Critical Illness Polyneuropathy & Myopathy In Children

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Objectives

- Definition of CIP and CIM
- Spectrum of the Diseases
- Manifestations of each type
- High Risk Cases
- Diagnosis
- Management
Critical Illness Neuropathy and Myopathy

- Critical illness Polyneuropathy (CIP), first described by Bolton and colleagues in 1986
- Most common acquired neuromuscular condition in adult ICU
- Almost affects 50% of patient with sepsis and multi-organ dysfunction syndrome (MODS)

Neurology Clin 28(2010)961-977
Spectrum of manifestation

- Critically ill patient
- Symmetric weakness
- Flaccidity
- Different degree of muscle atrophy
- Reduction or absence of deep tendon reflexes
- Distal loss of sensation
- Facial and ophthalmic muscle are less affected
- Different degree of encephalopathy
- Symptoms may start after 3 days of illness
Neuromuscular Weakness Related to Critical Illness

Critically ill

Flaccid weakness

ICU settings

Respiratory dysfunction, Ventilated

**Incidence:**
Adults, 25% of ICU patients.
Pediatrics, less common.
How common is critical illness polyneuropathy & myopathy?

- Early development of critical illness myopathy and neuropathy in patients with severe sepsis
- 48 patients with severe sepsis in ICU
- Abnormal nerve conduction study (NCS) in 63%
- 50% of patients developed neuromuscular dysfunction

*Neurology*, 2007 68:1529-1535
Onset time of critical illness myopathy and/or neuropathy during intensive care unit (ICU) stay


- Multi-center study
- 92 ICU patients
- Daily measurements of the action potential amplitude and nerve conduction velocity
- 30% developed either CIMP or CINP
What About Children?
How common is Critical illness myopathy and neuropathy?

- All children admitted to PICU of Sick Children Hospital of Toronto over 1 year were evaluated 3 times/week
- Age 3 months to 17 years
- Muscle weakness, reduced DTR, inability to wean MV
- Incidence: **14/830 (1.7%)**
- 3 children under 3 years (0.7%) and 11 above 10 years of age (5.1%)

NEUROLOGY 2003;61:1779–1782
ICU Related Neuromuscular weakness

- Critical Illness Myopathy
- CI Polyneuropathy
- Mixed Type of Both
- Prolonged NMJ Blockade
- Others
  - GBS
  - Rhabdomyolysis
  - Cachectic myopathy
  - Myopathies
CRITICAL ILLNESS MYOPATHY
Type of Critical Illness Myopathy

• **Acute necrotizing myopathy**
  – Occur after sepsis and trauma
  – Generalized muscle weakness
  – High serum creatine kinase
  – Myoglobinurea

• **Myopathy associated with NMB or Corticosteroid**
  – Diffuse muscle weakness
  – Muscle atrophy
Incidence

- Acute RDS, 3%
- Organ Transplant, 7%
- Severe Sepsis, 33%
- MOF, 50%

IV Glucocorticoids
CRITICAL ILLNESS MYOPATHY

- Hyperglycemia
- Systemic Inflammatory Response
- Increase Severity of Disease

IV Steroid NMB

Strongest Factor
Rare without exposure
Risk Factors

- Sepsis
- SIRS
- Hyperosmolality
- TPN use
- GCS< 10
- ARDS
- Pancreatitis
- Burn
- Asthma
- Organ Transplantation
- Renal or hepatic Failure

Steroid
NMB
Aminoglycoside
Hyperglycemia
Muscle weakness in critically ill children
Neurology 2003;61: 1779-1782

- 840 Patient included
- 14 patients (Ave 12 y/o) developed weakness (1.7 %)
- Age distribution 3 < 3 years of age, 11 > more than 10
- Under 3 years (0.5 %)
- More > 10 years (5.1 %)
- Length of PCICU stay (4 days - 11 days)
- 12/14 (86 %) required ventilation > 5 days
- 9 / 14 received corticosteroid
- 9/14 received NMB
- 57 % were transplant patients
- 4/14 Died (29 %)
ICU, ventilated, Paralyzed

