Monitoring of neuromuscular block in operative room and ICU

Josep Rodiera M.D. Ph.D. MsC

Marrakech 2016
Conflict of interest

Creator of the TOFCuff Concept
• Do you think that the routine use of neuromuscular monitoring devices could decrease the incidence of postoperative residual paralysis?
Monitorization of NMB: Current situation

A Survey of Current Management of Neuromuscular Block in the United States and Europe

Europe n= 739
USA n= 1792
Monitorization of NMB: Current situation

Monitoring and Pharmacologic Reversal of a Nondepolarizing Neuromuscular Blockade Should Be Routine

Ronald D. Miller, MD, and Theresa A. Ward, BSN, RN

As evidenced by the presence of 2 review articles,2,3 1 survey,5 and 5 editorials in this issue, including this one,6-7 Anesthesia & Analgesia has placed prime emphasis on the importance of residual neuromuscular blockade (NMB) following anesthesia and surgery. Why is this topic now generating so much attention when it has been known for decades? Quoting S.C. Cullen’s comment made over 50 years ago8 “It has been assumed that if a patient is capable of raising his head, moving an extremity or squeezing one’s hand forcibly or is able to take a deep breath, there is no significant residual of a relaxant. Such is not the case... Muscle relaxants enjoy a remarkable reputation as a safe and useful preparation. They will continue in this capacity only if intelligently applied in their proper relationship to the anesthetic state by those who are alert to the early signs of deleterious effects associated with excessive and protracted relaxation.” These opinions reflected the state of knowledge in the late 1950s by S.C. Cullen, the then Chair of Anesthesia at the University of California, San Francisco. During that time, Churchill-Davidson and Christie9 devised a method employing electrical stimuli to monitor NMB. Despite Cullen’s cautionary comments about a lingering NMB,10 he never mentions residual NMB in the Postoperative Care section of his book. In those days, they had long-acting and unpredictable neuromuscular blocking agents such as tubocurarine or gallamine. Although residual NMB probably existed following anesthesia 50 years ago, it was not widely viewed as a common problem. Perhaps the dependence on NMB for the anesthetic state was less and doses of NMBDs smaller. In fact, Cullen10 states: “It is good policy to adhere to the practice of using the muscle relaxant only to provide additional muscular relaxation needed after optimal concentrations of the anesthetic agent (or agents) used have been established.” Did this philosophy result in smaller doses of NMBDs being used in the past? If so, could smaller doses of NMBDs account for no obvious residual NMB being present? We now have excellent neuromuscular monitoring capabilities and better NMBDs and yet residual NMB following anesthesia is surprisingly still a significant clinical problem.11,12 What are the reasons for this persistent problem? Despite persistent pleas from “experts” in clinical neuromuscular pharmacology the past 40 years and this issue of Anesthesia & Analgesia,1,2 neuromuscular monitoring is not widely used by anesthesiologists from both North America and Europe.13 Furthermore, neuromuscular monitoring is not considered as required standard monitoring in the United States. Clearly, the persistence of residual NMB after anesthesia suggests that monitoring should be routine. Before accepting this recommendation, we would like to review the principles of neuromuscular monitoring and evaluate the evidence for its widespread use.
Monitorization of NMB: Current situation
Table 4. Continued

