Viewing Time

The program will take up to one hour to complete.

Target Audience

This program is designed for primary care physicians.

Other health care professionals working with patients and their families may also find this program of interest.

Faculty Disclosure

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Pain in the NICU: A Closer Look at Non-Emergent Intubations

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Pain in the NICU: A Closer Look at Non-Emergent Intubations

A lecture presenting the historical background, embryology, and physiology of pain in a neonate, as well as the physiological effects and importance of premedication of non-emergent intubations in the NICU.

Program Objectives

Upon completion of this program, participants should be able to:

- Understand the historical background, embryology, and physiology of pain in a neonate.
- Understand the adverse physiologic effects of endotracheal intubation.
- Recognize the importance of premedication for non-emergent intubations in the NICU.

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Receiving CME Credit

To receive CME credit you must view the entire program and complete the evaluation form at the end.

Pain in the NICU: A Closer Look at Non-Emergent Intubations

Kari Roberts, M.D.
Pediatric Grand Rounds
February 14, 2008

Outline:

I. Introduction
II. Historical Background
III. Embryology
IV. Intubation: Physiologic Responses
V. Intubation: Current Practice
VI. Research Study

Premedication for Non- Emergent Neonatal Intubations: A Randomized, Controlled Trial Comparing Atropine and Fentanyl to Atropine, Fentanyl and Mivacurium

Pediatrics. 2006; 118(4): 1583-1591

"It is a contradiction that most of us do not notice- we routinely impose pain on sick and vulnerable infants."

McGrath
"The Social Context of Pain"
Clinics in Perinatology, 2002

Sick neonates are among the most vulnerable members of our society.

- No ability to protect themselves
- No ability to ask for something to ameliorate pain
- No ability to protest about their pain experiences

However…..

Newborns in the NICU are subject to numerous painful procedures:

- Heel sticks
- Venipunctures
- Lumbar puncture
- Line placement
- Chest tube placement
- Intubation
- ETT suction
- Injections

Pain in newborns is often unrecognized and undertreated.

1997: Survey of Canadian NICUs

- n= 239 babies
- Total of 2134 invasive procedures over 1 week
- Approximately 9 procedures/baby/week
- Pain medication given 0.8%

Historical:

- Plato (400 BC): All feelings was essentially painful
- Felix Wurtz, M.D. 1600's:
  "If a new skin in old people be tender…what shall we think of a Child, which stayed not in the womb its full time? Surely it is twice worse with him."
- 1970's:
  - Rudimentary knowledge of how to safely anesthetize
  - Inadequate monitoring equipment (no oximeters, EKG monitors)
  - Belief that dosage requirement of anesthesia needed for neonates was much greater than for older children
  - Fear of hypotension and bradycardia with anesthesia
  - Belief that newborns didn't feel pain

Changing beliefs and attitudes about neonatal pain over past 20 years.

Survey pediatric anesthesiologists in UK and Ireland

- 1988: Purcell- Jones
  - Newborns did not feel pain: 13%
  - Neonates did not feel pain: 7%
  - Undecided: 23%
- 1996: de Lima
  - Universal agreement that newborns and neonates felt pain

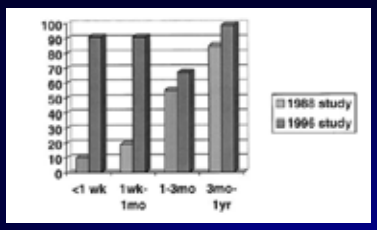


Fig. 1. Percentage of pediatric anesthetists reporting that they always or usually used systemic opioids in babies of different ages following major surgery.

Purcell-Jones G, et al. *Pain*. 1988; 33:181–7
de Lima J, et al. *BMJ*. 1996; 313:787

Why the change in beliefs?

"Change is a social process that requires social influence as well as scientific and technical knowledge."

"Lobbying, especially by parents, produces powerful social and public pressure that can (and has) resulted in rapid changes in health care."

