59 Pain Assessment and Management

The neonates communicate their pain and stress through a number of autonomic, motor and behavioral cues. The caregivers in NICU must recognize these cues and modify the environment to reduce stress, pain and facilitate self-regulatory mechanism to promote organization of the neonate.

There are four subsystems, which need continuous positive influence from the environment as well as synchronized functioning to optimize well-being and growth during hospital stay and following discharge. Table 59.1 (a to d) lists the subsystems and the associated organized and disorganized behaviour.[1]

The sub-systems are:

a. Autonomic and visceral subsystem
b. Motor subsystem
c. State of attention/interactive subsystem
d. Self-regulatory subsystem

Table 59.1a: Organized and disorganized behaviour in autonomic and visceral subsystem

Parameter	Organized	Disorganized behavior behaviour
Respiratory rate	Stable	Very fast/ very slow or with pauses
Heart rate	Stable	Very fast or very slow
Skin color	Pink	Blanching
Oxygen saturation	Normal	Gasping/ blue around the lips
Other signs	Absent	Yawning, startles, tremors, twitches, sneezing, coughing drooling, spitting, vomiting, gagging, straining as if passing bowel

Table 59.1b: Organized and disorganized behaviour in motor subsystem

Parameter	Organized	Disorganized behavior behaviour
Tone	Normal	Flaccidity in trunk, extremities, stiffening or arching and hyperextension
Posture	Maintains flexed posture	All limbs are extended
Movement	Slow regulated, controlled smooth movements	Jerky movements/ very slow movements, flailing movements of the arms and legs
Other signs	Nil	Arching body, finger splay, foot splay, fisting of hands, salute, high arm guard, sitting on air, tongue protrusion.

Table 59.1c: Organized and disorganized behaviour in attention and interactive sub-system

Organized behaviour	Disorganized behavior
Neonate is in deep sleep or quiet and alert, maintains eye contact, mouth pursing, cooing, smiling, consolable	Neonate is in active sleep state, twitching, fussy, frowning grimacing, irritable, crying, eyes rolling upward, averting eye gaze, gaping, sleepless

Table 59.1d: Behaviour in self-regulatory subsytem*

Organized behaviour	Disorganized behavior
This system helps the preterm infants to calm and soothe themselves in stressful situations. An infant who can self-regulate will have longer duration of undisturbed sleep; have better organized learning and coping mechanism during different painful experience. *Self -regulatory signs are finger clasping, clasping of blanket or sheet, fingers in the mouth with or without sucking, foot clasp, and feet against the bassinet for support.*	Neonate will be fussy, irritable and unable to interact with the environment positively.

**Observing an infant over a period of time is crucial. These cues are indicators if infants are ready for the activity, calmed before an activity is continued or not ready to engage at all. The older the infant, the more is their use of self-calming or self-regulatory techniques to organize themselves.*

Every health care facility caring for neonates should implement a comprehensive pain prevention program which should

include routine assessment of pain, minimizing procedures which can cause pain, effective use of non-pharmacological and pharmacological techniques for prevention of pain during routine procedures and complete pain relief during major surgeries.

Prevention of pain is not only important from ethical perspective but also to prevent long term deleterious consequences.

Pain assessment

Assessment of pain, an integral part of any pain prevention program is challenging in neonates. Use the Premature Infant Pain Profile (PIPP; Table 59.2) for assessment of acute pain.[1]

Table 59.2: Premature infant pain profile (PIPP)[7]

SN	Parameters	Score			
		0	1	2	3
1.	Gestation of infant	36wks	32-35[6/7]	28-31[6/7]	28 wks
2.	Score behavioral state before the procedure (15 sec)	Active awake *Eyes-open Facial movements+*	Quite awake *Eyes- open No facial movements*	Active sleep *Eyes-closed Facial movements+*	Quite/ sleep *Eyes closed No facial movements*
3.	Record baseline HR and find out maximum HR during the procedure	0-4/min increase	5-14/min	15-24/min	25/min
4.	Record baseline SO_2 and find out minimum SO_2 during the procedure	0-2.4% fall	2.5-4.9% fall	5-7.4% fall	7.5% fall
5.	Observe the infant for 30 sec immediately after the procedure (for brow bulge, eye squeeze and nasolabial furrow)	None (0-9% of time)	Min (10-39% of time)	Moderate (40-69% of time)	Maximum (70% of time)

