Premedication for Non-Emergency Endotracheal Intubation in the Neonate

Committee on Fetus and Newborn Section on Anesthesiology and Pain Medicine American Academy Of Pediatrics

Praveen Kumar, MBBS, DCH, MD, FAAP
Children’s Memorial Hospital, Chicago
Workshop on Perinatal Practice Strategies
Phoenix, AZ  April 5, 2009
Goals

- Is premedication necessary for non-emergency endotracheal intubation in neonates?
- What should be the recommended safe and effective strategy?
Is Premedication Necessary?

- Do neonates feel pain?
- Is endotracheal intubation painful?
- Is awake intubation associated with adverse outcomes?
- Is use of premedication safe and effective in controlling pain and minimizing the risks of adverse outcomes associated with awake intubation?
Do Neonates Feel Pain?

It was widely believed that the ability to experience pain was related to intelligence, memory and rationality; thus like lower species, babies lacked the mental capacity to suffer pain.
Parent Magazine, April 12, 1987

It may be a matter of life or death

Should Infants Have Surgery Without Anesthesia?
There are risks with anesthesia, and “it doesn’t do any good to have a dead patient who doesn’t feel pain.”
Biological Aspects of Neonatal Pain

- Cutaneous sensory receptors
- Nociceptive nerve endings density
- Pain pathways
- Cortical and subcortical centers
- Neurochemical systems for pain transmission
Physiologic Responses to Pain

Cardiorespiratory Changes

↑ in Heart rate
↑ in Respiratory rate
↑ in Blood pressure
↓ decrease in O2 Saturations

Hormonal Changes

↑ in Cortisol
↑ in Catecholamines
↑ in Growth Hormone
↑ in Glucagon
↓ in Insulin secretion
Is Endotracheal Intubation Painful?

- No pain (0-2): head u/s, chest x-ray, diaper change
- Discomfort (2-4): nasal prongs, eye exam (no manipulation), nasal/oral suction, NG tube, extubation
- Real pain (4-6): tracheal suction, umbilical cath, bladder cath, S/Q injection, remove CVL/art line
- More pain (6-7): heel stick, I/M injection, venipuncture, peripheral IV, remove chest tube
- Lots of pain (7-8): arterial puncture, tracheal intubation, arterial catheter, CVL catheter
- Unbearable pain (8-10): circumcision, lumbar puncture, chest tube placement, bone marrow biopsy
Advantages of Using Premedication for Intubation

- Better pain control
- Minimizes cardiorespiratory and hormonal changes associated with awake intubation
- Fewer attempts at intubation
- Reduces time needed to intubate
- Reduces incidence of airway trauma
- More humane

Byrne E, MacKinnon R. Arch Dis Child. 2006;91:79
Carbajal R, Eble B, Anand KJS. Semin Perinatol; 2007; 31:309
Is Premedication Necessary?

- Do neonates feel pain?  **YES**
- Is endotracheal intubation painful?  **YES**
- Is awake intubation associated with adverse outcomes?  **YES**
- Is use of premedication safe and effective in controlling pain and minimizing the risks of adverse outcomes associated with awake intubation?  **YES**
Considerable variations in use
More frequently used in term neonates than preterm neonates.
More frequently used for “difficult” intubations.
More frequently used in Level III units compared to Level II units.
Practice of Premedication Use for Elective Intubation in Neonates

- More frequently used in NICUs with written guidelines
- Morphine and fentanyl are the most commonly used drugs while muscle relaxants are used only rarely
- Procedural pain in newborns is still underestimated and inadequately managed
Role of Different Premedication Agents

- Opioids or anesthetics reduce pain and can attenuate increases in blood pressure
- Vagolytics prevent vagal bradycardia
- Muscle relaxants either alone or in combination with other agents decrease the time, number of attempts, and can also minimize increases in ICP

Carbajal R, Eble B, Anand KJS. Semin Perinatol; 2007; 31:309
The combination of a sedative or analgesic agent with a vagolytic and muscle relaxant maintains blood pressure, heart rate, ICP and oxygen saturations closest to baseline.

Carbajal R, Eble B, Anand KJS. Semin Perinatol; 2007; 31:309
Gaps in Knowledge

- Optimal pharmaceutical agents and precise doses based on gestational age
- Pharmacokinetics and pharmacodynamics of premedication drugs in the newborns
- Alternative routes of administration
- An ideal sequence of premedication
Proposed Recommendations

- Premedication should be used for *all* endotracheal intubations in newborns *except* emergent intubation during resuscitation.