McGrath, 2002

Jeffrey Lawson Story

1985: Born 1 pound, 11 oz
PDA ligation surgery

Jeffrey had holes cut on both sides of his neck, another cut in his right chest, an incision from his breastbone around to his backbone, his ribs pried apart, and an extra artery near his heart tied off. This was topped off with another hole cut in his left side for a chest tube. This operation lasted hours. Jeffrey was awake through it all. The anesthesiologist paralyzed him with Pavulon, a curare drug that left him unable to move, but totally conscious. When I questioned the anesthesiologist later about her use of Pavulon, she said Jeffrey was too sick to tolerate powerful anesthetics. Anyway, she said, it had never been demonstrated to her that premature babies feel pain. [13]

Lawson JR. Letter to the editor. *Birth*, 1986

1986: *Washington Post* ran Jeffrey Lawson story

1996: American Pain Society established "Jeffrey Lawson Award" to recognize advocacy in pediatric pain

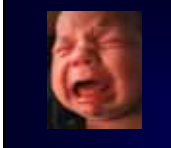
Leora Kuttner, PhD, 2007
Bonnie Stevens, PhD RN, 2006
Lonnie K. Zeltzer, MD, 2005
Patricia A. McGrath, PhD, 2004
Gary A. Walco, 2003
Kenneth D. Craig, 2002
Charles B. Berde, 2001
Kanwaljeet S. Anand, 2000
Lucia Benini, 1999
Neil L. Schechter, 1998
Joann Eland, 1997
Jill Lawson, 1996


Dennis Turk presents the Jeffrey Lawson Award to Lonnie Zeltzer.

Research

1985: Dr Anand reviewed prevalence of minimal anesthesia for surgical correction of PDA
- n=1157 neonates
- 77% given muscle relaxant without analgesia

Pilot study:
- Massive stress response occurred in all babies.
- Deep anesthesia substantially blunted stress response and may contribute to better clinical outcomes



Do neonates feel pain?



Embryology:

- 6 wks: Developing sensory neurons begin to synapse with the interneurons in the dorsal horn of the spinal cord
- Sensory neurons grow peripherally:
  - 7 wks: perioral to face
  - 15 wks: trunk and proximal arms/ legs
  - 20 wks: remaining cutaneous and mucosal surfaces
- By 20 weeks the peripheral and ascending pain pathways are mature

- Number of nociceptive (pain sensing) nerve endings is equal to or greater in density than those in adult skin
- Pain inhibitory tracts not fully functional
  ➔ increased transmission of painful stimuli

Result…

Newborns may actually experience *more* pain than adults

So, newborns feel pain…

But do they remember it?

Babies exposed to painful stimuli may have some memory of the experience:

Taddio, 1997. n=87
- Reaction to routine vaccination at 4 or 6 months of age
- Circumcised vs uncircumcised

Results:
Circumcised infants exhibited higher percentage of:
- cry duration
- facial action
- visual analog pain scale

Taddio, 2002. n=42

- Compared response to venipuncture for newborn screening test
- IDM babies who underwent repeat heel sticks during first 24-36 hrs of life vs no heel-stick

Results:

IDM babies showed:

- More grimacing during skin cleansing (22% vs 0%)
- Higher median scores for
  - grimacing
  - crying
  - visual analog pain scale

Concluded babies learn to anticipate pain and exhibit more intense pain responses

So, newborns feel pain…
Newborns remember it.

What can we do to improve the experience?

Intubations:

- Tracheal intubation is a procedure frequently performed in the NICU
- Often part of initial resuscitation or performed emergently for apnea
- However, often performed on semi-elective basis for air leaks, worsening respiratory distress, accidental extubation, or prior to surgical procedures
- Current practice:
  - Ranges from "awake intubation" (without pre-medication) to any number of combinations of meds

Studies:

Physiologic changes during intubation:

- **HR**
- **BP**
- **SaO_2**
- **ICP**

Heart Rate:

Bradycardia reported in response to awake and anesthesized intubation.

