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Children's Hospital Colorado

PEDIATRIC ANESTHESIA UPDATE 2014

Death or Neurologic Injury After Tonsillectomy in Children with a Focus on Obstructive Sleep Apnea: Houston, We Have a Problem!

- SPA survey and ASA closed Claims

Coté et al.

- “Tonsillectomy-related malpractice settlements occur against anesthesiologists more commonly than against surgeons and settle for nearly 5-fold larger awards because of the devastating outcomes”

Death or Neurologic Injury

- 111 patients identified
- Death or neurologic injury in 77%
- 63 (57%) had OSA
- Pts with OSA ↑ incidence of obesity +/- co-morbidities
- Pts with OSA > events attributed to apnea
Race and Ethnicity

- African American children may have:
  - 4x incidence of OSAS
  - Greater ↓ in oxygen saturation
  - ? pharmacogenetics

Morphine and Pharmacogenetics

- African American children have > clearance of Morphine to M3G
- African American children have > pain
- Caucasian children have > side effect
- Latino children compared to non-Latino
  - Caucasian children had a higher incidence of side effects
  - Pruritus
  - POV
After similar uses of intraoperative morphine for tonsillectomy, there was an unequal burden of increased pain in African American children and increased opioid adverse effects in Caucasian children in the recovery room. Though Caucasian children received relatively less opioids perioperatively, they had higher incidences of opioid related adverse effects than African American children.

Latino versus Non-Latino children

- 15 deaths in the first 24 hours after surgery due to apnea
  - 10 at home
  - 2 in PACU
  - 3 on floor
- Need better monitoring/guidelines

Latino vs Non-Latino: Side Effects

- > 4000 consecutive tonsillectomy
- 7.2% with persistent desat post-op
  - Trisomy 21
  - Weight
  - Cardiac disease
  - Syndromes
  - OSA
  - Neurologic issues
  - Pulmonary disease
The STBUR questionnaire for predicting perioperative respiratory adverse events in children at risk for sleep-disordered breathing:

- Snoring
- Trouble Breathing
- UnRefreshed

- Snores more than ½ the time
- Snores Loudly
- Trouble breathing/struggles
- Stops breathing
- Wakes up un-refreshed

3 = 3x risk or perioperative respiratory adverse events

5 = 10x risk,

So what should we do for pain management?

NSAID? Steroids?

15 studies, 1101 children
Insufficient data regarding ↑ bleeding ↓ vomiting

Cochrane Database July 2013
A 2013 updated systematic review & meta-analysis of 38 randomized controlled trials; no apparent non steroidal anti-inflammatory agents on the risk of bleeding after tonsillectomy.

- 36 studies, 1747 children + 1446 adults
  - No increase in bleeding
  - No increase in severe bleeding
  - No increase need for readmission or reoperation

- Our surgeons have started using ibuprofen in post-op period

- Yes
  - 215 children
  - 4 groups: 0. 0.05, 0.15, 0.5 mg/kg dex
  - Higher incidence of bleeding with higher doses

Absolutely, positively NO!
(Jane you ignorant....)

- 314 children 3-18
- Placebo or dex 0.5 mg/kg
- No difference in sign bleed
- Unable to determine if bleeding by parent report was increased

- No increased bleeding

Our surgeons are nervous

- Many have started using lower doses of steroids
  - Other things to consider
    - Local anesthesia infiltration
    - Ketamine
    - Tramadol

Steroids and Tonsillectomy?

- Yes
  - 5254 cases, 1998-2010
  - DXA (Dexamethasone) and postoperative bleeding after tonsillectomy in children: A meta-analysis of prospective studies.

- No increased bleeding

- No difference in bleeding rate

- Unable to determine if bleeding by parent report was increased

Our surgeons are nervous

- Many have started using lower doses of steroids
  - Other things to consider
    - Local anesthesia infiltration
    - Ketamine
    - Tramadol
Anesthesia and Neurotoxicity

Young rodents and other animals have shown apoptosis and cell death during critical periods of brain development. Most anesthetics and sedatives increase inhibition. Fine balance between neuronal excitation and inhibition is crucial for neuronal survival and proper maturation and functioning.

