Residual neuromuscular blockade and adverse postoperative events

Glenn S Murphy, MD*

* Director, Cardiac Anesthesia and Clinical Research, NorthShore University HealthSystem. Clinical Professor, University of Chicago.

DISCLOSURE INFORMATION

- I have the following financial relationship to disclose: Consultant for: Merck & Co., Inc.
- I will not discuss off-label use and/or investigational use in my presentation

Residual neuromuscular blockade is an under-recognized and under-treated patient safety issue that can adversely affect patient outcomes in the early recovery period after general anesthesia.

A survey of current management of neuromuscular block in the United States and Europe

RESIDUAL NEUROMUSCULAR BLOCKADE:
AN IMPORTANT PATIENT SAFETY ISSUE

- What is the incidence of residual blockade?
- What are the clinical consequences of residual blockade?

INCIDENCE OF RESIDUAL BLOCKADE

- Incidence ranges from 2-64%
- Incidence determined by several factors:
  - How defined (TOF < 0.7, TOF < 0.9, signs/symptoms of weakness)
  - Method of measurement (AMG, EMG, MMG)
  - Time of measurement (immediately before extubation, PACU)
  - Type of NMBA used (intermediate-acting, long-acting)
  - Use of intraoperative neuromuscular monitoring
  - Degree of neuromuscular blockade maintained intra-operatively (TOF count of 1, 2, 3 or 4)
  - Type of anesthesia used
  - Use of reversal agents/dosage of reversal agents

INCIDENCE OF RESIDUAL BLOCKADE

- 1970s: 42% of patients administered long-acting NMBAs with reversal had TOF ratio < 0.7 (MMG) on arrival to the PACU (Viby-Mogensen J, et al. Anesthesiology 1979;50:539-41.)
**Table I. Incidence of residual neuromuscular blockade (2000-2008).**

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Number of patients</th>
<th>NM Reversal Site/time</th>
<th>Number NMBD monitoring used (%)</th>
<th>NM Reversal Definition</th>
<th>Incidence RNMB (%)</th>
<th>Type of anesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baillard et al. (27)</td>
<td>2000</td>
<td>568</td>
<td>Vecuronium (NS)</td>
<td>2</td>
<td>PACU &lt; 0.7</td>
<td>42% (AMG)</td>
<td>Inhalational</td>
</tr>
<tr>
<td>Bissinger et al. (20)</td>
<td>2000</td>
<td>83</td>
<td>Pancuronium (NS)</td>
<td>100</td>
<td>PACU &lt; 0.7</td>
<td>20% (AMG)</td>
<td>Inhalational and TIVA</td>
</tr>
<tr>
<td>Hayes et al. (22)</td>
<td>2001</td>
<td>148</td>
<td>Vecuronium (NS)</td>
<td>100</td>
<td>PACU &lt; 0.7</td>
<td>7%</td>
<td>Primarily inhalational</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Atracurium (NS)</td>
<td>100</td>
<td>PACU &lt; 0.8</td>
<td>52%</td>
<td>Primarily inhalational</td>
</tr>
<tr>
<td>McCaul et al. (28)</td>
<td>2002</td>
<td>40</td>
<td>Atracurium (NS)</td>
<td>100</td>
<td>PACU &lt; 0.8</td>
<td>65% (AMG)</td>
<td>NS</td>
</tr>
<tr>
<td>Kim et al. (2)</td>
<td>2002</td>
<td>602</td>
<td>Vecuronium (NS)</td>
<td>0</td>
<td>PACU &lt; 0.7</td>
<td>24.7% (AMG)</td>
<td>Inhalational</td>
</tr>
<tr>
<td>Gatke et al. (23)</td>
<td>2002</td>
<td>60</td>
<td>Rocuronium (NS)</td>
<td>0</td>
<td>PACU &lt; 0.7</td>
<td>16.7% (AMG)</td>
<td>TIVA</td>
</tr>
<tr>
<td>Baillard et al. (21)</td>
<td>2005</td>
<td>101</td>
<td>Vecuronium (NS)</td>
<td>45</td>
<td>PACU &lt; 0.9</td>
<td>9% (AMG)</td>
<td>Inhalational</td>
</tr>
<tr>
<td>Debaene et al. (3)</td>
<td>2003</td>
<td>526</td>
<td>Rocuronium (NS)</td>
<td>41</td>
<td>PACU &lt; 0.9</td>
<td>16% (AMG)</td>
<td>Inhalational</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Atracurium (NS)</td>
<td>60</td>
<td>PACU &lt; 0.9</td>
<td>45%</td>
<td>Inhalational</td>
</tr>
<tr>
<td>Baillard et al. (21)</td>
<td>2005</td>
<td>210</td>
<td>Vecuronium (NS)</td>
<td>60</td>
<td>PACU &lt; 0.9</td>
<td>3.5% (AMG)</td>
<td>Inhalational</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Atracurium (NS)</td>
<td>60</td>
<td>PACU &lt; 0.9</td>
<td>3.5% (AMG)</td>
<td>Inhalational</td>
</tr>
<tr>
<td>Kopman et al. (24)</td>
<td>2004</td>
<td>60</td>
<td>Cisatracurium (NS)</td>
<td>100</td>
<td>PACU &lt; 0.9</td>
<td>36.7% (AMG)</td>
<td>Inhalational</td>
</tr>
<tr>
<td>Murphy et al. (26)</td>
<td>2004</td>
<td>70</td>
<td>Pancuronium (NS)</td>
<td>100</td>
<td>PACU &lt; 0.9</td>
<td>83% (AMG)</td>
<td>Inhalational</td>
</tr>
<tr>
<td>Murphy et al. (25)</td>
<td>2005</td>
<td>120</td>
<td>Rocuronium (NS)</td>
<td>100</td>
<td>PACU &lt; 0.9</td>
<td>88% (AMG)</td>
<td>Inhalational</td>
</tr>
<tr>
<td>Cammu et al. (4)</td>
<td>2006</td>
<td>640</td>
<td>Mivacurium (NS)</td>
<td>11-12</td>
<td>PACU &lt; 0.9</td>
<td>38-47% (AMG)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Rocuronium (NS)</td>
<td>11-12</td>
<td>PACU &lt; 0.9</td>
<td>38-47 NS</td>
<td>NS</td>
</tr>
<tr>
<td>Maybauer et al. (23)</td>
<td>2007</td>
<td>338</td>
<td>Cisatracurium (NS)</td>
<td>100</td>
<td>Exubation &lt; 0.9</td>
<td>57% (AMG)</td>
<td>TIVA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Rocuronium (NS)</td>
<td>100</td>
<td>Exubation &lt; 0.9</td>
<td>44% (AMG)</td>
<td>TIVA</td>
</tr>
<tr>
<td>Murphy et al. (6)</td>
<td>2008</td>
<td>90</td>
<td>Rocuronium (NS)</td>
<td>100</td>
<td>PACU &lt; 0.9</td>
<td>30% (AMG)</td>
<td>Inhalational (TOF group)</td>
</tr>
</tbody>
</table>

