Pain in Newborns and Infants

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Studies indicate a lack of awareness among health care professionals of pain perception, assessment, and management in.

Fear of adverse reactions and toxic effects often contributed to the inadequate use of analgesics.

In addition, health care professionals often focused on treatment of pain rather than a systematic approach to reduce or prevent Several

PAIN MANAGEMENT MYTHS

- Neonates do not feel pain.
- Infants are less sensitive to pain than adults
- Neonates have no memory of pain.
- Children will tell you when they are having pain.
- If a child can be distracted, he is not in pain.
- Neonates are not able to tolerate the effects of analgesics.
- Narcotics can lead to addiction in children.
- Infants become accustomed to pain.

Newborns can’t remember pain
pain

So, what are the facts?

- Newborn infants have functional nervous systems which are capable of perceiving pain
- Physiologic means of assessing pain (VS) can be an unreliable predictor of pain
- Infants often develop an increase in signs of discomfort with repeated painful procedures
- Premature infants can have unpredictable responses to painful stimuli
- Unmanaged pain in the neonatal period can cause long term developmental complications

The Effects of Pain

- Physiological Effects
  - changes in vital signs, pupils
- Behavioral Cues
  - how the baby acts when she is in pain
- Hormonal/Metabolic Responses
  - what happens chemically

What can we do?

Common sense tells us that not all crying babies are in pain.

A chronically stressed baby in the NICU may not react at all to pain.

Premature Infant Pain Profile

- Facial Actions
  - Brow bulge
  - Eye squeeze
  - Nasolabial furrow
- Physiological Indicators
  - Heart rate
  - Oxygen saturation
- Context
  - Gestational age
  - Behavioral state
- Inter-rater reliability >.93

Premature Infant Pain Profile

Pain Score Flow Chart

Score 0-6 - No Action.

Score 7-12 - Non Pharmacological Intervention e.g. Positioning, Containment, Swaddling, Non-nutritive sucking.

Reassess in 30 Minutes for effectiveness of intervention.

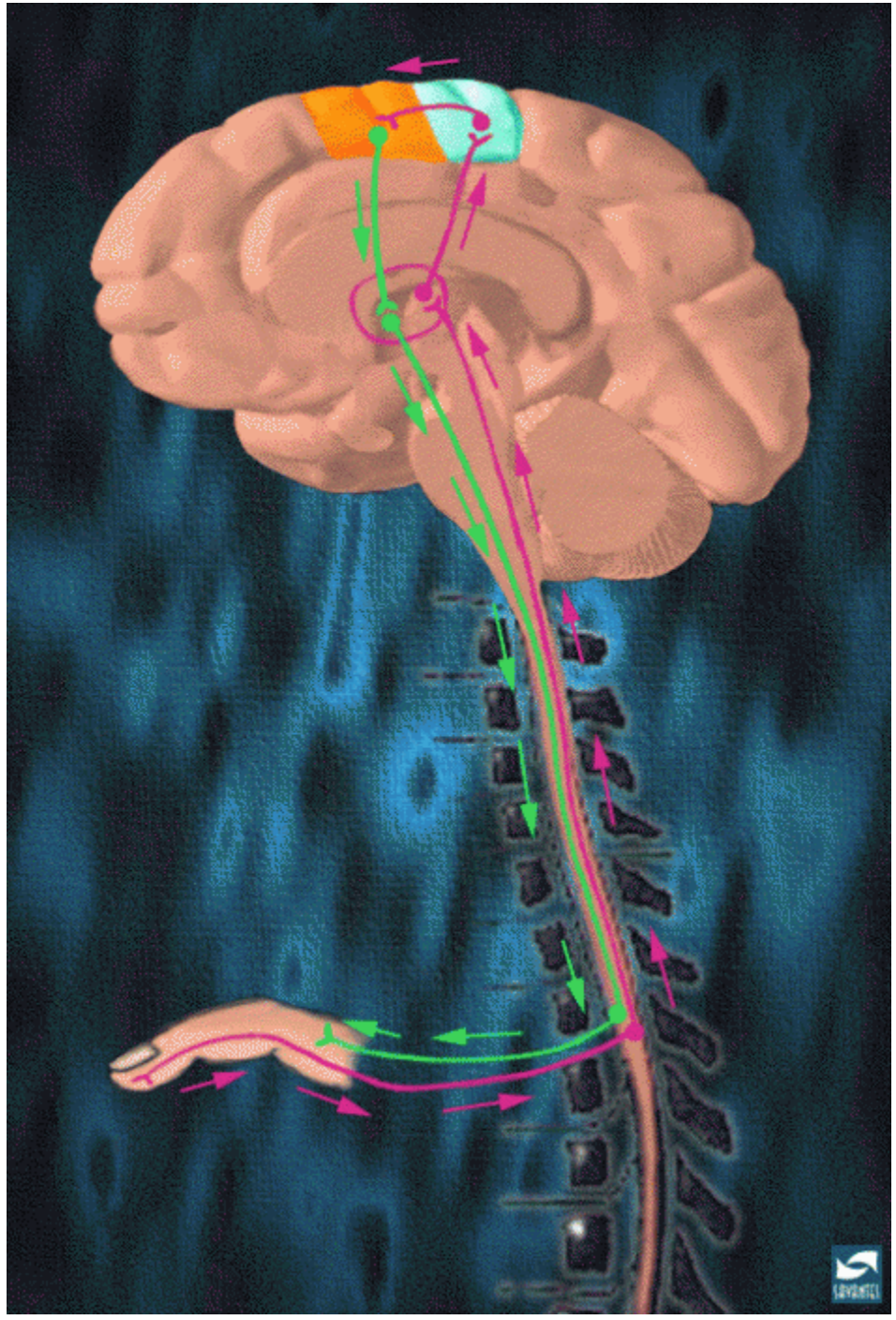
Score > 12 - Pharmacological Intervention e.g. Narcotics.