Health professionals should record PIPP score of all babies once/nursing shift and before the procedures. The issue of pain should be discussed on the rounds. The minimum score is 0 and maximum score is 21. Higher the score, greater the pain. Score <5: no pain; 6-10: moderate pain; and >10: severe pain

Preventing or reducing pain

General measures

Pain is managed most effectively by preventing, limiting or avoiding noxious stimuli. The following measures in combination are followed to minimize pain:

- Avoid bright light, loud noise
- Limit the number of painful procedures and handling
- Bundling of investigations and nursing interventions
- Swaddling, facilitated tucking, distraction measures like talking, music, etc.
- Tactile stimulation like stroking, caressing, massaging

Non-pharmacological measures

The environmental and behavioral interventions that do not use pharmacological agents are collectively called non-pharmacological measures. These include:

1. Sucrose/glucose solution induced analgesia
2. Breast feeding/breast milk supplementation
3. Skin to skin care
4. Non-nutritive sucking using pacifiers

The non-pharmacological measures are thought to alleviate pain by activating gate control mechanism, secretion of endogenous endorphins and diversion of attention.[2]

Sucrose analgesia

Sucrose administration is particularly useful for short procedures like venepuncture, heel prick, etc. Oral administration of concentrated sucrose solution (24% to 50%) acts by release of endogenous opiods like beta-endorphin. Analgesic effect lasts for 5-8 min and should be combined with other non-pharmacological measures for maximum benefit. Alternative to sucrose is dextrose, which is less commonly used.

Table 59.3: Dose of sucrose/dextrose for analgesia[6,9]

Concentration	For babies who are NPO	Preterm (<32 weeks)	Late PT/ Term
24% Sucrose / 25% Dextrose	0.1-0.2 mL	0.1-0.5 mL	0.2-1 mL
The sucrose solution is given orally by a syringe 2-3 min before procedure and may be repeated 1-2 min after the procedure. Intragastric administration has no analgesic effect			

Breast feeding and breast milk supplementation

Almost as effective as sucrose analgesia in reducing pain in newborns undergoing single painful procedure.

Table 59.4: Evidence supporting non-pharmacological analgesic measures in neonates

Agent	Evidence	
Sucrose (24%)	Cochrane meta-analysis 44 studies, 3496 infants	• Reduction in pain scores (PIPP) • Decreases physiological indicators of pain (heart rate increase) • Less behavioral indicators of pain (duration of cry, facial action)
Breast milk and breastfeeding	Cochrane meta-analysis 11 studies	• Less duration of cry, lesser increase in heart rate • Lesser PIPP score • Lesser increase in neonatal facial coding score • Breast feeding was better than breast milk supplementation
Non-nutritive sucking, skin to skin care, Swaddling, facilitated tucking, music	Systematic review 13 RCT 2 Meta-analysis	• Favorable effect on heart rate, respiration and oxygen saturation, on the reduction of motor activity, and on the excitation states after invasive measures • Non-nutritive sucking, swaddling and facilitated tucking are particularly useful • Combination of measures always provide better analgesia

Pharmacological measures

The pharmacological measures can be broadly divided into

- Local anesthetic agents
- Systemic agents: opioids, acetaminophen

Non-steroidal anti-inflammatory agents (NSAID) are generally not used in newborns as analgesics.

Local anesthetics

Local anesthesia is particularly useful for management of acute procedure related pain with the exception of heel lances.[1] It can be either topically applied on intact skin or injected subcutaneously.

The common topical preparations marketed are:

1. Eutectic mixture of local anesthetics (EMLA): is a mixture of two local anesthetics namely lidocaine and prilocaine that is available as 5% cream
2. Tetracaine (4%)
3. Liposomal lidocaine 4% cream

The dose of EMLA is 1-2 g with contact period of 30 min to 1 hour. Apply the cream over 2-3 cm^2 area with 1-2 mm thickness and cover with transparent (tegaderm) dressing. For maximal analgesic effect, the topical anesthetics should be combined with other non-pharmacological measures like sucrose analgesia or breast milk supplementation.

The major drawback is the delayed onset of action and a contact period of at least 1 hour prior to the procedure, which makes it unsuitable for emergent procedures. The risk of methemoglobinemia associated with repeated use of EMLA cream is not seen with newer preparations like tetracine gel.

For emergent procedures, subcutaneous local anesthetic injection (lidocaine hydrochloride 2%) is preferred over topical creams.

Opioids

The opioid drugs are the mainstay in the management of severe pain related to mechanical ventilation, endotracheal intubation and post surgical pain in neonates.

The two most commonly used agents are morphine and fentanyl.

