Management of Delirium in Hospice Patients

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Presentation Objectives

- Identify the clinical features of delirium
- Understand the underlying causes of delirium
- Compare and contrast between the medications that are commonly used to treat delirium in hospice care

Clinical Features of Delirium

Definition of Delirium

Acute state of mental confusion due to diffuse brain dysfunction characterized by cognitive failure

- Delirium is an urgent medical condition
- Delirium needs to be treated aggressively

Disease Burden

- Cause significant distress
- Impairs communication
- Complicates assessment
  - pain & other symptoms
- Increases risk of falls/injuries
- Results in extended hospital stays
- Condition may be reversible
  - 1/2 of the cases

Prevalence

50 – 75% of terminally ill patients

Delirium is a major cause of distress for:

- Patients
- Family
- Healthcare providers

Symptoms

- Hallucinations (visual, auditory, tactile)
- Delusions
- Confusion
- Agitation
- Tremor/myoclonus
- Insomnia **or** Sedation
- Withdrawal

Key Clinical Features

- Rapid onset: *within hours or days*
- Rapidly fluctuating course
- Reduced awareness of the environment
- Cognitive Impairment
- Behavior changes
- Emotional disturbances

Difficult to distinguish from dementia, depression and psychotic disorder except for the rapid onset and fluctuating course of symptoms

Categories

- Hyper-active
  - Confusion, Agitation, Aggression, Hallucinations, Myoclonus
  - Likely associated with drug use
- Hypo-active
  - Confusion, Sedation (rarely hallucinations or delusions)
  - Likely associated with dehydration and hepatic encephalopathy (difficult to detect)
  - Mistaken for depression (may mimic comatose state)
- Mixed
  - patient may transition back and forth b/w above

Diagnostic Tools

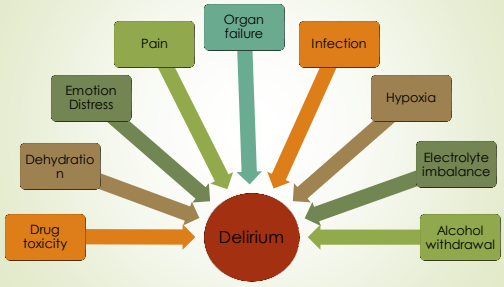
Nursing Delirium Screening Scale (NuDESC)	Mini Mental State Exam (MMSE)	Confusion Assessment Method (CAM)
• Diagnostic Tool • Can be used to monitor delirium severity	• Assess cognition • Not specific for delirium	• Diagnostic only • Does not assess severity

Possible Causes of Delirium

Who is at Greatest Risks?

- Older age
- Dementia
- Depression
- Alcoholism
- Vision/Hearing Impairment
- Mobility Impairment
- Dehydration
- Bladder Catheterization
- Malnutrition
- Infection
- Poorly managed pain
- Polypharmacy
- Terminal illness

Possible Causes at End of Life

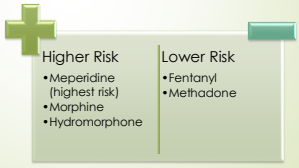


Drugs Causes Delirium

- Opioids
- Anticholinergic-type drugs
- Corticosteroids
- Benzodiazepines & sedative-hypnotics

Opioids Induced Neurotoxicity(OIN)

- OIN is a multifactorial syndrome that causes symptoms from mild confusion to hallucinations, delirium, and seizures
- All opioids may cause or contribute to delirium



Anticholinergics

- Dose-dependent
- Additive toxicity from multiple drugs

Drug Classes	Medication Examples (ABC score =3)
Antispasmodics (GI, GU)	Donnatal, Oxybutynin, Tolterodine, Dicyclomine
Antidepressants (older)	Amitriptyline, Nortriptyline, Paroxetine, Doxepin,
Drying Agents	Atropine, Scopolamine, Hyoscyamine
Antihistamines (older)	Diphenhydramine, Hydroxyzine, Meclizine
Muscle Relaxants	Methocarbamol, Cyclobenzaprine
Certain Antipsychotics*	Chlorpromazine, Olanzapine, Clonzapine, Quetiapine
Antimuscarinics	Benztropine, Trihexyphenidyl

