

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

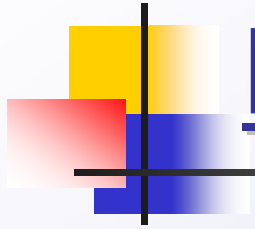
Should Infants
Have Surgery
Without
Anesthesia?



Medical Community Response

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

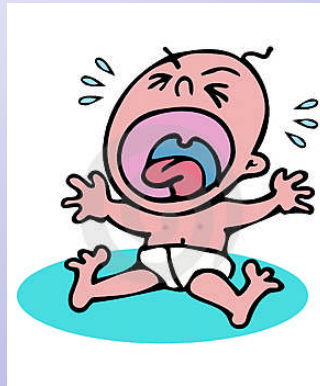


- Cutaneous sensory receptors
- Nociceptive nerve endings density
- Pain pathways
- Cortical and subcortical centers
- Neurochemical systems for pain transmission

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

Shah V, Ohlsson A. Clin Perinatol 2002;29:535

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*



Practice of Premedication Use for Elective Intubation in Neonates

- 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

Role of Different Premedication Agents

- 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.



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%



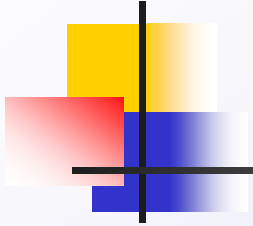
Results of Pre-meeting Survey

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

- Analgnesia: 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

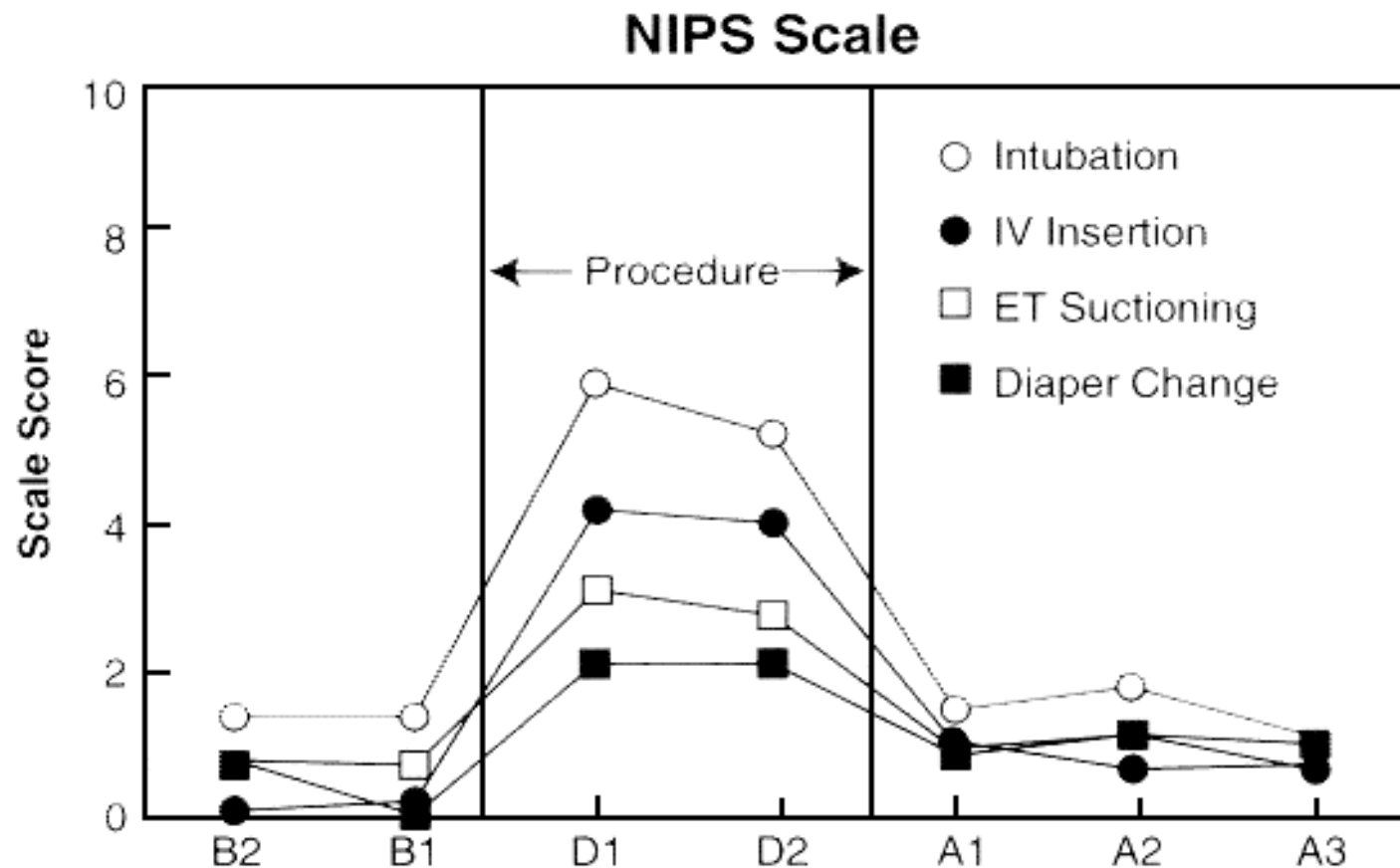
- Level A: Good scientific evidence suggests that the benefits of the clinical service substantially outweighs the potential risks. Clinicians should discuss the service with eligible patients.
- Level B: At least fair scientific evidence suggests that the benefits of the clinical service outweighs the 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?



