Acute vs. Maintenance

The objective of rapid and effective management of acute agitation, confusion and decompensation is to minimize the morbidities of the post-acute or chronic course, and thus reduce the occasions for pharmacologic temptation.

- Delirium
- Encephalopathy
- Psychosis
  - What kind?
  - Schizophrenia?
  - Manic?

What is it?
Agitated, Confused, Unreasonable, Nuts?

Think Encephalopathy

Diagnosis  Management

Delirium, et. al.

Delirium is common and associated with negative outcomes, including increases in length of stay, complications, cost, and mortality, decline in post-discharge cognitive function and independence, and readmission. Delirium is a subtype of encephalopathy. Reduction improves outcomes.

Signs and Symptoms

Confusion
Memory disorganization
  Contamination
  Sequencing
Acceleration
Perceptual distortion
Circadian disruption
Neural fatigue
Management and Reduction

• Care Interventions
  - Identification - Screening tools: CAM, Nu-Dex, History
  - Protocols, guidelines: Environment, deep, orientation
  - Monitoring: VS, sleep, hydration, elimination, motor
  - Documentation & communication

• Drugs
  - Antipsychotics
  - BZDP's
  - Anticonvulsants
  - As indicated for underlying conditions

Pharmacological Targets

Risks

- Self - falls, wandering, de-Foley-ating
- Others – Aggression, lability, disinhibition
- Restraint
- Drug effects
- Progression

The Setup

• Untreated encephalopathy has risks: complications, morbidity, mortality, readmission, longer hospital stay and chronic deterioration.
  - Antipsychotic and other drugs are effective for treatment, which improves outcomes.
  - BUT...
  - The drugs have risks.
Statements from Senator Herb Kohl:

"While antipsychotic drugs have been approved by the FDA to treat an array of psychiatric conditions, numerous studies have concluded that these medications can be harmful when used by frail elders with dementia who do not have a diagnosis of serious mental illness. In fact, the FDA issued 2 "black box" warnings citing increased risk of death when these drugs are used to treat elderly patients with dementia. Improper prescribing not only puts patients' health at risk, it also leads to higher health costs."

(Borrowed from Dave Lawless – sorry)

SO: Whatever you do...

...Is Wrong.
Antipsychotic Drugs

- Increased Mortality Risks
  - Old People:
  - Cardiovascular or Infectious Events
  - Young people:
  - Suicidality
  - (Extent to which attributable to drug is not clear)

Quetiapine

- Black Box Warnings
- Seroquel
- Dementia-Related Psychosis
  - not approved for dementia-related psychosis; incr. mortality risk in elderly dementia pts on conventional or atypical antipsychotics; most deaths due to cardiovascular or infectious events; extent to which incr. mortality attributed to antipsychotic vs. some pt characteristic(s) not clear
  - Suicidality
  - incr. suicidality risk in children, adolescents, and young adults w/ major depressive or other psychiatric disorders; suv risk vs. benefit in short-term studies of antidepressants vs. placebo, suicidality risk not incr. in pts >24 yrs, and risk decr. in pts >65 yrs; depression and certain other psychiatric disorders themselves assoc. w/ incr. suicide risk; observe all pts for clinical worsening, suicidality, or unusual behavior changes; advise families and caregivers of need for close observation and communication w/ prescriber; not approved for depression in pediatric pts

Haloperidol

Dementia-Related Psychosis

Not approved for dementia-related psychosis; incr. mortality risk in elderly dementia pts on conventional or atypical antipsychotics; most deaths due to cardiovascular or infectious events; extent to which incr. mortality attributed to antipsychotic vs. some pt characteristic(s) not clear

(But indicated for acute agitation)
Valproic Acid (Epocrates)

Hepatotoxicity
Serious or fatal hepatic failure reported, usually in 1st 6mo of tx preceded by malaise, weakness, lethargy, facial edema, anorexia, vomiting and loss of seizure control; incidence of fatal hepatotoxicity decr. considerably in progressively older pt groups >2 yo; monitor hepatotoxicity sx incl. LFTs at baseline and frequently thereafter especially in 1st 6mo

Pancreatitis
Life-threatening pancreatitis reported in children and adults; some cases hemorrhagic w/rapid progression from initial sx to death; cases reported shortly after initial use as well as after several years of use; advise pts to monitor for pancreatitis sx incl. abdominal pain, nausea, vomiting, and/or anorexia; D/C tx if pancreatitis diagnosis and start alternative tx as clinically indicated

Observed: Hyperammonemia

Stroke Risk


Alpha-2 & Muscarinic-1 affinity associated with higher stroke risk.