**REVIEW ARTICLE**

**Neuromuscular monitoring and postoperative residual curarization: a meta-analysis**

M. Naigub1†, A.F. Kopman3† and J.E. Ensor2

<table>
<thead>
<tr>
<th>Sub-population</th>
<th>Pooled rate of PORC§</th>
<th>Confidence interval</th>
<th>P-value</th>
<th>Heterogeneity Inconsistency† (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-acting (TOF&lt;0.7)</td>
<td>0.351</td>
<td>(0.25-0.46)</td>
<td>&lt; 0.001</td>
<td>86.7</td>
</tr>
<tr>
<td>Intermediate-acting (TOF&lt;0.7)</td>
<td>0.115</td>
<td>(0.07-0.17)</td>
<td>&lt; 0.001</td>
<td>85.9</td>
</tr>
<tr>
<td>Long-acting (TOF&lt;0.9)</td>
<td>0.721</td>
<td>(0.59-0.84)</td>
<td>&lt; 0.001</td>
<td>88.1</td>
</tr>
<tr>
<td>Intermediate-acting (TOF&lt;0.9)</td>
<td>0.413</td>
<td>(0.25-0.58)</td>
<td>&lt; 0.001</td>
<td>97.2</td>
</tr>
</tbody>
</table>

§ Pooled rate of PORC is the weighted average. The weight in the random-effect model takes into account both between and within studies variation.

† Inconsistency is the proportion of between studies variability that cannot be explained by chance.
CONCLUSIONS: NAGUIB, ET AL.

- There is a «continued high incidence of postoperative residual curarization reported from multiple academic centers» and that the incidence of this complication did not appear to be decreasing over time.

WHAT ARE THE CLINICAL CONSEQUENCES OF RESIDUAL BLOCKADE?

- Volunteer studies
  - NMBA infusions in awake subjects
- Clinical Studies → Databased
  - Large database investigations examining the association between NMBA use and adverse outcomes
- Clinical Studies → Residual block: postoperative complications
  - Residual block measured in PACU → adverse postoperative events

WHAT ARE THE CLINICAL CONSEQUENCES OF RESIDUAL BLOCKADE?

