Sedation of Short-Term Medical–Surgical ICU Patients

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Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult

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Maintaining an optimal level of comfort and safety for critically ill patients is a universal goal for critical care practitioners. The American College of Critical Care Medicine (ACCM) of the Society of Critical Care Medicine's (SCCM’s) practice guidelines for the optimal use of sedatives and analgesics was published in 1995 and recommended a tiered approach to the use of sedatives and analgesics, largely on the basis of expert opinion (1). These clinical practice guidelines replace the previously published parameters and include an evaluation of the evidence and expert opinion for a description of the methodology used to develop these guidelines (2).

This document is limited to a discussion of prolonged sedation and analgesia. Consistent with the previous practice guidelines, this document pertains to patients older than 12 years. The majority of the discussion focuses on the care of patients during mechanical ventilation. A discussion of regional techniques is not included. Appendix A summarizes the recommendations made herein.

ANALGESIA

Combined use of analgesics and sedatives may ameliorate the stress response in critically ill patients (7, 8). Pain may also contribute to pulmonary dysfunction through localized guarding of muscles around the area of pain and a generalized muscle rigidity or spasm that restricts movement of the chest wall and diaphragm (9). Effective analgesia may diminish pulmonary complications in postoperative patients (10).

Some patients recall unrelieved pain when interviewed about their ICU stays (3, 11, 12). The perception of pain can be influenced by several factors, such as the expectation of pain, prior pain experiences, and the intensity of the pain.
Prioritize analgesia

Sedation scale

Lorazepam for “most patients”

Sedation protocol
What’s ahead

1. Sedation protocols
2. Sedative choice
Sedation Protocols
DAILY INTERRUPTION OF SEDATIVE INFUSIONS IN CRITICALLY ILL PATIENTS UNDERGOING MECHANICAL VENTILATION

John P. Kress, M.D., Anne S. Pohlman, R.N., Michael F. O’Connor, M.D., and Jesse B. Hall, M.D.

ABSTRACT

Background Continuous infusions of sedative drugs in the intensive care unit may prolong the duration of mechanical ventilation, prolong the length of stay in the intensive care unit and the hospital, impede efforts to perform daily neurologic examinations, and increase the need for tests to assess alterations in mental status. Whether regular interruption of such infusions might accelerate recovery is not known.

Methods We conducted a randomized, controlled trial involving 128 adult patients who were receiving mechanical ventilation and continuous infusions of sedative drugs in a medical intensive care unit. In the intervention group, the sedative infusions were interrupted until the patients were awake, on a daily basis; in the control group, the infusions were interrupted only at the discretion of the clinicians in the intensive care unit.

Results The median duration of mechanical ventilation was 4.9 days in the intervention group, as compared with 7.3 days in the control group (P = 0.004), and the median length of stay in the intensive care unit was 6.4 days as compared with 9.9 days, respectively (P = 0.02). Six of the patients in the intervention group (8 percent) underwent diagnostic testing to assess changes in mental status, as compared with part pressure of arterial carbon dioxide to reach 50 mm Hg or higher), can cause patients substantial discomfort, necessitating high levels of sedation.

In many intensive care units, sedatives are infused continuously. As compared with intermittent bolus infusion, this approach provides a more constant level of sedation and may increase patients’ comfort. However, administration of sedatives by continuous infusion has been identified as an independent predictor of a longer duration of mechanical ventilation as well as a longer stay in the intensive care unit and in the hospital.

Continuous infusion of sedatives has other disadvantages. Extended sedation may limit clinicians’ ability to interpret physical examinations. It may be difficult to distinguish changes in mental status that are due to the action of a sedative from those that are due to neurologic injury. Therefore, clinicians may be compelled to order diagnostic studies to rule out new neurologic injury when patients do not awaken rapidly after the sedative infusion is discontinued.

