

Neonatal Centered Care Advances in Neonatal Pain Management

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Disclosure



- I am an employee of the Nutrition Health Institute, Abbott Laboratories Speakers Bureau

Objectives

- Recall two patient behaviors that can be used to assess pain that are not included in most Neonatal Pain Scales.
- Describe the benefit of acetaminophen in the management of post-operative pain in neonates.
- List medications that can be safely used in the elective intubation of neonates.

It's Complicated

Effective Pain Assessment and Management in Neonates

- **Team work**-surgeon, anesthesiologist, Neonatologist, Nursing
- **Knowledge** of pain behaviors, tools and pharmacologic treatment options
- **Systems** that improve safety-order sets, Smart pumps
- Use of tools and all other data in the context of care
- Excellent Communication
- Attention to detail

It's Complicated

- Pharmacokinetics of the drugs
- Development of "Tolerance"
- Individual differences in infants pain tolerance
- Assessment barriers
- Pain sources that have no "older patient" comparison i.e. gastrochisis silo/repair
- Personal bias about the presence and harm of pain
- Fear of adverse consequences in the use of pain treatments

Effects of inadequate analgesia

- **Gastrointestinal**
 - ↓'d gut motility
 - Delay in return of bowel function
- **Genitourinary**
 - ↓'d urine output
 - Urinary retention
 - Potential for fluid overload
- **Cardiovascular**
 - ↑'d heart rate
 - ↑'d blood pressure
 - ↑'d cardiac output
 - hyper coagulation
- **Pulmonary**
 - ↓'d tidal volume, ↓'d cough, ↑'d splinting
 - Hypoxia, atelectasis

Effects of inadequate analgesia

- **Immune System**
 - Impaired immune function
 - Exaggerated stress response
- **Metabolic**
 - Hyper metabolism
 - Decreased insulin secretion
 - Protein catabolism
 - Metabolic acidosis
 - ↓'d glucose stores (especially neonates)

Inadequately Treated Pain Conclusion

“It is bad for you.”

“What you see may be
because of pain, not the
medication used to treat the
pain”



Barriers to Assessment

- Prolonged effect of neuromuscular blockade
- Extreme prematurity
- Physiologic changes that are compatible with condition/disease as well as pain-THINK PAIN
- Non-verbal population
- Lack of consensus in health care providers
- Parents less likely to have knowledge of infant's pain behaviors

Pain Tools

- Multiple tools exist
- Some use only behavioral indicators such as cry or tone
- Others use physiologic indicators such as HR and blood pressure
- Some use a combination of both
- In a setting with monitoring, use a tool with Physiologic indicators

Pain Tools

- CRIES-behavior /physiologic-Term Post-op
- NIPS-behavior, state, tone, pattern of respiration
- COMFORT-behavior and physiologic-nonverbal post-op critical care
- PIPP-gestational based, state, facial expression, saturation change
- N-PASS-behavioral, physiologic, credit for immaturity, allows sedation assessment

Physiologic Responses to Pain

Clinical J Pain, 26 (9) 2010

- Change in respirations
- Increase/decrease blood pressure
- Increase/decrease in heart rate
- Loss of HR variability
- Color change
- Decreased skin perfusion-pallor and mottling
- Decrease in oxygen saturation
- Palmar sweating

Assessment of Functional Capacity

- Very few Pain Tools incorporate the concept of “Shutdown” in assessment
- All infants move and have tone
- Severe pain is associated with a patient who does not move, has decreased tone and does not have “social contact”



N-PASS

- Select a box that describes the infant for each category in the pain section
- Includes assessment for over sedation
- Range is 0-10
- Cannot be used if infant paralyzed
- Credit given for very immature infants
- Limits-no category for “shut down”

