Clinical practice guidelines for pain, agitation, delirium, sedation and mobilisation in the intensive care unit: A Rapid Review

Citation

Contact
cc@monashhealth.org

Executive Summary

Background
The Program Medical Director for Critical Care has requested a review of clinical practice guidelines for pain, agitation, delirium, sedation and mobilisation in the intensive care unit (ICU) to inform future implementation of a new clinical practice guideline in the ICU.

Objectives
The objective of this review was to review and summarise current clinical practice guidelines for pain, agitation, delirium, sedation and mobilisation in the intensive care unit (ICU).

Findings
A total of 4432 results were screened, if which 1 clinical practice guidelines was included in this review. This guideline had a working group that was based in the United States, and produced on behalf of The American College of Critical Care Medicine. It is worthwhile pointing this out as recommendations in this guideline were assessed for strength via a consensus process taking the evidence and risk/benefits into account. Therefore, any consensus decision is likely to reflect the clinical context of the individuals (e.g. U.S. setting only).

<table>
<thead>
<tr>
<th>Author</th>
<th>Date</th>
<th>Country</th>
<th>Endorsed</th>
<th>Pain</th>
<th>Sedation</th>
<th>Agitation</th>
<th>Delirium</th>
<th>Mobilisation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barr et al.¹</td>
<td>2013</td>
<td>U.S.</td>
<td>✓*</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

*This guideline was reviewed and endorsed by American College of Chest Physicians and the American Association for Respiratory Care; are supported by the American Association for Respiratory Care; and have been reviewed by the New Zealand Intensive Care Society.
Background

The Program Medical Director for Critical Care has requested a review of clinical practice guidelines for pain, agitation, delirium, sedation and mobilisation in the intensive care unit (ICU) to inform future implementation of a new clinical practice guideline in the ICU.

Objectives

The objective of this review was to review and summarise current clinical practice guidelines for pain, agitation, delirium, sedation and mobilisation in the intensive care unit (ICU).

Search strategy

The TRIP database and Google were searched by one author (CJ). In addition, a suite of other clinical practice guideline sources were also searched. Search terms can be found in Tables 1 & 2, and inclusion/exclusion criteria in Table 3. Papers identified were screened using inclusion and exclusion criteria established a priori. Searches of the TRIP database and the internet (using Google) were screened by one reviewer in consultation with colleagues as necessary.

NOTE: The evidence product is a Rapid Review, and as a result, all searches are restricted to only include the most recent evidence, which is defined as being that produced in the last five years.

Table 1. Topic search terms and relevant resource

<table>
<thead>
<tr>
<th>Topic</th>
<th>TRIP database search terms</th>
<th>Google search terms</th>
</tr>
</thead>
</table>
### Table 2. Clinical practice guideline source and search terms

<table>
<thead>
<tr>
<th>Source</th>
<th>Search terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Institute for Health and Care Excellence (NICE) <a href="https://www.nice.org.uk/">https://www.nice.org.uk/</a></td>
<td>pain OR delirium OR agitation OR sedation OR mobilisation AND ICU OR “intensive care unit”</td>
</tr>
<tr>
<td>National Guideline Clearinghouse <a href="https://www.guideline.gov/">https://www.guideline.gov/</a></td>
<td>pain OR delirium OR agitation OR sedation OR mobilisation AND ICU OR “intensive care unit”</td>
</tr>
<tr>
<td>BMJ Best Practice <a href="https://bestpractice.bmj.com/">https://bestpractice.bmj.com/</a></td>
<td>pain OR delirium OR agitation OR sedation OR mobilisation AND ICU OR “intensive care unit”</td>
</tr>
<tr>
<td>Scottish Intercollegiate Guidelines Network (SIGN) <a href="http://www.sign.ac.uk/">http://www.sign.ac.uk/</a></td>
<td>pain OR delirium OR agitation OR sedation OR mobilisation AND ICU OR “intensive care unit”</td>
</tr>
<tr>
<td>College of Physicians and Surgeons of Ontario <a href="http://www.cpso.on.ca/Policies-Publications/CPGs-Other-Guidelines">http://www.cpso.on.ca/Policies-Publications/CPGs-Other-Guidelines</a></td>
<td>pain OR delirium OR agitation OR sedation OR mobilisation AND ICU OR “intensive care unit”</td>
</tr>
</tbody>
</table>

