Rational Management of Neuromuscular Blockers

Michael Rieker, DNP, CRNA, FAAN
Director, Nurse Anesthesia Program
Wake Forest School of Medicine

Why monitor?

- To determine onset of block and readiness for intubation or procedure start.
- To guarantee paralysis when patient movement would be deleterious
- To assess ability to reverse relaxants.
- To time recovery to coincide with end of surgery
- To ensure adequate recovery and readiness for extubation.

Extubation Criteria- Good reason to monitor

- Former standard was TOF ratio > .7
  - Associated with eye-opening, hand grasp, and acceptable recovery of spirometry parameters
- Recent studies have shown that at .7, pharyngeal dysfunction may persist
- Clinical tests show poor sensitivity (~12%) to detect residual blockade
- Have to "fail" 8 clinical tests just to achieve 50% sensitivity (Cammu, et. al, 2006)
- Clinical tests poorly specific. May be weak even if TOFR > 0.9
- TOFR of 0.9 is now accepted level of recovery/extubation

(Un)reliability of clinical indicators

To participate:
text wfunap to phone number 22333

The single most important aspect of neuromuscular monitoring centers around recovery issues.

F Donati. Residual paralysis: a real problem or did we invent a new disease? Can J Anesth 2013; 60:714-29
Complications of Residual Relaxation

Patients with Postoperative Pulmonary Complications

<table>
<thead>
<tr>
<th></th>
<th>Pancuronium</th>
<th>Vecuronium or Atracurium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOFR &gt; 0.7</td>
<td>167</td>
<td>8</td>
</tr>
<tr>
<td>TOFR &lt; 0.7</td>
<td>59</td>
<td>10</td>
</tr>
<tr>
<td>%</td>
<td>4.8</td>
<td>16.9 *</td>
</tr>
</tbody>
</table>

Recovery from residual relaxation (TOFR < 0.7)

How “primed” does the recovered patient remain?

Older patients are at more risk

- Residual blockade 60% in elderly and 30.0% in younger patients.
- Airway obstruction, hypoxemic events, symptomatic weakness, pulmonary complications, and prolonged PACU stay were more common in elderly.
- Most adverse events were observed in patients with residual blockade (young and old)

Older patients are at more risk

- 1,444 patients retrospective review in Australia
- Neostigmine reversal was associated with more pulmonary complications with increasing age and ASA status, and
- Greater PONV overall
- Sugammadex group: very low complications

Duration of Drug May be Key

- PORC is lower in patients receiving intermediate-acting relaxants.
  - Incidence of T4/T1 < .9 greater in vecuronium vs. cisatracurium.
Implications of residual relaxation

- Decrease of inspiratory retropalatal and retroglossal upper airway volume
- Attenuation of the normal increase in anteroposterior upper airway diameter during forced inspiration
- Decrease in genioglossus activity during maximum voluntary tongue protrusion


Complications of Residual Relaxation

- Posterior cricoarytenoid muscles return to function 5 minutes after lateral cricoarytenoid muscle.


Residual relaxation prolongs PACU stay


Is reversal mandatory?

- Short-acting drugs make spontaneous recovery (without reversal) feasible.
- Advantages: cost, nausea?, side-effects

Complications of Residual Relaxation

- 57,000 cases
- 2,846 (5%) had SpO₂ < 90% after extubation or were re-intubated.
- Vecuronium, roc, and cis connected to increased risk for respiratory events
- Neither PNS monitoring nor reversal reduced the incidence of events.
- Vlessides, M. Neuromuscular Blockers Linked to Post-Op Breathing Problems Anesthesiology News (04/01/12) Vol. 38, No. 4
Is reversal mandatory?

- To challenge things further...
  - PNS subjective measurement tests (tactile/visual) very specific, but not very sensitive
    - 95% of pts who demonstrate fade do have residual relaxation.
    - Complete recovery >.9 seen in only 50% of pts who appear to have no fade.
  - Patients not reversed show up in PACU with residual blockade

So we need to reverse, right?

- 164 patients paralyzed using vecuronium, atracurium, or rocuronium
  - Of those not reversed, 60% showed residual relaxation (TOFR < 0.8)


So we need to reverse… right?

- 640 patients
  - 40% did not exceed TOFR > 0.9 even after reversal
  - 15% did not exceed TOFR > 0.7


Incidence of residual relaxation

- 1,571 patients from 32 hospitals in China.
  - Routine practice
  - 41% were < 0.7; and 17% were < 0.9
  - Longer lead time with neostigmine and longer interval since last NMB dosing were associated with less PORC.

