Muscle relaxation in seniors

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All diseases run into one, old age.

Ralph Waldo Emerson
(1803 – 1882)

The last birthday that's any good is 23.

Andy Rooney
(1919 – 2011)

My diseases are an asthma, and a dropsy, and what is less curable, seventy-five.

Samuel Johnson
(1709 – 1784)
NMBA as a part of balanced anesthesia

balanced anesthesia

- hypnosis
  - inhalation
  - intravenous
- analgesia
  - opioids
- NMB
  - NMBA

- must sleep
- must not feel pain
- muscles must be adequately relaxed
NMBA = powerful tool

✔ introduction of NMBAs into clinical practice enabled the development of many surgical disciplines

✖ a drug with potentially lethal effect
Paradoxically ...
„A milestone in anesthesia [d-tubocurarine chloride]”

By their very nature, surgical patients are “sick” - some more so than others.
The population is aging

In elderly there are many physiological and patophysiological changes that can influence both PK and PD of many drugs
Proportion of seniors in the group of operated patients (CR)
In 2012, 810 million people were aged 60 or over. By 2050, the number will reach two billion.

Two people celebrate their sixtieth birthday every second. An annual total of almost 58 million sixtieth birthdays.
Physiological and patophysiological changes (different PK $\rightarrow$ PD)

elderly

- **ill** (more often, more severely)
- **co-morbidities**
- **higher ASA PS classification**
- **medication** (compensation, interaction, polypragmasia)
- **different body composition**
  - total body water - decreased
  - lean body weight - decreased
  - total body fat - increased
Physiological and patophysiiological changes
(different PK → PD)

elderly

• changes in organ functions
  • kidneys – decreased blood flow
  • liver – decreased blood flow
• circulation
  • circulation time – increased
  • cardiac reserve – decreased

• enzyme activity – decreased
Changed reactivity to drugs in elderly
(mechanisms)

1. binding to plasma proteins
2. changes in composition of body tissues
3. metabolism of drugs
4. pharmacodynamic parameters
Motor end plate

Neuromuscular junction in elderly

morphology and physiology

- decreased number of motor units
- increased number of nicotinic receptors in motor units
- proliferation of extrajunction receptors
- reduction of the amount of ACh in motoneurons
- decreased concentration of ACh receptors at the motor end plate
- increase in the distance between the axon a motor end plate
- flattening of the folds of the motor end plate
- decreased release of ACh from the preterminal axon in response to a neural impulse

× differences in the PD of the NMBAs do not appear to be due to changes in the neuromuscular junction
Neuromuscular junction in elderly
morphology and physiology

The $ED_{95}$ (dose of NMBA causing 95% neuromuscular block), is similar the elderly and young patients.

<table>
<thead>
<tr>
<th>NMBA</th>
<th>$ED_{95}$ (mg/kg)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>young</td>
<td>elderly</td>
</tr>
<tr>
<td>PANC</td>
<td>0.078</td>
<td>0.081</td>
</tr>
<tr>
<td>VEC</td>
<td>0.041</td>
<td>0.038</td>
</tr>
<tr>
<td>ROC</td>
<td>0.521</td>
<td>0.369</td>
</tr>
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</table>
Neuromuscular junction in elderly
morphology and physiology


• when elderly patients have the same plasma concentration of NMBA as do young adults, they also have the same degree of neuromuscular block

• differences in PD parameters, therefore, appear to be due to differences in pharmacokinetics of the NMBAs in the aged patient population.
Variability in effect of NMBA is high in all patients. In seniors, it may be further increased.
Variability of duration of action of neuromuscular-blocking drugs in elderly patients

S. R. Arain¹, S. Kern², D. J. Ficke¹ and T. J. Ebert¹

¹Department of Anaesthesiology, Medical College of Wisconsin and Zablocki VA Medical Center, Milwaukee, WI, and ²University of Utah Medical Center, Salt Lake City, UT