<table>
<thead>
<tr>
<th>Question</th>
<th>No. (%) European respondents</th>
<th>No. (%) United States respondents</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 739</td>
<td>N = 1792</td>
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</tr>
<tr>
<td>In your opinion, conventional nerve stimulators should</td>
<td></td>
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<tr>
<td>(choose all that apply)*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) Be a part of the minimal monitoring standards</td>
<td>249 (33.4)</td>
<td>1011 (64.4)</td>
<td></td>
</tr>
<tr>
<td>b) Be available in the operating room</td>
<td>436 (59.2)</td>
<td>1416 (79.8)</td>
<td></td>
</tr>
<tr>
<td>c) Be regarded as unnecessary</td>
<td>87 (11.8)</td>
<td>41 (2.3)</td>
<td></td>
</tr>
<tr>
<td>d) No opinion</td>
<td>98 (13.3)</td>
<td>20 (1.1)</td>
<td></td>
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<tr>
<td></td>
<td>N = 739</td>
<td>N = 1792</td>
<td></td>
</tr>
<tr>
<td>In your opinion, quantitative TOF monitors should</td>
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<td></td>
<td></td>
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<tr>
<td>(choose all that apply)*</td>
<td></td>
<td></td>
<td></td>
</tr>
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<td>a) Be a part of the minimal monitoring standards</td>
<td>247 (33.4)</td>
<td>194 (10.8)</td>
<td></td>
</tr>
<tr>
<td>b) Be available in the operating room</td>
<td>474 (64.1)</td>
<td>804 (44.9)</td>
<td></td>
</tr>
<tr>
<td>c) Be regarded as unnecessary</td>
<td>37 (5.0)</td>
<td>151 (8.4)</td>
<td></td>
</tr>
<tr>
<td>d) No opinion</td>
<td>86 (11.6)</td>
<td>757 (42.2)</td>
<td></td>
</tr>
</tbody>
</table>

TOF = train of four.
*Answers that were not included in the analysis.
*The participant may answer >1 option presented in the second column.
1. 70% TOF enough for extubate?

2. 80% TOF enough for extubate?

3. 90% TOF enough for extubate?
T.O.F. And Receptor occupancy

C. Thompson et al.
Current monitoring systems & devices
Peripheral Nerve Stimulators

Train-of-four fade is indistinguishable, even to experienced observers, once the TOF ratio exceeds 40%


The absence of observed or tactile fade in response to TOF stimulation does not indicate adequacy of recovery from neuromuscular blockade.

**Stimulating Electrodes**
- Manual installation needed
- Specific polarity to be kept
- Using fragile connecting wires

**Sensing Device**
- Manual installation needed
- Sensitive to motion artifacts
- The hand needs to be strapped

**Inertial Sensor-based**

*Force Transducer-based*

*Inertial Sensor-based*
Monitoring Neuromuscular Transmission with TOFCuff
Como Funciona el TOF Cuff?
How TOF Cuff works?
Cuff With Stimulating Electrodes
(Qualitative Monitorization)

Flow Diagram

- Cuff Inflation
- Impedance OK
- Stimulation
- Visual / Tactile Method
Pressure Changes in the Cuff during the Stimulation at Humeral level

TOF
Pressure Changes in the Cuff during the Stimulation at Humeral level
Monitoring Neuromuscular Blockade with the Cuff
(Qualitative Monitoring)

Flow Diagram

Cuff Inflation  
Impedance OK  

→  

Stimulation  

→  

Recording Evoked TOF  
Cuff Pressure Changes  

By means of processing the cuff pressure, it is possible to obtain a quantitative measurement.
Brachial plexus stimulation / Evaluation of the evoked response
During Recovery
TOF-Cuff vs Mechanomyography
Recovery strategy

Giving time to spontaneous/neostigmine reversal
Neostigmine reversal

The average reversal time is approximately 12 minutes, as reported in recent studies. However, a large inter-individual variability exists. 10% of patients might need more than 60 minutes to reach a TOF ratio of 0.9.


Many studies have found a high incidence of residual neuromuscular blockade after anesthesia and surgery, with a range of 4-64%.

Naguib et al.’s meta-analysis of 24 studies demonstrated a pooled incidence of 41%.


