Improving sedation-analgesia quality using novel technology: A technology development journey

Tim Walsh
Professor of Critical Care, Edinburgh University
Declarations and Funding

Funding

• Chief Scientists Office, Scotland
• Unrestricted funding GE Healthcare

Personal

• No personal financial benefit/income; no shares
• Consultancy and collaborative work with GE Healthcare to Edinburgh University
Background

- Unnecessary deep sedation associated with adverse patient outcomes
  

- Early deep sedation (first 48 hours) associated with higher ICU mortality
  

- Agitation increases nursing workload, anxiety, and the risk of adverse events
  

- Pain is prevalent in ICU patients and frequently recalled by ICU survivors
  
Protocol-directed sedation to reduce duration of mechanical ventilation

Published:
6 January 2015

Authors:

Primary Review Group:
Anaesthesia, Critical and Emergency Care Group

Review question

We reviewed the evidence to determine if the use of protocol-directed sedation reduced the duration of mechanical ventilation (method to mechanically assist breathing) in critically ill people.

Background

Determining the sedation needs of critically ill people is an important part of critical care to assist recovery and ensure humane treatment. Protocol-directed sedation is one management strategy that has been proposed as a method of reducing sub-optimal sedation (both under- and over-sedation). Protocol-directed sedation is sedation that is administered by a nurse, pharmacist or other member of the healthcare team according to general principles outlined in a protocol (document). The initial order for protocol-directed sedation is provided by a medical officer or physician. The aim of protocol-directed sedation is to improve patient outcomes, for example reduce the length of time a person requires mechanical ventilation or remains in the intensive care unit.

Search date

The evidence is current to November 2013. We re-ran the search in October 2014. We will deal with any studies of interest when we update the review.

Study characteristics

We searched scientific databases for studies that examined protocol-directed sedation in adult intensive care patients. We identified two studies with 633 participants for inclusion in this review.

Key results

For 20 years, Cochrane has produced systematic reviews of primary research in human health care and health policy, and are internationally recognized as the highest standard in evidence-based health care resources. Read more...
Does daily sedation interruption reduce the time critically ill adults spend on breathing machines compared to other sedation strategies?

Published: 9 July 2014

Authors: Bury L, Rose L, McCullagh U, Ferguson DA, Ferguson ND, Mehta S

Primary Review Group: Anaesthesia, Critical and Emergency Care Group

Background: critically ill patients require life-support technologies such as mechanical ventilation (breathing machines) and can experience pain, anxiety, and sleep deprivation related to their illness. Good pain control and adequate sedation are important but too much sedative drug can increase the time on breathing machines and the chance of harmful effects such as pneumonia.

Medications that are available have many properties that make them difficult to use in critically ill patients. Without careful adjustments these properties can lead to a build up of drug in the body. These medications are given as continuous infusions, so that blood levels remain stable, and dose changes are left to clinician judgement. In order to avoid drug build up, several methods can be used to adjust doses. Some studies claim that an interruption, or stopping the drug for a period of time each day, will allow the body to clear the drugs and lead to patients being more awake and ready for earlier liberation from the breathing machine.

Search date: current to February 2014.

Study characteristics: we included nine studies involving 1282 critically ill patients receiving mechanical ventilation. Studies compared daily sedation interruption to strategies that did not include an interruption. Studies were conducted worldwide and involved both medical and surgical critically ill patients.

Key results: we did not find strong evidence that daily sedation interruption reduced the duration of mechanical ventilation, length of stay in the intensive care unit (ICU) or hospital, or the amount of drug used. The effect on adverse events such as accidental removal of the breathing tube or invasive devices, or the rate of delirium was uncertain. However, tracheostomy was performed less often in those who were managed with daily sedation interruption. Sedation practices are known to vary worldwide, and as such an analysis of studies conducted in North America showed a reduction in time on the breathing machine for those who were managed with daily sedation interruption compared to those who were not.
Implications of minimising sedation

- Tolerance of intubation and invasive ventilation
  - Analgesia
  - Antinociception
  - Airway reflexes

- Minimising risk of delirium

- Managing agitation

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

- Need for integrated approach
- Consider Pain, Agitation, and Delirium
- Need for monitoring/tracking tools to drive quality improvement

