Sedation and Ventilator Asynchrony

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Conflicts of interest

- none
Outline

- Sedation overview
- Circumstantial indictors
- How do sedatives influence asynchrony?
- Conclusion
Four years of work, wrap up meeting
sedation summary

- Light sedation is better
- Most sedatives worsen sleep quality
Sedation rather than drugs - a little pharmacology

- Sedatives are ubiquitously administered
- 20 to 95% of kinetic or dynamic pharmacotherapeutic determinants is genetic
- Drug-drug interactions also play a role
Cytochrome P450

Figure 1–4. The proportion of drugs metabolized by the major cytochrome P450 enzymes.
Figure 4. Pharmacogenetics of Nortriptyline.
Mean plasma concentrations of nortriptyline after a single 25-mg oral dose are shown in subjects with 0, 1, 2, 3, or 13 functional CYP2D6 genes. Modified from Dalén et al. with the permission of the publisher.
Mechanical ventilation

- Assumption it is uncomfortable
- Assumption dyspnea and asynchrony require pharmacological intervention
- As many as 1/4 of patients exhibit a high incidence of asynchrony during assisted ventilation; this, in turn, is associated with prolonged duration of mechanical ventilation.
Can we give him something?
managing asynchrony pharmacologically
Observational Study of Patient-Ventilator Asynchrony and Relationship to Sedation Level

Marjolein de Wit, MD, MS¹, Sammy Pedram, MD¹, Al M. Best, PhD², and Scott K. Epstein, MD³
The relationship between Richmond Agitation-Sedation Scale (RASS) and ineffective triggering index (ITI). For one unit decrease in RASS, ITI increased by 2.7%, p = 0.04.
Table 3
Relationship between ineffective triggering index and sedation levels

<table>
<thead>
<tr>
<th></th>
<th>ITI Mean</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Awake</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (n = 17)</td>
<td>2%</td>
<td>0.10%</td>
<td>0.04</td>
</tr>
<tr>
<td>No (n = 24)</td>
<td>11%</td>
<td>6.17%</td>
<td></td>
</tr>
<tr>
<td>CAM-ICU</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delirium absent (n = 8)</td>
<td>2%</td>
<td>0.11%</td>
<td>0.03</td>
</tr>
<tr>
<td>Delirium present (n = 14)</td>
<td>5%</td>
<td>1.12%</td>
<td></td>
</tr>
<tr>
<td>Coma (n = 13)</td>
<td>15%</td>
<td>8.22%</td>
<td></td>
</tr>
</tbody>
</table>

**RASS**
For each unit decrease in RASS, ITI increases by 2.7% 0.04

CI: confidence interval
ITI: Ineffective Triggering Index
CAM-ICU: Confusion Assessment Method for the Intensive Care Unit
RASS: Richmond Agitation-Sedation Scale
Impact of Ventilator Adjustment and Sedation-Analgesia Practices on Severe Asynchrony in Patients Ventilated in Assist-Control Mode*.
Chanques, Gerald; Kress, John; Pohlman, Anne; Patel, Shruti; Poston, Jason; Jaber, Samir; Hall, Jesse

DOI: 10.1097/CCM.0b013e31828c2d7a
Figure 1. Measurement of breath-stacking asynchrony index (AI) and tidal volume. Ventilator flow/time and pressure/time waveforms were recorded and analyzed to detect breath-stacking asynchrony. A stacked breath was defined as a subsequent inspiratory flow triggered before any complete expiration. AI was calculated as the ratio between the sum of stacked breaths divided by the sum of stacked breaths and normal breaths recorded during the same period, expressed in percentage. In this example, AI was 50%. Tidal volume was measured using the computer software as the calculation of area under the flow/time waveform.
Impact of Ventilator Adjustment and Sedation-Analgesia Practices on Severe Asynchrony in Patients Ventilated in Assist-Control Mode*.
Chanques, Gerald; Kress, John; Pohlman, Anne; Patel, Shruti; Poston, Jason; Jaber, Samir; Hall, Jesse
Figure 3. Individual change of breath-stacking index compared with baseline according to interventions decided by the primary care team. This figure shows individual changes in breath-stacking asynchrony index according to interventions decided by the primary care team (Wilcoxon test). The breath-stacking asynchrony index was calculated as the ratio between the sum of stacked breaths, which was divided by the sum of stacked breaths and normal breaths recorded during the same period, expressed in percentage.
The Association Between Ventilator Dyssynchrony, Delivered Tidal Volume, and Sedation Using a Novel Automated Ventilator Dynasense.