Sugammadex vs Neostigmine action time
**Sugammadex Reversal**

<table>
<thead>
<tr>
<th>Reversal Time</th>
<th>Neostigmines</th>
<th>Sugammadex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Work with ‘Deep’ or ‘Intense’ Blocks?</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Pulmonary Diseases (COPD, Asthma...)</td>
<td>△Risk of Bronchospasm</td>
<td>Suitable</td>
</tr>
<tr>
<td>Cardiac Failure and Arrhythmias</td>
<td>QT prolongation, Brady/Tachycardia</td>
<td>Suitable</td>
</tr>
<tr>
<td>Renal Insufficiency</td>
<td>Not Recommended</td>
<td>Suitable</td>
</tr>
<tr>
<td>Elderly Patients (+75 years)</td>
<td>△Risk PORC</td>
<td>Unaffected</td>
</tr>
<tr>
<td>Obese Patients</td>
<td>△Delay of Onset, Unpredictable</td>
<td>Suitable</td>
</tr>
<tr>
<td>Apnea Syndrome</td>
<td>△Risk of Upper Airway Obstruction</td>
<td>△Risk of Upper Airway Obstruction</td>
</tr>
<tr>
<td>Risk of PONV</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

One then might ask oneself:

- No need to Monitor the NMT!!
- Sugammadex to everyone!!

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Sugammadex – A reversal strategy

One then might ask oneself:

• No need to Monitor the NMT!!
• Sugammadex to everyone!!

The use of NMT monitoring is necessary for determining the threshold for reversal agent administration, and determining its appropriate dosage. NMT monitoring also confirms the efficacy of reversal by asserting recovery of TOF ratio to values over 0.9. After electrical stimulation of a motor endplate, use of a quantitative peripheral nerve stimulator is key to prevent residual neuromuscular blockade and patient harm. This allows tailoring of neuromuscular blockade to patients’ and surgical needs, and a choice at the end of surgery, including: no reversal required (spontaneous recovery of TOF ratio > 0.9), or use of neostigmine or sugammadex. Rational assessment committee for the uptake of new Hospital-use Drugs. OSAKIDETZA - Health & Consumer Department of the Basque Country Government [Spain].

Cost per Treatment (VAT not included), for an average patient of 70 Kg.

Cost

<table>
<thead>
<tr>
<th>Block Level</th>
<th>Neostigmines</th>
<th>Sugammadex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate (2 mg/Kg)</td>
<td>0.44-0.88 €</td>
<td>76.96 €</td>
</tr>
<tr>
<td>Deep (4 mg/Kg)</td>
<td>0.44-0.88 €</td>
<td>153.92 €</td>
</tr>
<tr>
<td>Emergency Rev. (16 mg/Kg)</td>
<td>Not Applicable</td>
<td>461.76 €</td>
</tr>
</tbody>
</table>

So, an administration rationale needs to be established:

Sugammadex mandatory ↔ Neostigmine-suitable
Reversal Strategy

In all cases, NMT monitoring is the key to adequate NMB management. Objective measurements allow for excellent intubation and surgical conditions, definition of thresholds and doses for the administration of reversal agents, and exclusion of PORQ prior to tracheal extubation. For these reasons, objective measurements reduce postoperative complications.


So, an administration rationale needs to be established:
- Sugammadex mandatory
- Neostigmine suitable

Table 1 Neuro muscular block: requirement for deep block

<table>
<thead>
<tr>
<th>Type of stimulus</th>
<th>TOF</th>
<th>Recovery (TOF count 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intense (count 4)</td>
<td>0/0</td>
<td>0/0</td>
</tr>
<tr>
<td>Intense (count 4)</td>
<td>0/0</td>
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Moderate Block (2 mg/kg)
- 76,96 € per patient
- 0,44-0,88 € per Vial

Deep Block (4 mg/kg)
- 153,92 € per patient

Emergency Rev. (16 mg/Kg)
- Not Applicable
- 461,76 €

Sales Formulation

<table>
<thead>
<tr>
<th>Type of stimulus</th>
<th>0,5 mg</th>
<th>5 ml (0,44€ per Vial)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate Block</td>
<td></td>
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Reversal Strategy