Blauer, T. Gertsman, D. *Clin J Pain* 1998; 14:39-47



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

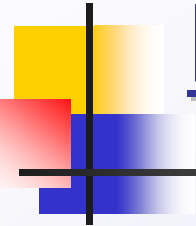
- Newborns are anatomically and functionally incapable of feeling pain
- There is no evidence that neonatal pain has any long-term adverse effects
- Side effects of drugs outweigh the benefits



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



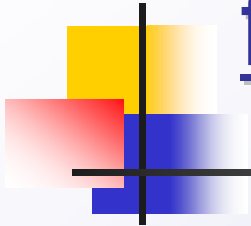
Author	Ziegler et al	Whyte et al	Simon et al	Lago et al
Study Period	1991	1998	2001	2003
Country	USA	UK	France	Italy
No. of Units	74	239	75	90
Level of Care	III	II & III	III	II & III
Premedication use (Routinely or Sometimes)	16%	37%	37% (real use)	77%
Units with policies and protocols	N/R	14%	20%	25%

Practice of Premedication Use for Elective Intubation in Neonates



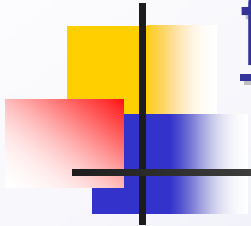
Author	Sarkar et al	McKechnie et al	Gharavi et al	Carbajal et al
Study Period	2005	2005	2005	2006
Country	USA	UK	Austria Germany Switzerland	France
No. of Units	78	192	225	13
Level of Care	III	II & III	II & III	III
Premedication use (Routinely or Sometimes)	72%	N/R	83%	59% (real use)
Units with policies and protocols	24%	70%	44%	N/R

Frequently Used Premedications for Intubations in Newborn



<u>Author</u>	<u>Whyte et al 2000</u>	<u>Lago et al 2005</u>	<u>Sarkar et al 2006</u>	<u>McKechine et al 2005</u>	<u>Gharavi et al 2005</u>
<u>Sedatives/Analgesics</u>					
Morphine	√	√	√	√	√
Fentanyl	√	√	√	√	√
Diamorphine	√	x	x	√	x
Pethidine	x	x	x	x	x
Diazepam	√	√	x	x	√
Midazolam	√	√	√	√	√
Lorazepam	x	x	√	x	x
Ketamine	√	√	x	x	√
Phenobarbitol	√	x	√	x	x
Chloral Hydrate	x	√	x	x	x
Tramadol	x	√	x	x	x
Lidocaine	x	√	x	x	√