IV steroid, several days

CIM

Diagnostic Criteria

Failure to wean MV not related to cardiopulmonary disease

Flaccid Proximal Quadriparesis

Normal sensation, DTR normal/Decreased

Increased CK (around day 4), 50-80%, might be without CIM

Electrophysiologic Study, Nerve conduction study, EMG

Muscle Biopsy, Electronic Microscope (Loss of Myosin)
Pathology

- Scattered atrophic fibers
- Loss of ATPase activity
- Loss of Myosin
- Loss of myosin thick filaments
Figure 1 Direct muscle stimulation

Zink, W. et al. (2009) Critical illness polyneuropathy and myopathy in the intensive care unit
*Nat. Rev. Neurol.* doi:10.1038/nrneurol.2009.75
Management Strategy

Critically Illness Myopathy

- Increase Severity of Disease
- Hyperglycemia
- SIRS
- Aggressive Management
- Insulin (80-110, 4.4-6.1)
- D/C or Decrease IV Steroid and NMB ASAP
- Aggressive Management

IV Steroid
Prevention

Management
- Supportive
- Rehabilitation
- Avoid the Occurrence

Prognosis
- Recovery within wks to months
- Variable residual weakness
- ICU stay, Morbidity, Mortality
ICU Related Neuromuscular weakness

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- Polyneuropathy
- Mixed Type of Both
- Prolonged NMJ Blockade
- Others
  - GBS
  - Rhabdomyolysis
  - Cachectic myopathy
  - Myopathies
CRITICAL ILLNESS POLYNEUROPATHY
Mechanism
(not clear)

Axonal Degeneration
70 %

Intact Nerves, 30 %

Damaged myelin
Critical illness

Neuropathy

Sepsis

Major Factors

High Sugar

SIRS

Low Alb
<table>
<thead>
<tr>
<th></th>
<th>CIM</th>
<th>CIP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence</strong></td>
<td>More common</td>
<td>Less common</td>
</tr>
<tr>
<td><strong>Major Factor</strong></td>
<td>IV steroid</td>
<td>Severe Sepsis, SIRS, MOF</td>
</tr>
<tr>
<td><strong>Onset</strong></td>
<td>Several days of IV steroid</td>
<td>After 1-2 wks of SIRS (average 28 days)</td>
</tr>
<tr>
<td><strong>Motor System</strong></td>
<td>Proximal</td>
<td>Involves distal</td>
</tr>
<tr>
<td><strong>Sensory Function</strong></td>
<td>Preserved</td>
<td>Affected</td>
</tr>
<tr>
<td><strong>DTR</strong></td>
<td>Usually normal</td>
<td>Usually absent</td>
</tr>
<tr>
<td><strong>Facial M and Cranial N</strong></td>
<td>Preserved</td>
<td>Usually Preserved</td>
</tr>
<tr>
<td><strong>Prognosis</strong></td>
<td>Better, Wks to Months, Residual weakness</td>
<td>Wks to Months, Residual weakness May remain quadriplegic</td>
</tr>
<tr>
<td><strong>Management</strong></td>
<td>Supportive, Preventive, Insulin</td>
<td>Supportive, Preventive, Insulin</td>
</tr>
</tbody>
</table>
It is difficult to differentiate CIM from CIP clinically.
Major electroneurographic features in axonal and demyelinating neuropathy

- **Normal nerve**
  - Nerve action potential: normal amplitude and conduction velocity

- **Axonal neuropathy**
  - Nerve action potential: reduced amplitude, normal conduction velocity

- **Demyelinating neuropathy (Guillain-Barré syndrome)**
  - Nerve action potential: reduced conduction velocity, normal amplitude
- Loss of myelinated nerve fibers
- Degenerating myelin
- Clusters of Schwann cell without nerve fibers
Limitation To Sensory & Motor Function Assessment

• Sedation
• Paralytic Agents

• Intubation
• Neonates and Infants

• Critical Illness
• Mixed Type

It is difficult to differentiate CIM from CIP clinically.
Management Strategy

- CIP
- Hyperglycemia
- SIRS
- Low Alb

- Increase Severity of Disease
- Insulin (80-110, 4.4-6.1)
- Maintain normal Albumin levels?
- Aggressive Management
- Aggressive Management
Prevention