- Bradycardia associated with laryngeal stimulation and increased vagal tone
- Bradycardia common with use of succinylcholine
- Bradycardia prevented by use of atropine

Babies dependent on HR for their cardiac output
CO= HR x SV

Blood Pressure:

Awake intubation causes fluctuations in blood pressure and an acute hypertensive response:

Belfort 1993: n=17 neonatal piglets

- BP increased 45% with intubation
- Remained elevated for 14 minutes

Marshall 1984: n=10 preterm infants

- BP increased 47% when trachea intubated

Blood pressure:

Changes in BP modulated by pre-medication:

Khammash 1993. n=28

- BP increased by 20% if using atropine alone
- BP increased by 4% above baseline with atropine/fentanyl/succinylcholine

SaO_2:

Awake intubation is associated with more severe and prolonged hypoxia.

Anesthesia and paralysis reduces number of attempts and time to successful intubation, thereby reducing severity and duration of hypoxia.

Author	Drugs	Successful First Attempts	Time
Cook-Sather[7]	Awake (no medication) vs thiopental/succinylcholine	64% vs. 87%	63 sec vs. 34 sec
Barrington[8]	Atropine vs. Atropine/succinylcholine		129 sec vs. 53 sec
Pokela[6]	Pethidine vs. Alfentanyl/succinylcholine	30% vs. 70%	120 sec vs. 60 sec
Bhutada[9]	Awake (no medication) vs. Thiopental		5.08 min vs. 2.7 min
Khammash[4]	Atropine vs. Atropine/ Fentanyl/Succinylcholine		50 sec vs. 24 sec
Oei[13]	Awake (no medication) vs. Atropine/Morphine/Succinylcholine		595 sec vs. 60 sec
Barrington[14]	Atropine/Fentanyl/Succinylcholine	88%	

Intracranial Pressure:

Changes in anterior fontanelle pressure (AFP) reflect changes in ICP.

Friesen, 1987. n=12

- Atropine: Increase AFP of 197%
- Atropine/pancuronium: No change AFP

Friesen, 1987

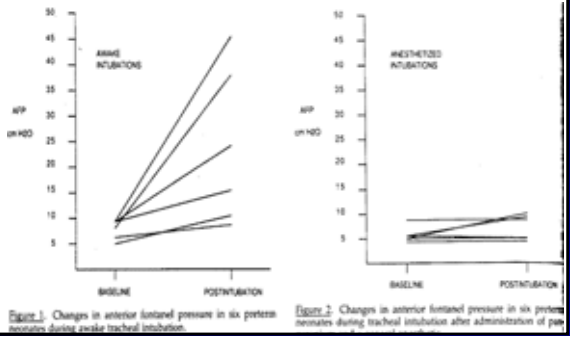


Figure 1. Changes in anterior fontanel pressure in six preterm neonates during awake tracheal intubation.

Figure 2. Changes in anterior fontanel pressure in six preterm neonates during tracheal intubation after administration of pan

Intracranial Pressure:

- Barrington, 1989. n=20.
  - Atropine: Statistically significant increase ICP
  - Atropine/succinylcholine: No change ICP
- Millar, 1994. N=13
  - Atropine: Statistically significant increase ICP
  - Atropine/thiopentone/succinylcholine: No change

Millar, 1994

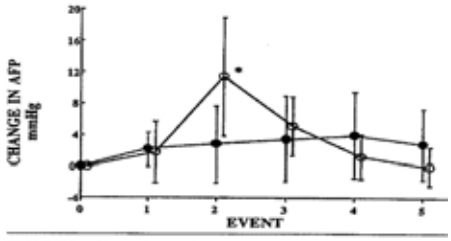


FIGURE 3 Change in anterior fontanelle pressure (AFP) from baseline in the awake (○) and anaesthetised groups (●) (* $P < 0.05$). Events: 0 = baseline, 1 = post-atropine, 2 = laryngoscopy, 3 = post-intubation, 4 = 1 minute post-intubation, 5 = 5 minutes post-intubation.

Summary of Physiologic Effects of Intubation:

- HR: Bradycardia
- BP: HTN
- SaO_2: Hypoxia
- ICP: Increased

Effects can be blunted with premedication

Summary:

- Atropine blocks bradycardia associated with endotracheal intubation
- Muscle relaxants attenuate increase in ICP
- Atropine, analgesic, and muscle relaxant maintain HR, BP, SaO_2, and ICP closest to baseline

Sounds like premedication is a good idea…
Is anyone using it?

