Analgosedation: What Strategy is Best?

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The facts

• Despite the efforts to optimize sedation and comfort of ICU’s patients:
  – More than 50% of patients from several studies recalled experiencing moderate to extreme pain, anxiety, fear and inability to sleep during ICU stay.
  – Managing sedation is an important unmet challenge in ICUs worldwide.
  – Pain management is often left aside despite major interventions
  – There is no gold standard regarding pharmacological options for managing pain and sedation

Bartel B: New Sedation Practices in the Adult Intensive Care Unit: Analgosedation; South Dakota Medicine
The target

• Identification of the critically ill patient´s need for pain relief and correct level of sedation decreases the risk of complications and reduces the LOS.

• Personalized pain treatment and sedation in the ICU also improve the patient´s comfort and raise the tolerance threshold for ICU treatment
Under Sedation:
- Pain
- Self extubation
- Misery
- Awake
- Aware

Over Sedation:
- Ventilator associated pneumonia
- Long-term decrease in cognitive function
- Hemodynamic instability
- Increased LOS and cost
- Post traumatic stress disorder

Balanced:
- Titration
- Pain
- Sedation
- Delirium

Reduced pain
- Decreased anxiety
- Managed delirium
- Amnesia
- Recovery
Sedation – Analgesia Model

• Patients are given constant sedatives to relieve anxiety or distress, with extra analgesia given to relieve pain.
• There is a tendency of oversedation between 40-60% of the patients
• There are several adverse effects of the drugs use in the sedation model
Sedation-Analgesia Model

• Recent publications have found that there are advantages of sedation protocols, assessment scales and daily interruptions of sedatives.

• However there is a great heterogeneity in sedation practices across countries

• Ideally, patients need to be awake or only lightly sedated unless there is a clinical need for deep sedation

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### Recall of ICU Stay in Patients Managed With a Sedation Protocol or a Sedation Protocol With Daily Interruption

**TABLE 4. Characteristics of Patients Who Reported That They “Did Not Remember Being in the ICU” and Those Who Did on Day 28**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Remember Being in ICU $(n = 88)$</th>
<th>Patients Who Reported They “Did not Remember Being in the ICU” $(n = 31)$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr), mean (sd)</td>
<td>57.6 (15.5)</td>
<td>53.5 (16.4)</td>
<td>0.22</td>
</tr>
<tr>
<td>Female</td>
<td>42 (47.7)</td>
<td>10 (32.3)</td>
<td>0.14</td>
</tr>
<tr>
<td>Randomization group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protocolized sedation</td>
<td>42 (47.7)</td>
<td>19 (61.3)</td>
<td>0.19</td>
</tr>
<tr>
<td>Protocolized sedation plus daily sedation</td>
<td>46 (52.3)</td>
<td>12 (38.7)</td>
<td></td>
</tr>
</tbody>
</table>
Pain in the ICU

• Two possible origins:
  – Acute pain from the basal illness
  – Acute pain from ICU procedures

• Reasons for untreated pain:
  – Underestimate pain in the sedated patient
  – Lack of knowledge of specific assessment tools
Pain: The unmet player

Determinants of Procedural Pain Intensity in the Intensive Care Unit
The Europain® Study
### Determinants of Procedural Pain Intensity in the Intensive Care Unit
#### The Europain® Study

Table 2: Differences in Pain Intensity from before the Procedure to during the Procedure

