragmented sleep
  - Involuntary movements rare
  - Orientation often impaired
- **Delirium**
  - Sudden acute onset
  - Positive diurnal variation
  - Reduced awareness, impaired attention
  - Immediate/recent memory impaired
  - Disorganized, fragmented, incoherent thought process
  - Disruption of sleep
  - Often asterixis or tremor
  - Usually impaired orientation for some time
  - Hypoactive/hyperactive
Case Study #1

While on call you receive a call from a patient’s wife at 10pm Saturday evening. The wife states that TJ is very restless and not making sense. He is trying to get out of bed and keeps removing his oxygen.

The on-call book reveals the following:

TJ is a 79 yo male, admitting diagnosis of end stage COPD.

Current Meds:
Duoneb® q 4hrs, lisinopril 10mg QD, furosemide 40mg qd, HCTZ 25mg QD, terazosin 2mg QHS
PRN meds: Roxanol® 5mg q4h prn, Ativan® 1mg q4h prn

Sundowning

- Onset/exacerbation of delirium in the evening/night with improvement or disappearance during the day
  - Mid-later stages of dementia
  - Possible causes: tire easily, lack of sensory stimulation, frustrated or unfamiliar caregiver, disrupted sleep/wake cycle

- Non-drug treatment options
  - Encourage daytime activity, reduce evening activity, nightlight, reduce caffeine intake, bedtime toileting, melatonin, light therapy

- Drug treatment options
  - Most aimed at regulating circadian rhythm
  - Benzodiazepines/hypnotics
  - Neuroleptics
**Assessment of Anxiety, Agitation and Delirium**

- Assessment points
  - Pain severity
  - Anxiety/agitation severity
  - Physical assessment
  - Observations of family and caregivers
  - Sleep pattern
  - Appetite
  - Depression
  - Suffering

**Assessment of Anxiety, Agitation and Delirium**

- MMSE (Mini-Mental Status Examination)
  - Easy and reliable
  - Tests for:
    - Cognition, which includes orientation, registration, attention and calculation, recall, visual–spatial ability and language

  *Note: Many hospice patients may have physical, visual or hearing impairments that negatively impact results.*

**Assessment for Delirium**

- CAM (Confusion Assessment Method)
  - Easy, sensitive, specific and reliable for rapid detections of delirium.

  Positive detection if 1 and 2 are present with 3 or 4.

  1) Acute onset and fluctuating course
  2) Inattention, distractibility
  3) Disorganized thinking, illogical or unclear ideas
  4) Alteration in consciousness
Case Study #1: What questions should you ask?

- Have you given any doses of the Ativan® or Roxanol®? If so, how much and when?
  - Medication related/adverse effects
  - Pain
- Are bathroom habits normal?
  - Constipation, diarrhea/electrolyte imbalance, urinary retention
- Are there any signs of fever?
  - Infection

Overall Goals of Therapy

- Reverse physical, environmental, psychiatric causes
- Improve QOL (i.e. decrease signs/symptoms)
- Prevent harm to patient, caregiver
- Minimize adverse effects

Treatment Options for Anxiety, Agitation and Delirium
Non-Pharmacologic Therapy

- Reduce isolation
- Short term counseling
- Gentle reassurance/reorientation
- Appropriate lighting
- Calm environment
  - Music, aroma, or pet therapy, meditation, familiar belongings
- Remove/increase stimulation
- Massage or pastoral care
- Temperature/climate control

Treatment Considerations

Underlying medical etiology should be determined and treated when possible.

For Example:
- Correct electrolyte disturbance
- Treat infection
- Remove medication causing adverse effect

Pharmacologic Therapy

- Benzodiazepines
- Antihistamines
- Neuroleptics
- Valproic acid
- Antidepressants
- Opiates
Benzodiazepines

- USE: Anxiety and/or agitation without psychosis; anxiety-induced dyspnea, insomnia, seizures
- MOA: Enhances action of GABA
  - Inhibitory neurotransmitter that produces a calming effect
- SE: Sedation, paradoxical reactions (e.g. restlessness, aggression, severe agitation), dizziness, weakness, ataxia

Benzodiazepines: Considerations in the Elderly

- Start low, go slow
- Avoid benzodiazepines with longer half-lives
  - Diazepam, clonazepam, flurazepam
  - Prolonged sedation, increased risk for falls and fractures
- Use smallest dose possible
  - Increased sensitivity to effects
- Monitor for adverse effects
  - Paradoxical CNS stimulation: hostility, nightmares, excitability, restlessness, insomnia, anxiety

Antihistamines

- USES: Pruritis; anxiety
  - Useful if allergy, intolerance or contraindication to benzodiazepine
- MOA: Compete with histamine for H₁ receptors
- SE: Drowsiness, anticholinergic symptoms (e.g. dry mouth, constipation, urinary retention, etc.)
- EXAMPLES: Hydroxyzine HCL/pamoate; diphenhydramine
  - May be useful in pts. with history of alcohol abuse
  - Short acting agents preferred over long acting (i.e. diphenhydramine)
Antihistamines: Considerations in the Elderly