Surveys:

Five Surveys conducted in NICU's looking at pre-medication for non-emergent intubations:

- Zeigler, Todres: *Am J Dis Child*. 1992
- Fernandez, Rees: *Canadian Med J*. 1994
- Whyte: *Arch Dis Child*. 2000
- Vogel: *Paediatric Res*. 2000
- Sarkar: *J Perinatology*. 2006

Zeigler and Todres, 1992

n= 101 University- affiliated NICU's in U.S.
Atropine:

- 100% denied routine use of atropine
  - 82% unnecessary
  - 22% not beneficial
  - 15% contraindicated (dry secretions, mask bradycardia from hypoxia)
  - 4% efficacy not proven

Sedatives:

- 84% never/ rarely
- 13% sometimes
- 3% routinely

Muscle Relaxants:

- 97% never/rarely
- 3% sometimes
- 0% routinely

Fernandez and Rees, 1994

n= 30 Canadian Level 3 NICU's

Sedation:
- 73% never/ rarely

Analgesia:
- 84% never/rarely

Muscle relaxant:
- 20% used alone to facilitate intubation

Whyte, 2000

n= 241 NICU's in United Kingdom

Sedation:
- 63% never/rarely
- 37% used
  - 66% Morphine
  - 9% Fentanyl
  - 11% Diazepam
  - 6% Midazolam

Muscle Relaxant:
- 22% used (always co-administered with sedation)

14% written policy

Vogel, 2000

n=263 neonatologists in Canada

Premedication used to some degree:
- 68% Group I (< 30 wks gestation)
- 76% Group II (30-37 wks gestation)
- 87% Group III (>37 wk gestation)

Reasons for not using premedication:
- Insufficient evidence (49%, 33%, 31%)
- No need (31%, 30%, 23%)
- Lack of comfort (17%, 26%, 23%)

Sarkar, 2006

n= 78 University- affiliated NICU's in U.S.

Premedication used
- Always: 44%
- Some: 28%
- Never: 28%

Atropine: 16%
Paralytic: 25%
Atropine/ Analgesic/ Paralytic: 12.5%

Sarkar, 2006

Analgesic
- Morphine or Fentanyl alone: 57%
- Morphine or Fentanyl plus Versed: 27%
- Versed alone: 12%
- Ativan alone: 4%

Paralytic:
- Mivacurium: 50%
- Succinylcholine: 21%
- Vecuronium: 14%
- Pancuronium: 14%

But is pre-medication safe?

Barrington and Byrne, 1998

Recorded incidence of complications for 253 consecutive intubations after instituting a routine policy for pre-medication with atropine/fentanyl/succinylcholine.
- n=194 without incident (77%)
- n=28 required two attempts (11%)
- n=22 required 3+ attempts (9%)
- n=9 required second attempt with smaller ETT (4%)
- n=4 chest wall rigidity (1%).
  - 3 resolved with succinylcholine administration

Medications are safe, feasible, and humane

"It is inconceivable that we should ever go back to a practice of allowing infants to cough, gag, choke, and struggle against a laryngoscope and endotracheal tube."

Barrington, 1998

Pre-medication Pros and Cons:

Pros:
- Less time to intubate
- More first attempt success
- Decreased frequency and duration of hypoxia
- Blunts HTN response
- Avoid increase ICP
- More humane

Cons:
- Time to insert IV
- Time to draw up meds
- Time to administer meds
- Pain with IV insertion
- Risk of adverse side effects of analgesics
- Airway concerns with muscle relaxants

Pilot Data

n=62
November 2002- August 2003

Data Collected:
- Premedication used
- Level of intubator (Intern, senior resident, NNP, fellow, staff)
- Time to intubate
- Number of attempts

Pilot Data

- Premedication being used 74%
  Alone or in combination:
  - Morphine 52%
  - Fentanyl 30%
  - Midazolam 35%
  - Pavulon 2%

Pilot Data

- Time to intubated ≤2 min: 34%
- Number of attempts ≤2: 53%
- Average Time: 4 min 54 sec
  (10sec- 18 min 3sec)
- Average 2.53 attempts/ infant