- Current technologies (most studied Bispectral Index; BIS) not recommended except:
  - during neuromuscular paralysis
  - therapeutic deep sedation
Table 1. The Richmond Agitation-Sedation Scale (RASS)

<table>
<thead>
<tr>
<th>Score</th>
<th>Term</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>+4</td>
<td>Combative</td>
<td>Overtly combative, violent, immediate danger to staff</td>
</tr>
<tr>
<td>+3</td>
<td>Very agitated</td>
<td>Pulls or removes tube(s) or catheter(s); aggressive</td>
</tr>
<tr>
<td>+2</td>
<td>Agitated</td>
<td>Frequent nonpurposeful movement, fights ventilator</td>
</tr>
<tr>
<td>+1</td>
<td>Restless</td>
<td>Anxious but movements not aggressive or vigorous</td>
</tr>
<tr>
<td>0</td>
<td>Alert and calm</td>
<td></td>
</tr>
<tr>
<td>−1</td>
<td>Drowsy</td>
<td>Not fully alert, but has sustained awakening (eye opening/eye contact) to voice (&gt;10 seconds)</td>
</tr>
<tr>
<td>−2</td>
<td>Light sedation</td>
<td>Briefly awakens with eye contact to voice (&lt;10 seconds)</td>
</tr>
<tr>
<td>−3</td>
<td>Moderate sedation</td>
<td>Movement or eye opening to voice (but no eye contact)</td>
</tr>
<tr>
<td>−4</td>
<td>Deep sedation</td>
<td>No response to voice, but movement or eye opening to physical stimulation</td>
</tr>
<tr>
<td>−5</td>
<td>Unarousable</td>
<td>No response to voice or physical stimulation</td>
</tr>
</tbody>
</table>

Procedure for RASS Assessment

1. Observe patient
   - Patient is alert, restless, or agitated.

2. If not alert, state patient's name and say to open eyes and look at speaker.
   - Patient awakens with sustained eye opening and eye contact.
   - Patient awakens with eye opening and eye contact, but not sustained.
   - Patient has any movement in response to voice but no eye contact.

3. When no response to verbal stimulation, physically stimulate patient by shaking shoulder and/or rubbing sternum.
   - Patient has any movement to physical stimulation.
   - Patient has no response to any stimulation.

Score 0 to +4
Score −1
Score −2
Score −3
Score −4
Score −5

Adapted with permission.26

Ely EW JAMA 2003; 289: 2183
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### Procedure for RASS Assessment

1. **Observe patient**
   - Patient is alert, restless, or agitated. Score 0 to +4

2. **If not alert, state patient's name and say to open eyes and look at speaker.**
   - Patient awakens with sustained eye opening and eye contact. Score −1
   - Patient awakens with eye opening and eye contact, but not sustained. Score −2
   - Patient has any movement in response to voice but no eye contact. Score −3

3. **When no response to verbal stimulation, physically stimulate patient by shaking shoulder and/or rubbing sternum.**
   - Patient has any movement to physical stimulation. Score −4
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<td>Light sedation</td>
<td>Briefly awakens with eye contact to voice (≤ 10 seconds)</td>
</tr>
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<td>Moderate sedation</td>
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3. When no response to verbal stimulation, physically stimulate patient by shaking shoulder and/or rubbing sternum.
   - Patient has any movement to physical stimulation.  
   - Patient has no response to any stimulation.  

Adapted with permission.²⁶
Relation between BIS and RASS scores
Ely EW et al 2003; 289; 2983

![Graph showing the relation between BIS and RASS scores]
Comparison of two bispectral index algorithms in monitoring sedation in postoperative intensive care patients
Tonner, Peter H et al CCM 2005; 33: 580
BIS: importance of facial EMG

An assessment of the validity of spectral entropy as a measure of sedation state in mechanically ventilated critically ill patients

DOI 10.1007/s00134-007-0858-x
Log EMG power across different clinical sedation levels
Responsiveness of the frontal EMG for monitoring the sedation state of critically ill patients

T. S. Walsh¹*, T. P. Lapinlampi², P. Ramsay¹, M. O. K. Särkelä², K. Uutela² and H. E. Viertiö-Oja²
Cohort of patients regaining consciousness post routine cardiac surgery
Potential importance of encephalopathy

\[ P_k \text{ for 1-4 versus 5-6:} \]

