

The Diagnosis, Treatment, and Prevention of Delirium

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Introduction: Agitation and Delirium

- Medical and surgical inpatient floors, as well as intensive care units (ICUs), are filled with agitated and confused patients
 - While such units provide the forum for dramatic, lifesaving interventions...
 - They are uniquely stressful
 - high tension
 - danger
 - high technology
 - death



General Principles

- Don't assume psychiatric symptoms are due to a long-standing psychiatric disorder
- Don't assume that psychiatric symptoms are a reaction to being in a critical care environment
 - Initiate a search for the underlying cause of the symptoms
 - Identify the symptoms that require treatment
 - Treat symptoms as specifically as possible



Assessment of Mental Status

- Evaluate the ABCs
 - affect
 - behavior
 - cognition



The Mental Status Examination

- Appearance & behavior
 - hypervigilant, frightened, poor eye contact, agitated, psychomotorically retarded
- Speech
 - rambling, rapid, incoherent, fluent
- Mood
 - depressed, fearful, tearful, irritable, anxious, angry, apathetic



The Mental Status Examination

- Affect
 - despondent, anxious, perplexed, blunted
- Thought
 - paranoid, loose associations, hallucinating
- Cognition
 - disoriented, decreased concentration, confused, impaired memory



Screening Tests and Tools for Assessment of Cognition

- Mini-Mental State Examination
 MMSE
- Montreal Cognitive Assessment
 - MoCA
- Confusion Assessment Method for the ICU – CAM-ICU



Agitation

- Excessive, usually non-purposeful motor activity associated with internal tension
- Varies from mild restlessness to combativeness
- Can signify clinical deterioration
- "ICU psychosis" is a misleading term
 - Implies cause & effect between being in the ICU and becoming psychotic
 - Agitation, delirium, and psychosis are not the same



Delirium: Definition

- An organic brain syndrome with a clouded state of consciousness, distractibility, decreased attention, sensory misperceptions, and a fluctuating course
 - "Acute brain failure"



Delirium: Signs & Symptoms

- Clouded consciousness
- Perceptual disturbances
- Incoherent speech
- Disturbed sleep-wake cycle
- Increased or decreased activity
- Disorientation and memory impairment
 - A fluctuating course
 - Related to an organic factor



Delirium: Associated Features

- Anxiety
- Fear
- Irritability
- Depression
- Euphoria
- Apathy

 These features may steer clinicians to make another diagnosis



Treatment...

- Since treatment is predicated on the diagnosis
 - Identify the etiology as specifically as possible
 - Be sure to rule-out life-threatening causes



Delirium: Life-Threatening Causes

- Wernicke's encephalopathy; Withdrawal reactions
- Hypoxia; Hypoperfusion of the CNS
- Hypoglycemia
- Hypertensive encephalopathy
- Intracerebral hemorrhage; Infection
- Meningitis/encephalitis; Metabolic
- Poisoning
- Seizures



- Central nervous system
 - Vascular
 - hypertensive encephalopathy, intracranial hemorrhage, vasculitis, stroke
 - Neoplastic
 - space-occupying lesions, paraneoplastic syndrome
 - Seizure
 - post-ictal state, complex partial seizures



- Cardiopulmonary
 - Cardiac arrest
 - Congestive heart failure
 - Respiratory failure
 - Shock
- Infection
 - Meningitis/encephalitis
 - Sepsis

SYCHIATRY ACADEMY

Sub-acute bacterial endocarditis

- Endocrine/metabolic
 - Acid-base disturbance
 - Fluid/electrolyte imbalance
 - Diabetic ketoacidosis
 - Hypoglycemia
 - Hepatic failure
 - Renal failure
 - Thyroid dysfunction



- Intoxication/withdrawal
 - Alcohol
 - Anesthetics
 - Anticholinergics
 - Hallucinogens
 - Psychostimulants
 - Narcotics
 - Sedative-hypnotics



- Nutritional deficiency
 - Folic acid
 - Niacin (pellagra)
 - Thiamine (Wernicke's, Korsakoff's)
 - Vitamin B_{12} (pernicious anemia)
- Poisons
 - Carbon monoxide
 - Heavy metals (lead, mercury)
 - Toxins



Common Delirium-Inducing Drugs

- Antiarrhythmics
 - Lidocaine, mexiletine, procainamide, quinidine
- Antibiotics
 - Penicillin, rifampin
- Anticholinergics
 - Atropine



Common Delirium-Inducing Drugs

- Antihistamines
 - Non-selective: diphenhydramine, promethazine
 - H₂ blockers: cimetidine, ranitidine
- Beta-blockers
 - Propranolol
- Narcotics
 - Meperidine, pentazocine



Treatment of Agitation

- Correct metabolic and systemic abnormalities
- Eliminate drug toxicity
- Remove the offending agent(s)
- Administer appropriate antidote(s)
 - e.g., Physostigmine, naloxone, flumazenil



Treat Drug Withdrawal

- Obstacles to prompt treatment
 - Emergent admissions may result in sudden discontinuation of abused drugs
 - History of use may be difficult to establish in intubated or unconscious patients
 - Physical signs of withdrawal are non-specific
 - No laboratory tests can confirm the diagnosis



