Anesthesiology Practice & Seizures

Barbara Van de Wiele MD
Clinical Professor, Vice Chair & Director
Neurosurgical Anesthesiology
UCLA Department of Anesthesiology and
Perioperative Medicine
1. Incidence, etiology and management of perioperative seizures
2. Antiepileptic medication side effects and drug interactions
3. Key issues for anesthesia care in patients with seizure disorders
Seizures

- **Partial Seizure**
  - Start in a focal area
- **Generalized Seizures**
  - Involve entire brain at outset
  - Always accompanied by LOC
- **Seizure disorder or epilepsy**
  - Two or more seizures without a clear cause (such as alcohol withdrawal)
Incidence:

- 1 seizure / lifetime: 10% of people worldwide
- Worldwide: 50 million people have epilepsy
- Active epilepsy in the US: 4-10/1000
Incidence: Perioperative

- All patients undergoing anesthesia
  - 3 in 10,000
- All patients with a seizure disorder undergoing anesthesia
  - 3 in 100
Akavipat P et al. The Thai Anesthesia Incidents Study of perioperative convulsion. *Journal of the Medical Association of Thailand* 88:106-12, 2005

- Prospective cohort study
- All anesthetics in 28 hospitals X 1 yr n=173,000
- Incidence 3/10K


- Retrospective review
- All patients with documented seizure disorder admitted for surgery
- n=641
<table>
<thead>
<tr>
<th>Factor</th>
<th>Increases likelihood of perioperative seizure in patients with seizure disorder?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of Anesthesia</td>
<td>No (General vs Regional vs MAC)</td>
</tr>
<tr>
<td>Frequency of seizures</td>
<td>Yes</td>
</tr>
<tr>
<td>Number of AEDs</td>
<td>Yes</td>
</tr>
<tr>
<td>More recent seizure</td>
<td>Yes</td>
</tr>
<tr>
<td>Subtherapeutic AEDs</td>
<td>Yes</td>
</tr>
</tbody>
</table>


- Retrospective analysis
- Prospectively data
- CPB 2004-2010
- n = 11,529
- Postoperative convulsive seizures: 100 pts (0.9%)

**RISK FACTORS for SEIZURES after CARDIAC SURGERY**

- Age
- Female gender
- Redo cardiac surgery
- Ascending aorta calcification
- Congestive heart failure
- Deep hypothermic circ arrest
- Duration of aortic cross-clamp
- Tranexamic acid

<table>
<thead>
<tr>
<th></th>
<th>Observation n=61 #(#)</th>
<th>Prophylaxis n=62 #(#)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>All seizure events</td>
<td>11(18)</td>
<td>15 (24)</td>
<td>NS</td>
</tr>
<tr>
<td>Early seizure &lt;30 days</td>
<td>5(8)</td>
<td>6(10)</td>
<td>NS</td>
</tr>
<tr>
<td>Seizures within 24 hours</td>
<td>2(3)</td>
<td>1(2)</td>
<td>NS</td>
</tr>
<tr>
<td>Seizures within 3 days</td>
<td>3(5)</td>
<td>2(3)</td>
<td>NS</td>
</tr>
<tr>
<td>Seizures within 1 week</td>
<td>5(8)</td>
<td>2(3)</td>
<td>NS</td>
</tr>
<tr>
<td>Early clinically significant seizures</td>
<td>2(3)</td>
<td>1(2)</td>
<td>NS</td>
</tr>
</tbody>
</table>
Conte et al. Analysis of propofol remifentanil infusion for tumor surgery with intraoperative brain mapping J. Neurosurg Anesthesiol 2010

<table>
<thead>
<tr>
<th>Intraoperative Complication</th>
<th>Overall n (%)</th>
<th>Asleep Awake n=135</th>
<th>Asleep Asleep n=103</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Seizure</td>
<td>54 (23)</td>
<td>22(16)</td>
<td>32(31)</td>
</tr>
<tr>
<td>Treated seizures</td>
<td>16 (7)</td>
<td>10(7)</td>
<td>6(6)</td>
</tr>
</tbody>
</table>

- Analysis of 238 consecutive procedures 2005-2008
- Propofol remifentanil anesthesia
Incidence and Etiology of Seizures during Anesthesia Care

- Stroke
- Intracranial tumor
- Eclampsia
- Porphyria
- Uremia
- Drug withdrawal
- Drug intoxication
- Electrolyte abnormalities
Treatment of Perioperative Seizures

1. Give O2, VS, IV, ECG, pulse ox, check ABG and glucose
   - Lorazepam 2 mg IV, repeat to max 0.1 mg/kg
   - Fosphenytoin IV 20 mg/kg IV max rate 150 mg/min