N-PASS: Neonatal Pain, Agitation and Sedation Scale

Assessment Criteria	Sedation		Normal	Pain/Agitation	
	-2	-1	0	1	2
Crying Irritability	No cry with painful stimuli	Moans or cries minimally with painful stimuli	Appropriate crying Not irritable	Irritable or crying at intervals Consolable	High-pitched or silent continuous cry Inconsolable
Behavior State	No arousal to any stimuli No spontaneous movement	Arouses minimally to stimuli Little spontaneous movement	Appropriate for gestational age	Restless, squirming Awakens frequently	Arching, kicking Constantly awake or arouses minimally/no movement/not sedated
Facial Expression	Mouth is lax No expression	Minimal expression with stimuli	Relaxed Appropriate	Any pain expression intermittent	Any pain expression continual
Extremities Tone	No grasp reflex Flaccid tone	Weak grasp Decrease muscle tone	Relaxed hands and feet Normal tone	Intermittent clenched toes, fist, or finger spica Body is not tense	Continual clenched toes, fist, or finger spica Body is tense
Vital Signs HR, RR, BP, SaO2	No variability with stimuli Hypoventilation or apnea	<10% variability from baseline with stimuli	Within baseline or normal for gestational age	Increase 10-20% from baseline SaO2 76-80% with stimulation-quick increase	Increase >20% from baseline SaO2 <70% with stimulation- slow increase Out of sync with vent

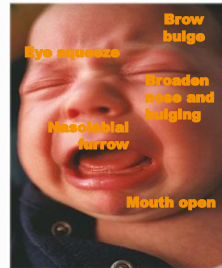
Additional Assessment Essential to Effective Management

- **Length** of the surgical procedure
- **Pre-existing disease** state-sepsis, peritonitis
- **Tissues and nerves involved**-thoracotomy v. abdominal incision
- Amount of dissection-**tissue inflammation**
- Use of **local anesthesia**-incision instillation of local anesthetic with epinephrine
- Use of **blocks, caudal, epidurals**

“Pain Assessment should be comprehensive and multidimensional, including contextual, behavioral *and* physiological indicators”

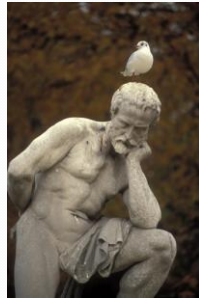
Dr. K.J.S. Anand
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Pain Assessment in Neonates



“Think outside the Tool”

- Use all the information that is available to you
- If there is a clear pain source, treat it
- Do not wait for the score to be high, preempting pain will require less drug



AAP Guideline

Committee on Fetus and Newborn, Prevention and Management of pain in the neonate: An Update Pediatrics 2006; 118;2231.

- Routine assessments for the detection of pain
- Reduce the number of painful procedures
- Prevent/reduce acute pain from invasive procedures performed at the bedside
- Anticipate and treat postoperative pain following surgery
- Avoid chronic pain/stress during neonatal intensive care

Approach

AAP Committee Prevention and Management of Pain in Neonates

- Preemptive analgesia for any anticipated painful procedure
- Elimination of unnecessary noxious stimuli or painful procedures
- Active involvement of the parents in helping their baby cope with the procedure
- A combination of nonpharmacologic methods and pharmacologic agents to prevent and reduce neonatal pain

“..that every health care facility caring for neonates implement an effective pain-prevention program and use pharmacologic and non-pharmacologic therapies for the prevention of pain associated with procedures” AAP Policy

Statement Pediatrics 2007,119 (2):425.



Pharmacokinetics “The Moving Target”



- Opiates and sedatives are cleared slower in an immature infant
- Clearance improves with post conceptual age, reaches adult levels at about 1 month
- Amount of drug needed to achieve goal increases with time (tolerance)
- There are **significant** individual differences

Baby Heroin Bottle-Diamorphine Pharmacokinetics



- Therapeutic doses rarely effect blood pressure, cardiac rate and rhythm
- Histamine release is rare in neonates

Single Dose Morphine

Pharmacokinetics in Prematures

- 20 infants studied, 26-40 Weeks
- Given a single dose of Morphine 0.1mg/kg
- Distribution half-life: Preterm vs. Term
- 50+-35 minutes/19 +- 8 minutes
- Elimination half-life: Preterm vs. Term 10+- 3.7 hours/6.7+-4.8 hours
- Bhat, R. et al, J Peds, 1990.