Volunteer studies
- Adverse affects on respiratory system
- Unpleasant symptoms of muscle weakness

ACCELEROMETRY OF ADDUCTOR POLLICIS MUSCLE PREDICTS RECOVERY OF RESPIRATORY FUNCTION FROM NEUROMUSCULAR BLOCKADE

Matthias Eikermann, MD,* Harald Groeben, MD,† Johannes Hüsing, PhD,‡ Jorge Peters, MD§

At a TOF ratio of 0.5
- FVC ↓ to 78% baseline
- FIV₁ ↓ to 53% baseline
- FEV₁ ↓ to 75% baseline
- Upper airway obstruction observed in 2/3 subjects
- Ability to swallow impaired in 6 of 12 subjects

At a TOF ratio of 0.83
- FVC ↓ to 94% baseline
- FIV₁ ↓ to 84% baseline
- Impaired in ½ subjects

THE INCIDENCE AND MECHANISMS OF PHARYNGEAL AND UPPER ESOPHAGEAL DYSFUNCTION IN PARTIALLY PARALYZED HUMANS

Pharyngeal videogradiography and simultaneous manometry after

- Methods
  - 20 subjects studied during swallowing
  - Fluoroscopy and manometry used to evaluate pharyngeal and esophageal function at TOF of 0.6 - > 0.9
- Results
  - Pharyngeal dysfunction observed 28, 17, and 20% of subjects at TOFs of 0.6, 0.7 and 0.8

Pharyngeal dysfunction

Premature leakage
Penetration of contrast from mouth to pharynx
Incomplete bolus clearance
Penetration of contrast to the laryngeal inlet
Retention of contrast from clearance, mouth to pharynx

Data are parts of total count of swallows with pharyngeal dysfunction (n = 74)

![Graph showing mmHg vs TOF] *p < 0.01

RESIDUAL BLOCK-HYPOXIC VENTILATOR CONTROL

- Increase in ventilation during hypoxia mediated primarily by chemoreceptors of the carotid bodies

**Hipoxic ventilator response**

![Graph showing HVR mL/min/%SpO2 for Atracurium, Pancuronium, and Vecuronium](image)

- **Atracurium**
  - Control
  - TOF 0.70
  - TOF > 0.90

- **Pancuronium**
  - Control
  - TOF 0.70
  - TOF > 0.90

- **Vecuronium**
  - Control
  - TOF 0.70
  - TOF > 0.90


EFFECTS OF PARTIAL PARALYSIS ON THE SWALLOWING REFLEX IN CONSCIOUS HUMANS

Shiroh Isono, MD,* Tohru Ide, MD,* Tetsuo Kochi, MD,* Tadanobu Mizugichi, MD,† Takashi Nishino, MD‡

- 8 awake volunteers given «priming» dose of pancuronium (0.02 mg/kg)

Results

- All 8 subjects reported blurred vision/difficulty keeping their eyes open within 2 minutes of injection
- 5 subjects reported difficulty swallowing
- 3 subjects reported difficulty moving jaw
- TOF ratio at this time: 0.82

FUNCTIONAL ASSESSMENT OF THE PHARYNX AT REST AND DURING SWALLOWING IN PARTIALLY PARALYZED HUMANS: SIMULTANEOUS VIDEOMANOMETRY AND MECHANOMYOGRAPHY OF AWAKE HUMAN VOLUNTEERS.

Lars I. Ericsson MD, PhD,* Eva Sundman MD,† Rolf Olssen MD, PhD,‡ Lena Nilsson MD,† Hanne With MD, PhD,† Olle Ekberg MD, PhD,§ Richard Kuylenstierna MD PhDII

- 14 awake volunteers given a vecuronium infusion
- Titrated to a TOF ratio of 0.7
- Results
- At a TOF ratio of 0.7, all 14 volunteers complained of:
  - Diploplia
  - Dysarthria
  - Subjective difficulty swallowing

RELATIONSHIP OF THE TOF FADE RATIO TO CLINICAL SIGNS AND SYMPTOMS OF RESIDUAL PARALYSIS IN AWAKE VOLUNTEERS


- Methods
  - Infusion of mivacurium in 10 healthy volunteers to achieve TOF ratio of 0.65 to 0.75 → recovery to TOF ratio 0.85-0.90
  - Patients carefully examined for signs/symptoms of muscle weakness
Glenn S Murphy. Residual neuromuscular blockade and adverse postoperative events

• Results
  – Recover TOF ratios of 0.70-0.75
    ◆ Diplopia/visual disturbances,
    ◆ ↓ grip strength
    ◆ Inability to maintain incisor teeth apposition
    ◆ Inability to sit without assistance
    ◆ Severe facial weakness
    ◆ Inability to drink from a straw
    ◆ Difficulty speaking
    ◆ General weakness/tiredness
  – TOF ratio of 0.85-0.9
    ◆ Visual problems, generalized fatigue
  – TOF ratio of 0.90-1.00
    ◆ Visual problems
  – Causes of death were determined by the team at each hospital