- Individuals who perform intubations should be:
  - Experienced in the use of bag/mask ventilation and/or laryngeal mask airway
  - Knowledgeable about the effects of laryngoscopy and intubation as well as the risks and benefits of premedication
Proposed Recommendations

- These infants should be monitored for:
  - Cardiorespiratory vitals including BP
  - Oxygen saturation and end-tidal carbon dioxide

- Medications with rapid onset and short duration of action are preferable.
  - Give analgesics.
  - Consider vagolytic agents and rapid onset muscle relaxants.
  - Avoid sedatives without analgesics.
  - Do not use muscle relaxants without analgesics.

- If IV access is not available, consider alternative routes.
Results of Pre-meeting Survey

All neonates irrespective of gestational age and birth weight are capable of perception and transmission of painful stimuli.

Agree 96%
Somewhat agree 4%
Disagree 0%
Results of Pre-meeting Survey

Neonates demonstrate physiologic, behavioral and hormonal responses to painful interventions similar to those seen in older children and adults.

Agree 61%
Somewhat agree 26%
Disagree 12%
Results of Pre-meeting Survey

Pain and its management in neonatal period have no consequences for later pain-related behavior and perception.

Agree 0%
Somewhat agree 5%
Disagree 95%
Results of Pre-meeting Survey

Pain control in neonates is only indicated for operative procedures but not really necessary for brief and infrequent procedures such as intubation, chest tube insertion and lumbar puncture.

Agree 0%
Somewhat agree 11%
Disagree 89%
Neonatal pain is currently being underestimated and undertreated in most NICUs.

Agree      58%
Somewhat agree 39%
Disagree   4%
Thank you for your attention!

Praveen Kumar
p-kumar@northwestern.edu
Anesthesia Definitions

- **Analgesia**: blocking the *conscious* sensation of pain
- **Hypnosis**: producing unconsciousness
- **Amnesia**: preventing *memory* formation
- **Paralysis**: preventing unwanted movement or muscle tone
- **Obtundation**: of reflexes, preventing exaggerated autonomic reflexes
Levels of Anesthesia

- **General anesthesia**
- Deep *sedation*/analgesia
- Moderate *sedation*/analgesia or conscious sedation
- Minimal *sedation* or *anxiolysis*
Levels of Evidence

- Level I: Evidence obtained from at least one properly designed randomized controlled trial.
- Level II-1: Evidence obtained from well-designed controlled trials without randomization.
- Level II-2: Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.
- Level II-3: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled trials might also be regarded as this type of evidence.
- Level III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.
Categories of Recommendations

- **Level A:** Good scientific evidence suggests that the benefits of the clinical service substantially outweigh the potential risks. Clinicians should discuss the service with eligible patients.

- **Level B:** At least fair scientific evidence suggests that the benefits of the clinical service outweigh the potential risks. Clinicians should discuss the service with eligible patients.
Categories of Recommendations

- **Level C**: At least fair scientific evidence suggests that there are benefits provided by the clinical service, but the balance between benefits and risks are too close for making general recommendations. Clinicians need not offer it unless there are individual considerations.

- **Level D**: At least fair scientific evidence suggests that the risks of the clinical service outweighs potential benefits. Clinicians should not routinely offer the service to asymptomatic patients.
Is Endotracheal Intubation Painful?

Limitations of Current Studies

- Small number of patients
- Variable drug regimen and combinations
- Variable outcome measures
- Limited data on short-term and/or long-term outcomes
Perceived Barriers to the Use of Premedication for Intubation

- Newborns are anatomically and functionally incapable of feeling pain
- There is no evidence that neonatal pain has any long-term adverse effects
- Side effects of drugs outweigh the benefits
Perceived Barriers to the Use of Premedication for Intubation

- Concerns about maintaining an adequate airway after premedication
- Intubation can be done quickly and does not require premedication
- Administration of drugs takes too much time
# Practice of Premedication Use for Elective Intubation in Neonates

<table>
<thead>
<tr>
<th>Author</th>
<th>Ziegler et al</th>
<th>Whyte et al</th>
<th>Simon et al</th>
<th>Lago et al</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country</td>
<td>USA</td>
<td>UK</td>
<td>France</td>
<td>Italy</td>
</tr>
<tr>
<td>No. of Units</td>
<td>74</td>
<td>239</td>
<td>75</td>
<td>90</td>
</tr>
<tr>
<td>Level of Care</td>
<td>III</td>
<td>II &amp; III</td>
<td>III</td>
<td>II &amp; III</td>
</tr>
<tr>
<td>Premedication use ( Routinely or Sometimes)</td>
<td>16%</td>
<td>37%</td>
<td>37% (real use)</td>
<td>77%</td>
</tr>
<tr>
<td>Units with policies and protocols</td>
<td>N/R</td>
<td>14%</td>
<td>20%</td>
<td>25%</td>
</tr>
</tbody>
</table>
### Practice of Premedication Use for Elective Intubation in Neonates

