Subclinical Seizures

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5 minute Friday
October 14, 2016
Significance of Neonatal seizures

Neonatal seizures may be the first and only clinical sign of a central nervous system disorder in a newborn.

Seizures may indicate the presence of a treatable condition prompting important evaluation and treatment.

Seizures may contribute to further brain injury.
Definition of neonatal seizures

**Definition:** Paroxysmal behavior caused by hypersynchronous discharge of a group of neurons.

May be classified as:

- **Clinical only seizure:** Sudden paroxysm of abnormal clinical changes with no correlation with simultaneous EEG seizure

- **EEG only seizure (sub-clinical seizure):** Definite EEG seizure not accompanied by any visible clinical signs

- **Electro-clinical seizure:** Definite clinical seizure signs simultaneously coupled with EEG seizure
Epidemiology of Neonatal Seizures

- Seizures occur most frequently in newborn period than any other time of life, up to 80% in the first week of life.
- Reported incidence varies 1.5 to 5 per 1,000 newborns, is higher with decreasing gestation age and increasing acuity of illness.
- True incidence may be significantly underestimated due low accuracy of diagnosis based on clinical signs and lack of population-based studies using conventional EEG (cEEG).
Diagnosis of neonatal seizures

Historically, the diagnosis of seizures was most often made based on clinical signs. However, EEG studies have demonstrated:

• Not all clinically suspicious events are epileptic seizures
• Most neonatal seizures are sub-clinical

Inaccurate seizure diagnosis has important consequences:

• Neonates with subclinical seizures are undertreated without cEEG screening
• Infants with suspicious activity that is not associated with EEG events may be exposed to unnecessary medications
Differentiating seizures from non-seizure events

**Purpose:** To determine the gap between EEG seizure burden, video recorded clinical findings, and clinical documentation of seizures by neonatal clinicians

**Method:** 51 infants at risk for seizures were monitored with video EEG and clinical documentation at bedside

**Results:**
- 9 had EEG seizures and 3 had clinical seizures
- Of 526 EEG seizures, only 34% had clinical manifestations
- Of 177 clinical seizures, only 27% had EEG seizures

Percentage time electrographic seizures had clinical signs recognized by clinicians

**Definition:** Persistence of electrographic seizures despite suppression of ≥50% clinical seizures

**Methods:** 50 newborns with EEG and clinical seizures treated with either phenobarbital or phenytoin.

**Results:**
- 24 had no EEG or clinical seizures.
- 26 had persistent seizures:
  - 5 EEG only
  - 10 ≥ 50% suppression clinical seizures
  - 11 < 50% suppression clinical seizures

**Conclusion:** 58% newborns had “uncoupling” with only or predominantly EEG seizures following treatment with anticonvulsants.

Treatment of subclinical seizures

- **Purpose:** To determine if treatment of both clinical and EEG seizures reduces EEG seizure duration and decreases brain injury.

- **Methods:** Term infants with HIE and seizures were randomized to treatment both clinical and subclinical seizures (Group A) or treatment only clinical seizures (Group B).

- **Results:**
  
<table>
<thead>
<tr>
<th>Group</th>
<th>Median seizure duration (minutes)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A (n=19)</td>
<td>196 ± 340</td>
<td>P=NS</td>
</tr>
<tr>
<td>Group B (n=14)</td>
<td>503 ± 1084</td>
<td></td>
</tr>
</tbody>
</table>

- **Conclusions:** Significant relationship between seizure duration and MRI severity scores.

Conclusions:

- Trend towards reduction in seizure duration when clinical and subclinical seizures were treated.
- In addition, more brain injury was seen with longer seizure duration, supporting the assumption that seizures enhance existing brain injury.
Treatment of subclinical seizures

**Purpose:** Determine impact of treating EEG seizures vs. clinical seizures on seizure burden, MRI, and neurodevelopmental outcome

**Methods:** Newborns with HIE were randomized to either
- Treatment of EEG seizures (ES)
- Treatment of clinical seizures (CS)
All were monitored with cEEG and those with status epilepticus were excluded.

**Results:**
- 35 of 69 (51%) developed seizures
- Total seizure burden significantly lower in ES group (p=.02)
- Total number of seizures and time to treatment lower in ES (p=.04)
- Significant association seizure burden and MRI injury score (p<.03)
- Increasing seizure burden correlated with lower Bayley scores (p=.03)

**Conclusions:** EEG monitoring and treatment of EEG seizures reduces seizure burden. Increasing seizure burden is associated more severe brain injury and lower Bayley III scores.

**Speculation:** Early detection and treatment of EEG seizures may reduce cumulative seizure burden leading to less brain injury by MRI and improved neurodevelopmental outcome.

aEEG data with raw EEG trace enabled detection of 85% of seizure burden making it a reasonable option when cEEG is not available.