Anticholinergic Burden

- Direct effect on CNS(confusion, agitation)
- Indirect peripheral effects:
  - *Urinary retention*
  - *Blurred vision*
  - *Constipation*
- Additive risk with multiple anticholinergics
- Geriatrics: increased sensitivity

"Hot – Dry – Mad"

Steroid Induced Psychosis

- Common steroids
  - Prednisone (Deltasone)
  - Dexamethasone (Decadron)
  - Methylprednisolone (Medrol)
- Dexamethasone is preferred more often in palliative care
  Prednisone 40mg = Dexamethasone 6mg
- Risk of delirium (The Boston Collaborative Drug Surveillance Study)

Prednisone Dose	Dexamethasone Dose	Steroid Psychosis Incidence
<40mg/day	<6mg/day	1.3%
40-80 mg/day	6-12mg/day	5% incidence
>80mg/day	>12mg/day	18%

Benzodiazepines

- Benzodiazepines may increase confusion & worsen delirium
- Long-acting versions more likely to accumulate to toxic level
- Limit benzodiazepines use to:
  - Hyperactive delirium not responding to antipsychotics
  - Delirium associated with alcohol or drug withdrawal
  - Intractable delirium where palliative sedation is indicated

Long Acting	Short Acting
Diazepam (Valium)	Alprazolam (Xanax)
Clonazepam (Klonopin)	Lorazepam (Ativan)
Temazepam (Restoril)	Oxazepam (Serax)

Treatment Strategies for Delirium

Treatment Strategies

- TREAT underlying medical causes
- Treatment can improve/resolve delirium
- Improvement can occur even in last week of life
- Lack of intervention or treatment shown to have deleterious impact to the caregivers

Non-Pharmacological Approaches

- **Investigate possible causes**
- **Corrective action to address causes if possible**
- Create calm comfortable environment
- Provide orienting objects (clock, calendar)
- Have family members present
- Limit room & staff changes
- Allow for uninterrupted rest/sleep at night
- Consider 1 on 1 nursing/aide observation prn

Pharmacological Approach

Hyper-active Delirium	• Antipsychotics (drug of choice) • Benzodiazepines (limited role) • Re-hydration
Hypo-active Delirium (Depends on goals of tx)	• Non-sedating antipsychotic • Stimulant therapy • Re-hydration

Antipsychotics

Drugs of Choice for the Treatment of Delirium

- Initial phase:
  - Rapid dose titration to control symptoms Q1h prn
  - Titrate to effect within first 24h
- Maintenance phase:
  - 2/3 to 1/2 of the initial phase dose in 2 to 3 divided doses
  - Allow time to identify and/ or resolve delirium causes
- Taper & D/C (if possible):
  - Taper over 3 – 5 days if symptoms completely resolve

Haloperidol (Haldol)

Most Preferred Antipsychotic for Delirium

- High potency
- Low sedative activity
- Low anticholinergic side effects
- Variety of dosage forms
  - Oral concentrate 2mg/ml
  - Injection solution 5mg/ml
  - Oral tablets : 0.5mg, 1mg, 2mg, 5mg, 10mg (crushable)
- Flexible route of administration (PO, SL, SC, IV)
- Most studied antipsychotic for delirium
- Lowest cost

Haloperidol Dosing

Aggressive approach (for severe agitation):
- Adult: 2mg Q6h routine & 2mg Q1hr prn **(1)**
- Geriatric: 0.5 -1 mg Q6h routine & 0.5mg Q1h prn

Conservative approach:
- Adult: 1 - 2mg Q4 prn **(2)**
- Geriatric: 0.25 - 0.5mg Q4h prn

Routes of administration: PO, SL, SC, IV
Caution for IV route (hypotension, cardiac toxicity)

(1) Dept of Palliative Care, MD Anderson Cancer Center University of Texas
(2) American Psychiatric Association Guidelines