• Results
  – Data collected on 599,548 anesthetics
  – Mortality rates when NMBAs were used (1:370) were
    6x higher than when NMBAs were avoided (1:2,100)
  – 63% of the deaths involving NMBAs were caused by
    respiratory failure

DEATH ATTRIBUTABLE TO ANAESTHESIA:
A 10-YEAR SURVEY (1967-1976)


• Methods
  – Mortality data collected over 10 years at Groote Schuur Hospital, Cape Town
  – Examined data from 240,483 anesthetics

• Results
  – Frequency of death to which anesthesia contributed was
    0.22 per 1,000 anesthetics
  – Anesthetic deaths were attributed to:
    1. Hypovolemia
    2. Respiratory inadequacy following myoneural block
    3. Complications of tracheal extubation
    4. Inadequate postoperative care and supervision

CRITICAL RESPIRATORY EVENTS IN THE POST-
ANESTHESIA CARE UNIT: PATIENT, SURGICAL
AND ANESTHETIC FACTORS

D. Keith Rose MD, FRCPC,* Marsha M. Cohen, MD, FRCPC,†‡§ Dan F. Wigglesworth, BSc,* Don P. DeBoer, M. Math†

• Methods
  – Prospectively collected data on 24,157 PACU patients
    who received a GA over a 33-month period
  – A critical respiratory event (CRE) defined as unan-
    ticipated
    ◆ Hypoxemia
    ◆ Hypoventilation
    ◆ Airway obstruction requiring an intervention
  – Patient, surgical, and anesthetic risk factors identified