Reassess in 15-30 Minutes for effectiveness of intervention.

Facial expression of physical distress and pain in the infant

PIPP Scale

	0	1	2	3
GA	> / = 36 Wks	32-35 6/7 Wks	28-31 6/7 Wks	< / = 28 Wks
Behavioral State	Active/Awake	Quiet/Awake	Active/Sleep	Quiet/Sleep
HR	0-4 Beats/ Minute Inc	5-14 Beats/ Minute Inc	15-24 Beats/ Minute	25 Beats or > Inc
O2 Sats	0-2.4% Decrease	2.5-4.9% Decrease	5-7.4% Decrease	7.5% or > Decrease
Brow Bulge	None	Minimum	Moderate	Maximum
Eye Squeeze	None	Minimum	Moderate	Maximum
Nasolabial Furrow	None	Minimum	Moderate	Maximum



Prolonged Effects of Pain

- Preterm infants show prolonged hyperalgesia within an area of local tissue damage and secondary hyperalgesia in the contralateral limb.
- Circumcision results in increased pain behavior 3 months later.
- Birth trauma linked to increased acute stress responses to pain in infancy.

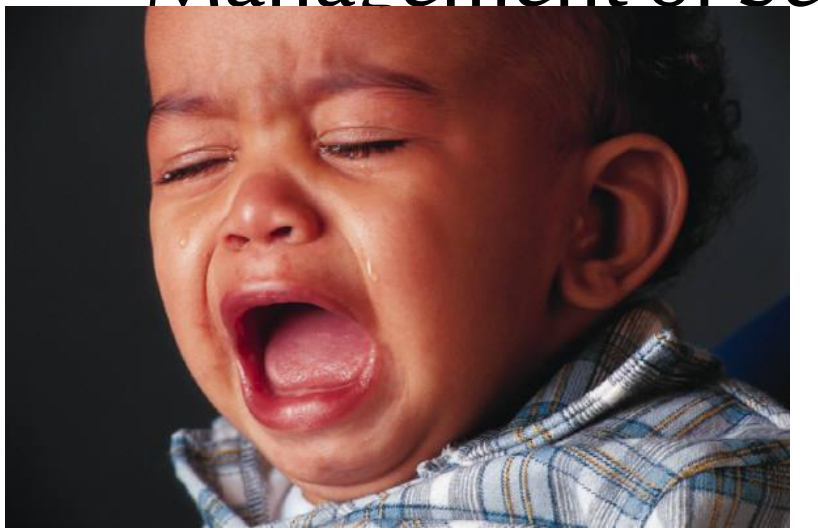
Long Term Effects of Untreated Pain

- Some experts believe that untreated pain in the newborn period forces abnormal pathways to form in the brain
- This aberrant brain activity results in impaired social/cognitive skills and specific patterns of self- destructive behavior
- Studied MRI's of newborns-reactions to pain transferred into similar electrical reactions to any kind of stressful situation

Avoid Painful Procedures

- Painful or stressful procedures should be minimized and, when appropriate, coordinated with other aspects of the neonate's care.
- Skillful placement of peripheral, central, or arterial lines reduces the need for repeated intravenous punctures or intramuscular injections.
- Thus, in some such cases, the risk-benefit balance may favor the more invasive indwelling catheters. Whenever possible, validated noninvasive monitoring techniques (e.g., pulse oximetry) that are not tissue damaging should replace invasive methods.

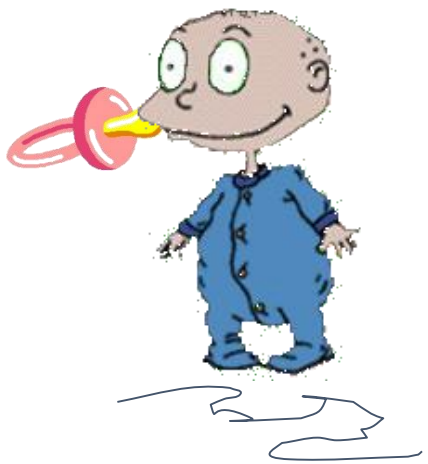
Management of Severe Pain



- developmental support
- parental involvement
- pharmacological management

  - medications given on a prn basis result in peaks and valleys of pain relief
  - pain is better controlled if medication is given prior to the climax of pain
  - continuous drip or regularly scheduled doses maintain a constant level of analgesia