Research Trial

- Prospective, randomized, controlled trial
- 2 Centers: DHMC and UC-San Diego
- Hypothesis:
  1. Premedication for non-emergent intubations would reduce the duration of hypoxia
  2. Increase the number of successful intubations with attempts ≤ 2 and time ≤ 2 minutes

Research Trial

Eligibility: NICU patients who required *non-emergent* intubation and had IV access

Exclusion criteria:
- Known airway or cardiorespiratory anomalies
- Renal or hepatic insufficiency
- Known neuromuscular disorder
- Hemodynamically unstable

Medications

Control Group:
- Anti-cholinergic: Atropine
- Sedative/Analgesic: Fentanyl

Study Group:
- Anti-cholinergic: Atropine
- Sedative/Analgesic: Fentanyl
- Muscle Relaxant: Mivacurium

Analysis

Videotapes:
- Time
  - Duration from *first* insertion of laryngoscope until laryngoscope is removed after *successful* intubation
- Number of attempts
- Duration of action of mivacurium
- Potential areas of improvement
  - Personnel
  - Equipment
  - Positioning
  - Technique

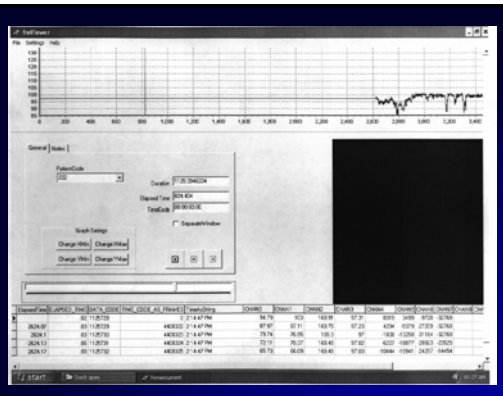
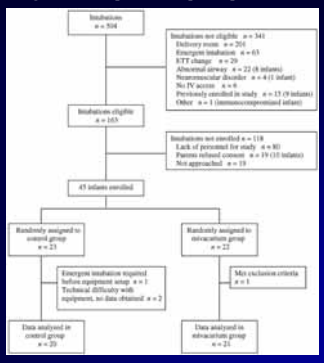


Figure 1. Trial profile and participant flow



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PEDIATRICS

TABLE 1 Baseline Characteristics

Variable	Control Group (n = 20)	Mivacurium Group (n = 21)	P
Birth weight, mean ± SD (range), g	1627 ± 1215 (685–4990)	1420 ± 901 (640–4270)	.538
Weight at time of procedure, mean ± SD (range), g	1687 ± 1187 (754–4990)	1556 ± 912 (660–4270)	.692
Gestational age, mean ± SD (range), wk	30.2 ± 4.9 (24.3–42.0)	29.7 ± 4.3 (24.7–38.1)	.737
Adjusted age, mean ± SD (range), wk	31.6 ± 4.2 (27.1–42.0)	31.0 ± 3.9 (25.0–38.6)	.652
Age at time of procedure, mean ± SD (range), d	9.6 ± 16.7 (0–65)	9.4 ± 16.8 (0–74)	.967
Study center, n (%)			.623
Children's Hospital at Dartmouth	8 (40)	10 (48)	
University of California San Diego Medical Center	12 (60)	11 (52)	
Male, n (%)	9 (45)	13 (62)	.278
5-min Apgar score, median (range)	9 (3–9)	8 (3–9)	.120
Initial intubation, n (%)	13 (65)	12 (57)	.606
FIO_2 before procedure, mean ± SD	0.56 ± 0.30	0.67 ± 0.31	.276
Reason for intubation, n (%)			1.000
Respiratory distress	14 (70)	14 (67)	
Apnea	3 (15)	3 (14)	
Self-extubation	0 (0)	1 (5)	
Preoperative	3 (15)	3 (14)	
Level of training of first intubator, n (%)			.877
Intern	11 (55)	9 (43)	
Resident	5 (25)	7 (33)	
NNP	1 (5)	1 (5)	
Fellow	3 (15)	4 (19)	