### Table 3. Inclusion/Exclusion criteria

| Population | Include: Adults  
Exclude: Neonatal, paediatric, adolescent |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Interventions</td>
<td>Include: Pain, agitation, delirium, sedation, mobilisation</td>
</tr>
</tbody>
</table>
Outcomes | Include: Assessment and management  
Exclude: All other outcomes  
--- | ---  
Context | Include: Patients in the intensive care unit  
Exclude:  
--- | ---  
Types of evidence | Include: Clinical practice guidelines  
Exclude: All other types of evidence  
--- | ---  
Limits | Date: Since 2013 (last 5 years)  
Language: Publications in English.

Quality Appraisal
An internationally recognised appraisal tool, AGREE II\(^2\), was used to determine if each guideline was developed using an evidence-based approach. Two key criteria were used to appraise each guideline on their evidence-based process and content. The AGREE II criteria includes:

- Criterion 7: Were systematic methods used to search for evidence?
- Criterion 12: Is there an explicit link between the recommendations and the supporting evidence?

Each guideline was given one point for each criteria, with a possible total of 2 points. If the guideline did not meet the criteria, it was given a zero. If required, a full appraisal using all criteria can be conducted for the future.

NOTE: Where required, all guidelines and their background documentation were searched to determine if an evidence-based approach was used in the development process. It should also be noted that if the guideline did not meet Criteria 7 or 12, that does not necessarily mean that the recommendations in the guideline were not informed by evidence, but that, an explicit evidence-based method was not used or information explaining this process could not be explicitly determined.

Results
Search results
A total of 4432 results were screened (3358 results from TRIP & 1047 from Google). Of these, 18 results were explored, with 12 full-text items retrieved. A total of 1 clinical practice guidelines are included in this review\(^1\). This guideline had a working group that was based in the United States, and produced on behalf of The American College of Critical Care Medicine\(^1\). It is worthwhile pointing this out as recommendations in this guideline were assessed for strength via a consensus process taking the evidence and risk/benefits into account. Therefore, any consensus decision is likely to reflect the clinical context of the individuals (e.g. U.S. setting only).
Summary of findings

Table 4 provides a summary of the clinical practice guideline found in this report. In regards to the quality of evidence provided, high quality was based on the evidence being high quality randomised controlled trials; moderate quality was based on randomised controlled trials with significant limitations, or high-quality observational studies; and low quality refers to observational studies only.

Table 4. Summary of Barr et al., 2013

<table>
<thead>
<tr>
<th>Topic and subheading</th>
<th>Recommendation</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain and Analgesia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence of pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>i. Adult medical, surgical, and trauma ICU patients routinely experience pain, both at rest and with routine ICU care.</td>
<td>Moderate</td>
<td></td>
</tr>
<tr>
<td>ii. Pain in adult cardiac surgery patients is common and poorly treated; women experience more pain than men after cardiac surgery.</td>
<td>Moderate</td>
<td></td>
</tr>
<tr>
<td>iii. Procedural pain is common in adult ICU patients.</td>
<td>Moderate</td>
<td></td>
</tr>
<tr>
<td>Pain assessment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>i. We recommend that pain be routinely monitored in all adult ICU patients.</td>
<td>Moderate</td>
<td></td>
</tr>
<tr>
<td>ii. The Behavioral Pain Scale (BPS) and the Critical-Care Pain Observation Tool (CPOT) are the most valid and reliable behavioral pain scales for monitoring pain in medical, postoperative, or trauma (except for brain injury) adult ICU patients who are unable to self-report and in whom motor function is intact and behaviors are observable. Using these scales in other ICU patient populations and translating them into foreign languages other than French or English require further validation testing.</td>
<td>Moderate</td>
<td></td>
</tr>
<tr>
<td>iii. We do not suggest that vital signs (or observational pain scales that include vital signs) be used alone for pain assessment in adult ICU patients.</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>iv. We suggest that vital signs may be used as a cue to begin further assessment of pain in these patients, however.</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>Treatment of pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>i. We recommend that pre-emptive analgesia and/or non-pharmacologic interventions (e.g., relaxation) be administered to alleviate pain in adult ICU patients prior to chest tube removal.</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>ii. We suggest that for other types of invasive and potentially painful procedures in adult ICU patients, pre-emptive analgesic therapy and/or non-pharmacologic interventions may also be administered to alleviate pain.</td>
<td>Low</td>
<td></td>
</tr>
</tbody>
</table>
iii. We recommend that intravenous (IV) opioids be considered as the first-line drug class of choice to treat non-neuropathic pain in critically ill patients.  

