Peripheral and respiratory muscle weakness in ICU: causes and consequences

Greet Hermans

Promotor: Prof Dr M Decramer
Co-promotor: Prof Dr G Van den Berghe
Prof G Gayan-Ramirez
Introduction

Muscle weakness in ICU

limbs

respiratory muscles

impaired rehabilitation

delayed weaning
Muscle weakness in ICU

Most frequent cause:

CIP = acute and primary axonal motor and sensory neuropathy

CIM = acute primary myopathy

Incidence:

± 50% in sepsis, MOF, prolonged mechanical ventilation

Bolton 1986
Zochodne 1986, Lacomis 2000
Stevens, 2007

CIP/CIM
Muscle weakness in ICU

Associated with:
- Increased ICU stay
- Increased hospital stay
- Increased mortality

Diagnosis:
- No universally accepted criteria

Risk factors:
- CIP/CIM

High suspicion

- Duration of ICU stay/MV
- Persistent SIRS/MOF
- Hyperglycemia
- Corticosteroids
- Neuromuscular blockers
- Hypoalbuminemia
- Parenteral nutrition
- Hyperosmolarity
- ERR

Low suspicion
Pathophysiology

‘just another organ failure’

Muscle weakness in ICU

Prognosis:
recovery within weeks to months
most severe: incomplete or not occur at all
de Seze, 2000

Prevention/therapy:
reducing risk factors:
aggressive sepsis treatment, CS, NMBA
physiotherapy

CIP/CIM
Insulin therapy protects the central and peripheral nervous system of intensive care patients

G. Van den Berghe, MD, PhD; K. Schoonheydt, MD; P. Becx, MD; F. Bruyninckx, MD; and P.J. Wouters, MSc
Muscle weakness in ICU

**VIDD: animal experiments:**

Controlled mechanical ventilation induces atrophy and weakness of the diaphragm

**Mechanisms:**

- Muscle atrophy
- Oxidative stress
- Structural injury
- Myofiber remodelling
Muscle weakness in ICU

VIDD in humans?

- Critically ill patients have reduced diaphragmatic muscle force
  Watson 2001, Laghi 2003

- Diaphragm of organ donors shows atrophy and increased oxidative stress after 18-69u CMV
  Levine 2008
1. Effect of Intensive Insulin Therapy on Neuromuscular Complications in a Medical ICU
Patients and Methods

• Prospectively planned subanalysis of large RCT comparing CIT versus IIT, in MICU
Patients and Methods

• Aim: assess impact of IIT on CIP/CIM and prolonged MV, pt in ICU ≥ 7 days

  – Diagnosis CIP/CIM: EMG/NCS

  – Diagnosis PMV: ≥ 14d
- **Intention-to-treat**

- **Censored**

- **Uncensored**

  *Hermans et al, AJRCCM 2007*
Results

1. CIP/CIM
MVLR:

**IIT** is independent protector (**p=0.02**) 
Nor glycemia, nor insulin d independently explain benefit

AJRCCM 2007, Hermans et al
2. Prolonged Mechanical Ventilation
MVLR:

**IIT is independent protector (p=0.01)**

Beneficial effect of IIT is due to insulin dose

↓ CIP/CIM does not entirely explain beneficial effect on PMV

AJRCCM 2007, Hermans et al
Conclusion

IIT reduces the electrophysiological incidence of CIP/CIM and the need for prolonged mechanical ventilation, also in medical patients, in ICU for at least 7 days.
1 Intensive Insulin Therapy (IIT) versus Conventional Insulin Therapy (CIT)

1.1 Occurrence of CIP/CIM

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>IIT Events</th>
<th>IIT Total</th>
<th>CIT Events</th>
<th>CIT Total</th>
<th>Weight %</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
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</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
<td>M-H, Fixed, 95% CI</td>
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<td>M-H, Fixed, 95% CI</td>
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<tr>
<td>1.1.1 In total population randomised</td>
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<tr>
<td>Hermans 2007</td>
<td>81</td>
<td>595</td>
<td>107</td>
<td>605</td>
<td>49.6%</td>
<td>0.77 [0.59, 1.00]</td>
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<tr>
<td>Van den Berghe 2005</td>
<td>46</td>
<td>765</td>
<td>109</td>
<td>783</td>
<td>50.4%</td>
<td>0.43 [0.31, 0.60]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>1360</td>
<td>1388</td>
<td>100.0%</td>
<td></td>
<td></td>
<td>0.60 [0.49, 0.74]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>127</td>
<td>216</td>
<td></td>
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</tr>
<tr>
<td>Heterogeneity: Chi² = 7.20, df = 1 (P = 0.007); I² = 86%</td>
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<tr>
<td>Test for overall effect: Z = 4.88 (P &lt; 0.00001)</td>
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<tr>
<td>1.1.2 In screened patients</td>
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</tr>
<tr>
<td>Hermans 2007</td>
<td>81</td>
<td>208</td>
<td>107</td>
<td>212</td>
<td>52.1%</td>
<td>0.77 [0.62, 0.96]</td>
<td></td>
</tr>
<tr>
<td>Van den Berghe 2005</td>
<td>46</td>
<td>181</td>
<td>109</td>
<td>224</td>
<td>47.9%</td>
<td>0.52 [0.39, 0.69]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>389</td>
<td>436</td>
<td>100.0%</td>
<td></td>
<td></td>
<td>0.65 [0.55, 0.77]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>127</td>
<td>216</td>
<td></td>
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</tr>
<tr>
<td>Heterogeneity: Chi² = 4.68, df = 1 (P = 0.03); I² = 79%</td>
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<tr>
<td>Test for overall effect: Z = 4.86 (P &lt; 0.00001)</td>
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</tbody>
</table>
2. Effect of Intensive Insulin Therapy in *routine daily care practice* on Neuromuscular Complications
Patients and Methods

