Management of delirium in mechanically ventilated patients

Advances in Critical Care Medicine

King Hussein Cancer Center
Outline:

- Introduction
- Prevalence of delirium in ICU
- Why it is important to screen and early manage delirium?
- Delirium Pathophysiology
- Delirium risk factors
- How to manage delirious patient in ICU?
- Conclusion
Delirium is a disturbance of consciousness with inattention accompanied by a change in cognition or a perceptual disturbance, such as visual hallucinations, that develops over a short period (hours to days) and fluctuates over time. (American Psychiatric Association, 2000)

Types of Delirium:
- Hyperactive 1%
- Hypoactive 35%
- Mixed 64%
The prevalence of delirium in ICU (in multi center study) was 32.2% (Sallluh et al 2010).

Study found an incidence of delirium of only 20% in no intubated ICU patients (Van Rompaey B et al, 2008), whereas another study found an incidence of 83% in mechanically ventilated patients (Ely EW et al, 2001).

Delirium occurs in 60% to 80% of mechanically ventilated patients (Ely, Inouye, et al., 2001; Ely et al., 2004; McNicoll et al., 2003; Pandharipande et al., 2008).
Why it is important to screen and early manage delirium?

- Delirious patient had a 10-day increase in median length of stay and a 2-fold increased risk of remaining hospitalized (Dasta, 2005).

- Length of stay is considered the major driver of the increased costs on ICU care.

- Increase time on ventilator (9 vs. 4 days)------(Ely, et al 2001)

- Delirium accelerate dementia, 25% patients that do not cover from delirium will have long term cognitive impairment (Cole et al, 2003).
Why it is important to screen and early manage delirium?

- The presence of delirium has important prognostic implications; in mechanically ventilated patients it is associated with a 2.5-fold increase in short-term mortality and a 3.2-fold increase in 6-month mortality.

Delirium Pathophysiology

- Medications
  - Alcohol withdrawal
- Stroke
- Dopamine Activation
- Cholinergic Inhibition
- Cytokine Excess
- Serotonin Activation
- Medications
  - Substance withdrawal
- Medications
  - Medical illness
  - Surgical Illness
- Reduced GABA Activity
- GABA Activation
- Glutamate Activation
- Cortisol Excess
- Serotonin Deficiency
  - Tryptophan depletion
  - Phenylalanine elevation
  - Surgical Illness
  - Medical Illness
- Hepatic Failure
- Glucocorticoids
  - Cushing's Syndrome
  - Surgery
  - Stroke
- Benzodiazepines
- Benzodiazepine and Alcohol Withdrawal

Intracranial
- Hematoma
- Hemorrhage
- Meningitis
- Encephalitis
- Cerebral abscess
- Tumor

Respiratory
- Hypoxemia
- Hypercapnia

Endocrine
- Hyperthyroidism
- Addison disease
- Hypothyroidism
- Hyperparathyroidism
- Cushing syndrome

Metabolic
- Acid base disturbances
- Electrolyte imbalances (hypoglycemia)

Delirium Risk Factors
Higher APAHE score
Organ failure
Liver encephalopathy
Uremic encephalopathy
Septic shock
Drug related
Alcohol withdrawal
Drug induced
Higher pain scores at rest was associated with an increased risk of delirium over the first 3 postoperative days (adjusted risk ratio 1.20, p=0.04)
Constipation
Sleep deprivation

Delirium Risk Factors
Delirium Risk Factors

- Elderly
- Higher APAHE
- Organ Failure
- Drug related
- Septic shock

Liver encephalopathy
Uremic encephalopathy

Higher pain scores at rest was associated with an increased risk of delirium over the first 3 postoperative days (adjusted risk ratio 1.20, p=0.04).
Lorazepam Is an Independent Risk Factor for Transitioning to Delirium in Intensive Care Unit Patients


Figure 3. Probability of Transition to Delirium

Anesthesiology, V 104, No 1, Jan 2006
Risk factors you can’t control...

Age
Each year ↑ risk by 2%

Illness Severity
each APACHE point ↑ risk by

![Graph showing the probability of transitioning to delirium with age and APACHE II score.](image)

- Probability of Transitioning to Delirium with Age
  - Age (years) vs. Probability
  - p=0.04

- Probability of Transitioning to Delirium with APACHE II Score
  - APACHE II Score vs. Probability
  - p=0.01
The Impact of Postoperative Pain on the Development of Postoperative Delirium

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

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2002 SCCM - Clinical Practice Guidelines

<table>
<thead>
<tr>
<th>Patient Comfort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
</tr>
<tr>
<td>Sedation</td>
</tr>
<tr>
<td>Delirium</td>
</tr>
</tbody>
</table>

What to do?????