### RESULTS: ANESTHETIC MANAGEMENT FACTORS ASSOCIATED WITH CRITICAL RESPIRATORY EVENTS

<table>
<thead>
<tr>
<th>Management</th>
<th>n*</th>
<th>Rate of critical respiratory events</th>
<th>Relative risk</th>
<th>95% Confidence interval</th>
<th>Adjusted relative odds</th>
<th>95% Confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Premedication</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Sedative</td>
<td>2,611</td>
<td>2.0</td>
<td>1.87</td>
<td>(1.37-2.55)</td>
<td>2.00</td>
<td>(1.49-2.69)</td>
</tr>
<tr>
<td>Opioid ± sedative</td>
<td>3,432</td>
<td>2.6</td>
<td>2.51</td>
<td>(1.95-3.23)</td>
<td>1.76</td>
<td>(1.24-2.49)</td>
</tr>
<tr>
<td>No premedication§</td>
<td>17,631</td>
<td>1.0</td>
<td>1.0</td>
<td></td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td><strong>Induction agent</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Thiopental</td>
<td>18,230</td>
<td>1.6</td>
<td>3.86</td>
<td>(2.5-5.9)</td>
<td>2.46</td>
<td>(1.56-3.89)</td>
</tr>
<tr>
<td>Propofol§</td>
<td>5,158</td>
<td>0.4</td>
<td>1.0</td>
<td></td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td><strong>Sedative</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any benzodiazepine</td>
<td>13,634</td>
<td>1.5</td>
<td>1.26</td>
<td>(1.02-1.60)</td>
<td>1.28</td>
<td>(0.99-1.64)</td>
</tr>
<tr>
<td><strong>Inhalation agent</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Enflurane</td>
<td>12,682</td>
<td>1.4</td>
<td>1.09</td>
<td>(0.88-1.36)</td>
<td>‡</td>
<td>‡</td>
</tr>
<tr>
<td>Isoflurane§</td>
<td>9,765</td>
<td>1.4</td>
<td>1.0</td>
<td></td>
<td>‡</td>
<td>‡</td>
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<tr>
<td><strong>Atiemic</strong></td>
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<td></td>
</tr>
<tr>
<td>Droperidol ≥ 0.01 mg·kg</td>
<td>6,089</td>
<td>1.8</td>
<td>1.36</td>
<td>(1.06-1.73)</td>
<td>1.05</td>
<td>(0.76-1.45)</td>
</tr>
<tr>
<td>Droperidol ≤ 0.01 mg·kg</td>
<td>5,433</td>
<td>1.1</td>
<td>0.87</td>
<td>(0.64-1.16)</td>
<td>1.29</td>
<td>(0.97-1.71)</td>
</tr>
<tr>
<td>No droperidol§</td>
<td>12,120</td>
<td>1.3</td>
<td>1.0</td>
<td></td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td><strong>Opioid</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Only fentanyl</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 1 - ≤ 2 µg·kg⁻¹·h⁻¹</td>
<td>8,595</td>
<td>1.1</td>
<td>0.76</td>
<td>(0.58-0.99)</td>
<td>1.07</td>
<td>(0.79-1.43)</td>
</tr>
<tr>
<td>Only fentanyl</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 2 µg·kg⁻¹·h⁻¹</td>
<td>3,529</td>
<td>1.3</td>
<td>0.91</td>
<td>(0.65-1.28)</td>
<td>1.87</td>
<td>(1.26-2.79)</td>
</tr>
<tr>
<td>Fentanyl, morphine combination</td>
<td>1,167</td>
<td>1.3</td>
<td>0.95 (1.40-2.73)</td>
<td>1.56</td>
<td>(1.06-2.29)</td>
<td></td>
</tr>
<tr>
<td>Alternate narcotic choices</td>
<td>1,167</td>
<td>1.3</td>
<td>0.9 (0.53-1.53)</td>
<td>0.98</td>
<td>(0.54-1.77)</td>
<td></td>
</tr>
<tr>
<td>Fentanyl ≤ 1 µg·kg⁻¹·h⁻¹ or nil§</td>
<td>8,694</td>
<td>1.4</td>
<td>1.0</td>
<td>–</td>
<td>1.0</td>
<td>–</td>
</tr>
<tr>
<td><strong>Ventilation/muscle relaxant</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spontaneous-mask</td>
<td>4,620</td>
<td>0.3</td>
<td>0.21</td>
<td>(0.12-0.36)</td>
<td>0.68</td>
<td>(0.34-1.31)</td>
</tr>
<tr>
<td>Spontaneous-tracheal intubation</td>
<td>388</td>
<td>1.8</td>
<td>1.26 (0.60-2.67)</td>
<td>2.21</td>
<td>(0.95-5.13)</td>
<td></td>
</tr>
<tr>
<td>Controlled with</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atracurium ≥ 0.25 mg·kg⁻¹·h⁻¹</td>
<td>1,252</td>
<td>3.4</td>
<td>2.3 (1.61-3.29)</td>
<td>2.17</td>
<td>(1.40-3.34)</td>
<td></td>
</tr>
<tr>
<td>Vecuronium ≥ 0.04 mg·kg⁻¹·h⁻¹</td>
<td>7,844</td>
<td>1.4</td>
<td>0.95 (0.73-1.25)</td>
<td>1.19</td>
<td>(0.87-1.62)</td>
<td></td>
</tr>
<tr>
<td>Pancuronium ≥ 0.02 mg·kg⁻¹·h⁻¹</td>
<td>1,399</td>
<td>2.2</td>
<td>1.52 (0.74-2.01)</td>
<td>1.45</td>
<td>(0.91-2.33)</td>
<td></td>
</tr>
<tr>
<td>Any combination</td>
<td>1,010</td>
<td>1.8</td>
<td>1.22</td>
<td>(1.02-2.26)</td>
<td>1.28</td>
<td>(0.81-2.00)</td>
</tr>
<tr>
<td>Controlled with low-dose§</td>
<td>7,074</td>
<td>1.5</td>
<td>1.0</td>
<td>–</td>
<td>1.0</td>
<td>–</td>
</tr>
</tbody>
</table>

CLINICAL INVESTIGATIONS

IMPACT OF ANESTHESIA MANAGEMENT CHARACTERISTICS ON SEVERE MORBIDITY AND MORTALITY

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• Methods
  – Case-control study → identify risk factors related to anesthesia management for mortality or coma within 24 hours of surgery
  – Data were collected (1995-1997) on all patients undergoing GA (869,483 patients) in 3 of 12 provinces in The Netherlands
  – Cases: Patients who remained comatose or died

• Results
  – 807 «cases» and 883 matched «controls» were analyzed
  – The most significant risk factor identified in the analysis was related to neuromuscular management
  – Reversal of the effects of muscle relaxants was associated with a marked reduction (odds ratio, 0.10; 95% CI, 0.03-0.31) in mortality and coma

CONCLUSIONS: ADVERSE RESPIRATORY EFFECTS OF NMBAS-DATABASE STUDIES

• Several large database studies have examined anesthetic-related causes of major morbidity and mortality. Postoperative respiratory failure due to neuromuscular management was the primary cause of adverse outcomes in many of these investigations
• Limitation: The presence or absence of residual blockade not determined in these investigations
• Data is suggestive, not conclusive

WHAT ARE THE CLINICAL CONSEQUENCES OF RESIDUAL BLOCKADE?