2. Additional Fosphenytoin 10mg/kg
   - Valproate 30mg/kg/IV or proceed to step 3

3. Intubate start EEG monitoring
   - Midazolam 0.2 mg/kg IV then infusion 0.1 mg/kg/hr
   - Propofol 1-2 mg/kg/hr then 2mg/kg/hr
   - Pentobarbital 5 mg/kg at 50 mg then infusion 1mg/kg/hr

Work up of Perioperative Seizure

Clinical Assessment
- Medical history
- Clinical context
- Seizure morphology

Consultation

Diagnostic Testing
- Laboratory studies:
  - electrolytes, calcium, magnesium, urine tox screen, AED levels if indicated
- Neuroimaging:
  - In patients who have risk factors for acute intracranial pathology e.g. acute head trauma, history of anticoagulation, malignancy, and focal seizure, new focal deficit, altered mental status, headache
- Other Diagnostic Testing
# Anesthesia Care of Patients with Epilepsy

## Work up for Epilepsy Surgery
- Imaging (MRI, PET)
- Wada Testing
- Magnetoencephalography
- EEG electrode placement
- Depth electrode placement
- Subdural Grid Placement

## Surgery for Epilepsy
- Focal Resection
- Temporal Lobectomy
- Hemispherectomy
- Corpus Callosotomy
- Deep Brain Stimulation
- Vagal Nerve Stimulator Placement
- Laser Ablation of seizure foci

## Surgery Unrelated to Epilepsy
1. Incidence, etiology and management of perioperative seizures
2. Antiepileptic medication side effects and drug interactions
3. Key issues for anesthesia care in patients with seizure disorders
### Antiepileptic Drugs (AEDs)

#### “Classic”
- Phenytoin (Dilantin)
- Carbamazepine (Tegretol)
- Valproic Acid (Depakote)
- Phenobarbital (Luminal)
- Ethosuximide (Zarontin)
- Primidone (Mysoline)
- Benzodiazepines

#### “Newer”
- Topiramate (Topomax)
- Oxcarbazepine (Trileptal)
- Zonisamide (Zonagran)
- Levetiracetam (Keppra)
- Lamotrigine (Lamictal)
- Felbamate (Felbatol)
Cytochrome P450

Enzyme inducers
- Carbamazepine
- Phenytoin
- Phenobarbital
- Primidone
- Oxcarbazepine
- Topamax

Enzyme inhibitors
- Valproic Acid
Plasma Concentration

- Cardiovascular drugs
  - Amiodarone
  - Beta blockers
  - Calcium channel antagonists
- Neuromuscular blockers
- Benzodiazepines
Time to onset and recovery after 0.6 mg/kg Rocuronium (2X ED95)

<table>
<thead>
<tr>
<th></th>
<th>Phenytoin N=18</th>
<th>Control N=18</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>2.3±.9</td>
<td>1.9±.5</td>
<td>NS</td>
</tr>
<tr>
<td>10% Recovery</td>
<td>20.5±5.8</td>
<td>27.2±5.5</td>
<td>P&lt; .001</td>
</tr>
<tr>
<td>25% Recovery</td>
<td>23.8±5.5</td>
<td>31.1±5.6</td>
<td>P&lt; .001</td>
</tr>
<tr>
<td>75% Recovery</td>
<td>30.6±6.7</td>
<td>39.3±6.2</td>
<td>P&lt; .001</td>
</tr>
<tr>
<td>90% Recovery</td>
<td>32.5±7.3</td>
<td>41.2±6.1</td>
<td>P&lt; .001</td>
</tr>
</tbody>
</table>


Table 2. Neuromuscular Transmission Data

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Anticonvulsant group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lag time</td>
<td>0.9 ± 0.4</td>
<td>16.2 ± 0.4</td>
</tr>
<tr>
<td>Onset</td>
<td>3.6 ± 0.9</td>
<td>3.5 ± 0.7</td>
</tr>
<tr>
<td>Maximal suppression</td>
<td>4.4 ± 1.4</td>
<td>4.7 ± 2.55</td>
</tr>
<tr>
<td>Recovery</td>
<td>26.3 ± 11.1</td>
<td>21.1 ± 5.2 (0.06)</td>
</tr>
<tr>
<td>T1 10%</td>
<td>10.3 ± 3.8</td>
<td>10.2 ± 4.6</td>
</tr>
<tr>
<td>T1 25%</td>
<td>20.0 ± 4.4</td>
<td>16.6 ± 5.0 (0.028)</td>
</tr>
<tr>
<td>T1 75%</td>
<td>41.0 ± 8.5</td>
<td>32.5 ± 7.6 (0.006)</td>
</tr>
<tr>
<td>T1 0%–25% recovery index</td>
<td>10.4 ± 2.1</td>
<td>8.7 ± 1.1 (0.01)</td>
</tr>
<tr>
<td>T1 25%–75% recovery index</td>
<td>21.2 ± 5.1</td>
<td>16.2 ± 3.7 (0.004)</td>
</tr>
<tr>
<td>T1% final, not corrected</td>
<td>71.0 ± 10.1</td>
<td>69.5 ± 6.6</td>
</tr>
</tbody>
</table>

Data are means ± SD; P values are in parentheses. All values are expressed in minutes.