- Monitor for excessive CNS and anticholinergic effects
  - Urinary retention, constipation, dry mouth, confusion, sedation, dry eyes
- Weigh benefit vs. risk
- Watch for concomitant use with drugs with similar anticholinergic effects
  - e.g. TCAs, GI antispasmodics
  - Additive effects can result

Typical Neuroleptics

- USE: Agitation with psychosis, delirium; nausea/vomiting; hiccups
- MOA: Dopamine inhibition
- SE: Extrapyramidal symptoms (EPS), drowsiness, dizziness, orthostatic hypotension, QT prolongation, NMS
- EXAMPLES: Haloperidol; chlorpromazine

Atypical Neuroleptics

- USE: Agitation with psychosis, delirium
- MOA: Antagonizes D₂, 5-HT₂, H₁, and adrenergic α₁ receptors
- SE: EPS, somnolence, dizziness, postural hypotension, dry mouth, dyspepsia, weight gain, NMS
- EXAMPLES: Risperidone, quetiapine, olanzapine
  - Quetiapine may be more appropriate in patients with Parkinson’s Disease or other Parkinson’s-like movement related disorders due to minimized risk for development of EPS
**Typical VS. Atypical Neuroleptic Agents**

- Superiority of atypicals over typicals not yet been proven, although may produce less extrapyramidal symptoms (EPS) than typical neuroleptics
  - In patients > 65yo the risk is about 50%
  - EPS:
    - Dystonias (involuntary muscle spasms)
    - Akathisia (uncontrollable motor restlessness)
    - Rigidity and tremor
    - Tardive dyskinesias (chronic movement disorders)

**Neuroleptic Malignant Syndrome**

- Idiosyncratic reaction to neuroleptic use
- Emergent situation; can be fatal
- AIDS:
  - Altered mental status, muscle rigidity, hyperthermia, autonomic dysfunction, severe EPS
- Presentation
  - Usually develops within 3 days of drug initiation however, can develop at any time
  - May be seen after abrupt discontinuation or dose reduction of carbidopa/levodopa when used concomitantly with neuroleptics
- Differential diagnosis
  - Heat stroke, serotonin syndrome, malignant hyperthermia
- Predisposing factors
  - Organic brain disease, dehydration, exhaustion, hyperthermia

**Neuroleptics: Considerations in the Elderly**

- In general, neuroleptic use can lead to:
  - Cognitive impairment
  - Declines in ADLs
  - Falls/fractures
- Weigh benefit vs. risk and evaluate each drug’s profile since all neuroleptics are not created equal
  - Quetiapine (Seroquel®) best for Parkinson’s disease
  - Haloperidol palliative for nausea/vomiting
  - Chlorpromazine more sedating than haloperidol
FDA Advisory for Atypical Neuroleptics

- FDA has determined that the treatment of behavioral disorders in elderly patients with dementia with atypical antipsychotic medications is associated with increased mortality.
  - Deaths were varied but most appeared to be cardiovascular or infectious in nature.
- All manufacturers must include a Boxed Warning and a Bolded Warning.
- Weigh risks vs. benefits.
- For more information see the FDA website:
  - www.fda.gov/cder/drug/advisory/antipsychotics.htm
  - www.fda.gov/cder/drug/information/antipsychotics/default.htm

Mood stabilizers/anticonvulsants

- USE: Manic depressive (Bipolar) disorder, chronic aggression/behavior disturbances, seizures (anticonvulsants only).
- EXAMPLES: Lithium; Valproic acid/valproate (Depakote®); Carbamazepine (Tegretol®)
- Various side effects (depends on specific agent); Many drug interactions.
- Valproic acid/valproate:
  - Better tolerated and wider therapeutic index compared to lithium.
  - Common side effects are GI related, however, hematologic toxic effects can occur and frequent monitoring is recommended.
    - Aplastic anemia, thrombocytopenia
    - Numerous DIs
      - i.e. Increase in free fraction of unbound warfarin by up to 36%.
- Carbamazepine:
  - Dosage adjustments required in elderly.
    - Clearance reduced by 40%.
  - Significant potential for serious drug interaction.
  - Extensive side effect profile.

Considerations in the Elderly

Mood stabilizers/anticonvulsants
Antidepressants

- **USE:** Depression; GAD
- **MOA:**
  - **SSRIs:** inhibition of 5-HT
  - **TCAs:** unknown, may involve 5-HT and NE
  - **Tetracyclics:** unknown, but does not involve MAO inhibition
  - **Remeron®:** unknown, but enhances noradrenergic and 5-HT activity
- **INTERACTIONS:** Various and drug specific

Opioids

- **USE:** Pain management
- **Assess for presence of untreated pain syndrome**
  - Thoroughly evaluate and assess the patient to determine if pain is causing the agitation and not another unmanaged issue.

*Thank you for your participation!*

**QUESTIONS?**
References

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- Kaye P. Notes on Symptom Control in Hospice and Palliative Care. 2003; 35, 298