Olanzapine, clozapine, chlorpromazine, thioridazine

Drug Risks

Antipsychotics
- Anticholinergic – hypotension, syncope
- Extrapyramidal – dystonia, dyskinesia, akathisia
- Neurologic – NMS, seizures, suicidality
- Endocrine/metabolic – hyperglycemia, DM, weight gain, hypothyroidism
- Cardiac – Q-T prolongation, torsade de pointes
- Hematologic – agranulocytosis, leukopenia
- Allergic – Stevens-Johnson
**Drug Risks**

**Benzodiazepines**
- Oversedation - circadian disruption, aspiration, hypoxemia, respiratory depression
- Confusion
- Agitation/ disinhibition
- Sleep disruption - REM deprivation, confusion, apnea
- Seizures
- Syncope/falls
- Hypotension/tachycardia
- Blood dyscrasias
- Dependence

**However –**

**Encephalopathy is not Good for You**
- Severity and duration associated with worse outcomes – in hospital and post-hospital.

**Outcome Risks**

**Increased levels of:**
- Serotonin metabolites
- Dopamine metabolites
- Interleukin-8
- Cortisol
- Lactate
- CSF protein
- Acetylcholinesterase
Outcome Risks

- Increased LOS
- Excessive drug use
- Hospital-acquired complications: infection, aspiration, skin breakdown, falls
- Cardiac dysrhythmias
- Respiratory depression
- Stroke
- Death
- Permanent cognitive loss
- Increased post-hospital utilization

Balance

Encephalopathy Reduction

- Prevention – history of risk factors
- Identification – faster is better
- Diagnosis – contributory conditions
- Control – reduce severity
- Management – reduce duration
Encephalopathy Risk Factors

- Age over 65
- Severe illness
- History of MI or heart surgery
- Current or past addiction
- History of Stroke or brain injury (including craniotomy)
- Dementia
- History of encephalopathy
- Depression
- Multiple medical conditions
- History of neuropsychiatric illness
- Sensory impairment
- Renal or hepatic impairment
- Polypharmacy
- Functional dependence
- Autoimmune disease
- Malnutrition
- Dehydration
- Malnutrition
- Functional dependence
- Autoimmune disease

Encephalopathy Identification and Diagnosis

- Under-identification is most common problem
- History of Risk Factors
- Clinical Recognition
- Screening instruments: CAM, Nu-DESC

Diagnosis of Underlying Conditions

“History is 90% of Diagnosis”

Acute
e.g., Toxic, Metabolic, Vascular, Trauma

Subacute
- Malnutrition, Infection,
- Progressive
- Dementias, Substance abuse

Relapsing
- Schizophrenia, Bipolar
In-Hospital Contributing Factors

• 3 or more new drugs
• Infection
• Electrolyte disturbance
• Pain
• Hypoxia
• Sleep deprivation/fragmentation
• Surgery
• Environmental stimulus level
• Alcohol or drug withdrawal
• Restraints

Neuron Fatigue

Bedside Screening Instruments

• Advantages:
  o Early identification;
  o Standardized;
  o Monitoring measures.

Precautions: They have to be documented, communicated, and responded to: diagnosis documented, orders written, etc. Something has to happen.
Confusion Assessment Method (CAM)

Scoring: Yes or No;
YES, if “Yes” to Features 1 and 2, plus “Yes” to either 3 or 4

I. FEATURE 1: Mental Status Change
- Mental status different from baseline
- New confusion/disorientation
- Mental status fluctuation – confusion comes/goes

II. FEATURE 2: Inattention
- Easily distracted or has difficulty keeping track of conversation
- Spell W-O-R-L-D backwards OR
- Count backwards from 20 to 1

IV. FEATURE 3: Disorganized Thinking
- Rambling, irrelevant conversation OR
- Continually switches subjects OR
- Have patient state reason for admission OR
- Have patient state year, where they are
V. FEATURE 4: Altered Level of Consciousness
- Hyperalert – vigilant
- Lethargic – drowsy, but arousable
- Stupor – difficult to arouse
- Coma

Fig 1. The Nursing Delirium Screening Scale (NuDESC). Scores are scaled from 0 to 11 based on the presence and severity of each symptom and individual ratings are added to obtain a total score per shift. The first four items of the NuDESC are included in the GDS. This scale may be reproduced without permission. For clinical use only.