Maybe we need to reverse more conservatively?

- 120 patients maintained at TOF= 2
- Reversed with TOF 2-4 using neostigmine
- Patients met extubation criteria
- Before extubation, 58% had TOFR <0.7
- 88% had TOFR < 0.9
- In PACU, 8% were < 0.7; 32% < 0.9


Neostigmine after recovery may impair neuromuscular function

- Neostigmine after recovery increases upper airway collapsibility and impairs the genioglossus electromyogram in response to negative pharyngeal pressure.

Herbstreit, Frank; Zingales, Daniela; Ochterbeck, Christof; Petes, Jurgen; Eikermann, Matthias. *Anesthesiology.* 113(6):1280-1288, December 2010.

Confused yet?

Can we compensate with more effective monitoring?

### Methods of stimulation

<table>
<thead>
<tr>
<th>Mode</th>
<th>Characteristics</th>
<th>Main Uses</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single Twitch</td>
<td>0.2 ms in duration</td>
<td>Onset Monitor depolarizing block</td>
<td>Divide twitch height by height of control twitch prior to relaxation. Depression of twitch relates to degree of block.</td>
</tr>
</tbody>
</table>
| Train Of Four         | 4 stimuli 500 ms apart | Onset, Maintenance, Recovery, Extubation (ratio) \ No potentiation (freq. use O.K.) | 1. Count responses to determine block of 75-100% (4/4 response)  
2. Compare height of fourth to first twitch (T4/T1 or TDF ratio) >0.9 = adequate pulmonary function for extubation. |
Limitations of PNS information

<table>
<thead>
<tr>
<th>Mode</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head lift</td>
<td>TOF &lt; .7</td>
<td>TOF &lt; .9</td>
</tr>
<tr>
<td></td>
<td>19</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>85</td>
<td>87</td>
</tr>
<tr>
<td>TOF</td>
<td>TOF &lt; .7</td>
<td>TOF &lt; .9</td>
</tr>
<tr>
<td></td>
<td>27</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>98</td>
<td>99</td>
</tr>
</tbody>
</table>

Sensitivity and specificity of head lift and TOF ratio to detect TOF ratios < .7 or .9.


Methods of stimulation

<table>
<thead>
<tr>
<th>Mode</th>
<th>Characteristics</th>
<th>Main Uses</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetany 50 Hz</td>
<td>0.2 ms repeated</td>
<td>Exubation; IDs of residual block (no fade) = ready for extubation (not necessarily complete reversal)</td>
<td>5-second sustained response</td>
</tr>
<tr>
<td></td>
<td>q 20μs</td>
<td></td>
<td>Indicate muscle strength</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>equivalent to 5-second head lift.</td>
</tr>
<tr>
<td>Tetany 100 Hz</td>
<td>0.2 ms repeated</td>
<td>Exubation; more sensitive, but less specific.</td>
<td>5-second sustained response</td>
</tr>
<tr>
<td></td>
<td>q 10μs</td>
<td>Can cause fade in absence of relaxant</td>
<td>Indicate muscle strength</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>equivalent to 5-second head lift.</td>
</tr>
</tbody>
</table>

Benefit of Double Burst Stimulation

<table>
<thead>
<tr>
<th>Pancuronium guided by</th>
<th>Mean TOFR in PACU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical criteria</td>
<td>0.53</td>
</tr>
<tr>
<td>TOF</td>
<td>0.67</td>
</tr>
<tr>
<td>Double Burst</td>
<td>0.81</td>
</tr>
</tbody>
</table>

Benefit of Double Burst Stimulation

Pancuronium guided by: Mean TOFR in PACU

Clinical criteria 0.53

TOF 0.67

Double Burst 0.81


Limitations of PNS information

<table>
<thead>
<tr>
<th>Mode</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head lift</td>
<td>TOF &lt; .7</td>
<td>TOF &lt; .9</td>
</tr>
<tr>
<td></td>
<td>19</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>85</td>
<td>87</td>
</tr>
<tr>
<td>TOF</td>
<td>TOF &lt; .7</td>
<td>TOF &lt; .9</td>
</tr>
<tr>
<td></td>
<td>27</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>98</td>
<td>99</td>
</tr>
<tr>
<td>DBS</td>
<td>TOF &lt; .7</td>
<td>TOF &lt; .9</td>
</tr>
<tr>
<td></td>
<td>35</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>98</td>
<td>99</td>
</tr>
</tbody>
</table>

Sensitivity and specificity of head lift, TOF ratio and Double burst stimulation to detect TOF ratios < .7 or .9.