- “Low risk” encephalopathy: 0.90 (0.02)
- “High risk” encephalopathy: 0.70 (0.04)
The “traffic light” concept

- Familiar warning colours to alert clinical staff to absolute values and trends

- **Red (RASS -5)**
  - “warning”
  - “stop”
  - “danger”
  - “be alert”...etc

- **Amber**
  - “intermediate state”

- **Green (RASS ≥ -3)**
  - “continue”
  - “Go”
  - “OK”...etc
Derivation of “best cut-off values” to discriminate “higher” from “lower” probability of over-sedation

In absence of likely encephalopathy:
Cut-off RI 35:  Sensitivity 90%
Specificity 79%

RED: \( \leq 20 \)
AMBER: 20-40
GREEN: \( \geq 40 \)
Responsiveness colour in relation to RASS score

**Algorithm**
Canadian J Neurol Sciences 2014, 41(5):611-619

**Validation and “Traffic light cut-offs”**
J Crit Care 2014, 29(5):886.e881-887
Reasons for an “unresponsive“ patient based on fEMG activity (Red/Amber)

• Muscle paralysis
• Normal sleep
• Illness associated coma
  – Liver failure
  – Hypoxic brain injury
  – Traumatic brain injury
  – Severe metabolic encephalopathy
• Drug-induced coma
  – Excessive dosing of sedative drugs
  – Accumulation of sedative drugs
• Decreased levels of patient stimulation
Excessive sedation
A randomized controlled proof-of-concept trial of early sedation management using Responsiveness Index monitoring in mechanically ventilated critically ill patients

Markus Kaila, Kirsty Everingham, Petteri Lapinlampi, Petta Peitola, Mika O K Särkelä, Kimmo Uutela and Timothy S. Walsh

- Reduction in time with “Red” Responsiveness Index
- Reduction in time to extubation
- Increase in extubations during 48 hrs intervention period
Staff education, regular sedation and analgesia quality feedback, and a sedation monitoring technology for improving sedation and analgesia quality for critically ill, mechanically ventilated patients: a cluster randomised trial


Summary

Background Optimal sedation of patients in intensive care units (ICUs) requires the avoidance of pain, agitation, and unnecessary deep sedation, but these outcomes are challenging to achieve. Excessive sedation can prolong ICU stay, whereas light sedation can increase pain and frightening memories, which are commonly recalled by ICU survivors. We aimed to assess the effectiveness of three interventions to improve sedation and analgesia quality: an online education programme; regular feedback of sedation–analgesia quality data; and use of a novel sedation-monitoring technology (the Responsiveness Index [RI]).
Sedation Quality Assessment Tool (SQAT)

**Denominator data**

**Pain behaviours:** facial expression; limb relaxation; ventilator synchrony

**Sedation state:** agitation; calm/cooperative; unresponsive

**Clinical status justifying deep sedation:** advanced ventilation; therapeutic cooling; brain injury

Completed for every 12 hours (nursing shift)  
“DESIST care period” (unit of quality)
Primary outcome
Proportion of DESIST care periods with optimum sedation
Care period without agitation, excessive sedation, poor limb relaxation, or poor ventilator synchronisation

Secondary outcomes
A Primary outcome sedation quality components
Proportion of all DESIST care periods with:
1. agitation
2. excessive sedation
3. poor relaxation
4. poor ventilator synchronisation

B Patient-level sedation outcomes
Number of DESIST care periods per mechanically ventilated patient with:
1. optimum sedation
2. agitation
3. excessive sedation
4. poor relaxation
5. poor ventilator synchronisation
Study Design: modified cluster randomised trial
Setting: 8 ICUs in Scotland

<table>
<thead>
<tr>
<th>45 weeks</th>
<th>8 weeks</th>
<th>45 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-implementation baseline period</td>
<td>Implementation phase</td>
<td></td>
</tr>
</tbody>
</table>

- **Group 1:**
  - Education package
  - Existing local feedback

- **Group 2:**
  - Education package
  - Enhanced process feedback
  - Introduced into ICU

- **Group 3:**
  - Education package
  - Existing local feedback
  - Responsiveness technology
  - Introduced into ICU

- **Group 4:**
  - Education package
  - Enhanced process feedback
  - Introduced into ICU
  - Responsiveness technology
  - Introduced into ICU
Sample size