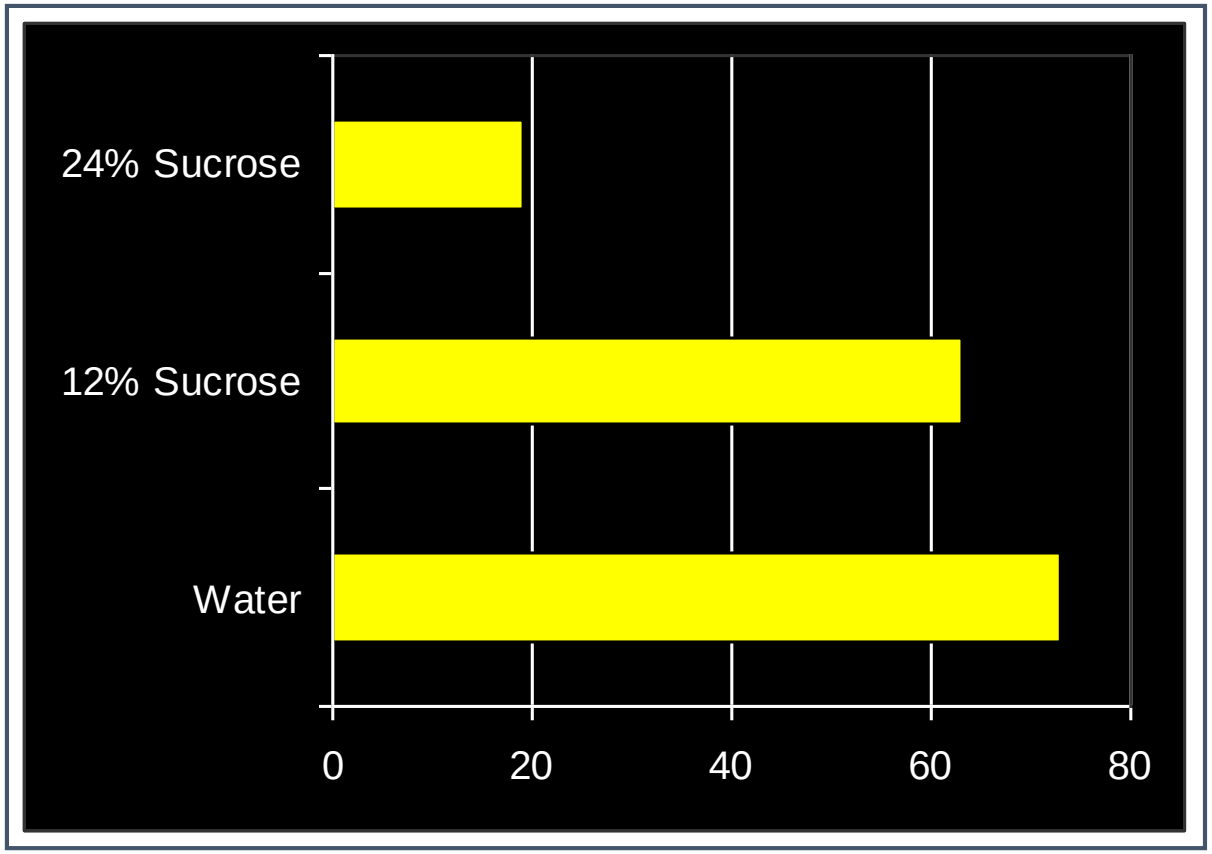
Non-nutritive sucking



- Tested during heelstick procedure
  - Heelstick caused no effect on respiratory rate and oxygen saturations
  - Sucking reduced time of crying and heart rate increases

--Corbo, et al. Biol Neonate, 2000

Effect of Oral Sucrose Solution on Venipuncture Pain



Time crying (sec)

Abad, et al
Acta Paediatr, 1996

روشهای دارویی مدیریت درد در نوزادان

Sucrose (sweet-tasting liquids (most commonly sucrose) are effective analgesics in both term and preterm infants)

- Its dose is 0.1 to 1 mL of 24% sucrose(or 0.2–0.5 mL/kg) was administered 2 minutes before a painful procedure and the effects lasted ~ 4 minutes (AAP 2015).

●24 to 26 weeks PMA – 0.1 mL

●27 to 31 weeks PMA – 0.25 mL

●32 to 36 weeks PMA – 0.5 mL

●37 to 44 weeks PMA – 1 mL

●45 to 60 weeks PMA – 2 mL (Anand 2019)

- An additive analgesic effect has been noted when sucrose is used in conjunction with other nonpharmacologic measures, such as nonnutritive sucking, skin to skin contact and swaddling.