<table>
<thead>
<tr>
<th>Author</th>
<th>Sarkar et al</th>
<th>McKechnie et al</th>
<th>Gharavi et al</th>
<th>Carbajal et al</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country</td>
<td>USA</td>
<td>UK</td>
<td>Austria</td>
<td>France</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Germany</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Switzerland</td>
<td></td>
</tr>
<tr>
<td>No. of Units</td>
<td>78</td>
<td>192</td>
<td>225</td>
<td>13</td>
</tr>
<tr>
<td>Level of Care</td>
<td>III</td>
<td>II &amp; III</td>
<td>II &amp; III</td>
<td>III</td>
</tr>
<tr>
<td>Premedication use ( Routinely or Sometimes )</td>
<td>72%</td>
<td>N/R</td>
<td>83%</td>
<td>59% (real use)</td>
</tr>
<tr>
<td>Units with policies and protocols</td>
<td>24%</td>
<td>70%</td>
<td>44%</td>
<td>N/R</td>
</tr>
</tbody>
</table>
# Frequently Used Premedications for Intubations in Newborn

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sedatives/Analgesics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>Diamorphine</td>
<td>√</td>
<td>x</td>
<td>x</td>
<td>√</td>
<td>x</td>
</tr>
<tr>
<td>Pethidine</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Diazepam</td>
<td>√</td>
<td>√</td>
<td>x</td>
<td>x</td>
<td>√</td>
</tr>
<tr>
<td>Midazolam</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>x</td>
<td>x</td>
<td>√</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Ketamine</td>
<td>√</td>
<td>√</td>
<td>x</td>
<td>x</td>
<td>√</td>
</tr>
<tr>
<td>Phenobarbitol</td>
<td>√</td>
<td>x</td>
<td>√</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Chloral Hydrate</td>
<td>x</td>
<td>√</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Tramadol</td>
<td>x</td>
<td>√</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>x</td>
<td>√</td>
<td>x</td>
<td>x</td>
<td>√</td>
</tr>
</tbody>
</table>
**Frequently used Premedications for Intubations in Newborns**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle Relaxant</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Succinylcholine</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>x</td>
</tr>
<tr>
<td>Atracurium</td>
<td>√</td>
<td>x</td>
<td>x</td>
<td>√</td>
<td>x</td>
</tr>
<tr>
<td>Pancuronium</td>
<td>√</td>
<td>x</td>
<td>√</td>
<td>√</td>
<td>x</td>
</tr>
<tr>
<td>Vecuronium</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Miracurium</td>
<td>x</td>
<td>√</td>
<td>√</td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Vagolytics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atropine</td>
<td>x</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>x</td>
</tr>
</tbody>
</table>
AAP Publications

- **Policy statements** - organizational principles to guide and define the child health care system and/or improve the health of all children
- **Clinical reports** - guidance for the clinician in rendering pediatric care
- **Technical reports** - background information to support AAP policy
Systematic Reviews and Meta-analyses

Randomized Controlled Double Blind Studies

Randomized Controlled Double Blind Studies

Cohort Studies

Case Control Studies

Case Series

Case Reports

Ideas, Editorials, Opinions

Animal research

In vitro ('test tube') research
Median Numbers, Interquartile Ranges, and Extreme Values of Painful Procedures Performed per Day of Neonatal ICU or Pediatric ICU hospitalization