• Retrospective analysis of EMG/NCS:
  – performed in MICU and SICU
  – because of weakness/weaning failure
  – from 1998-2006, eliminating RCTs
Results
Glycemic control
Mean glycemia before and after IIT (mean±SD)

Hermans et al, Crit Care 2009
Electrophysiological data
Spontaneous electrical activity before and after IIT

MVLR: IIT = independent protector \( p < 0.0001 \)

Hermans et al, Crit Care 2009
Myopathic pattern present on EMG before and after IIT

Hermans et al,Crit Care 2009
SNAPs UL before and after IIT

% of normal

- Total population before IIT
- Total population after IIT
- Surgical population before IIT
- Surgical population after IIT
- Medical population before IIT
- Medical population after IIT

*p-value ≤ 0.05 before versus after

Hermans et al, Crit Care 2009
Prolonged mechanical ventilation
## Risk for prolonged mechanical ventilation

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycemic control, IIT</td>
<td>0.40 (0.22-0.72)</td>
<td>0.002</td>
</tr>
<tr>
<td>ICU type, medical</td>
<td>0.35 (0.18-0.67)</td>
<td>0.002</td>
</tr>
<tr>
<td>On admission blood glucose</td>
<td>0.99 (0.99-1.002)</td>
<td>0.4</td>
</tr>
<tr>
<td>Gender, female</td>
<td>0.74 (0.48-1.12)</td>
<td>0.2</td>
</tr>
<tr>
<td>N of d treatment with norepinephrine, per d added</td>
<td>1.16 (1.11-1.22)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cumulative dose hydrocortisone equivalent, per mg added</td>
<td>1.00 (1.00-1.00)</td>
<td>0.9</td>
</tr>
<tr>
<td>Treatment with aminoglycosides, yes</td>
<td>1.72 (1.003-2.96)</td>
<td>0.05</td>
</tr>
<tr>
<td>N of d treatment with NMBAs (≥1 bolus or drip), per day added</td>
<td>1.15 (1.04-1.27)</td>
<td>0.007</td>
</tr>
<tr>
<td>Number of days treatment with dialysis, per day added</td>
<td>1.09 (1.03-1.15)</td>
<td>0.004</td>
</tr>
<tr>
<td>Bactaemia, yes</td>
<td>2.11 (1.26-3.55)</td>
<td>0.005</td>
</tr>
<tr>
<td>...</td>
<td></td>
<td>...</td>
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</tbody>
</table>
Conclusion

IIT reduces the electrophysiological incidence of CIP/CIM and the need for prolonged mechanical ventilation, also in routine daily practice.
3. Measuring diaphragmatic force in ICU
Methodology

BAMPS
TwPdi = TwPabd - TwPes
Results

1. Patients
Consent obtained
N=25

No stimulation performed
N=8
Reasons:
- n=3: balloon placement impossible
- n=1: extubated
- n=2: instable/DNR code
- n=1: valve broken
- n=1: consent withdrawn

Stimulation performed
N=17

Paired measurement
N=7

1 measurement
N=3

No measurement
N=7
Reasons:
- Technical problems n=5
- Intolerance n=1
- Abd contraction n=1
2. Reproducibility
# Between-occasion coefficient of variation

<table>
<thead>
<tr>
<th>Patient</th>
<th>Mean value Pdi</th>
<th>Number of measurements</th>
<th>Time span</th>
<th>Coefficient of variation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>12.2</td>
<td>2</td>
<td>24h</td>
<td>1.9 %</td>
</tr>
<tr>
<td>Patient 4</td>
<td>11.7</td>
<td>2</td>
<td>24h</td>
<td>15.5 %</td>
</tr>
<tr>
<td>Patient 5</td>
<td>8.7</td>
<td>2</td>
<td>48h</td>
<td>6.5 %</td>
</tr>
<tr>
<td>Patient 6</td>
<td>15.6</td>
<td>2</td>
<td>48h</td>
<td>2.0 %</td>
</tr>
<tr>
<td>Patient 7</td>
<td>9.5</td>
<td>2</td>
<td>120h</td>
<td>16.6 %</td>
</tr>
<tr>
<td>Patient 9</td>
<td>10.0</td>
<td>2</td>
<td>24h</td>
<td>16.3 %</td>
</tr>
<tr>
<td>Patient 10</td>
<td>20.5</td>
<td>4</td>
<td>24h</td>
<td>9.3 %</td>
</tr>
</tbody>
</table>

**mean**  
12.6  
2.3  
9.7 %
3. Relationship between TwPdi and duration of mechanical ventilation
Duration of mechanical ventilation

\[ R = 0.69 \]
\[ p = 0.038 \]
Conclusion

1. Similar reproducibility of BAMPS Pdi on ICU as in healthy volunteers

2. Logarythmic decline of TwPdi with increasing duration of MV
3. Future perspectives

1. Mechanistic approach:
   200 muscle biopsies: effects IIT

2. New potential intervention:
   EPaNIC

3. Diagnostic approach:
   Clinical evaluation muscle force in ICU
ICC = 0.95 (0.92-0.97)
Thank you:

Promoters:

G Van den Berghe
M Decramer
G Gayan-Ramirez
Thank you:

**Electrophysiologist:**
F Bruyninckx

**Neurologists:**
P Van Damme
M Schrooten
W Robberecht

**ICU teams:**
Nurses
Trainees
Residents
Staff members

**Study nurses:**
P Wouters
and team

**Physiotherapists:**
B Clerckx
T Vanhullebusch
C Robbeets
R Gosselink

**ICU Lab:**
I Vanhorebeek
S Derde