Efficacy of Antipsychotics

- Conclusions from a systematic review of pooled data from 3 large randomized, blinded studies:

- Haloperidol vs. Olanzapine & Risperidone for Delirium:
  1. No difference in efficacy for *delirium*
  2. No difference in incidence of adverse effects *at low dosage*
  3. High dose Haloperidol was associated with increased EPS

(Low dose Haloperidol defined: 4mg/day or less)
(High dose Haloperidol defined: 5mg/day or greater)

Ref: Cochrane Database Syst Rev. 2007 Apr 18;(2):CD005594

Comparison of Antipsychotics

Antipsychotic	Usual daily adult dose (mg)	Side Effects				
		Sedation	EPS	Anticholinergic Effects	Orthostatic Hypotension	Weight gain
Haloperidol	1 to 100	+	+++ +	+	+	0
Chlorpromazine	30 to 800	+++	++	++	+++	0
Risperidone*	4 to 16	+	++	0 to +	++	+++
Quetiapine*	50 to 800	++	0	0 to +	++	+++
Olanzapine*	5 to 20	++	+	++	++	++++

*Atypical Antipsychotics
ESP = extrapyramidal side effects

Atypical Antipsychotics

- Less EPS risk
  - Parkinson's disease
  - History of drug induced EPS
- Less risk for QTc interval prolongation
  - Cardiac disease
  - Bradycardia
  - Low potassium &/or magnesium levels

Common Generic Atypicals Used for Delirium	Common Initial Dose
Risperidone (Risperdal)	1mg BID
Quetiapine (Seroquel)	50mg BID
Olanzapine (Zyprexa)	5 mg daily

Benzodiazepines

Benzodiazepines are used only:
- Palliative sedation (in severely agitated pt)
- Alcohol or sedative-drug withdrawal
- Lack of response to antipsychotics

Benzodiazepines may worsen delirium:
- Excessive sedation
- Increased confusion
- Ataxia
- Disinhibition (worsened hyperactivity)

Drugs: Lorazepam (Ativan), Alprazolam (Xanax), Clonazepam (Klonopin), Diazepam (Valium, Diastat), Midazolam (Versed)

Lorazepam (Ativan)

Advantages
- Prompt onset
- Short –acting
- Various dosage-forms: tablet, oral concentrate 2mg/ml, injection solution
- Inexpensive

Initial Dosage
- 0.5mg – 2mg Q 1 – 2 hours prn (PO, SL, IV)
- May use in combination with Haloperidol
  - increased sedation & decreased EPS potential

Palliative Sedation

- Indications
  - For severe hyperactive delirium
  - Terminal patients
  - Not responding to antipsychotics
- Treatment can be used with antipsychotic or alone for palliative sedation:
  - Benzos: Lorazepam or Midazolam (PO, SL, SC, IM, IV)
  - Phenobarbital (PO, rectal, SC,IV)

Examples of starting dose:
- Midazolam (Versed) 0.5-1mg/hr infusion IV or SC
- Phenobarbital 100mg rectal Q8 -12 hr

Stimulant Therapy

- Treatment option for hypo-active delirium
- Goal of maximize alertness & ability to interact
- Methylphenidate (off label use)
  - 10mg to 60mg/day in 1 or 2 divided doses
  - Limited evidence to guide therapy
  - Associated with significant risks for terminal patients
    - hallucinations, agitation, tachycardia

Re-hydration

- Oral, IV, SC
- IV/SL re-hydration may prolong life
  - May not align with the goals of therapy for terminal patients
- Risks of worsening dyspnea or edema
  - CHF
  - Renal impairment

Summary

- Delirium is common in palliative care patients
- Treatment focus on finding the cause and symptom control
- Always review the patient's medication regimen
- Ensure adequate pain control
- Prompt control of agitation in delirium is essential
- Primary drug for agitation is haloperidol
- Benzodiazepines has limited role
- Atypical antipsychotics are for patients at high risk for EPS