iv. All available IV opioids, when titrated to similar pain intensity endpoints, are equally effective.  

v. We suggest that nonopioid analgesics be considered to decrease the amount of opioids administered (or to eliminate the need for IV opioids altogether) and to decrease opioid-related side effects.  

vi. We recommend that either enterally administered gabapentin or carbamazepine, in addition to IV opioids, be considered for treatment of neuropathic pain.  

vii. We recommend that thoracic epidural anesthesia/analgesia be considered for postoperative analgesia in patients undergoing abdominal aortic aneurysm surgery.  

viii. We provide no recommendation for using a lumbar epidural over parenteral opioids for postoperative analgesia in patients undergoing abdominal aortic aneurysm surgery, due to a lack of benefit of epidural over parenteral opioids in this patient population.  

ix. We provide no recommendation for the use of thoracic epidural analgesia in patients undergoing either intrathoracic or nonvascular abdominal surgical procedures, due to insufficient and conflicting evidence for this mode of analgesic delivery in these patients.  

x. We suggest that thoracic epidural analgesia be considered for patients with traumatic rib fractures.  

xi. We provide no recommendation for neuraxial/regional analgesia over systemic analgesia in medical ICU patients, due to lack of evidence in this patient population.  

### Sedation & Agitation

<table>
<thead>
<tr>
<th>Depth of sedation vs. clinical outcomes</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>i. Maintaining light levels of sedation in adult ICU patients is associated with improved clinical outcomes (e.g., shorter duration of mechanical ventilation and a shorter ICU length of stay [LOS]).</td>
<td>Moderate</td>
</tr>
<tr>
<td>ii. Maintaining light levels of sedation increases the physiologic stress response, but is not associated with an increased incidence of myocardial ischemia.</td>
<td>Moderate</td>
</tr>
<tr>
<td>iii. The association between depth of sedation and psychological stress in these patients remains unclear.</td>
<td>Low</td>
</tr>
<tr>
<td>iv. We recommend that sedative medications be titrated to maintain a light rather than a deep level of sedation in adult ICU patients, unless clinically contraindicated.</td>
<td>Moderate</td>
</tr>
</tbody>
</table>
## Monitoring depth of sedation and brain function

1. The Richmond Agitation-Sedation Scale (RASS) and Sedation-Agitation Scale (SAS) are the most valid and reliable sedation assessment tools for measuring quality and depth of sedation in adult ICU patients. **Moderate**

2. We do not recommend that objective measures of brain function (e.g., auditory evoked potentials [AEPs], Bispectral Index [BIS], Narcotrend Index [NI], Patient State Index [PSI], or state entropy [SE]) be used as the primary method to monitor depth of sedation in noncomatose, nonparalyzed critically ill adult patients, as these monitors are inadequate substitutes for subjective sedation scoring systems. **Moderate**

3. We suggest that objective measures of brain function (e.g., AEPs, BIS, NI, PSI, or SE) be used as an adjunct to subjective sedation assessments in adult ICU patients who are receiving neuromuscular blocking agents, as subjective sedation assessments may be unobtainable in these patients. **Moderate**