American Academy of Pediatric. Prevention and Management of Procedural Pain in the Neonate: An Update.2015
Kanwaljeet JS Anand. Prevention and treatment of neonatal pain. 24th Sep 2019.

Sucrose

- موارد استفاده: نمونه گیری از پاشنه پا,پانکچرشریانی یا وریدی,قراردادن NGT,تزریق عضلانی و یا زیر جلدی, معاینه ROP و در ترکیب باسایر آنالژیک ها در LP, قرار دادن CV Line, inter osseous accessوختنه کردن نوزادان
- مزایایی سوکروز:

  کاهش طول مدت گریه کردن
  کاهش تغییرات فیزیولوژیک به درد مثل SPO2,HR
  کاهش تغییرات چهره نوزاد در پاسخ به درد
  کاهش اسکور درد

- کنتراندیکاسیون های ساکارز

  انتروکولیت نکروزان

  فیستول نای تراشه

  عدم وجود رفلکس بلع

  عدم تحمل فروکتوز یا ساکارز

- **Local anesthetics**

*Lidocaine infiltration: It is usually administered as either a 0.5 mL/kg subcutaneous infiltration of a 1% (10mg/mL) solution or 0.25 mL/kg infiltration or a 2% (20 mg/mL) solution to a maximum dose of 3 to 5 mg/kg.