Clinical studies

Residual block measured in PACU → adverse postoperative events
• Adverse respiratory events
• Prolonged PACU LOS
• Unpleasant symptoms of muscle weakness

POSTANESTHESIA CARE UNIT RECOVERY TIMES AND NEUROMUSCULAR BLOCKING DRUGS: A PROSPECTIVE STUDY OF ORTHOPEDIC SURGICAL PATIENTS RANDOMIZED TO RECEIVE PANCRUONIUM OR ROCURONIUM

Glenn S Murphy, MD, Joseph W Szokol, MD, Mark Franklin, MD, Jesse H. Marymont, MD, Michael J Avram, PhD, and Jeffery S Vender, MD

• Objective: to assess the effect of choice of NMBA (long-or intermediate-acting) on postoperative recovery
• Methods
  – 70 patients undergoing orthopedic surgical procedures randomized to receive pancuronium or rocuronium
  – NM monitoring and reversal used in all subjects
  – TOF ratios quantified with acceleromyography (AMG) on arrival to PACU and at + 30 minutes
  – Episodes of hypoxemia measured (SpO₂ < 93 or 90%)

MURPHY, ET AL. RESULTS

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rocuronium group</th>
<th>Pancuronium group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Train-of-four-ratio &lt; 0.9 at:</td>
<td>10</td>
<td>29</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>PACU arrival</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 min after</td>
<td>1</td>
<td>11</td>
<td>0.003</td>
</tr>
<tr>
<td>PACU arrival</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients having episodes of</td>
<td>10</td>
<td>21</td>
<td>0.015</td>
</tr>
<tr>
<td>SpO₂ &lt; 93%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SpO₂ &lt; 90%</td>
<td>7</td>
<td>15</td>
<td>NS</td>
</tr>
<tr>
<td>Need for oxygen therapy</td>
<td>4</td>
<td>10</td>
<td>NS</td>
</tr>
</tbody>
</table>


RESIDUAL NEUROMUSCULAR BLOCKADE AND CRITICAL RESPIRATORY EVENTS IN POSTANESTHESIA CARE UNIT

Glenn S. Murphy, MD
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Jesse H. Marymont, MD
Steven B. Greenberg, MD
Michael J. Avram, PhD
Jeffery S. Vender, MD

Hypothesis: Patients with evidence of severe respiratory impairment in the PACU would have a higher incidence of residual block compared to matched controls without CREs
METHODS

- **Design**: Case-control study with prospectively defined cases
- All cases during the 1-year study period with the outcome of interest in the PACU (CRE) were identified
  - **CRE**:
    1) Upper airway obstruction requiring intervention
    2) Mild-mod (90-93% SpO2) or severe (< 90% SpO2) hypoxemia on > 3L NC/min not responsive to intervention
    3) Signs respiratory distress/impending ventilatory failure
    4) Patient requiring re-intubation
    5) Evidence of aspiration
- If CRE identified by PACU nursing, study investigator immediately contacted and TOF ratio quantified using acceleromyography


MURPHY, ET AL. RESULTS

- Data was collected on 7,459 patients undergoing GA during the 1-year period
- CREs identified in 61 patients (0.8%)
- Control and CRE groups evenly matched for all preoperative and intraoperative variables
- Multiple logistic regression analysis revealed the only preoperative or intraoperative factor associated with CREs was residual block

### Critical respiratory event group

<table>
<thead>
<tr>
<th>Critical respiratory event group</th>
<th>Control group</th>
<th>Difference (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Train-of-four ratio</td>
<td>0.62 ± 0.20</td>
<td>0.98 ± 0.07</td>
<td>-0.36 (-0.43 to -0.30) &lt; 0.0001</td>
</tr>
<tr>
<td>Degree of NM Blockadeb</td>
<td>4 (9.5%)</td>
<td>38 (90.5%)</td>
<td>-81.0% (-90 to -66) &lt; 0.0001*</td>
</tr>
<tr>
<td>Acceptable</td>
<td>7 (9.5%)</td>
<td>4 (9.5%)</td>
<td>7.1% (-9 to 24) &lt; 0.366*</td>
</tr>
<tr>
<td>Severe</td>
<td>31 (73.8%)</td>
<td>0 (0%)</td>
<td>73.8% (99 to 85) &lt; 0.0001*</td>
</tr>
</tbody>
</table>

*The 95% confidence interval for the difference between the population means was calculated from all pairwise data. The P value given is the probability determined by the two-sided paired t-test for the difference between means.*

* The 95% confidence interval for the difference was calculated using the Nam restricted maximum likelihood estimation (RMLE) score. The P value given is the probability determined by McNemar’s two-sided hypothesis test about the difference.

b Degree of residual NM blockade classified as acceptable neuromuscular recovery 0 (TOF ratio 0.90), mild to moderate 1 (0.70 TOF ratio 0.90), or severe 2 (TOF ratio 0.70).

