# Anxiety, Agitation and Delirium in the Hospice Population

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## Disclosures

- Dr. Garner discloses his employment as
  - Regional Medical Director for VistaCare
- VistaCare has provided commercial support for this activity
- Palliative medicine frequently involves the use of medications for “off-label” purposes. Such use may be discussed during this presentation.

## Objectives

- Discuss the spectrum of behavioral disturbances from anxiety, to agitation, and finally delirium
- Describe the pathophysiologic basis for such behavioral disturbances
- Discuss the pharmacologic management of such disturbances

## Behavioral Disturbances: Anxiety

- Restless, edgy, 'keyed up'
- Tires easily
- Trouble concentrating
- Irritability
- Muscle tension
- Trouble sleeping
- Usually not associated with change in mental status

## Behavioral Disturbances: Agitation

- Excessive restlessness, increased mental and physical activity, severe motor restlessness usually **associated** with anxiety and/or delirium
- Dis-inhibiting agitated delirium will frequently exacerbate the condition 'bad reaction to benzodiazepines'? Or wrong drug

## Delirium: Past History

- Delirium, even into the 19th century by Osler, has been thought to be a 'tired or sleepless' state best treated by sedation.
- Delirium is not usually a disorder of sleep and does not respond well to 'more bed rest'; sedation is not treatment of choice
- Opiates, not only are ineffective sedatives, may precipitate or accelerate a delirious state

## Behavioral Disturbances: Delirium

- Clinical state of acute onset with fluctuating disturbances in cognition, mood, attention, arousal and self-awareness
  - Usually reversible if cause is identified
  - Medications are the most common cause in the elderly;
  - Infection, hypoxia, metabolic disturbance, anticholenergic excess, cytokines (IF-a)-(IL-2)-(TNF), may also precipitate delirium at any age.
  - Any significant medical condition or trauma predisposes one to delirium at any age

## Delirium +/- Agitation: dementia?

- Dopamine/Norepinephrine balance?
- Paucity of Serotonin 5H-T
- Acute onset with similar change in neurotransmitter balance to Alzheimer's disease

## Delirium Treatment: Difficulties in Data Collection

- Very little evidence based data due to multi-factorial causation/association
- Informed consent issues are complicated by acute onset and frequently severe nature of the disorder
- Only one randomized, controlled trial identified; in AIDS population
- Historically, sedation has been initiated, blurring outcome measures

## Delirium:Management

- Identify/treat early and avoid precipitating factors
  - Sedatives, opiates, anticholinergics, visual/hearing impairment, sleep deprivation, dehydration, immobility, cognitive impairment, infection, change in environment
- Neuroleptics for agitation with/without low dose short-acting benzodiazepines for anxiety are mainstays in treatment
- Behavioral modification and situational re-orientation is synergistic with medical management

## Case study: A

- 88 yo. Retired physician with Alzheimer's dementia PPS has been 40%
  - Sudden presentation of agitation and intermittent delirium, frequent falls over past 4 days
  - Totally bed bound x 24h
  - Rigidity, increased temperature, torticollis reported
  - Medication: past 24h haloperidol 5-10mg q4hrs
    - (extrapyramidal sx. Consider adding anticholinergic or atypical antipsychotic medication)

## Delirium: Medication/Dosing

- Haloperidol (IV,IM,SQ,PO,PR,depo)
  - Start low 0.25-0.5 mg BID, increase as needed
  - Up to 500mg/24 hr IV has been used
  - Non-sedating, anti-emetic at lower doses
  - Consider diphenhydramine (25mg TID) or benztropine (1mg BID) for extrapyramidal effects at higher doses.
  - Consider atypical agent for dosing longer than a few months especially at higher doses or if sedation is desired and not obtained with benzodiazepines.

## Delirium: Medication/Dosing

- Chlorpromazine (IV,IM,SQ,PO,PR)
  - 25-50mg starting dose
  - Sedating
  - Increased risk of extrapyramidal side effects, strongly anticholinergic, antimuscarinic may slow GI motility
  - Powerful anti-emetic at lower doses

## Delirium: Medication/Dosing

- Risperidone
  - Mildly sedating
  - Low incidence of extrapyramidal effects
  - Dosing 0.5-1mg BID

## Delirium:Medication/Dosing

- Olanzepine
  - Sedative and anxiolytic effects
  - Low incidence of extrapyramidal side effects
  - May stimulate appetite, increase weight gain
  - Starting dose in elderly or impaired excretion
    - 2.5mg HS, increase HS dose or change to BID/TID as symptoms dictate
    - Consider adding low dose benzodiazepine when agitation controlled
- Clozapine, Quetiapine, Ziprasidone with similar safety profile

## Case Study:B

- 42-yo male, multiple brain metastasis unknown primary. Increase in agitated delirium past 5 days. Increased delirium after rapid increases in pain medications/anxiolytics. On dexamethasone. Excellent response initially to Haloperidol up to 10mg Q 4hours IV. Now 3:00 AM with escalation in delirium, agitation.
- Now what?

## Case Study: C

- Patient hitting and pushing staff at nursing home, calling out, screaming. Now is uncontrollable requires two staff to keep in bed, violent behavior. Started on lorazepam 2mg Q2h prn last PM. No other meds.

## Medications: Anxiolytics

- Benzodiazepines
- Mechanism + inhibitory transmitter activity at GABA receptor site.
  - Short/Long activity
  - Metabolytes
  - Onset of action/Duration
  - Mode of administration
  - Sedation

## Medications: Trazodone

- Improve quality/quantity of sleep
- Sedation is useful side effect + wt gain possible
- Start 25-50mg QHS 1.5-2hrs before sleep increase if needed 100-150 mg.
- Decreases ruminative thought process.
- Priapism possible at higher doses
- 450 mg and up for depression (not recommended)

## Medications:Anxiolytics

- Buproprion
- Mirtazapine
  - Sedating at lower doses (15mg 1-2 times daily)
  - Strong anti-emetic effects, appetite stimulant

# Medications

- Buspirone
  - Weak 5-HT and NE uptake blocker
  - ? Decrease in agitation from GABA or 5-HT pathways
  - Slower onset than benzodiazepines