Using the Drugs
- Making Choices
- Keeping it Simple
- Playing with Others
One way to judge drug choices

- Alcohol withdrawal syndrome “type indicator,” a symptom-based assessment tool used to guide treatment decisions and monitor clinical response. The type indicator groups symptoms into categories.7,8

- Type A symptoms are characterized by central nervous system excitation (e.g., anxiety and restlessness) caused by γ-aminobutyric acid (GABA) withdrawal. Type A symptoms are generally treated with GABA agonists, most commonly Type B symptoms (e.g., fever, diaphoresis, tremor, and elevated blood pressure) benzodiazepines.8,1

- Type B symptoms (e.g., fever, diaphoresis, tremor, and elevated blood pressure and heart rate) are caused by adrenergic excess from activation of the locus ceruleus due to a hyperglutamatergic state. Before treating a patient for type B symptoms, other causes of this cluster of symptoms should be ruled out, such as volume depletion, blood loss, and pain. For example tachycardia, which can be controlled with metoprolol.

- Type C symptoms (e.g., confusion, hallucinations, paranoia, and agitation) are caused by excess dopamine release through the mesolimbic tract and are treated with dopamine antagonists.

Antipsychotics

Not all the same; variations in –

Receptor affinities: dopamine D1 - 4; 5HT 1, 2a & c, 3; Alpha1; histamine H1; muscarinic 1 – 5...

Anatomical selectivity of action on each receptor: tuberoinfundibular; mesocortical; nigrostriatal...

Pharmacology and metabolism: absorption, peak level, halflife, receptor occupancy.

Antipsychotics

Typical (old) vs Atypical (newer)

Atypicals have:

- Stronger 5HT affinity
- More selective dopamine affinity
- More selective for anatomical tracts

Thought to account for differences in side effects
What I do, More or Less

Generic order content for encephalopathy in addition to, or absence of, specific orders for etiology being treated (e.g., withdrawal, hepatic, etc.). Dosing depends on monitoring data and severity, but basically:

- Haloperidol po/IM/IV prn for agitation
- Quetiapine qhs (or earlier: 1800 or 2000)
- Lorazepam if Haldol inadequate, or give with haloperidol if muscle rigidity/tremor/lessness associated with haloperidol doses. Monitor for increased confusion associated with lorazepam.
- Valproic acid 125-500 q12 h if aggressive or impulsive, not relieved by haloperidol, or if requiring >3 mg lorazepam/12 hours, or excessive sedation from haloperidol -lorazepam.

Document sleep-wake times.

Do not wake patient between 10 PM and 7 AM except as ordered.

Rationale

Gain control quick, then back off.

Not a prescription for specific treatment, but acute stabilization.

Haloperidol is familiar, has rapid onset, easily titrated and limits residual sedation. Best for hospital use for monitoring.

Lorazepam should be avoided, but backup sedation to haloperidol. Can be used for akathisia or dystonia.

Valproic acid has broad spectrum of receptor activity, does not add sedation and allows limiting of haloperidol dosing.

Quetiapine has the most normalizing effect on sleep architecture but poor daytime prn.

Treating Agitation

To reduce factors generating progression or permanent injury:

- Oxidative Stress: Neuron dysfunction
- Kindling: Autonomic instability
- Cardiovascular risk: Immune dysfunction

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Side Effect Management

“Agitation” or “impulsivity” may be akathisia. Check for cogwheeling & tongue fasciculation.

Observe timing of episodic agitation – is it lorazepam? Need data on nighttime sleep-wake-mental status.

Dyskinesia, rigidity, dystonia – try to avoid anticholinergics (Benadryl, Cogentin). Try low-dose lorazepam, back down haloperidol, consider beta-blocker, DA agonist if necessary.

Non-pharmacological Management

Environmental, Stimulus, and Circadian management is the mainstay, and the most influential on outcome.

Nursing carries the ball and must have training and standard guidelines to follow.

Documentation and communication is key.

It takes a team.