- 1600 patients (800 per study period; target 100 per site per period)
- Modelled with various ICC values
- Assumed 70% optimum sedation rate pre-intervention, detecting 25% improvement at patient level (80% power; P = 0.05)

Analysis

- multilevel generalised linear regression mixed model
- 3 levels
  - ICU
  - Patient
  - DESIST care period
- Adjustment for ICU; time period (pre-intervention or post-implementation); ICU by time period interaction; age, sex and APACHE II score
DESIST Responsiveness monitoring

- Monitoring supplied to all ICUs (sufficient for all ventilated patients)
- Training of staff and subsequent support available
- Staff encouraged to use “red” RI as trigger to explore potential deep sedation (prompts on screen)
- No formal protocol linking RI number to sedative drug use
**DESIST Consort Diagram**

(Study totals)

**Total number of Screened Patients**

n = 9427

Excluded patients = 340

- Patient died 244
- Age <16 years 71
- For Palliative care 25

Inclusion Criteria not met = 5960

- Patient not receiving mechanical ventilation via ET tube or tracheostomy 3877
- Patient has received mechanical ventilation but has been discontinued at the time of screening 1132
- Extubation anticipated in the next 4 hours at time of screening 678
- Patient in whom the decision to withdraw treatment has been made at time of screening 194
- Patient already enrolled in the study in current hospital admission 79

**Eligible patients**

n = 3127

Unconsented patients = 1490

Reasons for not obtaining consent:

- No one available to give consent 270
- Lack of research staff 133
- Not approached 243
- Clinician refusal 109
- Consent not obtained within 48 hours of admission 380
- Other 355

Includes:

- Refusals
- Transferred out of ICU/hospital prior to consent
- Patients with a primary neurological diagnosis
- Family distress/inappropriate to approach
- NOK had cognitive issues

**Consented patients**

n = 1637

Randomised 296
Primary outcome and sedation quality outcomes at the DESIST care period level by intervention

Odds Ratio (95% CI)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Education</th>
<th>Process Feedback</th>
<th>Responsiveness Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free from excessive sedation</td>
<td>1.08 (0.78-1.51)</td>
<td>0.65 (0.45-0.94)</td>
<td>1.59 (1.09-2.31)</td>
</tr>
<tr>
<td>Agitation</td>
<td>1.13 (0.69-1.84)</td>
<td>1.27 (0.74-2.15)</td>
<td>0.84 (0.51-1.39)</td>
</tr>
<tr>
<td>Poor relaxation</td>
<td>0.83 (0.60-1.15)</td>
<td>0.98 (0.68-1.41)</td>
<td>1.26 (0.88-1.80)</td>
</tr>
<tr>
<td>Poor synchronisation</td>
<td>0.96 (0.74-1.50)</td>
<td>0.91 (0.61-1.35)</td>
<td>1.55 (1.05-2.30)</td>
</tr>
<tr>
<td>Optimum sedation (primary outcome)</td>
<td>1.13 (0.86-1.48)</td>
<td>0.74 (0.54-1.00)</td>
<td>1.44 (1.07-1.95)</td>
</tr>
<tr>
<td>p=0.392</td>
<td></td>
<td>p=0.052</td>
<td>p=0.017</td>
</tr>
<tr>
<td>Day with sedation-related adverse event</td>
<td>0.52 (0.30-0.92)</td>
<td>1.08 (0.57-2.04)</td>
<td>1.78 (0.94-3.37)</td>
</tr>
<tr>
<td>Patient had sedation-related adverse event</td>
<td>0.56 (0.32-0.99)</td>
<td>1.15 (0.61-2.15)</td>
<td>1.91 (1.02-3.58)</td>
</tr>
</tbody>
</table>

Figure 3: Estimates of effects of each intervention on sedation–analgesia quality measures at the care period level, and sedation-related adverse events

Figure shows OR with 95% CIs. For the sedation–analgesia quality measures, OR > 1 indicates an increase in the outcome with the intervention (improvement); for the sedation-related adverse event outcomes, an OR < 1 indicates a decrease in the outcome with the intervention (improvement). Data from all ICUs were combined in a single statistical model to explore the independent effects of each of the three interventions. Results are from multilevel generalised linear model to estimate the effects of each intervention. OR=odds ratio.
Process evaluation