Hemodynamic Effects of IV Morphine

- 30 ventilated Infants 27-31 wk., 800-1680 grams
- Loaded 100 mcg/kg/h for 2 hours
- No change in cerebral or cardiac Doppler parameters
- MAP 44 +- 6 mm Hg fell to 42+-4 down 4%, HR 148+-12 fell to 140 +-16 down 5%

Hemodynamic Effects of IV MS

Sabatino, et al, early Human Development, 47, (1997)

- Summary: A loading dose of morphine over 2 hours did not have any significant effect on MABP or cerebral and cardiac hemodynamics
- No Adverse effects were noted that could be attributed to morphine therapy

IV Morphine Postop

Intermittent bolus vs continuous infusions

- 83 infants: 56 continuous infusion, 27 intermittent bolus as needed
- Ventilation compared by pulse ox, blood gases and CO₂ response curves
- Pain scored every four hours

Drip vs Bolus

Lynn, A.M et al, Pain, 88 (2000) 89-95.

- Findings: Bolus group had more pain scores showing distress 32% vs. 13%
- Time Sats <90: Infusion 2.3%, Bolus 2.5%
- Supplemental O₂: Infusion 2, bolus 0
- PCO₂: Infusion 43 +-6, bolus 42 +-6
- Morphine clearance improves with age, 0-7 days 9.8 ml min kg, 31-90 days, 23.9 ml min kg

Selecting a Dose

Practical Considerations

- Gestational and post-conceptual age
- Opiate *experienced* or *naïve*
- Response to previous painful procedures
- Surgical procedure-type, length, tissues and nerves cut or traumatized
- Use a broad range for infusion 0.005 mg/kg/hr. and increase as clinically indicated
- Use "breakthrough/rescue" initially until pain relief achieved

Effect of IV Paracetamol on Postoperative Morphine Requirements in Neonates and Infants Undergoing Major Noncardiac Surgery
Ceelie, She, et al, JAMA, 2013; 309 (2)

- 71 Neonates in an Intensive Care Unit
- Loaded with morphine 30 " before the end of surgery
- Randomized to continuous morphine or intermittent IV Tylenol for 48 hours after surgery
- Cumulative morphine dose in Tylenol group was 121 (99-264 mcg/kg)
- Cumulative morphine dose in the non Tylenol group was 357 (220-605 mcg/kg)
- P<.001 between groups

Pain Management IV Tylenol

- Current dosing recommendation:
 - Load with 20 mg/kg IV over ~15 minutes
 - 10 mg/kg IV every 6 hours
 - New FDA approval in the US, used in Europe for over a decade
 - Not much published compatibility data
 - Dose not mask fever
 - No reports of hepatic injury when used for post-operative pain management

Nurse Controlled Analgesia

Paediatric Anaesthesia, 20 (2), 2010

- Prospective study of patient who received "Nurse Controlled Analgesia (NCA)
- 18 centers in the United Kingdom
- Effectiveness, morphine requirements, side effects and serious complications recorded
- 10,079 patients-1 day-20 years
- 510 Neonates
- Average duration of therapy was 43.7 hours

Nurse Controlled Analgesia

- A demand-led alternative for patients too young or unable to use PCA
- Administered by trained personnel
- Designed to provide safe, potent, convenient and flexible pain control
- Typical "background" infusions supplemented with 10-20 mcg/kg bolus options when necessary and assessed by nursing staff

Nurse Controlled Analgesia

Pediatric Anesthesia 20,2010

- Initiated by pediatric anesthesia
- Institutional protocol
- NCA required that nurses completed training in management of post-operative pain
- All assessments included an evaluation of over sedation
- Narcan was included in order sets, Smart Pumps and lockouts were included in all institutions

Nurse Controlled Analgesia

- 98% used morphine (1.8% replaced with other agents)
- 4.5% depression of respiration
- 0.4% serious adverse effects-no deaths
- Analgesia rated as "good" or "very good" in 98% of all cases
- Conclusion: NCA is safe and effective for management of post-op pain

"Analgesia is therefore "titrated" to the requirements of each individual, who, because of their relative immaturity, are likely to include many of those at highest risk of under treatment or adverse effects"



NCA Conclusions

- Used for 20 years in United Kingdom and now considered a Standard technique of post-operative pain management
- Since 1996 used on all aged infants
- Major advantage is flexibility that allows rapid and significant changes to the dose of analgesia in response to pain and in **anticipation of pain**