Management
- Supportive
- Rehabilitation
- Avoid the Occurrence

Prognosis
- Recovery within wks to months
- Variable residual nerve dysfunction for years
- May remain quadriplegic
- ICU stay, Morbidity, Mortality
PROLONGED NEUROMUSCULAR JUNCTION BLOCKADE
ICU Related Neuromuscular weakness

- Critical Illness Myopathy
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PERSISTENT PARALYSIS IN CRITICALLY ILL PATIENTS AFTER LONG-TERM ADMINISTRATION OF Vecuronium

Table 1. Renal and Liver Function in Patients with Prolonged Neuromuscular Blockade and in Those without Such Blockade after Long-Term Administration of Vecuronium.

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Sex</th>
<th>Duration of Prolonged Blockade</th>
<th>Creatinine Clearance</th>
<th>Liver Function*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>&gt;168† hr</td>
<td>4.8 ml/min</td>
<td>Normal</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>40 hr</td>
<td>&lt;4.8 ml/min</td>
<td>Impaired</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>32 hr</td>
<td>&lt;4.8 ml/min</td>
<td>Impaired</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>31 hr</td>
<td>7.8 ml/min</td>
<td>Normal</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>&gt;8† hr</td>
<td>22.2 ml/min</td>
<td>Normal</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>7 hr</td>
<td>0 ml/min</td>
<td>Impaired</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>6 hr</td>
<td>30.0 ml/min</td>
<td>Impaired</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>Absent</td>
<td>Normal</td>
<td>Liver failure</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>Absent</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>Absent</td>
<td>20.0 ml/min</td>
<td>Impaired</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>Absent</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>Absent</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>13</td>
<td>F</td>
<td>Absent</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>14</td>
<td>M</td>
<td>Absent</td>
<td>&lt;4.8 ml/min</td>
<td>Impaired</td>
</tr>
<tr>
<td>15</td>
<td>M</td>
<td>Absent</td>
<td>13.2 ml/min</td>
<td>Impaired</td>
</tr>
<tr>
<td>16</td>
<td>M</td>
<td>Absent</td>
<td>0 ml/min</td>
<td>Liver failure</td>
</tr>
</tbody>
</table>

- 16 critically ill received Vecuronium
- NMB > 2 days
- 7/16 had prolonged paralysis > 6 hours after stopping NMB
- 7/7 had renal impairment
- High serum Mg level
- Liver impairment
- Acidosis
Prolonged use (days) of paralytic agents

Renal or hepatic insufficiency

Prolonged circulation of drug metabolites

Bind irreversibly to acetylcholine receptors

Inhibiting neuromuscular transmission

Flaccid Paralysis
Paralytic Agents

Aminosteroid
- Pancuronium
  - Degenerated in the kidney and the liver into active metabolite
  - affected by renal, hepatic and cardiac insufficiency
- Vecuronium
  - Degenerated in the blood into inactive metabolite
  - Not affected by renal, hepatic or cardiac insufficiency

Benzylisoquinolone
- Cisatracorium
- Doxaurium
Diagnosis and Management

- **Anti-Ach-erase**
  - Pyridostigmin

- **Clinical Improvement**

- **Support Diagnosis**

- **Rx Management**

- **Avoidance**
  - Aminosteroid Agents

- **Use**
  - Anti-acetyl cholinesterase Agents
Preventive measures

- Avoid use of muscle relaxant
- Monitor muscle strength during paralysis
- Daily interruption of sedation and paralysis
- Monitoring of brain activity
- Remember risk factors: NMB, Aminoglycoside, steroid, Renal failure
Conclusion

• Critical illness neuromyopathy is frequently under-diagnosed
• Sepsis and MOF are risk factor
• Steroid, NMB, hyperglycemia, aminoglycoside are potential incriminating factors
• Early recognition and Diagnosis are important
• Management is based on preventive and supportive measures
The magic spinach is not yet there

Thanks