Roberts, K. D. et al. Pediatrics 2006;118:1583-1591

PEDIATRICS

Results

TABLE 2 Hypoxia Results

Variable	Control Group (n = 20)	Mivacurium Group (n = 21)	P
Incidence of saturation below threshold, n (%)*			
Sao_2 ≤ 85%	19 (95)	17 (81)	.343
Sao_2 ≤ 75%	13 (65)	11 (52)	.530
Sao_2 ≤ 60%	11 (55)	5 (24)	.041
Sao_2 ≤ 40%	5 (25)	1 (5)	.093
Incidence of saturation exceeding 30 s below threshold, n (%)*			
Sao_2 ≤ 85%	16 (80)	13 (62)	.306
Sao_2 ≤ 75%	11 (55)	6 (29)	.086
Sao_2 ≤ 60%	3 (15)	3 (14)	1.000
Sao_2 ≤ 40%	2 (10)	1 (5)	.606
Duration of saturation below threshold, mean ± SD (range), s			
Sao_2 ≤ 85%	135 ± 166 (0–736)	108 ± 126 (0–386)	.571
Sao_2 ≤ 75%	63 ± 108 (0–476)	36 ± 65 (0–190)	.368
Sao_2 ≤ 60%	25 ± 59 (0–256)	12 ± 33 (0–138)	.389
Sao_2 ≤ 40%	11 ± 31 (0–136)	4 ± 17 (0–76)	.342

*Incidence is defined as ≥1 event meeting definition during intubation procedure.

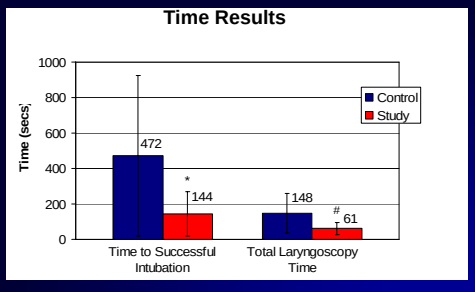
Roberts, K. D. et al. Pediatrics 2006;118:1583-1591

PEDIATRICS

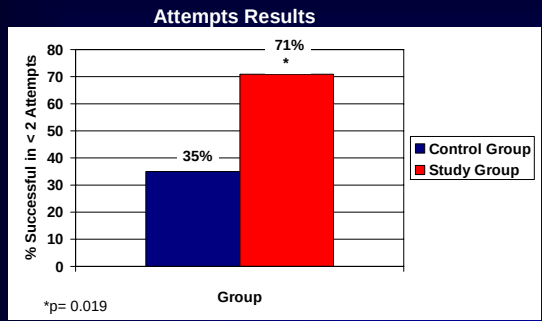
Results

- Heart Rate
  - Change from baseline similar between groups
  - HR < 100
    - n=4
    - Range 74-92 bpm
    - Maintained HR > 100 in 5/6 infants with SaO2 < 40%

Blood Pressure
  - Change from baseline similar between groups



*p=0.003, #p=0.002



*p= 0.019

Results

- Complications
  - Difficulty with bag-mask ventilation n=3
  - Pneumothorax n=1
  - Mouth/lip lacerations n=2
  - Aspiration n=1

Duration of mivacurium:
11 min 26 sec (5-22 minutes)

Results: Summary

Premedication with a muscle relaxant compared to without a muscle relaxant…

- Decreased incidence of SaO2 ≤ 60%
  (55% vs 24%, p=0.041)
- Threefold decrease in total procedure time
  (472 sec vs 144 sec, p=0.003)
- Twofold decrease in total laryngoscope time
  (148 sec vs 61 sec, p=0.002)
- Intubation successful in ≤ 2 attempts more than twice as often
  (35% vs 71%, p=0.019)

Recommendations

1. Premedication with atropine, fentanyl/ morphine, and muscle relaxant should be considered for *all* non-emergent intubations in the NICU
   Ensure proper personnel present
2. Use of atropine for *all* non-emergent intubations in the NICU
3. Using Rocuronium as muscle relaxant

Recommendations

4. Use of premedication order set in computer
5. Flowchart for intubation "protocol"
6. Videotape procedures
   - Review with team after procedure
   - Pediatric resident noon conference
   - Respiratory therapist conferences

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