Standardized Pain Management

Furdon, et al, J Perinat Neonat Nurs 1998

Outcome Measures: Pre/Post Protocol

- Effectiveness, amount of drug, side effects, post-op weight gain, days to extubation and mean length of stay
- Protocol: Initial opiate bolus-continuous drip opiate for 48-72 hours (procedure variable)

Standardized Post-op Pain Management Protocol

- Results:
 - ⌚ More infants received an analgesic over the first 3 post-op days
 - ⌚ Less overall opiate was used
 - ⌚ Fewer infants had adverse side effects
 - ⌚ Post-op weight gain was less
 - ⌚ Decreased hours to extubation/Mean LOS

Post-Operative Pain Protocol

- **Around the clock** opiates for 48-72 hours for all major chest or abdominal procedures (No prn)
 - PDA ligation
 - Exploratory laparotomy
 - NEC-Ostomy
 - TEF repair
 - Ostomy takedown

Post Operative Pain Protocol

- Drip started within 1 hr. of last opiate in OR
- Starting Morphine dose based on:
 - Opiate experienced or naïve factored into dosing
 - Length of surgery
 - Local anesthetic in OR-incision/caudal?
 - Degree of tissue manipulation
 - Co-morbidities-peritonitis, NEC, infection
 - Anesthesia/Surgeon

Post-Operative Pain Management Conclusions

- Use a protocol to guide initial treatment
- Use drip for moderate to severe pain
- Preempt pain and do not wait for scores
- Meet with the surgeon and anesthesiologist about intraoperative management and the procedure
- Anticipate a “prn bolus” option until the drip dose is determined to be adequate for each infant
- Implement the use of scheduled Acetaminophen to “potentiate” the opiates and improve pain management

PRN stands for “Patient Receives Nothing”

Dr. Stefan Friedrichsdorf, Director of Pain Medicine,
University of Minnesota

Procedural Pain Management Options

- Non-Pharmacologic
- Oral sucrose (breast milk)
- Topical anesthetics-4% Lidocaine
- Subcutaneous anesthetics-Lidocaine
- Systemic non-opiates-Acetaminophen
- Systemic opiates-Fentanyl, morphine
- Systemic sedatives
- Combinations of the above

Topical Anesthetics

Biran, V. et al, “Analgesic effects of EMLA cream and oral sucrose during venipuncture in preterm infants”. *Pediatrics* 2011; 128:e63.

- Pain behaviors reduced as an adjunct to nerve block in circumcision
- Reduced pain in venipuncture and arterial puncture
- No effect on heel stick
- Reduced pain in spinal tap
- Mild transient skin irritation is rare
- Application requires occlusion-LNX 20 minutes, EMLA 60 minutes
- Level of anesthesia for 45-60 minutes

Lidocaine-1%

- Local instillation effective for:
 - Venipuncture or arterial puncture
 - Circumcision
 - Infiltration of incision site preoperatively
 - Chest tube insertion
 - Tap procedures for fluid-peritoneal or pleural
 - Toxicity can occur if used in high doses and multiple sites

Sucrose for Procedural Pain

Linda Franck, Children's Medical Ventures Educational Booklet, Vol1,NO.1,2000.

- Analgesic effects-primarily mediated through opioid pathways
- Efficacy-supported in many studies over the past decade AAP/CPS support
- Safety-No adverse effects reported except choking in very low birth weight infants
- 24% solution is hyperosmolar but has been shown to not grow bacteria, or fungus

Sucrose for Procedural Pain

- Dose and mode of delivery-Small amounts on a the tongue or a pacifier
- NG administration is not effective
- Felt to be synergistic with non-nutritive sucking
- Drops as needed-repeat during procedure
- Heel stick, venipuncture, immunization, tape removal, NG insertion, dressing changes, bladder catheterizations etc.
- Non-procedural use-Pain behaviors that cannot be managed with interventions such as diaper change etc.