Frequently used Premedications for Intubations in Newborn



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<u>Muscle Relaxant</u>					
Succinylcholine	√	√	√	√	x
Atracurium	√	x	x	√	x
Pancuronium	√	x	√	√	x
Vecuronium	√	√	√	x	x
Miracurium	x	√	√	x	x
<u>Vagolytics</u>					
Atropine	x	√	√	√	x

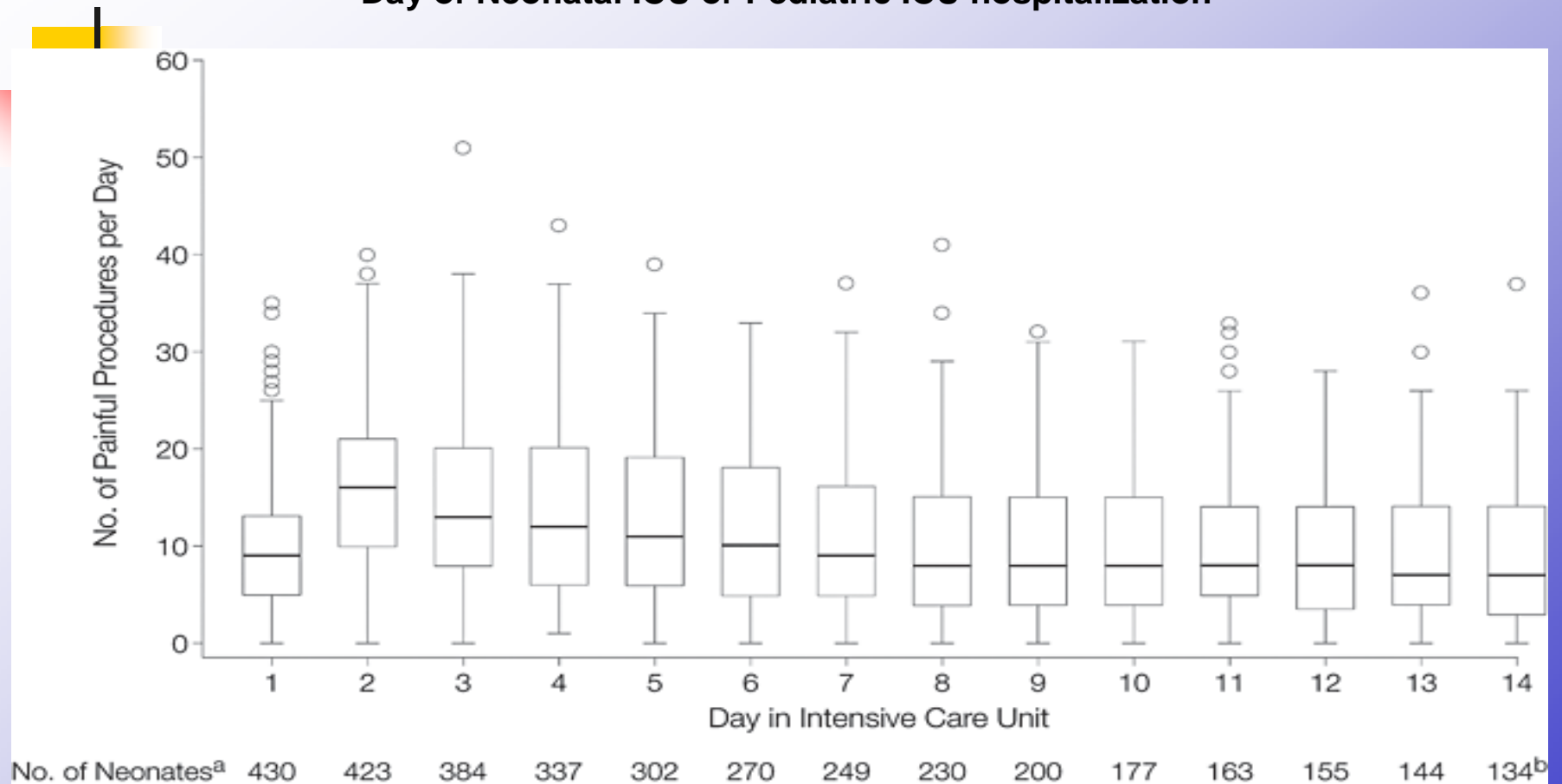


AAP Publications

- 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



Median Numbers, Interquartile Ranges, and Extreme Values of Painful Procedures Performed per Day of Neonatal ICU or Pediatric ICU hospitalization



Carbajal, R. et al. JAMA 2008;300:60-70.

Table 2. Analgesic Treatment of the 20 Most Frequent Painful Procedures Performed in 430 Neonates^a

Procedure	Procedures, No. (%)	Specific Analgesia Prior to Procedure, %			Nonspecific Concurrent Continuous Analgesia, %	Some Form of Analgesia, % ^c
		Nonpharmacological Only	Pharmacological Only	Nonpharmacological, Pharmacological, or Both ^b		
Nasal aspiration	12 269 (28.9)	5.4	0.9	6.3	31.6	36.5
Tracheal aspiration	9883 (23.3)	4.2	2.3	6.6	51.9	55.5
Heel stick	8396 (19.8)	42.5	1.2	44.0	24.7	62.2
Adhesive removal	5376 (12.7)	19.5	0.8	20.7	30.1	48.0
Gastric tube insertion	1037 (2.4)	10.9	0.6	11.5	13.1	23.4
Venipuncture ^d	757 (1.8)	66.6	3.8	71.9	22.3	81.6
