Hospital Delirium: New Evidence in Diagnosis & Treatment

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Key Questions

1. Based on new data is it time to begin using melatonin/melatonin agonists to prevent delirium?

2. What tests should we order more, or less, of to evaluate hospital-onset delirium?

3. Are we helping or harming when we treat delirium with antipsychotics?
Clinical Case
Gertrude’s Tragic Tale

- 88 y/o woman admitted for back pain after a fall onto her sacrum.
  - No head trauma or LOC
- X-ray demonstrates thoracic compression fracture.
- Admit for pain control, inability to ambulate.

PMH
- Mild Alzheimer’s Dementia
- Insomnia
- HTN
- Urge incontinence
- Depression

Medications
- Lisinopril 10mg daily
- Aspirin 81 mg daily
- Amitriptyline 50mg qhs
- Oxybutinin 5mg bid

Gertrude is confused
- Knows the day of the week but no recollection of the list of her home medications
- “Honey, I don’t have to know that at my age” when asked for the year.
  - With great effort can say months of the year backwards
  - Asks you whether you are a “real doctor” to be asking questions like that to a woman with a broken back
- Tells you a bright and animated story about the havoc her dog caused to her apartment the last time she was hospitalized

Is Gertrude Delirious?

There are Some Who Think the Hospital Is a Fancy Hotel
“Ultra-brief” Delirium Screen

- What is the day of the week?
- Months of Year Backwards

Sensitivity of 93%
Specificity of 64%

Prevention of Delirium
Non-pharmacologic measures

- Modifiable risk factor
- Prospective Intervention
  - Visual Impairment ➜ Visual aides, adaptive equip
  - Hearing Impairment ➜ Amplifiers, adaptive equip
  - Cognitive impairment ➜ Orienting communication
  - Immobility ➜ Early mobilization, reduce restraints
  - Dehydration ➜ Oral hydration
  - Sleep deprivation ➜ Uninterrupted sleep, non-pharmacologic aides

JHM 2015;10:645-650
NEJM 1999;340:669-676
JAGS 2009;57:2029-2036
One of Hebb's sensory deprivation subjects at McGill.

Sensory Deprivation

Declassified 1983 CIA Training Manual

“Deprivation of sensory stimuli induces stress and anxiety.”

“Some subjects progressively lose touch with reality, focus inwardly, and produce hallucinations, delusions, and other pathological effects.”

1984 revision states: “Deliberately causing these symptoms is a serious impropriety.”

Accessed 2/28/09 at http://www.gwu.edu/~nsarchiv/NSAEBB/NSAEBB27/02-02.htm from National Security Archive Database

Sensory Deprivation

One of Hebb's sensory deprivation subjects at McGill.
Mobility

- One study reveals 30% of elderly patients had initial order for "bed-rest"
- Gertrude's activity order reads "ad lib"
- Translate this:

Elderly Patients Spend the Majority of Their Hospital Time Immobile

- Another study found the median amount of time standing or walking:
  - 43 minutes
- Translation:
  - "Ad lib" means 97% of the time immobile

What About Restraints?

Restraint chains used to control mentally ill patients, and documentation regarding Pennsylvania Hospital's purchase of such restraints in 1751 and 1752.
RESTRAINT USE

- Restraints ARE appropriate for behavior that is a risk to life or to necessary medical care
- Restraints associated with significant injuries
- Restraints associated with 4 fold increased risk of delirium
- Distraction Vest

Journal of Gerontol Nurs 2001;27:40-45
Clin Geriatr Med 2008;24:467-466

Sleep Deprivation

Consequences of lack of sleep in healthy volunteers include “impaired attention” and “irritability”

- Noise
- Vital signs
- Light
- Illness
- Phlebotomy
- Skin care

No longer accepts submissions in this category due to deleterious health effects

Could you sleep?

Prevention

- Warm Milk Before Bed Part of Original Delirium Prevention Protocol
- What is special about warm milk?
  - Melatonin

Magical Milk Sleeping Potion
New Evidence for Prevention
Melatonin or Melatonin Agonists

- 1 small trial of melatonin agonist Ramelteon
  - 67 pts
- Dramatically less delirium
  - 3% vs 32%; P = 0.03

Exogenous Melatonin for Delirium Prevention: a Meta-analysis of Randomized Controlled Trials.incl Neursci. 2015.


Gertrude’s Tragic Tale

- The three days later Gertrude is still drowsy at midday
  - Can not remember day of the week.
- Loses track of the conversation in mid sentence
  - No longer can recite months of year backwards.
- She becomes more confused
  - Trying to get out of bed
  - Pulling at her IVs

Is she delirious now?