• DESIST Responsiveness monitoring
  – time between intubation and starting monitoring median 21 hours (IQR: 11, 34)
  – median duration of monitoring was 66 hours (27, 139).
  – First RI recorded was: red 59% (range 50-66% across ICUs), amber 12% (range 4-17%), and green 28% (range 25-38%).
  – Median time to first recording green RI 9 hours (4, 23).
  – RI value red for 35% of monitoring time (range 23-48% across ICUs)

• Qualitative data
  – Perceived by many as user friendly and a useful bedside prompt to all staff to review sedation management.
  – Mixed views
  – Some staff did not understand the concept and questioned its utility and validity.
  – Some found its presence at the bedside intrusive.
<table>
<thead>
<tr>
<th>Sedation–analgesia quality measure at care period level</th>
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<tr>
<td><strong>Primary outcome</strong></td>
</tr>
<tr>
<td>Optimal sedation</td>
</tr>
<tr>
<td>Baseline: 61.6%</td>
</tr>
<tr>
<td>Education: 64.4%</td>
</tr>
<tr>
<td>Education plus process feedback: 57.1%</td>
</tr>
<tr>
<td>Education plus responsiveness monitoring: 72.3%</td>
</tr>
<tr>
<td><strong>Components of primary outcome</strong></td>
</tr>
<tr>
<td>Free from excessive sedation</td>
</tr>
<tr>
<td>Baseline: 85.5%</td>
</tr>
<tr>
<td>Education: 86.5%</td>
</tr>
<tr>
<td>Education plus process feedback: 80.6%</td>
</tr>
<tr>
<td>Education plus responsiveness monitoring: 91.0%</td>
</tr>
<tr>
<td>Free from agitation</td>
</tr>
<tr>
<td>Baseline: 97.3%</td>
</tr>
<tr>
<td>Education: 97.6%</td>
</tr>
<tr>
<td>Education plus process feedback: 98.1%</td>
</tr>
<tr>
<td>Education plus responsiveness monitoring: 97.2%</td>
</tr>
<tr>
<td>Free from poor relaxation</td>
</tr>
<tr>
<td>Baseline: 90.3%</td>
</tr>
<tr>
<td>Education: 88.6%</td>
</tr>
<tr>
<td>Education plus process feedback: 88.4%</td>
</tr>
<tr>
<td>Education plus responsiveness monitoring: 90.7%</td>
</tr>
<tr>
<td>Free from poor synchronisation</td>
</tr>
<tr>
<td>Baseline: 94.5%</td>
</tr>
<tr>
<td>Education: 94.8%</td>
</tr>
<tr>
<td>Education plus process feedback: 94.3%</td>
</tr>
<tr>
<td>Education plus responsiveness monitoring: 96.6%</td>
</tr>
<tr>
<td><strong>Sedation-related adverse events</strong></td>
</tr>
<tr>
<td>Proportion of days on which a sedation-related adverse event occurred</td>
</tr>
<tr>
<td>Baseline: 2.0%</td>
</tr>
<tr>
<td>Education: 1.1%</td>
</tr>
<tr>
<td>Education plus process feedback: 1.1%</td>
</tr>
<tr>
<td>Education plus responsiveness monitoring: 1.9%</td>
</tr>
<tr>
<td>Patient experienced a sedation-related adverse event</td>
</tr>
<tr>
<td>Baseline: 17.6%</td>
</tr>
<tr>
<td>Education: 10.7%</td>
</tr>
<tr>
<td>Education plus process feedback: 12.1%</td>
</tr>
<tr>
<td>Education plus responsiveness monitoring: 18.6%</td>
</tr>
</tbody>
</table>

Predictions are for the average patient in the intensive care unit enrolled in the study (age 60 years, 60% male, APACHE II score 22).

Table 4: Predicted percentages from modelling effects of interventions on sedation–analgesia quality measures at care period level and sedation-related adverse events
Conclusions

• Continuous Responsiveness Index monitoring is a promising novel technology to assist decision-making during ICU sedation-analgesia

• RI has been specifically developed to detect deeper sedation states and encourage sedation review and reduction

• Future trials should test its effects on other important outcomes such as duration of ventilation and assess cost-effectiveness.