<table>
<thead>
<tr>
<th>Procedure</th>
<th>N (%)</th>
<th>Preprocedural Pain Intensity Median (IQR)</th>
<th>Pain Intensity During the Procedure Median (IQR)</th>
<th>Difference Median (IQR)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest tube removal</td>
<td>292 (6.1)</td>
<td>2 (0–4)</td>
<td>5 (3–7)</td>
<td>2.5 (0.5–4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Wound drain removal</td>
<td>75 (1.6)</td>
<td>2 (0–4)</td>
<td>4.5 (2–7)</td>
<td>2 (0–4.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Arterial line insertion</td>
<td>199 (4.1)</td>
<td>1 (0–2.5)</td>
<td>4 (2–6)</td>
<td>2.75 (0–5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Endotracheal suctioning</td>
<td>767 (15.9)</td>
<td>1 (0–4)</td>
<td>4 (1–6)</td>
<td>1.5 (0–4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Tracheal suctioning</td>
<td>302 (6.3)</td>
<td>1 (0–3.5)</td>
<td>4 (1–6)</td>
<td>1 (0–4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Peripheral intravenous insertion</td>
<td>315 (6.5)</td>
<td>1 (0–3)</td>
<td>3 (1–5.5)</td>
<td>1 (0–3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Peripheral blood draw</td>
<td>328 (6.8)</td>
<td>0.5 (0–3)</td>
<td>3 (1–5)</td>
<td>1 (0–3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Turning</td>
<td>873 (18.1)</td>
<td>1.75 (0–4)</td>
<td>3 (0.25–6)</td>
<td>1 (0–2.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Respiratory exercises</td>
<td>439 (9.1)</td>
<td>2 (0–4)</td>
<td>3 (1–5)</td>
<td>1 (0–2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Positioning</td>
<td>371 (7.7)</td>
<td>1 (0–4)</td>
<td>3 (0–5)</td>
<td>1 (0–2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Wound care</td>
<td>301 (6.3)</td>
<td>2 (0–4)</td>
<td>3 (1–6)</td>
<td>0.5 (0–2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mobilization</td>
<td>526 (10.9)</td>
<td>1 (0–3)</td>
<td>2 (0–5)</td>
<td>0 (0–2)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

**Definition of abbreviation:** IQR = interquartile range.
Pain intensity was scored on a 0–10 numerical rating scale.
*Wilcoxon signed rank sum test.
Fig. 1 The multidimensionality of pain and other symptoms.

Pain in the ICU

- Successful analgesia starts with identifying and managing conditions that contribute to pain, well before the use of any medications.
- Insomnia, anxiety and delirium can amplify the pain experience and also require prompt treatment.

Azzam & Abdulkader: “Pain in the ICU A Psychiatric Perspective” (2013) J of Intensive Care Medicine, 28 (3) 140
Clinical recommendations

Figure 1. Visual Analog scale (VAS) and Numerical Rating scale (NRS). Adapted from Breivik et al.,\textsuperscript{24} with permission.

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facial expression</td>
<td>Relaxed</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Partially tightened (eg, brow lowering)</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Fully tightened (eg, eyelid closing)</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Grimacing</td>
<td>4</td>
</tr>
<tr>
<td>Upper limbs</td>
<td>No movement</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Partially bent</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Fully bent with finger flexion</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Permanently retracted</td>
<td>4</td>
</tr>
<tr>
<td>Compliance with ventilation</td>
<td>Tolerating movement</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Coughing but tolerating ventilation most</td>
<td></td>
</tr>
<tr>
<td></td>
<td>of time</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Fighting ventilator</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Unable to control ventilation</td>
<td>4</td>
</tr>
</tbody>
</table>

Total score 3-12

\textsuperscript{*} Adapted from Payen et al.,\textsuperscript{35} with permission.
# Clinical recommendations