Alcohol & Sedative-Hypnotics

Alcohol withdrawal

- Benzodiazepines, phenobarbital, neuroleptics

- Sedative-hypnotic withdrawal
 - Symptom-onset a function of half-life; the longer the half-life the longer the latency
 - Symptom frequency and intensity greatest with half-life of 10-20 hours
 - Treatment best with a longer half-life agent



Narcotic Withdrawal

- Syndrome generally mild
 - Discomfort; delirium uncommon
 - Treatment involves replacement with a longer half-life agent of the same class
 - Clonidine is effective in reducing symptoms



Haloperidol

- A high-potency agent
- Trivial effects on heart rate, blood pressure, respiratory drive
- Often used IV despite lack of FDA approval for IV use
- Used IV it precipitates with phenytoin and heparin;

– Flush the IV line first

• Dose used depends on symptom severity



Haloperidol

- Onset of action: 10-30 minutes
- Hypotension, if it occurs, is associated with hypovolemia
- High-dose use associated with QTc prolongation and Torsades de Pointes
- Extrapyramidal side effects are rare with IV use



Haloperidol

- Titrate the dose to the symptoms
 - If mild, use 0.5-2 mg
 - If moderate, use 5-10 mg
 - If severe, use 10 mg or more
- Repeat doses when necessary, every 15-30 minutes
- Adjust dose to clinical course



Other Neuroleptics

- Droperidol
 - More sedating than haloperidol
 - Lowers blood pressure more than haloperidol
- Chlorpromazine
 - More anticholinergic, more apt to induce hypotension, and more likely to induce arrhythmias than haloperidol



Atypical Antipsychotics

- Olanzapine
- Quetiapine
- Risperidone
- Clozapine
- Ziprasidone



Alternative Agents for Agitation...

- Dexmedetomidine
 - Highly selective alpha-2 adrenoreceptor agonist with sedative and analgesic properties
- Valproate
 - Especially when irritability or impulsivity present
- Propofol



Alternative Agents for Agitation

- Narcotics
 - Morphine typically used
- Paralytics
 - If used, sedation still required
- Benzodiazepines
 - Lorazepam
 - used PO, SL, IV; has no active metabolites
 - Midazolam
 - rapidly-acting; causes amnesia and respiratory depression



Benzodiazepines...

- Midazolam
 - half-life, 1-12 hrs; 2 mg; fast
- Oxazepam
 - half-life, 5-15 hrs; 15 mg; slow
- Lorazepam
 - half-life, 10-20 hrs; 1 mg; intermediate
- Alprazolam
 - half-life, 12-15 hrs; 0.5 mg; intermediate-fast



Benzodiazepines...

- Chlordiazepoxide
 - half-life, 5-30 hrs; 10 mg; intermediate
- Clonazepam
 - half-life, 15-50 hrs; 0.25 mg; intermediate
- Diazepam
 - half-life, 20-100 hrs; 5 mg; fast
- Flurazepam
 - half-life, 40 hrs; 5 mg; fast
- Clorazepate
 - half-life, 30-200 hrs; 7.5 mg; fast



Benzodiazepines

- Diazepam
 - IV: onset, 2-5 min; starting dose, 2-5 mg
 - PO: onset, 10-60 min; starting dose, 2-5 mg
- Lorazepam
 - IV/IM: onset, 2-20 min; starting dose, 1-2 mg
 - SL: onset, 2-20 min; starting dose, 0.5-1 mg
 - PO: onset, 2-60 min; starting dose 0.5-1 mg



Non-Pharmacological Treatment

- Re-orientation
- Adjustment of physical environment
- Reassurance
 - Determine why are the patient is anxious to guide interventions
 - Clarify misconceptions
 - Remain calm



Prevention of Delirium

- Minimize risk factors for delirium
- Monitor lab values and vital signs
 - e.g., Oxygenation, hematocrit, blood pressure, drug levels
- Administer antipsychotics prophylactically
 - Administration of olanzapine reduced incidence of post-operative delirium from 41% to 15% in elderly joint replacement patients



Conclusion

- Medically-oriented psychiatric consultants can help evaluate and manage critically ill patients as well as prevent psychiatric and neuropsychiatric symptoms
 - Psychopharmacologic skills
 - Psychotherapeutic skills
 - Medical knowledge



Selected References...

- Stern TA, Herman JB, Slavin PL, editors. <u>The MGH Guide</u> <u>to Primary Care Psychiatry, 2[/]e</u>. McGraw-Hill, New York, 2004.
- Stern TA, Celano CM, Gross AF, et al: The assessment and management of agitation and delirium in the general hospital. Prim Care Companion J Clin Psychiatry 2012; 12(1): e1-e11.
- Stern TA, Freudenreich O, Smith FA, Fricchione GF, Rosenbaum JF, editors. <u>Massachusetts General Hospital</u> <u>Handbook of General Hospital Psychiatry, 7/e</u>. Elsevier, Philadelphia, 2018.



Selected References...

- Larsen KA, Kelly SE, Stern TA, et al: Administration of olanzapine to prevent postoperative delirium in elderly joint replacement patients: a randomized controlled study. Psychosomatics 2010; 51: 409-418.
- Jain FA, Brooks JO, Larsen KA, et al: Individual risk profiles for postoperative delirium after joint replacement surgery. Psychosomatics. 2011; 52: 410-416.



Thank You...

• Questions?