1st
Prevent................................................................................................................

...........

Identify the etiologies and try to modify the risk factors
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....................................................................................................................
....................................................................................................................

2nd
Treat ICU delirium.........................................................................................
Critical Care Nurses’ Role in Implementing the “ABCDE Bundle” Into Practice

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ABCDE bundle

- Has multiple evidenced based components which are interdependent where:
  - A: Awakening
  - B: Breathing
  - C: Coordination and Choice of sedation
  - D: Delirium monitoring
  - E: Early mobility and exercise

That aims to standardized care process and decrease delirium.
Pharmacologic

- Haloperidol

- Recommended first line treatment by Society of Critical Care Medicine and the American Psychiatric Association.
### Table 2 Clinical trials evaluating antipsychotics in critically ill patients with delirium.

<table>
<thead>
<tr>
<th>Author, year</th>
<th>No. of patients</th>
<th>Inclusion criteria</th>
<th>Interventions</th>
<th>Blinding</th>
<th>Randomization</th>
<th>Primary endpoint</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reade [84], 2009</td>
<td>20</td>
<td>Mechanical ventilation, inability to extubate because of agitation</td>
<td>Dexmedetomidine 0.2-0.7 mcg/kg/h (loading dose was optional) Haloperidol 0.5-2 mg/h (loading dose was optional)</td>
<td>No</td>
<td>Computer-generated random sequence</td>
<td>Time from commencement of study drug to extubation</td>
<td>Patients on dexmedetomidine were extubated sooner than those on haloperidol: 9.9 (IQR 7.3-24) vs. 42.5 (IQR 23.2-117.8) hours, P = 0.016.</td>
</tr>
<tr>
<td>Girard [85], 2010</td>
<td>101</td>
<td>Mechanical ventilation, abnormal level of consciousness, receipt of sedative or analgesic medications</td>
<td>Haloperidol 5 mg Ziprasidone 40 mg placebo. Second dose administered 12 hours after the first if QT &lt; 500 msec; then every 6 hours.</td>
<td>Yes</td>
<td>Computer-generated, permuted-block randomization scheme</td>
<td>Number of days alive without delirium or coma. P = 0.66. Haloperidol: 14 (IQR 6-18) days Ziprasidone: 15 (IQR 9.1-18) days Placebo: 12.5 (IQR 1.2-17.2) days</td>
<td>No significant difference in number of days alive without delirium or coma. P = 0.66. Haloperidol: 14 (IQR 6-18) days Ziprasidone: 15 (IQR 9.1-18) days Placebo: 12.5 (IQR 1.2-17.2) days</td>
</tr>
<tr>
<td>Devlin [86], 2010</td>
<td>36</td>
<td>ICU patients with delirium and an order for as-needed haloperidol</td>
<td>Quetiapine 50 mg every 12 hours titrated upwards on a daily basis if haloperidol was needed. Placebo.</td>
<td>Yes</td>
<td>Computer-generated random sequence</td>
<td>Time to first resolution of delirium</td>
<td>Time to first resolution was shorter with Quetiapine therapy than with placebo, P = 0.001. Quetiapine: 1 (IQR 0.5-3) days Placebo: 4.5 (IQR 2-7) days</td>
</tr>
<tr>
<td>Skrobik [87], 2004</td>
<td>73</td>
<td>ICU patients with delirium</td>
<td>Haloperidol 2.5-5 mg every 8 hours Olanzapine 5 mg daily</td>
<td>Only those assessing outcomes</td>
<td>Even/odds day basis</td>
<td>Not specified</td>
<td>No difference in delirium index scores, P = 0.83. No difference in benzodiazepine use, P = 0.9.</td>
</tr>
</tbody>
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IQR, interquartile range.
Conclusion:

- Delirium is often invisible unless you look for it.
- Delirium increases both hospital stay and mortality in pts. who are mechanically ventilated.
- 1st Prevent ............. 2nd Treat ICU delirium.
- Delirium is a multifactorial phenomena, but sleep deprivation is a universal experience that may contribute to ICU delirium.