استفاده در کاهش دردهای نمونه گیریهای شریانی ووریدی,کاتتریزاسیون شریانی و وریدی,ختنه, post operative analgesia.

*Topical anesthetics (Eutectic Mixture of Local Anesthetics (EMLA)): it be used 30 to 60 minutes before the procedure

- It is only approved for infants ≥ 37 weeks gestation.
- املا سبب کاهش درد در LP و ونوپانکچر می شود ولی درنمونه گیری پاشنه پا موثر نیست.

عارضه: مت هموگلوبینمی (در نوزادان شایع نیست),واکنش پوستی به صورت قرمزی,تعریق وBlanching

Opioid therapy

*__Morphine__ (Morphine is the most commonly used opioid for neonatal analgesia, often used as a continuous infusion in ventilated or postoperative infants, or intermittently to reduce the acute pain associated with invasive procedures. Its effectiveness and safety for these indications has not been established, but remains under active investigation.)

با آنکه انفوزیون مداوم مورفین سنکرونیزاسیون نوزاد با ونتیلاتور را بهبود میبخشد ولی در نوزادان پره ترم توصیه نشده است.

دریافت کنندگان مورفین اسکور درد کمتر در PIPP داشته وتغیرات HR, RR نیز کمتر بوده است. از طرفی عوارضی مثل هیپوتانسیون,احتباس ادراری ,باقی ماندن طولانی مدت زیرونتیلاتور با تجویز این دارو مشاهده شده و مدت زمان طولانی لازم بوده تا نوزاد به تغدیه کامل برسد و تحمل Poداشته باشند.

استفاده از پروتکل و دوز مناسب Parent/nurse-control باعث کاهش عوارض مورفین می شود.

Example of morphine nurse-controlled analgesia (NCA) protocol in clinical use

Weight	Drug and dose	Concentration
Up to 50 kg	Morphine 1 mg/kg made up to 50 ml with 0.9% sodium chloride or 5% glucose	1 ml = 20 mcg/kg (Max 4 hrly dose: 20 ml)

	Suggested initial programme	Loading dose (ml)	Background infusion (ml/h)	Bolus dose (ml)	Lockout (min)
NCA	standard	2.5 or 5	0, 0.2, 0.5 or 1	0.5 or 1	20 or 30
NCA	in ICU areas	2.5 or 5	0, 0.2, 0.5 or 1	0.5 or 1	5
NCA	neonates & infants <5 kg	1 or 2.5	0	0.5	20

(Courtesy of Great Ormond Street Hospital Pain Management Service)

Carachi P, Williams G. Acute pain management in the neonate. Anaesthesia & Intensive Care Medicine. 2020 Feb 1;21(2):99-104.

*__Fentanyl__ (fentanyl provides rapid analgesia with minimal hemodynamic effects in term and preterm newborn)

*__Remifentanil__ (It has a chemical structure similar to that of fentanyl, but has twice its analgesic potency with an ultra-short duration of action (3–15 minutes). Remifentanil is used for pain relief during brief procedures such as central line placement or tracheal intubation.)

- مطالعه ای نشان داده که استفاده از رمی فنتانیل در ایبنتوباسیون سریع معادل
- مورفین +میدازولام است.

موارد استفاده از رمی فنتانیل:

اینتوباسیون الکتیو

آنالژزی بعداز جراحی بخصوص جراحی قلب

پولمونای هایپرتانسیون در زمینه (MAS,هرنی دیافراگماتیک و CHD)

Non-opioid therapies

- Benzodiazepines (are commonly used in NICU's, but they have no analgesic effects. These drugs provide sedation and muscle relaxation, making them useful for non-invasive procedures such as imaging studies and as an adjunct for motion control in invasive procedures.