Recovery = recovery from the initial bolus of cisatracurium. Other recovery parameters were obtained after termination of the infusion.

Other AED interactions

- Increased narcotic requirements
- Increase in demethylation of meperidine to normeperidine


Other AED interactions

• **Increased metabolism of corticosteroids**

• **Decreased plasma concentration of midazolam after oral administration**
  – Backman J et al: Concentrations and effects of oral midazolam are greatly reduced in patients treated with carbamazepine or phenytoin. Epilepsia, 1996

• **Attenuation of ketamine effects**
Other AED Side Effects

• Trileptal: Hyponatremia

• Zonagran and Topiramate: Acidosis

• Phenytoin: Hypotension

• Additive Sedation: Leviteracetam, Phenobarbital
1. Incidence, etiology and management of perioperative seizures
2. Antiepileptic medication side effects and drug interactions
3. Key issues for anesthesia care in patients with seizure disorders
Perioperative Management of AEDs

- Avoid disruption of AED medication schedule
- Continue PO till surgery
- Resume ASAP after surgery
- Substitute parenteral drugs
Proconvulsant and anticonvulsant effects of anesthetics
### IV agents

<table>
<thead>
<tr>
<th></th>
<th>PRO</th>
<th>ANTI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiopental</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Methohexital</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etomidate</td>
<td></td>
<td>+++</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td>Ketamine</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Propofol</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Opioids</td>
<td></td>
<td>+++</td>
</tr>
</tbody>
</table>

- Benzodiazepines are anticonvulsant
- Thiopental is anticonvulsant
- Methohexital and Etomidate are proconvulsant but...
- Propofol is anticonvulsant but...
- Ketamine is anticonvulsant but...
- Some narcotics are proconvulsant but...

Kofke WA. Anesthetic management of the patient with epilepsy or prior seizures. Curr Opin Anaesthesiol 23(3):391-9, 2010
### Inhalation Agents

<table>
<thead>
<tr>
<th></th>
<th>PRO</th>
<th>ANTI</th>
</tr>
</thead>
<tbody>
<tr>
<td>N2O</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Halothane</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Enflurane</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Isoflurane</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Sevoflurane</td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Desflurane</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

- Ethrane and sevoflurane are proconvulsant under certain conditions
  - $> 1.5$ MAC, rapid changing concentration and hypocapnia
- Desflurane and isoflurane are anticonvulsant

Kofke WA. Anesthetic management of the patient with epilepsy or prior seizures. Curr Opin Anaesthesiol. 23(3):391-9, 2010
# Anti Seizure Anesthesia Plan

## Well Controlled Seizures
- Continue AEDs
- Consider premedication with benzodiazepine
- Avoid non therapeutic hyperventilation
- Avoid triggering agents*
- If use Sevoflurane < 1.5 MAC
- Pay attention during induction and emergence

## Poorly Controlled Seizures
- Continue AEDs
- Consider premedication with benzodiazepines
- Avoid non therapeutic hyperventilation
- Avoid triggering agents*
- ? Sevoflurane
- Pay attention
- Consider avoiding NMB
- Consider intraop monitoring
- Factor urgency of procedure
- Consider consultation

*Etomidate, methohexital, large bolus doses of alfentanil, remifentanil, fentanyl
Mapping Seizure Foci
Endo T. Effects of sevoflurane on ECOG in patients with Intractable temporal lobe epilepsy J Neurosurg Anesthesiol 14:2002
# Diagnostic Pharmaco-activation

- Fentanyl -10mcg/kg
- Alfentanil 30-50mcg/kg
- Remifentanil (1-2.5 mcg/kg)
- Methohexital 0.3-0.5 mg/kg
- Etomidate (.05-o.1 mg/kg)
Electrocorticography

Avoid
- Benzodiazepine
- Potent Inhalation Agents

Maybe
- Nitrous oxide
- Propofol

OK
- Narcotics
- Dexmedetomidine
- Droperidol
Summary

- Seizures are rare perioperative events
- May herald serious underlying conditions or metabolic abnormalities
- Non neurologic events can mimic seizures
- Prolonged seizures are lifethreatening
- AEDs have important interactions
- ASAP = Stable AEDs + appropriate anesthetics
Thank You