3D-CAM: Derivation and Validation of a 3-Minute Diagnostic Interview for CAM-Defined Delirium

A Cross-sectional Diagnostic Tool Study

Sens 95%
Spec 94%
**TESTING**

- Chem7, CBC
- U/A, CXR and/or Blood Gas - driven by clinical cues
- Troponin, EKG
- Extensive testing of limited value unless driven by a specific clinical suspicion

**LOW YIELD STUDIES**

- EEG
  - If clinical evidence of seizures
- LP
  - For fever with nuchal sign
- Brain CT/MRI?

220 patients with hospital onset delirium
- Excluded if focal findings or head trauma
- 6 of scans were positive (2.7%)
- 4 bleeds and 2 were mass or infarcts
- Half of the positive scans were on anticoagulation
- All positive scans resulted in change in management
  - All had NS or neurology consults
  - 2 had anticoagulation reversed
  - 2 had change to palliative care


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**What is an acceptable miss rate?**

**How do you apply the results of this research to your practice?**
Practical Approach

1. **Remove Problem Medications**
   Particularly Anticholinergic, Benzodiazepines, and minimize Narcotics

2. **Treat Withdrawal**
   Alcohol or benzodiazepines

3. **Correct Metabolic Disturbances**
   Electrolytes, glucose, hydration

4. **Reduce Level of Invasion**
   Indwelling urinary catheters and lines

5. **Assess and Treat Infection**
   Particularly new UTI or pneumonia

6. **Improve Environment and Mobility**

7. **Adaptively Treat Pain**
   Uncontrolled pain is more potent delirium trigger than narcotics.
   Scheduled may be better than prn. Maximize non-narcotic Therapy

Problematic Medications

- **Sedative/Hypnotics**
  - Diazepam, Lorazepam, Zolpidem

- **Narcotics**
  - No good evidence that one narcotic is better than another
  - Except Meperidine which is clearly the worst

- **Antihistamines**
  - Diphenhydramine, hydroxyzine, H2 blockers

- **Anticholinergic Medications**
  - Promethazine, Cyclobenzaprine, Oxybutynin, Amitriptyline
  - Combinations of medications with partial anticholinergic activity
    - Prednisolone
    - Theophylline
    - Digoxin
    - Furosemide

Medical Therapy for Delirium

- No good evidence that cholinesterase inhibitors (donepezil, rivastigmine) are effective

- No good evidence that Benzodiazepines are effective EXCEPT in alcohol withdrawal

- Antipsychotics may decrease degree and duration of delirium
  - The evidence for this is not strong
“The prescribing practitioner should not prescribe antipsychotic medications for the treatment of older adults with postoperative delirium who are not agitated and threatening substantial harm to self or others.”

AMERICAN GERIATRICS SOCIETY 2014 GUIDELINES

When All Else Fails.....

ANTIPSYCHOTICS

Typical Antipsychotics (Haloperidol)
- Extra-pyramidal side effects with high doses
- Haloperidol 0.25 – 0.5mg PO/IM BID or pm q 4h.

Atypical Antipsychotics (Risperidone, Olanzapine, Quetiapine)

Unsafe Use
- IV Haloperidol has specific FDA black box warning
  - Recommends EKG monitoring when used
- “QTP and TdP almost uniformly take place in patients with concomitant risk factors and with cumulative doses > 2 mg”
- IV Haloperidol often prescribed unsafely
  - 1 in 5 patients received 5mg or more for first dose
  - 20% had no baseline EKG
  - 16% had Qtc > 500 BEFORE first dose
  - Only 42% received care concordant with safe prescribing

JHM 2010;5;E8-E16
JAGS 2013;61:160-61
Antipsychotics associated with increased mortality in dementia

- Lowers seizure threshold
- Prolongs QTc

9% treated with antipsychotics

QTC >500 after treatment in a quarter of pts

Almost half had new antipsychotic prescription on discharge

What is an example of another medication which gets started with appropriate indication in the hospital...

PPIs

But gets inappropriately continued on hospital discharge?
What you start...gets continued

DART-AD
- Randomized Placebo-Controlled Drug Withdrawal Study
- 165 dementia patients on an antipsychotic
  - Half had it substituted for placebo

No difference in mortality at first (1 yr)
21% vs. 25%

After 5 years mortality was higher in the group who continued antipsychotics
38% vs. 54%

"Side Effects May Include Lawyers"

Johnson & Johnson to pay $2 billion in settlement over antipsychotic drugs in nursing homes

Pharmaceutical giant Johnson & Johnson and some subsidiaries will pay more than $2.3 billion to settle claims that they inappropriately promoted antipsychotic drugs for use in nursing homes, the U.S. Department of Justice announced Monday. The agreement is one of the largest ever of its kind, and will also settle charges that the companies paid kickbacks to the nation's largest long-term care pharmacy, Omnicare.
Always ask yourself if the cure is worse than the disease.

Mahalo
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