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Description and Score</th>
</tr>
</thead>
</table>
| Facial expression | No muscular tension observed. Relaxed, neutral: 0  
Presence of frowning, brow-lowering, orbit tightening, and levator contraction. Tense: 1  
All of the above facial movements plus eyelids tightly closed. Grimacing: 2 |
| Body movement | Does not move at all (does not necessarily mean the absence of pain). Absence of movements: 0  
Slow, cautious movements, touching or rubbing the pain site, seeking attention through movements. Protection: 1  
Pulling at tube, attempting to sit up, moving limbs or thrashing, not following commands, striking at staff, trying to climb out of bed. Restlessness: 2 |
| Muscle tension (evaluated by passive arm flexion and extension) | No resistance to passive movements. Relaxed: 0  
Resistance to passive movements. Tense, rigid: 1  
Strong resistance to passive movements, inability to complete them. Very tense or rigid: 2 |
| Ventilator compliance (if intubated) or vocalization (if not intubated) | Alarms not activated, easy ventilation. Tolerating ventilation or movement: 0  
Alarms stop spontaneously. Coughing but tolerating ventilator: 1  
Asynchrony: blocking ventilation, alarms frequently activated. Fighting ventilator: 2  
Talking in normal tone or no sound: 0  
Sighing, moaning: 1  
Crying out, sobbing: 2 |

Total score  
0-8

*Adapted from Gélinas et al.39 with permission.*
Analgo sedation

Is it the right answer?
Analgo-Sedation

- The ICU is an hostile environment
- Pain is often the root cause of distress
  - Anxiety
  - Dyspnea
  - Delirium
  - Sleep deprivation
Analgosedation

• The primary goal is to address pain and then add a hypnotic agent if necessary
  – Analgesia based sedation
  – Analgesia first sedation

• It is an approach to ICU sedation that may ameliorate significant patient safety concerns associated commonly with sedative agents.

• Puts a focus on the unmet need of providing adequate pain relief.

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Analgosedation

• The trials reviewed by Devabhakthuni et al (2012) showed that:
  – Comparing the use of remifentanil to propofol or midazolam, the approach of using remifentanil alone in continuous infusion:
    • Led to optimal patient comfort studies
    • None of the remifentanil studies used daily sedation interruption
    • Patients treated with this model were more likely to be weaned from ventilation more quickly, spend less time on ventilator support, and have a shorter ICU length of stay.

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Analgosedation

• There has been also drawbacks in the analgosedation model:
  – Delirium has also been found to be associated with morphine administration.
  – Recall for unpleasant events before regaining consciousness, nightmares and hallucinations.
  – Immunosuppressive effects of opioids
  – Strong withdrawal effect following the discontinuation
  – Hyperalgesia and increased analgesic requirements following cessation of remifentanil infusions

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Analgosedation

• There are some concerns about the use of analgosedation if the patient:
  – Requires deeper levels of sedation (such as those with elevated intracranial pressure)
  – Ventilator disynchrony
  – Severe agitation
  – Other specific conditions
Analgesedation

• Which opioid is the best?
  – Remifentanil is the ideal based on its pharmacokinetic properties...
    • More important role in patients with neurologic conditions that require closer monitoring.
    • Cause hyperalgesia
  – Fentanyl is also a reasonable choice with similar outcomes when compared to remifentanil
  – Morphine accumulates in renal failure and has deleteriogenic effects

<table>
<thead>
<tr>
<th></th>
<th>Propofol</th>
<th>Fentanyl</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of mechanical ventilation (hrs)</td>
<td>46.7 (27.9–66.7)</td>
<td>46 (34.3–96.9)</td>
<td>0.19</td>
</tr>
<tr>
<td>ICU length of stay (days)</td>
<td>5 (4–8)</td>
<td>5 (3–7.3)</td>
<td>0.42</td>
</tr>
<tr>
<td>CPOT scores at goal</td>
<td>81%</td>
<td>84%</td>
<td>0.44</td>
</tr>
<tr>
<td>RASS scores at goal</td>
<td>41.2%</td>
<td>41.8%</td>
<td>0.94</td>
</tr>
<tr>
<td>RASS scores +1 to +4</td>
<td>19.1%</td>
<td>18.9%</td>
<td>0.95</td>
</tr>
<tr>
<td>RASS scores −2 to −5</td>
<td>39.7%</td>
<td>39.3%</td>
<td>0.91</td>
</tr>
<tr>
<td>Required rescue opioid</td>
<td><strong>56%</strong></td>
<td>34%</td>
<td>0.04</td>
</tr>
<tr>
<td>Rescue opioid dose (µg)</td>
<td><strong>150 (90–443.8)</strong></td>
<td>100 (25–232.5)</td>
<td>0.03</td>
</tr>
<tr>
<td>Required rescue benzodiazepine</td>
<td>24%</td>
<td>38%</td>
<td>0.19</td>
</tr>
<tr>
<td>Rescue benzodiazepine dose (mg)</td>
<td>6 (3.8–20)</td>
<td>8 (2–11.4)</td>
<td>0.74</td>
</tr>
</tbody>
</table>

