Approaching Intensive Care Unit Delirium
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Disclosure

- I do not have any relevant financial or non-financial disclosures.
- Some medications will be discussed for non-FDA labeled indications.

Clinical Practice Guidelines for the Management of Pain, Agitation, and Delirium in Adult Patients in the Intensive Care Unit

- Pain
- Agitation
- Delirium

- Use of analgesics
- Use of sedatives
- Use of antipsychotics

- Identification of patients at risk
- Early intervention
- Continual assessment

- Prevention of delirium
- Treatment of delirium

Restaurants and quotations will be used to reference the guidelines.

Grades for recommendations will appear in parentheses:
- Level A: Evidence from descriptive studies with high internal validity
- Level B: Evidence from randomized clinical trials
- Level C: Evidence from single-arm trials or smaller clinical trials

The strength of recommendations is denoted by "V" for "Very" and "A" for "Against".

Objectives

1. Discuss the impact of intensive care unit (ICU) delirium on patient outcomes.
2. Outline strategies for prevention and management of ICU delirium.

Defining Delirium

Delirium is defined as a disturbance of consciousness that is accompanied by a change in cognition that cannot be better accounted for by a preexisting or evolving dementia. - American Psychiatric Association

Risk Factors

- Disease severity
- Invasive devices

Delirium Across Continuum of Care

Prevalence of delirium
- Emergency room (8% to 19%)
- Acute care setting (30%)
- ICU (10% to 40%)
  - 15% in the first 24 hours
  - 32% each ICU day
  - 63% to 86% of those who are mechanically ventilated

Without Dementia With Dementia
Fig. 2: The interaction between patient vulnerability and precipitating factors in the development of delirium. Delirium vulnerability requires high risk and indicates a delirious state. Link arrow: High level vulnerability requires the involvement of precipitating factors.

- Genetics
- Demographics
- Advancing age
- Visual impairment
- Onchosis conditions
- Metabolic derangement
- Anemia
- Hypertension
- Depression
- Malignancy
- Immunosuppression, transplantation, or antithrombotic agents
- Medications
- Sedatives
- Psychotropic drugs with antiparkinson effects and propafenone
- Benzodiazepines or benzodiazepine withdrawal
- Diphenhydramine and anticholinergic
- Environmental
- Immobility
- Procedures such as catheter insertion
- Lack of sleep
- Overstimulation
- Lack of environmental orientation

- Prolonged ICU stay
- Prolonged mechanical ventilation
- Increased hospital stay
- Increased mortality
- Post-ICU cognitive impairment
- Increased catheter removal and self-extubation
MMSE 12-months after surgery

Long-term brain dysfunction

Question for audience

Which of the following is associated with ICU delirium?
A. Decreased ICU length of stay
B. Decreased hospital length of stay
C. Decreased mortality
D. Longer duration of mechanical ventilation

Prevention

“THINK” delirium!

- Toxic situations and medications
- Hypoxemia/Hypoglycemia
- Infection/sepsis/inflammation/immobility
- Nonpharmacological interventions
- K+ (potassium) and other electrolytes

Acronym to help you remember common modifiable risk factors that can be addressed in a newly delirious patient
ABCDE daily cycle

Vicious cycle

Optimize sedation

- Consider non-benzodiazepine-based sedation (dexmedetomidine or propofol) instead of benzodiazepines (+2E)
- Target light sedation (RASS 0 or -1) (+1B)
- Conduct SAs and SBIs daily (+1B)
- Consider analgesia-first sedation to decrease sedative exposure (+2B)

Haloperidol data conflicts

Randomized trials of haloperidol for delirium prevention

- Sleep deprivation is common in the ICU
  - Impaired wound healing and cellular immune function
  - Potentially cause of delirium and physiologic stress
- Promote sleep in adult ICU patients (+1C)
  - Control light and noise
  - Cluster nursing activities to provide uninterrupted time at night
  - Decrease stimuli at night (eye masks & ear plugs)
Sleep hygiene

The effect of earplugs during the night on the onset of delirium and sleep patterns in critically ill patients

- RCT of 120 non-delirious patients
- Intervention was earplugs at night
- Primary outcome was a decreased incidence of delirium or confusion

Treatment

- Non-benzodiazepine based sedation
- "Atypical antipsychotics may reduce the duration of delirium in adult ICU patients (C)"
  - Not recommended in patients at significant risk for torsades de pointes (2D)
  - Only a few small trials have been conducted (e.g., Deeks 2010)
  - Only consider after all other interventions have been attempted
- Do not use rivastigmine (-1B) (may increase mortality)

Dexmedetomidine

Figure 2. Daily Prevalence of Delirium Among Intubated Intensive Care Unit Patients Treated With Dexmedetomidine vs Midazolam

Quetiapine in 36 patients

First resolution of delirium

- Duration: Dexmedetomidine 36, Placebo 120, P value 0.000
- Recurrence of delirium after initial resolution: Quetiapine 22%, Placebo 44%, P value 0.29
- Hours of agitation, median: Quetiapine 6, Placebo 36, P value 0.02
No HOPE for haloperidol

- January 2013: "There is no published evidence that treatment with haloperidol reduces the duration of delirium in adult ICU patients (No evidence)"
- September 2013: HOPE-ICU study found no benefit from haloperidol for the prevention/treatment of delirium
  - No benefit for prevention/treatment of delirium
  - May prevent/treat acute episodes of agitation

<table>
<thead>
<tr>
<th></th>
<th>Haloperidol (n=27)</th>
<th>Placebo (n=27)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive, delirium-free, coma-free days in first 14 days*</td>
<td>5 (0-10)</td>
<td>6 (0-11)</td>
<td>0.53</td>
</tr>
<tr>
<td>Days in delirium</td>
<td>5 (2-8)</td>
<td>5 (1-8)</td>
<td>0.99</td>
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<tr>
<td>28-day mortality</td>
<td>28%</td>
<td>27%</td>
<td>n/a</td>
</tr>
</tbody>
</table>

* Primary outcome: Study planned to enroll 128 patients to detect a 2-day reduction in delirium days

Ongoing trials

- Wes Ely - MIND-USA (NCT01211522): RCT (n=900) from 2011 to 2016 comparing haloperidol, ziprasidone, and placebo for 14-day delirium/coma free days
- Pratik Panharipande - MENDS II (NCT01739933): RCT (n=500) from 2012 to 2016 comparing dexmedetomidine to propofol for 14-day delirium/coma free days
- Yoanna Skroblik - SKY-DEX (NCT01791296): RCT (n=100) from 2011 to 2014 comparing nighttime infusion of dexmedetomidine to placebo for incidence of delirium

Acknowledgments

- Publicly available educational material from www.icudelirium.org was used to develop this presentation.