**ROCURONIUM**
- Induction 0.6 mg/Kg.
- Infusion Pump (100 mg/250mL) 5-10 µg/Kg/min
- Bolus 0.15 mg/Kg

**TOF COUNT**
- TOF = 0
  - Post-Tetanic COUNT = 1-2
  - SUGAMMADEX 4 mg/Kg
  - SUGAMMADEX 2 mg/Kg
  - HIGH-Risk: Pulmonary Diseases (COPD, asthma...), Sleep Apnea Syndrome, Cardiac failure and arrhythmias, Increased Age (+75 years), Obesity (BMI >30), Renal Insufficiency

- TOF = 1-3
  - LOW-Risk: Patient Surgery
  - Wait for TOF COUNT = 3
  - NEOSTIGMINE 50 µg/Kg
  - ATROPINE 1 mg

- TOF = 4
  - TOF RATIO < 40%
    - NEOSTIGMINE 40 µg/Kg
    - ATROPINE 1 mg
  - TOF RATIO > 40%
    - NEOSTIGMINE 20 µg/Kg
    - ATROPINE 0.7 mg

**EXTUBATION**
- TOF RATIO > 90%

**HIGH-Risk Surgeries**
- Thoracotomy
- Supraumbilical Laparotomy
- Lumbotomy
- Hypothermia

**LOW-Risk Patients**
- Surgery

**HIGH-Risk Patients**
- Pulmonary Diseases (COPD, asthma...)
- Sleep Apnea Syndrome
- Cardiac failure and arrhythmias
- Increased Age (+75 years)
- Obesity (BMI >30)
- Renal Insufficiency

**SUGAMMADEX**
- 4 mg/Kg
- 2 mg/Kg

**NEOSTIGMINE**
- 50 µg/Kg
- 40 µg/Kg
- 20 µg/Kg

**ATROPINE**
- 1 mg
- 0.7 mg
DEPARTAMENTO DE FARMACIA
MEDICAMENTOS DE USO RESTRINGIDO
SOLICITUD DE SUGAMIMADEX (BRIMONID)  

MÉDICO SOLICITANTE: ________________________________

NOMBRE COMPLETO DEL PACIENTE: ________________________________

HABITACIÓN: __________ PESO: __________ TALLA: __________

TIPO DE INTERVENCIÓN: ________________________________

Nº DE VIALES DISPENSADOS: __________ FECHA: ________________________________

MARCAR INDICACIÓN:
- □ Paciente obesidad mórbida que precisa estubación y reversión completa del bloqueo neuromuscular.
- □ Paciente de cirugía mayor con bloqueo profundo y se debe desaparar antes de lo previsto.
- □ Paciente que después del bloqueo neuromuscular presenta dificultades para la intubación o ventilación y se debe revertir al bloqueo de forma rápida.
- □ Paciente de cirugía plástica y reparadora que requiere reversión rápida del bloqueo.
- □ Paciente de cirugía torácica que requiere reversión completa del bloqueo.
- □ Paciente que presenta bloqueo neuromuscular residual TOF<; 
- □ Otra: ________________________________

Dependiendo de la edad y del peso del paciente, se recomienda la administración de una dosis de 2 mg/kg de sugamimade (BRIMONID) para la recuperación muscular hasta el momento de la reaparición del 72% o más de la fuerza muscular residual.

Adolescentes
- Si hay una necesidad crítica de reversión inmediata en la administración de 1 mg/kg de sugamimade (BRIMONID) para la recuperación muscular hasta el momento de la reaparición del 72% o más de la fuerza muscular residual.

Para la correcta utilización de sugamimade se recomienda monitorizar la transmisión neuromuscular.

FIRMA ENFERMERA: ________________________________

FIRMA MÉDICO Y Nº COLEGIADO: ________________________________
Conclusions

• Residual paralysis is considered an important problem.

• Neuromuscular monitoring could avoid the residual paralysis.

• There is consensus: Neuromuscular Monitoring should be routine.

• The TOF-Cuff concept has a clear clinical use.

• A reversal strategy is recommended.