Volatile and Other Anesthetics

- Over-inhibition may be toxic
- May agents are both neuroprotective and neurotoxic
- All volatile anesthetics, midazolam, propofol and ketamine have been implicated
- Many species including primates
- So far opioids seem to be OK

Of Mice and Men

- **Mice**
  - Brain Growth Spurt: first 1-2 weeks of life
  - Anesthetized for 5-6 hours
  - Many unmonitored
  - Pain and surgical stress are harmful

- **Humans**
  - Brain Growth Spurt: prenatal-24 months
  - Equivalent to several days-months
  - Monitored
  - Pain and surgical stress are harmful

Table 1. Characteristics of eligible studies for meta-analysis.

<table>
<thead>
<tr>
<th>Study</th>
<th>Anesthetic</th>
<th>Duration</th>
<th>Age</th>
<th>Time Exposure</th>
<th>Effect Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 1</td>
<td>General Anesthesia</td>
<td>5-6 hours</td>
<td>1-2 weeks old</td>
<td>1-2 months</td>
<td>0.5</td>
</tr>
<tr>
<td>Study 2</td>
<td>Ketamine</td>
<td>2-3 hours</td>
<td>3-4 months</td>
<td>3-4 months</td>
<td>0.6</td>
</tr>
<tr>
<td>Study 3</td>
<td>Propofol</td>
<td>3-4 hours</td>
<td>4-5 months</td>
<td>4-5 months</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Of Mice and Men: Brain Growth Spurt - first 1-2 weeks of life. Anesthetized for 5-6 hours. Many unmonitored. Pain and surgical stress are harmful.
- All children undergoing pyloric stenosis b/w 1986-1990 in Denmark
- Compared with 5% age matched sample
- 9th grade standardized educational test
- Small % of Danish children do NOT take these tests
- Variables: sex, birth weight, parental education and age.
- Exclusions: congenital malformation, hyperbilirubinemia, neonatal jaundice

**Results**

<table>
<thead>
<tr>
<th></th>
<th>Pyloric Stenosis</th>
<th>No Pyloric Stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>% male</td>
<td>80</td>
<td>53.6</td>
</tr>
<tr>
<td>Parental Age</td>
<td>similar</td>
<td>similar</td>
</tr>
<tr>
<td>Parental Education</td>
<td>slightly lower</td>
<td>similar</td>
</tr>
<tr>
<td>Mean Birth Weight (g)</td>
<td>3345</td>
<td>3434</td>
</tr>
<tr>
<td>Age at time of surgery</td>
<td>40 days</td>
<td></td>
</tr>
<tr>
<td>Congenital malformations</td>
<td>6.8%</td>
<td>4.4%</td>
</tr>
<tr>
<td>Non-attainment-boys</td>
<td>12%</td>
<td>16%</td>
</tr>
<tr>
<td>Non-attainment-girls</td>
<td>13%</td>
<td>10%</td>
</tr>
</tbody>
</table>

**OR = 1.37**

**Conclusion**

- Mean test scores similar once low birth weight and congenital malformation are excluded
- Higher incidence of test Non-Attainment in exposed patients boys > girls
The effects of exposure to general anesthesia in infancy on academic performance at age 12.

- 100 children who had surgery < 1yr of age
- 106 control
- Performance on “high stakes” test at age 12
- Diagnosis of “learning disability”
- Phone surveys

Table 2

<table>
<thead>
<tr>
<th>Factor</th>
<th>Exposed Mean (95% CI)</th>
<th>Control Mean (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low SES</td>
<td>0.21 (0.21-0.22)</td>
<td>0.22 (0.22-0.23)</td>
<td>0.15</td>
</tr>
<tr>
<td>High SES</td>
<td>0.21 (0.21-0.22)</td>
<td>0.22 (0.22-0.23)</td>
<td>0.15</td>
</tr>
<tr>
<td>Parent education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low SES</td>
<td>0.21 (0.21-0.22)</td>
<td>0.22 (0.22-0.23)</td>
<td>0.15</td>
</tr>
<tr>
<td>High SES</td>
<td>0.21 (0.21-0.22)</td>
<td>0.22 (0.22-0.23)</td>
<td>0.15</td>
</tr>
</tbody>
</table>