Morphine

Morphine has slower onset of action with mean onset at 5 min with peak effect at 15 min. It is metabolized in the liver to morphine-3- glucoronide, an opioid antagonist and morphine-6-glucoronide a potent analgesic. Newborn babies especially preterm infants mainly produce morphine-3-glucoronide leading to emergence of tolerance after 2-3 days of therapy.

The observed side effects include hypotension, need for prolonged ventilation, delay in reaching full feeds, and rarely bronchospasm secondary to histamine release[12].

Fentanyl

Fentanyl is a synthetic opioid analgesic. It is 50 to 100 times more potent and more rapid in onset of action compared to morphine. Fentanyl is preferred over morphine in infants with hypotension as cardiovascular side effects are lesser. [2] The unique side effect of fentanyl is chest wall rigidity, especially if given as rapid intravenous bolus.

The other opioids used are methadone, sulfentanil, remifentanil etc, which are used for short procedures like endotracheal intubation and short neonatal surgeries.

Analgesia for specific procedures

Elective and semi-elective intubation

Intubation of neonates in awake state is associated with increase in heart rate, greater fall in oxygen saturations / heart rate, increased intracranial pressure, increased risk of IVH, airway trauma and failure of procedure especially, in in-experienced hands.[3]

The AAP committee on fetus and newborn recommends avoiding awake intubation of newborns except in emergent situations like delivery room intubation and in cases where intravenous access is unavailable.[4]

The AAP recommends

- Analgesic agents or anesthetic dose of a hypnotic drug should be given

- Vagolytic agents and rapid-onset muscle relaxants should be considered
- Use of sedatives alone such as benzodiazepines without analgesic agents should be avoided
- A muscle relaxant without an analgesic agent should not be used

Table 59.5: Sedation for elective intubation

The preferred regimen includes:
1. Inj. Fentanyl 1-4 mcg/kg, given slow IV over 3-5 min
2. Inj. Atropine 0.02 mg/kg (minimum dose should of 0.1 mg)
3. Inj. Vecuronium 0.1 mg/kg administered IV, 2-3 minutes prior to the procedure

Avoid using paralytic agents in case experienced person is unavailable for intubations

Mechanical ventilation

Mechanical ventilation is a painful and uncomfortable experience which might adversely affect the course of acute illness as well as long term neurodevelopment.[5] However, there is insufficient evidence for routine use of pharmacological measures in all ventilated infants.

Indications for continuous infusion of opioids in ventilated neonates are:

- Post operative patients especially in the first 48-72 hours
- Illnesses like meconium aspiration syndrome or congenital diaphragmatic hernia with PPHN
- Asynchrony or fighting with ventilator. Rule out causes like ventilator malfunction, tube block or inappropriate settings before the infant is sedated for this indication.

Avoid use of midazolam especially in preterm neonates. Do not use paralytic agents routinely in ventilated neonates.

Analgesia/sedation in ventilated neonates: what is the evidence? A Cochrane meta-analysis (2005) including 13 studies and 1505 infants concluded that there is insufficient evidence to recommend routine use of opioids. However, when used, morphine is safer than midazolam showing reduction in pain severity as noted by lower PIPP scores and there was no long term/ short term reduction in morbidity/mortality.

Tables 59.6 and 59.7 provide details on how to provide analgesia in different procedures.

Table 59.6 Analgesia measures for routine bedside procedures

Procedure	Analgesia measure recommended			
	General measures	Sucrose analgesia*	Breast milk*	Facilitated tucking / caressing
Venipuncture Sampling#	+	+	±	+
Heel prick#	+	+	+	+
Subcutaneous/ IM injection	+	+	+	+
Adhesive tape removal	+	+	+	+
IV cannulation	+	+	±	+

**Either sucrose analgesia or breast feeding can be adopted depending on the availability and feasibility; for slightly longer procedure sucrose analgesia is preferred over breast milk/breast feeding*

#Venipuncture should be the preferred mode of blood sampling as heel lance is more painful

Table 59.7: Analgesic measures for specific procedures[6]

Procedure	Intubated	Non-intubated
Arterial puncture/ cannulation Lumbar puncture PICC line placement	• Inj Morphine 0-1-0-2 mg/kg IV • EMLA cream locally • Sucrose analgesia	• EMLA cream locally • Sucrose analgesia • General measures
Chest tube placement	• Inj Morphine 0-1-0-2 mg/kg IV • Local infiltration with Lignociane 2% • Sucrose analgesia	• Inj Morphine 0.1 mg/kg IV* • Local infiltration with Lignociane 2% • Sucrose analgesia
Chest drain removal	• Inj Morphine 0.1- 0.2 mg/kg • Sucrose analgesia • General measures	• EMLA cream locally • Sucrose analgesia • General measures
ROP screening	• Inj Morphine 0.1- 0.2 mg/kg IV	• Local anesthetic eye drops

contd....