INTRAOPERATIVE ACCELEROMYOGRAPHIC MONITORING REDUCES THE RISK OF RESIDUAL NEUROMUSCULAR BLOCKADE AND ADVERSE RESPIRATORY EVENTS IN POSTANESTHESIA CARE UNIT

Glenn S. Murphy, MD,* Joseph W Szokol, MD,* Jesse H. Marymont, MD,* Steven B. Greenber, MD,† Michael J Avram, PhD,‡ Jeffery S. Vender, MD,§ Margarita Nisman BA,‖

- **Objective**: To assess the effect of AMG monitoring on the incidence of postoperative residual NMB
- **Hypothesis**: If AMG reduces the frequency of residual NMB, it should also reduce the incidence of associated adverse respiratory events
- **Results**
  - 185 patients randomized to AMG group or standard peripheral nerve monitoring (PNM) (qualitative TOF monitoring)
  - TOF group: Extubation when standard criteria met + no fade TOF
  - AMG group: Extubation when standard criteria met + TOF ratio > 0.8
  - During transport: Examined for hypoxemia + airway obstruction
  - On arrival to PACU: TOF ratios quantified with AMG

### Acceleromyography Conventional Difference

<table>
<thead>
<tr>
<th>Acceleromyography group</th>
<th>Conventional TOF Group</th>
<th>Difference (99% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Degree of neuromuscular blockade* Acceptable recovery Moderate</td>
<td>4 (4.5%)</td>
<td>15 (16.7%)</td>
<td>-12.2% (-25.2 to -0.4%) 0.014</td>
</tr>
<tr>
<td>Severe</td>
<td>0 (0%)</td>
<td>12 (13.3%)</td>
<td>-13.3% (-25.1 to -6.0%) &lt; 0.001</td>
</tr>
</tbody>
</table>

* Degree of residual neuromuscular blockade classified as acceptable neuromuscular recovery 0 (train-of-four [TOF] ratio 0.90), mild to moderate 1 (0.70 TOF ratio 0.90), or severe 2 (TOF ratio 0.70).

### Number

<table>
<thead>
<tr>
<th>Acceleromyography group</th>
<th>Conventional TOF group</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. with episodes of SpO2 90-93% during transport</td>
<td>0 (0%) 10 (21.1%)</td>
</tr>
<tr>
<td>No. with episodes of SpO2 &lt; 90% during transport</td>
<td>0 (0%) 10 (21.1%)</td>
</tr>
<tr>
<td>Lowest SpO2 during transport, %</td>
<td>96 (90-100) 4 (10-96)</td>
</tr>
<tr>
<td>No. requiring airway maneuver during transport</td>
<td>9 (10-90) 0 (0-10)</td>
</tr>
</tbody>
</table>

SpO2, arterial oxygen saturation measured by pulse oximetry

RESIDUAL NEUROMUSCULAR BLOCKADE IS A RISK FACTOR FOR POSTOPERATIVE PULMONARY COMPLICATIONS


- Objective: To determine the incidence of POPC following the use of pancuronium, atracurium, and vecuronium and to examine the effect of RNMB in the PACU on the incidence of POPC

BERG, ET AL. RESULTS

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Patients with POPC</th>
<th>Number of patients</th>
<th>Patients with POPC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TOF ≥ 0.7</td>
<td>167</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>TOF &lt; 0.7</td>
<td>59</td>
<td>10</td>
</tr>
</tbody>
</table>

*P < 0.02

POSTANESTHESIA CARE UNIT RECOVERY TIMES AND NEUROMUSCULAR BLOCKING DRUGS: A PROSPECTIVE STUDY OF ORTHOPEDIC SURGICAL PATIENTS RANDOMIZED TO RECEIVE PANCURONIUM OR ROCURONIUM

Glenn S. Murphy, MD,* Joseph W Szokol, MD,* Mark Franklin, MD,* Jesse H. Marymont, Md,* Michael J. Avram, PhD,† and Jeffery S. Vender, MD*

- Methods
  - 691 patients (abdominal, gynecologic, or orthopedic) randomized to receive pancuronium, atracurium, or vecuronium
  - NM management standardized; all patients reversed
  - TOF ratios measured in PACU with MMG and patients examined for signs of muscle weakness
  - Patients examined over post-operative day (POD) 1-6 for POPC
- Pneumonic infiltrate or atelectasis on chest X-ray (CXR)

POSTOPERATIVE RESIDUAL CURARIZATION FROM INTERMEDIATE-ACTING NEUROMUSCULAR BLOCKING AGENTS DELAYS RECOVERY ROOM DISCHARGE

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3 Universitaetsklinikum Essen, Essen, Germany
* Corresponding author. E-mail: meikermann@rics.bwh.harvard.edu