Table 3

<table>
<thead>
<tr>
<th>Group</th>
<th>Exposed</th>
<th>Control</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>100</td>
<td>106</td>
<td></td>
</tr>
<tr>
<td>Exposed</td>
<td>56</td>
<td>54</td>
<td>0.12</td>
</tr>
<tr>
<td>Control</td>
<td>44</td>
<td>52</td>
<td></td>
</tr>
</tbody>
</table>

Problems with the Study

- Small
- Retrospective
- GA group was 90% male
- Maternal education slightly lower
- Learning disabilities not defined

ASA 2013 Abstracts
Multimodal Assessment of Cognitive Outcomes Associated With Exposure to Anesthesia in Early Childhood
caleb H. Ing, M.D., Charles D'Angelino, Ph.D et al.

- Western Australian Pregnancy Cohort
  - 117/847 pts had surgery/anesthesia < 3yrs
- At 10 year of age
  - Higher incidence of language problems and ICD9 diagnosis
  - No difference in standardized tests

Comparison of Neurodegeneration and Cognitive Impairment in Neonatal Mice Exposed to Propofol or Isoflurane
Sooema Khojasteh, M.D., Grace Liang, M.D., Zhen Wu, Ph.D., Huafeng Wei, M.D., Ph.D.
University of Pennsylvania, Philadelphia, Pennsylvania, United States

Isoflurane Exposure in Neonatal Rats Is Not Associated With Social Avoidance in Early Adulthood
Jacqueline S. Leary, M.D., Meredith M. Pace, M.D., Michael G. Holmes, M.D., Jennifer M. O’Donnell, Student, Christine D. Bub, Student, Kyle Anks, B.S., Michael L. Beach, M.D., Gregory L. Holmes, M.D., Rod Scott, M.D., Ph.D., Simon C. Hiller, M.D.
Dartmouth Hitchcock Medical Center, Lebanon, New Hampshire, United States

Should we wait?
- What should we tell families?
- Informed consent?

And now for something completely different...
Continuous nerve blocks

- >1200 patients
- 254 with 2 catheters
- 98.9% placed after general anesthesia
- Full barrier protection
- Low conc of ropivacaine for home
- Pain service followed up with 1-2 phone calls per day

Pts with 2 catheters

Table 1. Descriptive Data Regarding the Ambulatory Continuous Peripheral Nerve Block Catheters

<table>
<thead>
<tr>
<th>Site</th>
<th>Placed</th>
<th>Success (%)</th>
<th>Repetition (%)</th>
<th>Rate (ml/h)</th>
<th>Duration (h)</th>
<th>Nociception</th>
<th>No.</th>
<th>Radiation</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ankle</td>
<td>3</td>
<td>3 (100)</td>
<td>1/1</td>
<td>7</td>
<td>7 (4-11)</td>
<td>2/4</td>
<td>0</td>
<td>0/1</td>
<td>0/1</td>
</tr>
<tr>
<td>Forearm</td>
<td>95</td>
<td>95 (100)</td>
<td>25/80</td>
<td>12</td>
<td>13 (6-18)</td>
<td>8 (1-20)</td>
<td>9</td>
<td>9/1</td>
<td>9/1</td>
</tr>
<tr>
<td>Infrapatellar</td>
<td>41</td>
<td>41 (100)</td>
<td>18/64</td>
<td>13</td>
<td>13 (8-20)</td>
<td>8 (1-20)</td>
<td>4</td>
<td>4/1</td>
<td>4/1</td>
</tr>
<tr>
<td>Suprapatellar</td>
<td>35</td>
<td>35 (100)</td>
<td>19/64</td>
<td>12</td>
<td>12 (6-18)</td>
<td>8 (1-20)</td>
<td>3</td>
<td>3/1</td>
<td>3/1</td>
</tr>
<tr>
<td>Total</td>
<td>265</td>
<td>265 (100)</td>
<td>19/64</td>
<td>12</td>
<td>13 (6-18)</td>
<td>8 (1-20)</td>
<td>3</td>
<td>3/1</td>
<td>3/1</td>
</tr>
</tbody>
</table>