Categorical data displayed as %.
Continuous data displayed as median (IQR).
ICU = intensive care unit; CPOT = Critical Care Pain Observation Tool; RASS = Richmond Agitation Sedation Scale.

Clinical recommendations

• A shift in current sedations practices to analgosedation should be considered in the care of mechanically ventilated ICU patients.

• Clinicians must avoid oversedation, which can be accomplished with the use of protocols and daily sedation interruptions.
  – Sedation interruptions should be targeted at achieving the lightest level of sedation possible to prevent excessive drug accumulation

Clinical recommendations

• When possible, analgesic effectiveness and requirements should be monitored through patient self-report.
  – Those unavailable to communicate, a validated assessment tool for pain should be use (visual analog pain scale or behavioral pain scale)

• Patient discomfort should be treated with analgesics such as remifentanil or fentanyl; leaving morphine reserved as a second-line agent due to its adverse effects.

Clinical recommendations

• The use of hypnotic agents such as propofol or dexmedetomidine should be considered in all patients requiring rescue therapy after the initiation of analgosedation.

• Benzodiazepines use should be kept to a minimum.

• The use of sparing agents such as acetaminophen or NSAIDs is currently under research

Clinical recommendations

• Anxiety, delirium and pain are not mutually exclusive, and treatment of one may exacerbate the other (eg: excessive ansiolytic administration promoting delirium)
  – Physicians must understand the relation of neuropsychiatric conditions of pain (multimodal sedation?)
  – Sedation protocols

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Conclusions

• Critical care improves and patients benefit when ICU clinicians practice thoughtful and systematic pain management.
• Guidance through protocols is the best strategy to minimize pain and improve comfort without oversedation.
• Analgosedation although promising, needs further clinical confirmation.
Analgosedation Pros and Cons

Advantages
• Reduction in hypnotics
• Less mechanical ventilation time
• Shorter ICU length of stay
• Rapid onset and offset of action
• Overall ICU cost savings?

Disadvantages
• Delirium
• Higher incidence of recall
• Nightmares
• Hallucinations
• Immunosuppression
• Withdrawal
• Hyperalgesia
Algoritmo para Sedación y Analgesia en TI

**Sedación**

- Corta
  - Evaluar con escalas 1B
  - Dexmedetomidina 1B
  - Sedación basada en la analgesia 1B
  - Propofol 1B

- Prolongada
  - Evaluar con escalas 1B
  - Interrupción diaria de la sedación 1B
  - Propofol 1B
  - Dexmedetomidina 1C
  - Lorazepam 1C
  - Midazolam 1C

**Agitación**

- Sí
  - Evaluar factores predisponentes 1B

- No
  - Evaluar con escalas de sedación y alcanzar objetivos 1B

**Dolor**

- Sí
  - Morfina 1C
  - Fentanilo 1C
  - Evaluar dolor cada 10-15 min. 1C
  - Remifentanilo 1C
  - Ajustar opioides 1C
  - Evaluar cada 4 horas con escalas y ajustar dosis 1C

- No
  - Evaluar causa de incomodidad: 1C
  - Hipoxia
  - Alteración metabólica
  - Reacción adverse a fármacos
  - Síndrome de abstinencia
  - Cama húmeda
  - Retención urinaria
  - Modo ventilatorio inadecuado

- Dexmedetomidina 1B
- Propofol 1B

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Hand Made

Thank you