Figure 1. Representative images of each type of dyssynchrony: double-triggered breaths are characterized by incomplete exhalation between breaths (arrow). Flow-limited breaths are characterized by the scooping of the pressure-time curve (arrow). Premature-ventilator-terminated breaths are characterized by the ventilator terminating the breath and then the patient making an immediate effort to take another breath (arrows). Finally, ineffective-triggered breaths are characterized as the patient making efforts to initiate a breath during the expiratory phase of the breath (arrows).
delivery of tidal volumes of greater than 10 mL/kg. Although ventilator dyssynchrony is reduced by deep sedation, potentially deleterious tidal volumes may still be delivered. However, neuromuscular blockade effectively eliminates ventilator dyssynchrony. *(Crit Care Med 2018; 46:e151–e157)*
Sedation during mechanical ventilation and opiate in co-sedation and opioid use.

Figure 2. a, fewer events of patient-ventilator asynchrony in the co-sedation group, expressed as the mean number of events/patient/day ($p = .04$).
Remifentanil effects on respiratory drive and timing during pressure support ventilation and neurally adjusted ventilatory assist

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ABSTRACT

We assessed the effects of varying doses of remifentanil on respiratory drive and timing in patients receiving Pressure Support Ventilation (PSV) and Neurally Adjusted Ventilatory Assist (NAVA). Four incrementing remifentanil doses were randomly administered to thirteen intubated patients (0.03, 0.05, 0.08, and 0.1 µg/Kg⁻¹/min⁻¹) during both PSV and NAVA. We measured the patient’s (Ti/Ttotₜₚₑₑ) and ventilator (Ti/Ttotᵦₑₑ) duty cycle, the Electrical Activity of the Diaphragm (EAdi), the inspiratory (Delayₚₑₑ) and expiratory (Delayₑₑ) trigger delays and the Asynchrony Index (AI).

Increasing doses of remifentanil did not modify EAdi, regardless the ventilatory mode. In comparison to baseline, remifentanil infusion > 0.05 µg/Kg⁻¹/min⁻¹ produced a significant reduction of Ti/Ttotₜₚₑₑ and Ti/Ttotᵦₑₑ by prolonging the expiratory time. Delayₚₑₑ and Delayₑₑ were significantly shorter in NAVA, respect to PSV. AI was not influenced by the different doses of remifentanil, but it was significantly lower during NAVA compared to PSV. In conclusion, remifentanil did not affect the respiratory drive, but only respiratory timing, without differences between modes.
Observing asynchronies

Candelaria de Haro, Rudys Magrans, Josefina López-Aguilar, Jaume Montanyà, Enrico Lena, Carles Subirà, Sol Fernandez-Gonzalo, Gemma Gomà, Rafael Fernández, Guillermo M Albaiceta, Yoanna Skrobik, Umberto Lucangelo, Gastón Murias, Ana Ochagavia, Robert M Kacmarek, Montserrat Rue, Lluís Blanch, for the Asynchronies in the Intensive Care Unit (ASYNICU) Group
<table>
<thead>
<tr>
<th>Patients</th>
<th>n = 79</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>63 [52, 75]</td>
</tr>
<tr>
<td>Sex (% men)</td>
<td>64.5%</td>
</tr>
<tr>
<td>Reason for admission n (%)</td>
<td></td>
</tr>
<tr>
<td>Acute respiratory failure</td>
<td></td>
</tr>
<tr>
<td>- sepsis</td>
<td>12 (15.2%)</td>
</tr>
<tr>
<td>- pneumonia</td>
<td>7 (8.7%)</td>
</tr>
<tr>
<td>- ARDS</td>
<td>5 (6.3%)</td>
</tr>
<tr>
<td>- COPD</td>
<td>3 (3.8%)</td>
</tr>
<tr>
<td>- congestive heart failure</td>
<td>2 (2.5%)</td>
</tr>
<tr>
<td>- Other</td>
<td>10 (12.7%)</td>
</tr>
<tr>
<td>Neurologic</td>
<td>15 (19%)</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>10 (12.7%)</td>
</tr>
<tr>
<td>Postsurgical</td>
<td>8 (10.1%)</td>
</tr>
<tr>
<td>Multiple trauma</td>
<td>6 (7.6%)</td>
</tr>
<tr>
<td>Neuromuscular disease</td>
<td>1 (1.3%)</td>
</tr>
<tr>
<td>Apache II</td>
<td>17 [10, 26]</td>
</tr>
<tr>
<td>SOFA at admission</td>
<td>7 [5.25, 10.75]</td>
</tr>
<tr>
<td>Length of MV (days)</td>
<td>6 [3, 10.5]</td>
</tr>
<tr>
<td>ICU stay (days)</td>
<td>10 [6, 18]</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>23 [11, 50]</td>
</tr>
</tbody>
</table>
Rate of ineffective inspiratory efforts during expiration by treatment group

Rate of double cycling by treatment group

p < 0.0001

p = 0.0004
Light sedation is better
Most sedatives worsen sleep quality
Augmenting sedation depth doesn’t help and probably worsens synchrony
Light sedation with opiates after ventilator adjustment requires study
Thank you