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td>CIS</td>
<td>0,1 mg/kg</td>
</tr>
<tr>
<td>ROC</td>
<td>0,6 mg/kg</td>
</tr>
<tr>
<td>VEC</td>
<td>0,1 mg/kg</td>
</tr>
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</table>

When used with sevoflurane/N₂O, there was a two-fold greater variability of duration of NMB in elderly patients receiving ROC or VEC compared with CIS.
## Elimination of NMBA

<table>
<thead>
<tr>
<th>NMBA</th>
<th>elimination via</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>kidney</td>
<td>liver</td>
<td>others</td>
<td></td>
</tr>
<tr>
<td>PAN</td>
<td>++++++</td>
<td>+</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>PIP</td>
<td>++++++</td>
<td>+</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>VEC</td>
<td>++</td>
<td>++</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>ROC</td>
<td>+</td>
<td>+++</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>ATR</td>
<td>+</td>
<td>--</td>
<td>++++++</td>
<td></td>
</tr>
<tr>
<td>CIS</td>
<td>+</td>
<td>--</td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>MIV</td>
<td>+/-</td>
<td>--</td>
<td>++++++</td>
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Correlation of Succinylcholine Duration of Action with Plasma Cholinesterase Activity in Subjects with the Genotypically Normal Enzyme

Jørgen Viby-Mogensen, M.D.*

elderly – decreased activity of plasma cholinesterase
the decrease is insufficient to prolong the effect of SUX

possible interactions – prolonged effect of SUX:
donepezil (Aricept)
  • therapy of Alzheimer disease
  • reversible inhibitor of AChE
  • biological half-time 70 hrs
Pharmacokinetics and Pharmacodynamics of Cisatracurium in Young and Elderly Adult Patients


- young (18–50 yrs) vs. elderly (over 65 yrs) patients
- CIS 0.1 mg/kg + 0.025 mg/kg boluses (or infusion)
- blood samples to determine CIS plasma concentration
- pharmacokinetics modeling
- TOF measurements

PK of CIS differs only marginally between young and elderly onset is delayed in elderly due to slower biophase equilibration

× limitation of this study: gender - less males (9/22) in younger group than in elderly group (19/14)
Onset time (sec)

influence of age

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CIS

ROC

VEC

Onset time (sec)

0 100 200 300

60-75

20-40

*p < 0.001

Onset time – prolongation in seniors


Mechanisms:

• lower cardiac output
• longer circulation time
• decrease blood flow to muscle
• slower equilibration of biophases

onset time can be shortened: ephedrin
onset time can be prolonged: BB
Reversal in elderly: neostigmine

data are not conclusive

most authors:
effect of NEO is longer than in younger
Reversal in elderly: sugammadex
(recommended dose is not age-dependent)

*Reversal with SUG 2 mg/kg at spontaneous recovery to $T_2$ after ROC 0.6 mg/kg

Data on file MSD (2008)
### PD of NMBAs in elderly (summary)

↑ = prolonged  ↔ = unchanged

<table>
<thead>
<tr>
<th></th>
<th>onset time</th>
<th>clinical duration</th>
<th>full recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SUX</strong></td>
<td>↑</td>
<td>↔</td>
<td>↔</td>
</tr>
<tr>
<td><strong>aminosteroids</strong> (ROC, VEC)</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td><strong>benzylisoquinolines</strong> (CIS, ATR)</td>
<td>↑</td>
<td>↔</td>
<td>↔</td>
</tr>
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NMB in elderly: safe use

- is the NMB actually necessary?
- proper dose of NMBA is enough!
- titration of the NMBA dose may be useful
- compared to younger patients:
  - doses of NMBA should not be larger than recommended in younger patients
  - intervals of administration should not be more frequent than used in younger patients
- which NMBA?
  - steroids – excellent reversal agent is available
  - benzylisoquinolines – effect less dependent on organ function
- prolonged duration of effect of the NMBA should be anticipated
- objective monitoring of NMB should be used
NMBA? YES
but
BE PREPARED! (not only in elderly)