Arterial puncture ^d	755 (1.8)	54.6	10.3	70.1	32.3	82.4
Intravenous cannula	576 (1.4)	67.5	2.4	71.2	18.4	80.2
Chest physiotherapy	551 (1.3)	6.5	1.6	8.2	30.9	37.4
Removal of intravenous line	491 (1.2)	41.3	1.4	43.8	22.4	60.1
Wound treatment	368 (0.9)	23.6	3.0	26.6	23.1	45.1
Tracheal extubation	280 (0.7)	4.3	2.1	6.4	12.5	17.1
Central catheter ^e	240 (0.6)	35.0	27.5	71.7	28.8	88.3
Finger stick	238 (0.6)	16.4	0.8	17.2	25.2	42.0
Venous umbilical catheter ^f	208 (0.5)	7.2	3.8	11.1	25.5	32.7
Bladder compression ^g	195 (0.5)	1.0	3.6	4.6	84.1	86.2
Chest tube drainage ^h	155 (0.4)	4.5	34.8	39.4	81.9	84.5
Tracheal intubation	101 (0.2)	0.0	41.6	42.6	29.7	59.4
Physiotherapy ⁱ	75 (0.2)	10.7	4.0	14.7	61.3	73.3
Subcutaneous injection	69 (0.2)	85.5	1.4	88.4	7.2	92.8
Miscellaneous ^j	323 (0.8)					
Total	42 413 (100)	18.2	2.1	20.8	34.2	50.9

^aData are proportions of procedures carried out with analgesic treatment. Blank space indicates not applicable.

^bThe 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.

^dFor blood sampling.

^ePeripherally inserted central catheter.

^fInvolves manipulation of the umbilical cord skin and usually a suture on the skin.

^gFor urine retention.

^hManeuvers to mobilize secretions.

ⁱOther than chest.

^jIncluding 16 chest tube placements and 38 lumbar punctures.