	• Local anesthetic eye drops • Sucrose analgesia • Post screen-paracetamol	• Sucrose analgesia • Post screen- paracetamol
ROP Laser surgery	• Inj Morphine 0.1- 0.2 mg/kg IV • Local anesthetic eye drops • Sucrose analgesia • Post OP- paracetamol 15 mg/kg q 6 hourly for 1-2 day	• Inj Morphine 0.1- 0.2 mg/kg IV* • Local anesthetic eye drops • Sucrose analgesia • General measures • Post OP-paracetamol 15 mg/kg q 6 hourly for 1-2 day
CT/ MRI- for sedation	• Inj Morphine 0.1- 0.2 mg/kg IV • Inj Midazolam 0.1- 0.3 mg/kg IV	• Oral Chloral hydrate 50-100 mg/kg • Oral Trichlophos- 20 mg/kg • IV Midazolam 0.1- 0.2 mg/kg IV single dose

**In non-ventilated babies while using opioids- Watch for apnea/ respiratory depression; IV Naloxone should be kept ready and used in case of respiratory depression or apnea (0.1 mg/kg or 0.25 ml/kg IV); Inj Fentanyl may be substituted for Inj Morphine; Dose 1-4 mcg/kg slow iv over 3-5 min*

*** Even ventilated patients on opioid infusion during procedures needs additional analgesic measures*

Table 59.8: provides details of different analgesic agents.

Table 59.8: Drugs and dosages of analgesic/sedative medications commonly used in NICU

Drug	Dose	Preparation/ administration	Pharmaco- logy	Adv effect
Morphine	Bolus:100-200 mcg/kg slow IV over 5 min Infusion: 10-20 mcg/ kg/hr IV	1 mL=15 mg. Dilute in NS/ 10D/5D to make a maximum concentration of 5 mg /mL Incompatible with phenytoin, phenobarbitone	Onset: 5 min Peak :15 min t½: 9 hrs	Respiratory depression Bradycardia Hypotension Ileus, Urinary retention Tolerance
Fentanyl	Bolus 1-5mc g/kg IV slow IV over 5-10 min Infusion 1-5 mcg/kg/	1 mL=50 mcg Dilute in NS/5D/10D Incompatible with phenytoin, phenobarbitone	50-100 times more potent than morphine Rapid onset; less	Respiratory depression Chest wall rigidity with rapid push

contd....

	hour IV		hypotension than morphine t½: 1-15 hrs	Urinary retention Tolerance
Midazolam	Bolus: 0.1-0.2 mg/kg slow IV IV Infusion: 0.01-0.06mg/kg/hour Intranasal/ sublingual route (dose 0.2-0.3 mg/kg) may also be used	1 mL=1 mg Dilute in– NS/5D /10D Incompatible with NaHCO3, fat emulsion	Sedation only, no analgesic effect t½: 4-6 hrs in term infants; preterm variable up to 22 hrs not recommended in neonates esp. preterm	Respiratory depression; Myoclonic jerk Hypotension (esp with rapid push)
Vecuronium	0.1 mg/kg	Available as powder (1 vial=10 mg/20mg) Dilute in 5D/NS to make 1 mg/mL)	Non depolarizing muscle relaxant Onset 1-2min; duration of action 1-2 hours Consider using during non emergent intubation as premedication	Respiratory depression Hypotension in ventilated Avoid routine use in ventilated neonates.
Paracetamol	10-15 mg/kg/dose PO 6-8 hrly 30 mg/kg/dose per rectal	Syp 5 mL= 125 mg Drops 1 ml=100 mg Suppositories 80 mg	Rectal route-erratic absorption	
Chloral hydrate	25-75 mg/kg PO/rectally	1ml=100mg	No analgesia, only sedation Administer with feeds (high osmolality, may cause GI intolerance)	Bradycardia Gastric irritation Contraindicated in hepatic/ renal dysfunction
EMLA cream	1- 2 g for 1hr	Lidocaine-prilocaine 5% (Eg. Oint Prilox available in India) 5g/30g with teg derm dressing	Delayed onset t½-1 hr; Not effective for heel lance	Methemo globinemia

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