The benefit of administering sedatives by continuous infusion must be balanced against these disadvantages. Daily interruption of sedative infusions to
Daily Interruption of Sedatives

Patients Receiving Mechanical Ventilation (%)

Control (n=60)
Protocol (n=68)

Adjusted p<.001

Daily Interruption of Sedatives

Ventilator time reduced by 2.5 days

Control (n=60)  Protocol (n=68)  Adjusted p<.001


Patients Receiving Mechanical Ventilation (%)

Time (Days)
Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial

ABC Trial
Awakening and Breathing Controlled Trial
336 randomized

168 to SAT
168 to control

SAT
Usual care

SBT
SBT

Four tertiary care MICUs in the U.S.

Patients Successfully Extubated (%) vs Days

Mean ventilator-free days, 14.7 versus 11.6 days
95% CI for the difference, 0.7 to 5.6 days; p=.02

ICU Length of Stay

SAT+SBT (n=167)

Control (n=168)

p=.01

Hospital Length of Stay


Patients Discharged from the Hospital (%)

SAT+SBT (n=167)

Control (n=168)

p = .04
One-Year Survival

- **SAT+SBT (n=167)**
- **Control (n=168)**

One-Year Survival

Patients Alive (%)

Control (n=168)

SAT+SBT (n=167)

NNT = 7

p = .01

A protocol of no sedation for critically ill patients receiving mechanical ventilation: a randomised trial

Thomas Strøm, Torben Martinussen, Palle Toft

Summary

Background Standard treatment of critically ill patients undergoing mechanical ventilation is continuous sedation. Daily interruption of sedation has a beneficial effect, and in the general intensive care unit of Odense University Hospital, Denmark, standard practice is a protocol of no sedation. We aimed to establish whether duration of mechanical ventilation could be reduced with a protocol of no sedation versus daily interruption of sedation.

Methods Of 428 patients assessed for eligibility, we enrolled 140 critically ill adult patients who were undergoing mechanical ventilation...
No Sedation: Design

113 randomized

55 to
Morphine PRN
Haloperidol PRN
6 hr propofol
Cont. propofol

58 to control
Morphine PRN
Cont. propofol
Ramsay 3–4
Daily

## No Sedation: Actual Management

<table>
<thead>
<tr>
<th>Management</th>
<th>No Sedation</th>
<th>Control</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continuous sedation, %</td>
<td>18%</td>
<td>100%</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Propofol, per hr</td>
<td>0 [0–0.52]</td>
<td>0.77 [0.15–1.65]</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Midazolam, per hr</td>
<td>0 [0–0]</td>
<td>0.003 [0–0.02]</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Morphine, per vent hr</td>
<td>0.005</td>
<td>0.005</td>
<td>0.39</td>
</tr>
<tr>
<td>Haloperidol, per vent</td>
<td>0 [0–0.01]</td>
<td>0 [0–0]</td>
<td>0.01</td>
</tr>
<tr>
<td>Extra staff needed, %</td>
<td>2.5±2.3</td>
<td>2.5±2.3</td>
<td>NR</td>
</tr>
<tr>
<td>Days required</td>
<td>2.5±2.3</td>
<td>2.5±2.3</td>
<td>NR</td>
</tr>
</tbody>
</table>

No Sedation: ICU Length of Stay

Control (n=58) vs Intervention (n=55)

p = .03

No Sedation: ICU Length of Stay

ICU stay reduced by 9.7 days

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Sedative Choice
A randomized trial of intermittent lorazepam versus propofol with daily interruption in mechanically ventilated patients*

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**Objective:** To compare duration of mechanical ventilation for patients randomized to receive lorazepam by intermittent bolus administration vs. continuous infusions of propofol using protocols that include scheduled daily interruption of sedation.

David Bar-Or et al.

ventilator-free survival, intensive care unit and hospital length of stay, and hospital mortality. Median ventilator days were significantly lower in the daily interruption propofol group compared with the intermittent bolus lorazepam group (5.8 vs.
Propofol Trial: Design

132 randomized

- 68 to propofol
  - Propofol
  - SAT

- 64 to lorazepam
  - Lorazepam
  - SAT

Propofol and Ventilator Time

Effect of Sedation With Dexmedetomidine vs Lorazepam on Acute Brain Dysfunction in Mechanically Ventilated Patients

The MENDS Randomized Controlled Trial

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Context Lorazepam is currently recommended for sustained sedation of mechanically ventilated intensive care unit (ICU) patients, but this and other benzodiazepine drugs may contribute to acute brain dysfunction, ie, delirium and coma, associated with prolonged hospital stays, costs, and increased mortality. Dexmedetomidine induces sedation via different central nervous system receptors than the benzodiazepine drugs and may lower the risk of acute brain dysfunction.