Nerve stimulators

- Various models; similar functions

- Increasing occurrence of automated monitors and new modalities
Nerve stimulators- Myographs

- Mechanomyography measures the force exerted by a muscle
- Relaxometer (Groningen University)
- Myograph 2000 (Biometer)

Nerve stimulators- Accelerometers

- Accelerometry- if mass is constant, acceleration is equal to force
- TOF-Guard (Biometer)
- TOF-Watch (Phillips Co.)

Nerve stimulators- Accelerometers vs. Myographs

- Wider variability in results
- Onset same; recover appears slower with accelerometer.
- Advantage: no preop calibration needed

Nerve stimulators- Accelerometers vs. Myographs

- Accelerometry performs better than DBS or tetanus, but does not reliably detect low degrees of residual paralysis
Accelerometry - Sensitivity

<table>
<thead>
<tr>
<th>TOFR by MMG</th>
<th>TOF</th>
<th>DBS</th>
<th>50Hz TET</th>
<th>100Hz TET</th>
<th>AMG</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1-0.19</td>
<td>71%</td>
<td>100%</td>
<td>42%</td>
<td>89%</td>
<td>100%</td>
</tr>
<tr>
<td>0.4-0.49</td>
<td>22%</td>
<td>95%</td>
<td>24%</td>
<td>75%</td>
<td>100%</td>
</tr>
<tr>
<td>0.5-0.59</td>
<td>8%</td>
<td>72%</td>
<td>6%</td>
<td>90%</td>
<td>100%</td>
</tr>
<tr>
<td>0.9-1.0</td>
<td>0%</td>
<td>4%</td>
<td>0%</td>
<td>59%</td>
<td>89%</td>
</tr>
</tbody>
</table>


Nerve stimulators - Kinemyography

- Neuromuscular Transmission Module (Datex)
- Like AMG, but measures degree of movement

New Technology

Tri-axial Accelerometry

Neuro-Trace III

New Technology

Phonomyography

- Phonomyography - measurement of low-frequency sounds created during muscle contraction.
- Preliminary results similar to MMG

Phonomyography

- Good agreement between mechanomyographic measurements at the adductor pollicis muscle and phonomyographic measurements at the thenar and the first dorsal interosseus muscles.
- Phonomyography of those two muscles could be used interchangeably with mechanomyography of adductor pollicis for clinical purposes.

Canadian Journal of Anaesthesia, 2004
What do you think?
Which of these is most reliable at reducing residual relaxation?
A. administer only a half-dose of relaxant (e.g. 0.3mg/kg rocuronium)
B. administer a double dose of neostigmine (e.g., 0.1 mg/kg)
C. monitor via train of four
D. monitor via double burst stimulation

Residual Relaxation is…
- Prevalent
- Associated with complications
- Difficult to detect
- Present regardless of monitoring or reversal

Minimizing residual relaxation
- Reduce dosage of drugs:
  - Low dose Rocuronium
  - Use ED_{50} or ED_{95} instead of intubating dose
- Use drugs with rapid elimination profiles; infuse for better control
  - Recovery index of Cis faster than Roc after infusion

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
<th>Time to TOFR recovery to 0.8 (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.15</td>
<td>13</td>
</tr>
<tr>
<td>0.22</td>
<td>16</td>
</tr>
<tr>
<td>0.3</td>
<td>27</td>
</tr>
</tbody>
</table>

Dose

Minimizing residual relaxation
- Spontaneous recovery prior to reversal does not guarantee complete reversal
- Provide additional time when possible
- Avoid long-acting drugs (Pancuronium)
  - Can achieve same stability with infusion of other agents

Practical Pearls
- Recognize limitations of “human interpreted” nerve stimulators- Low sensitivity for residual relaxation.
- Always monitor; automated monitors are best
Practical Pearls

• Reverse conservatively
  – TIVA: at least 2 twitches
  – Volatile: 4 twitches
  – If TOFR > .9 (determined quantitatively), do not reverse
  – Reverse with 15 minute lead time prior to extubation.


Summary

• Residual relaxation is a common problem, which may lead to complications.
• Human-interpreted PNS data is not sensitive to residual relaxation.
• Choice of PNS mode (such as double burst stim.), and monitoring site may improve decision-making process re: relaxants.
• Use of rapidly-metabolized drugs or lower doses of relaxants may improve safety.