- Midazolam (it is the most commonly used benzodiazepine in the NICU) A starting dose of 100 mcg/kg with a maintenance dose of 50-100 mcg/kg/hour can be used in neonates to provide sedation.

میدازولام:شروع اثر کوتاه مدت ولی sedation طولانی میدهد .به همین دلیل در نوزادان پره ترم توصیه نمی شود.

- Lorazepam—Lorazepam has also been used in the NICU, albeit not as routinely as midazolam.

Other Sedatives

- Phenobarbital—Phenobarbital is usually considered as the drug of choice for seizure control. There is sparse evidence for antinociceptive effects of phenobarbital in animals, but it has no significant analgesic effects in humans. It was used in conjunction with opioids for sedation, although there is little recent evidence that it is effective. Classically, it has been used for neonatal abstinence syndrome

- Propofol—Propofol has become popular as an anesthetic agent for young children, but it has not been studied extensively in neonates

- Ketamine—Ketamine is a dissociative anesthetic that provides analgesia, amnesia, and sedation. Although ketamine has been used extensively in older children, there have been limited studies in neonates.

- در جراحی و بعد از آن به عنوان آنالژزیک در نوزادان وشیرخواران استفاده میشوند.

_کتامین باعث ساپرشن تنفسی نمی شود وخاصیت برونکودیلاتوری دارد .
_کتامین با افزایش مختصر HR,RR باعث بهبود همودینامیک میشود و می تواند در نوزادان با همودینامیک ناپایدار مثل فتق دیافراگماتیک, CHD, ECMO مناسب باشد.

- Dexmedetomidine— It provides potent sedative and analgesic effects, while causing minimal respiratory depression. Although dexmedetomidine is approved for sedation of patients undergoing surgical or other procedures, the clinical experience using this drug in neonates is limited.

A phase II/III multicenter trial demonstrated dexmedetomidine is effective and well tolerated for sedating both preterm and term neonates (Chrysostomou C etal 2014)

دکسمدتومیدین یک داروی جایگزین امیدوار کننده برای آرام بخشی مداوم در نوزاد نارس است.
McPherson C etal 2017

- Chloral Hydrate— It is commonly used in European NICUs when sedation is required without analgesia. It is commonly used for radiological procedures, electroencephalography, echocardiography.

Acetaminophen (Paracetamol)

- it has been well studied in newborns. It is frequently used in conjunction with other pain relief to decrease opioid use, especially for post surgical pain. In infants, oral, rectal and intravenous formulations of acetaminophen have minimal adverse effects in infants.
- In both preterm and term infants, the clearance of acetaminophen is slower than older children, so oral/rectal dosing is required less frequently Single oral doses of 10 to 15 mg/kg may be given every 6-8 hours, 20 to 25 mg/kg can be given rectally at the same.
- IV acetaminophen dosage

•24 to 30 weeks gestation – 20 to 30 mg/kg/day

•31 to 36 weeks gestation – 35 to 50 mg/kg/day

•37 to 42 weeks gestation – 50 to 60 mg/kg/day

•1 to 3 months postnatal – 60 to 75 mg/kg/day

every 6 hours for infants at 32-44 weeks postmenstrual age

Every 6-8 hours for neonates between 23 and 32 weeks postmenstrual age.

Non-steroidal Anti-inflammatory Drugs (NSAIDS)

- There are little data on the analgesic effects of NSAIDS in neonates, although both ibuprofen and indomethacin have been used for ductal closure.

Hall RW, Anand KJ. Pain management in newborns. Clinics in perinatology. 2014 Dec 1;41(4):895-924.