4. We recommend that EEG monitoring be used to monitor non-convulsive seizure activity in adult ICU patients with either known or suspected seizures, or to titrate electrosuppressive medication to achieve burst suppression in adult ICU patients with elevated intracranial pressure. **High**

## Choice of sedative

1. We suggest that sedation strategies using non-benzodiazepine sedatives (either propofol or dexmedetomidine) may be preferred over sedation with benzodiazepines (either midazolam or lorazepam) to improve clinical outcomes in mechanically ventilated adult ICU patients. **Moderate**

## Delirium

### Detecting and monitoring delirium

1. We recommend routine monitoring of delirium in adult ICU patients. **Moderate**

2. The Confusion Assessment Method for the ICU (CAM-ICU) and the Intensive Care Delirium Screening Checklist (ICDSC) are the most valid and reliable delirium monitoring tools in adult ICU patients. **High**

3. Routine monitoring of delirium in adult ICU patients is feasible in clinical practice. **Moderate**

### Delirium risk factors

1. Four baseline risk factors are positively and significantly associated with the development of delirium in the ICU: pre-existing dementia, history of hypertension and/or alcoholism, and a high severity of illness at admission. **Moderate**

2. Coma is an independent risk factor for the development of delirium in ICU patients. **Moderate**

3. Conflicting data surround the relationship between opioid use and the development of delirium in adult ICU patients. **Moderate**
iv. Benzodiazepine use may be a risk factor for the development of delirium in adult ICU patients. 

v. There are insufficient data to determine the relationship between propofol use and the development of delirium in adult ICU patients.

vi. In mechanically ventilated adult ICU patients at risk of developing delirium, dexmedetomidine infusions administered for sedation may be associated with a lower prevalence of delirium compared to benzodiazepine infusions.

### Delirium treatment

1. There is no published evidence that treatment with haloperidol reduces the duration of delirium in adult ICU patients. 
   - No evidence

2. Atypical antipsychotics may reduce the duration of delirium in adult ICU patients. 
   - Low

3. We do not recommend administering rivastigmine to reduce the duration of delirium in ICU patients. 
   - Moderate

4. We do not suggest using antipsychotics in patients at significant risk for torsades de pointes (i.e., patients with baseline prolongation of QTc interval, patients receiving concomitant medications known to prolong the QTc interval, or patients with a history of this arrhythmia). 
   - Low

5. We suggest that in adult ICU patients with delirium unrelated to alcohol or benzodiazepine withdrawal, continuous IV infusions of dexmedetomidine rather than benzodiazepine infusions be administered for sedation to reduce the duration of delirium in these patients. 
   - Moderate

### Strategies for Managing Pain, Agitation, and Delirium to Improve ICU Outcomes

1. We recommend either daily sedation interruption or a light target level of sedation be routinely used in mechanically ventilated adult ICU patients. 
   - Moderate

2. We suggest that analgesia-first sedation be used in mechanically ventilated adult ICU patients. 
   - Moderate

3. We recommend promoting sleep in adult ICU patients by optimizing patients’ environments, using strategies to control light and noise, clustering patient care activities, and decreasing stimuli at night to protect patients’ sleep cycles. 
   - Low

4. We provide no recommendation for using specific modes of mechanical ventilation to promote sleep in mechanically ventilated adult ICU patients, as insufficient evidence exists for the efficacy of these interventions. 
   - No Evidence

5. We recommend using an interdisciplinary ICU team approach that includes provider education, pre-printed and/or computerized protocols and order forms, and quality ICU rounds checklists to facilitate the use of pain, agitation, and delirium management guidelines or protocols in adult ICUs. 
   - Moderate
Quality appraisal

Overall, the quality of the guidelines included in this review was high (Table 5).

Table 5. Quality appraisal of included guidelines

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Evidence-based?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Item 7</td>
</tr>
<tr>
<td>Barr et al., 2013</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Conclusions

This review found one high quality clinical practice guidelines that addressed pain, agitation, sedation and delirium in adults in the ICU. No guidelines were found for mobilisation.

References