- Observational study-246 consecutive patients
- TOF ratios measured on arrival to PACU
- Results
  - 22% of patients had TOF ratios < 0.9
  - PACU LOS was significantly longer in patients with TOF ratios < 0.9 (323 min) compared to those with TOF ratios > 0.9 (243 min, P = 0.026)
  - Patients with TOF ratios < 0.9 met discharge criteria 75 minutes later than those with TOF ratios > 0.9
  - Only age and residual block independently associated with PACU LOS
POSTANESTHESIA CARE UNIT RECOVERY TIMES AND NEUROMUSCULAR BLOCKING DRUGS: A PROSPECTIVE STUDY OF ORTHOPEDIC SURGICAL PATIENTS RANDOMIZED TO RECEIVE PANCURONIUM OR ROCURONIUM

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Table II. Muscular weakness in the PACU.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rocuronium group</th>
<th>Pancuronium group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upon arrival</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blurry vision</td>
<td>2</td>
<td>16</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Difficulty smiling</td>
<td>0</td>
<td>6</td>
<td>NS</td>
</tr>
<tr>
<td>Difficulty swallowing</td>
<td>0</td>
<td>7</td>
<td>NS</td>
</tr>
<tr>
<td>Facial numbness</td>
<td>0</td>
<td>4</td>
<td>NS</td>
</tr>
<tr>
<td>Generalized weakness</td>
<td>10</td>
<td>27</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Unable to do 5-s head lift</td>
<td>1</td>
<td>5</td>
<td>NS</td>
</tr>
<tr>
<td>Unable to do 5-s leg</td>
<td>1</td>
<td>6</td>
<td>NS</td>
</tr>
<tr>
<td>Unable to hold tongue blade</td>
<td>0</td>
<td>3</td>
<td>NS</td>
</tr>
</tbody>
</table>

RESULTS: NUMBER OF SYMPTOMS

- General weakness and visual symptoms (difficulty tracking objects with eyes and maintaining eye opening, blurry vision) were the most frequently described patient complaints related to RNB
- Overall weakness on 0-10 scale reduced by ~50% in the AMG group at all measurement intervals in PACU
- Average # of signs of muscle weakness 0 in both groups at all 4 measurement times
- Strong association between residual block (TOF ratio < 0.9) and symptoms of muscle weakness demonstrated by ROC analysis
- QOR scores significantly higher in AMG group compared to control group
- Conclusion: Supports recent editorial, «It is possible that rigorous management of residual blockade might lead to more patient comfort and more satisfaction».


INTRAOPERATIVE ACCELEROMYOGRAPHY MONITORING REDUCES SYMPTOMS OF MUSCLE WEAKNESS AND IMPROVES QUALITY OF RECOVERY IN THE EARLY POSTOPERATIVE PERIOD


- In previous clinical trials, we have observed that many patients with RNMB complain of symptoms of muscle weakness
- Hypothesis: The use of AMG monitoring, by reducing the incidence of RNB, will also reduce unpleasant symptoms of muscle weakness
- 155 patients randomized to AMG group or control group (standard PNS)
- Patients examined for 16 symptoms/11 signs of muscle weakness on PACU arrival and 20-, 40-, and 60- minutes later
- General weakness quantified on a 10-point scale at these times
- QOR assessed using 100- mm VAS score at PACU discharge

RESULTS

- General weakness and visual symptoms (difficulty tracking objects with eyes and maintaining eye opening, blurry vision) were the most frequently described patient complaints related to RNB
- Overall weakness on 0-10 scale reduced by ~50% in the AMG group at all measurement intervals in PACU
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- Conclusion: Supports recent editorial, «It is possible that rigorous management of residual blockade might lead to more patient comfort and more satisfaction».


CONCLUSIONS: CLINICAL STUDIES, RESIDUAL BLOCKADE AND ADVERSE OUTCOMES

- Observational and randomized trials have demonstrated that residual blockade in the PACU results in airway obstruction, hypoxemia, postoperative pulmonary complications, prolonged PACU LOS, and unpleasant symptoms of muscle weakness.
CONCLUSIONS: RESIDUAL NEUROMUSCULAR BLOCKADE: AN IMPORTANT PATIENT SAFETY ISSUE

• There is a high incidence of postoperative residual blockade reported in contemporary anesthesia practices.
• Volunteer studies demonstrate that small degrees of residual blockade are associated with upper airway obstruction, pharyngeal dysfunction and an increased risk of aspiration, impairment of the hypoxic ventilatory drive, and unpleasant symptoms of muscle weakness.

CONCLUSIONS (CONTINUED)

• Databased investigations suggest an association between residual blockade and major morbidity and mortality.
• Clinical studies have demonstrated that residual block in the PACU results in adverse respiratory events, prolonged PACU LOS, and unpleasant symptoms of muscle weakness.
• Methods to reduce the risk of postoperative residual blockade are needed in order to optimize patient recovery and improve patient safety.