Opioids

Drug	Advantages	Disadvantages
Morphine	Potent pain relief Better ventilator synchrony Sedation Hypnosis Muscle relaxation Inexpensive	Respiratory depression Arterial hypotension Constipation, nausea Urinary retention CNS depression Tolerance, dependence Long term outcomes not studied Prolonged ventilator use
Fentanyl	Fast acting Less hypotension	Respiratory depression Short half life Quick tolerance and dependence Chest wall rigidity Inadequately studied
Remifentanil	Fast acting Degraded in the plasma Unaffected by liver metabolism	

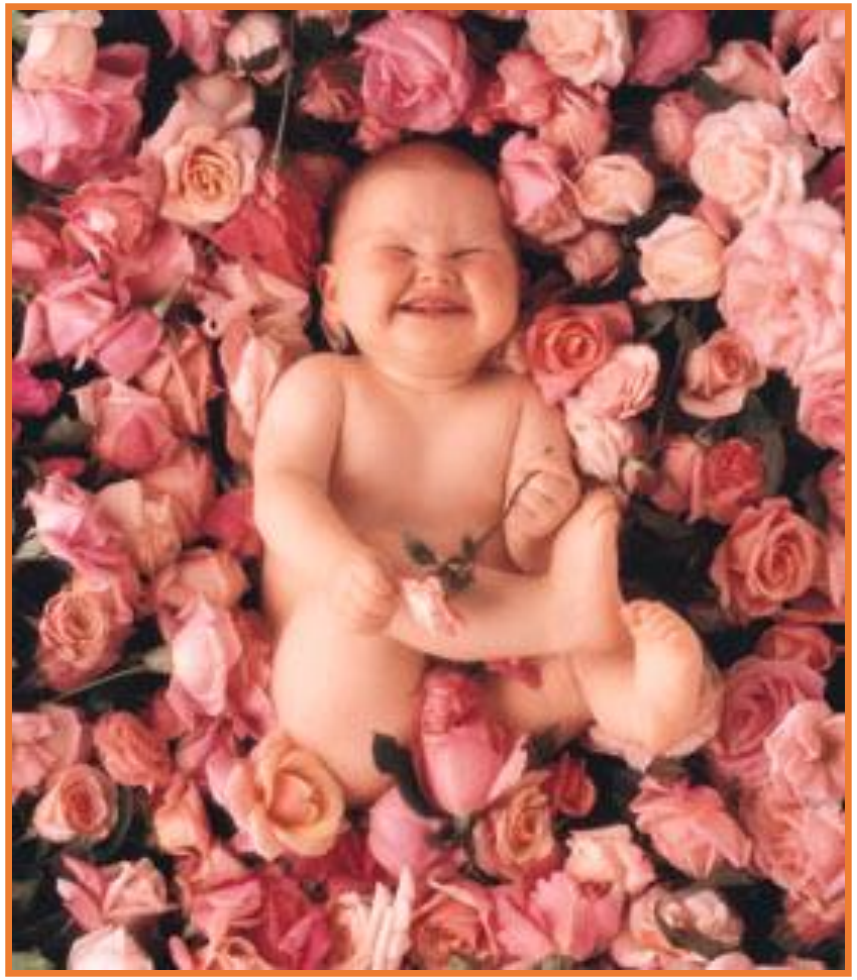
Hall RW, Anand KJ. Pain management in newborns. Clinics in perinatology. 2014 Dec 1;41(4):895-924.

Benzodiazepines

Drug	Advantages	Disadvantages
Benzodiazepines	Better ventilator synchrony Antianxiety Sedation Hypnosis Muscle relaxation Amnesia Anticonvulsant	No pain relief Arterial hypotension Respiratory depression Constipation, nausea Urinary retention Myoclonus Seizures CNS depression Tolerance, dependence Alters bilirubin metabolism Propylene glycol and benzyl alcohol exposure
Midazolam	Most studied benzodiazepine Quickly metabolized	Short acting Benzyl alcohol exposure
Lorazepam	Longer acting Better anticonvulsant	More myoclonus reported Propylene glycol exposure
Diazepam		Not recommended in the neonate

Hall RW, Anand KJ. Pain management in newborns. Clinics in perinatology. 2014 Dec 1;41(4):895-924.

Thanks for Listening



Because of
you…

Life is Good !

Thanks