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Procedures, No. (%)</th>
<th>Nonpharmacological Only</th>
<th>Pharmacological Only</th>
<th>Nonpharmacological, Pharmacological, or Both</th>
<th>Nonspecific Concurrent Analgesia, %</th>
<th>Some Form of Analgesia, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal aspiration</td>
<td>12,269 (28.9)</td>
<td>5.4</td>
<td>0.9</td>
<td>6.3</td>
<td>31.6</td>
<td>36.5</td>
</tr>
<tr>
<td>Tracheal aspiration</td>
<td>9,683 (23.3)</td>
<td>4.2</td>
<td>2.3</td>
<td>6.6</td>
<td>51.9</td>
<td>55.5</td>
</tr>
<tr>
<td>Heal stick</td>
<td>8,396 (19.8)</td>
<td>42.5</td>
<td>1.2</td>
<td>44.0</td>
<td>24.7</td>
<td>62.2</td>
</tr>
<tr>
<td>Adhesive removal</td>
<td>5,376 (12.7)</td>
<td>19.5</td>
<td>0.8</td>
<td>20.7</td>
<td>30.1</td>
<td>48.0</td>
</tr>
<tr>
<td>Gastric tube insertion</td>
<td>1,037 (2.4)</td>
<td>10.9</td>
<td>0.6</td>
<td>11.5</td>
<td>13.1</td>
<td>23.4</td>
</tr>
<tr>
<td>Venipuncture</td>
<td>757 (1.8)</td>
<td>66.6</td>
<td>3.8</td>
<td>71.9</td>
<td>22.3</td>
<td>81.6</td>
</tr>
<tr>
<td>Arterial puncture</td>
<td>755 (1.8)</td>
<td>54.6</td>
<td>10.3</td>
<td>70.1</td>
<td>32.3</td>
<td>82.4</td>
</tr>
<tr>
<td>Intravenous cannula</td>
<td>576 (1.4)</td>
<td>67.5</td>
<td>2.4</td>
<td>71.2</td>
<td>18.4</td>
<td>80.2</td>
</tr>
<tr>
<td>Chest physiotherapy</td>
<td>551 (1.3)</td>
<td>6.5</td>
<td>1.6</td>
<td>8.2</td>
<td>30.9</td>
<td>37.4</td>
</tr>
<tr>
<td>Removal of intravenous line</td>
<td>491 (1.2)</td>
<td>41.3</td>
<td>1.4</td>
<td>43.8</td>
<td>22.4</td>
<td>60.1</td>
</tr>
<tr>
<td>Wound treatment</td>
<td>368 (0.9)</td>
<td>23.6</td>
<td>3.0</td>
<td>26.6</td>
<td>23.1</td>
<td>45.1</td>
</tr>
<tr>
<td>Tracheal extubation</td>
<td>280 (0.7)</td>
<td>4.3</td>
<td>2.1</td>
<td>6.4</td>
<td>12.5</td>
<td>17.1</td>
</tr>
<tr>
<td>Central catheter</td>
<td>240 (0.6)</td>
<td>35.0</td>
<td>27.5</td>
<td>71.7</td>
<td>28.8</td>
<td>88.3</td>
</tr>
<tr>
<td>Finger stick</td>
<td>238 (0.6)</td>
<td>16.4</td>
<td>0.8</td>
<td>17.2</td>
<td>25.2</td>
<td>42.0</td>
</tr>
<tr>
<td>Venous umbilical catheter</td>
<td>208 (0.5)</td>
<td>7.2</td>
<td>3.8</td>
<td>11.1</td>
<td>25.5</td>
<td>32.7</td>
</tr>
<tr>
<td>Bladder compression</td>
<td>195 (0.5)</td>
<td>1.0</td>
<td>3.6</td>
<td>4.6</td>
<td>84.1</td>
<td>96.2</td>
</tr>
<tr>
<td>Chest tube drainage</td>
<td>155 (0.4)</td>
<td>4.5</td>
<td>34.8</td>
<td>39.4</td>
<td>81.9</td>
<td>84.5</td>
</tr>
<tr>
<td>Tracheal intubation</td>
<td>101 (0.2)</td>
<td>0.0</td>
<td>41.6</td>
<td>42.6</td>
<td>29.7</td>
<td>59.4</td>
</tr>
<tr>
<td>Physiotherapy</td>
<td>75 (0.2)</td>
<td>10.7</td>
<td>4.0</td>
<td>14.7</td>
<td>61.3</td>
<td>73.3</td>
</tr>
<tr>
<td>Subcutaneous injection</td>
<td>69 (0.2)</td>
<td>85.5</td>
<td>1.4</td>
<td>88.4</td>
<td>7.2</td>
<td>92.8</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>323 (0.8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>42,413 (100)</td>
<td>18.2</td>
<td>2.1</td>
<td>20.8</td>
<td>34.2</td>
<td>50.9</td>
</tr>
</tbody>
</table>

*a* Data are proportions of procedures carried out with analgesic treatment. Blank space indicates not applicable.

The proportion of procedures performed with no specific analgesia given prior to the procedure is obtained by subtracting the value of this column from 100 (for example, for Total, 100 − 20.8 = 79.2%).

*c* Some form of analgesia refers to the use of specific analgesia, nonspecific concurrent continuous analgesia, or both.

*d* For blood sampling.

*e* Peripherally inserted central catheter.

*f* Involves manipulation of the umbilical cord skin and usually a suture on the skin.

*g* For urine retention.

*h* Maneuvers to mobilize secretions.

*i* Other than chest.

*j* Including 16 chest tube placements and 38 lumbar punctures.