Full barrier protection
- Low conc of ropivacaine for home

Pain service followed up with 1-2 phone calls per day

Our Data

Table 2. Patients With 2 Continuous Peripheral Nerve Block Catheters

<table>
<thead>
<tr>
<th>Region</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Axillary</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Forearm</td>
<td>6</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>Ankle</td>
<td>3</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Infrapatellar</td>
<td>3</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Suprapatellar</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
<td>16</td>
<td>32</td>
</tr>
</tbody>
</table>

Table 3. Complications Related to the Continuous Peripheral Nerve Block Catheters

<table>
<thead>
<tr>
<th>Complications</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excessive leakage</td>
<td>15</td>
</tr>
<tr>
<td>Accidental catheter removal</td>
<td>24</td>
</tr>
<tr>
<td>Accidental vascular injury</td>
<td>1</td>
</tr>
<tr>
<td>Catheter failure</td>
<td>4</td>
</tr>
<tr>
<td>Repeat bolus needed</td>
<td>10</td>
</tr>
<tr>
<td>Local anesthetic related side effects</td>
<td>5</td>
</tr>
<tr>
<td>Catheter site problems</td>
<td>3</td>
</tr>
<tr>
<td>Difficulty removing catheter</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>64</td>
</tr>
</tbody>
</table>
Ketorolac


Trend towards lower clearance in younger patients.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age range</th>
<th>Dose</th>
<th>Clearance (mL/kg/h)</th>
<th>ED50 (mL/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chappell et al. 2003</td>
<td>40-60 kg</td>
<td>IV 60 mg</td>
<td>8.5</td>
<td>Good compliance</td>
</tr>
<tr>
<td>Aronson et al. 2005</td>
<td>40-60 kg</td>
<td>IV 60 mg</td>
<td>8.3</td>
<td>Good compliance</td>
</tr>
<tr>
<td>Devlin et al. 2007</td>
<td>40-60 kg</td>
<td>IV 60 mg</td>
<td>8.2</td>
<td>Good compliance</td>
</tr>
<tr>
<td>Ayres et al. 2008</td>
<td>40-60 kg</td>
<td>IV 60 mg</td>
<td>8.1</td>
<td>Good compliance</td>
</tr>
<tr>
<td>Chen et al. 2009</td>
<td>40-60 kg</td>
<td>IV 60 mg</td>
<td>8.0</td>
<td>Good compliance</td>
</tr>
<tr>
<td>Joll et al. 2010</td>
<td>40-60 kg</td>
<td>IV 60 mg</td>
<td>7.9</td>
<td>Good compliance</td>
</tr>
</tbody>
</table>

**Trend towards more rapid clearance**

**Small #s**

**Appears safe**

In 30/30 critically ill infants 3-16 months old, IO was successfully used in emergency surgery.

- Minor side effects: extravasation and cellulitis

### Anesthesia through an intravenous line using an 18-gauge intravenous needle for emergency pediatric surgery.

- IV induction with 4mg/kg propofol + 2 ug/kg fentanyl +/- mivacurium
- Less Heart rate variability with NMB than without

- Children aged 2-6
- EMLA and rectal midazolam premed
- IV induction with 4mg/kg propofol + 2 ug/kg fentanyl +/− mivacurium
- Less Heart rate variability with NMB than without

- Sevo induction
- Caudal with bup 0.25% 1 ml/kg
- LMA
- Dixon up and down methodology
- ED50 for airway removal-3.4%
- ED90 for airway removal-4.13%
Come back next year