Objective To determine whether dexmedetomidine reduces the duration of delirium and coma in mechanically ventilated ICU patients while providing adequate sedation as compared with lorazepam.

Design, Setting, Patients, and Intervention Double-blind, randomized controlled trial of 106 adult mechanically ventilated medical and surgical ICU patients at 2 tertiary care centers between August 2004 and April 2006. Patients were sedated with dexmedetomidine or lorazepam for as many as 120 hours. Study drugs were titrated to achieve the desired level of sedation, measured using the Richmond Agitation-Sedation Scale (RASS). Patients were monitored twice daily for delirium using the Confusion Assessment Method for the ICU (CAM-ICU).

Main Outcome Measures Days alive without delirium or coma and percentage of days spent within 1 RASS point of the sedation goal.
MENDS Trial: Design

106 randomized

54 to dexmedetomidine

52 to lorazepam

Dexmedetomidine – Accuracy of Sedation


\[ p = 0.04 \]

Patients within 1 of Target RASS (%)

- **Dexmedetomidine**
- **Lorazepam**

Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6
---|---|---|---|---|---

\[ p = 0.04 \]
Dexmedetomidine – Accuracy of Sedation

Median days within 1 of target RASS (%): 80 (58,100) vs. 67 (48,83), p = .04

Daily Risk of Delirium in MENDS


p = 0.02
Dexmedetomidine vs Midazolam for Sedation of Critically Ill Patients
A Randomized Trial

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Providing sedation for patient comfort is an integral component of bedside care for critically ill patients. Relief of pain and anxiety and reduction in the occurrence of delirium are important outcomes of sedation. Several randomized trials have demonstrated that dexmedetomidine, an 

Context  

γ-Aminobutyric acid receptor agonist medications are the most commonly used sedatives for intensive care unit (ICU) patients, yet preliminary evidence indicates that the α₂ agonist dexmedetomidine may have distinct advantages.

Objective  

To compare the efficacy and safety of prolonged sedation with dexmedetomidine vs midazolam for mechanically ventilated patients.

Design, Setting, and Patients  

Prospective, double-blind, randomized trial conducted in 68 centers in 5 countries between March 2005 and August 2007 among 375 medical/surgical ICU patients with expected mechanical ventilation for more than 24 hours. Sedation level and delirium were assessed using the Richmond Agitation-Sedation Scale (RASS) and the Confusion Assessment Method for the ICU.

Interventions  

Dexmedetomidine (0.2-1.4 μg/kg per hour [n=244]) or midazolam (0.02-0.1 mg/kg per hour [n=122]) titrated to achieve light sedation (RASS scores between −2 and +1) from enrollment until extubation or 30 days.

Main Outcome Measures  

Percentage of time within target RASS range. Secondary end points included prevalence and duration of delirium, use of fentanyl and open-label midazolam, and nursing assessments. Additional outcomes included duration of mechanical ventilation, ICU length of stay, and adverse events.

Results  

There was no difference in percentage of time within the target RASS range (77.3% for dexmedetomidine group vs 75.1% for midazolam group; difference, 2.2% [95% confidence interval (CI), −3.2% to 7.5%]; P=.18). The preva-
Daily Risk of Delirium in SEDCOM

Riker, et al. JAMA 2009;301:489-499

p < 0.001
Dexmedetomidine – Extubation

- Patients Mechanically Ventilated (%)

0 2 4 6 8 100

- Days

Midazolam
Dexmedetomidine

p = .01

Riker RR, et al. JAMA 2009;301(5):489-499
Looking back

1. Use sedation protocols
2. Avoid benzodiazepines