IV Start/Venipuncture

- Oral sucrose
- Containment
- Vein selection-hands more painful than antecubital
- When frequent blood draws are required consider a short term access such as an umbilical catheter or peripheral arterial line-Risk/Benefit discussion
- Batching of all lab draws-coordination of orders to reduce sticks

PICC Insertion



- Topical Lidocaine
- Low dose opiate
- Containment
- Oral sucrose

Spinal Tap

- Topical Lidocaine
- Lidocaine instillation
- Low dose opiate
- Low dose sedative
- Goals are patient comfort and ease of positioning to improve success of procedure

Chest Tube Insertion

- Lidocaine instillation-0.5-1% solution without epinephrine no more than 3-5 mg/kg
- Opiate IV-lower dose if not intubated
- Consider more opiate for chest tube removal
- Some pain source during duration of indwelling tube during handling and breathing

ROP Laser

Sammartine, M. et al, "Efficacy and safety of continuous intravenous infusion of remifentanyl in preterm infants undergoing laser therapy in retinopathy of prematurity: clinical experience" Paediatr Anaesth 2003; 13: 596.

- Topical anesthetic (proparacaine), oral sucrose and comfort care (containment) show minimal or no effects on pain behaviors
- Deep sedation recommended with short acting drugs like midazolam and fentanyl are most effective
- Consider orders for Romazicon and Narcan after the procedure is completed if sedation leads to apnea, bradycardia or desaturations
- Doses will need to be repeated due to the half life of the reversal agents compared to the drugs

"Should we reconsider awake intubations?"



Intubation

AAP Committee on Fetus and Newborn, Section on Anesthesiology and Pain Medicine, 2010

- Recommend premedication for nonemergency intubation in neonates
- Number of attempts reduced
- Time to intubation reduced
- Minimizes airway trauma
- Improved physiologic homeostasis-less bradycardia, desaturations, less increased in intracranial pressure

Intubation-Premedication

- Initial medication: Fast acting opiate: Fentanyl 2 mcg/kg given by slow IV push to avoid chest wall rigidity
- Second medication: Atropine 20 mcg/kg IV, wait for a 20 bpm risk in heart rate, blunts the vagal response and reduces secretions
- Last medication: Fast acting neuromuscular blockade agent-Succinylcholine 2 mg/kg IV push or Rocuronium 1 mg/kg -given when ready to insert tube (in hand/positioned)-duration minutes-an hour

Other Procedures

- ETT Suctioning
- NG insertion
- Bladder catheterization
- Dressing changes
- Heel sticks
- Eye exams
- IM or SQ injections
- Imaging procedures
- Reduce number of events with no routines
- Oral sucrose and containment

Reversal Option-Naloxone

- Specific Opioid antagonist, nonselective
- Half life shorter than morphine, may need to be repeated
- Intermittent small doses .05-.1 mg/kg to **reverse unacceptable effects**, try to maintain desirable effects

Recommendations

- Plan and discuss post-operative pain management for each infant-before they return from the OR
- **Treat infants who undergo major thoracic or abdominal procedures with continuous infusion morphine**
- **Add IV Acetaminophen to potentiate opiate**
- Consider an option of **nurse controlled analgesia and/or bolus** for "break through" pain but ultimately adjust continuous drip
- Treat all painful procedures and evaluate the need for them

Recommendations

- Do not rely only on Pain Tools as they all have shortcomings
- **Pain behaviors should be presumed to be pain until proven otherwise**
- **Listen to the nurse-and "Presume Good Will"** when they ask for additional medication it is her/his job to advocate for patient pain relief
- Work towards consensus on management of Non-major procedures-VP shunt, hernia repair, GT, anoplasty etc.

Conclusions

- Pain is bad for neonates
- Treatment protocols should be developed at a unit level and individualized based on gestation, pain source, opiate experience and more
- Nurses need to carefully consider pain source and use pain medications when pain sources exist
- Pain behaviors may mean pain even if you cannot define the source
- Sedatives do not have a direct effect on pain
- Pain treatment is complex

Pre-emptive Analgesia in the NICU

Grunau, R.E. et al, Seminars in Fetal and Neonatal Medicine 2006

- "It is very challenging to study effects of morphine or other analgesics or sedatives used pre-emptively in the NICU, even in RCT's, because humane care of infants currently requires physicians to treat those thought to be in pain, despite the knowledge gaps of long-term risks and benefits of these medications."

“Treating Pain in neonates is the right thing to do and is our job. We may not have all the answers but we can begin by advocating for every infant in our care and work towards a consensus and safe practice.”



<http://nursing.ucsf.edu/news/comforting-your-baby-intensive-care-professor-linda-franck-now-available-free-charge>



Now Available on iTunes

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