Pain management in the neonate

Murila FV

Martha Gatumbu

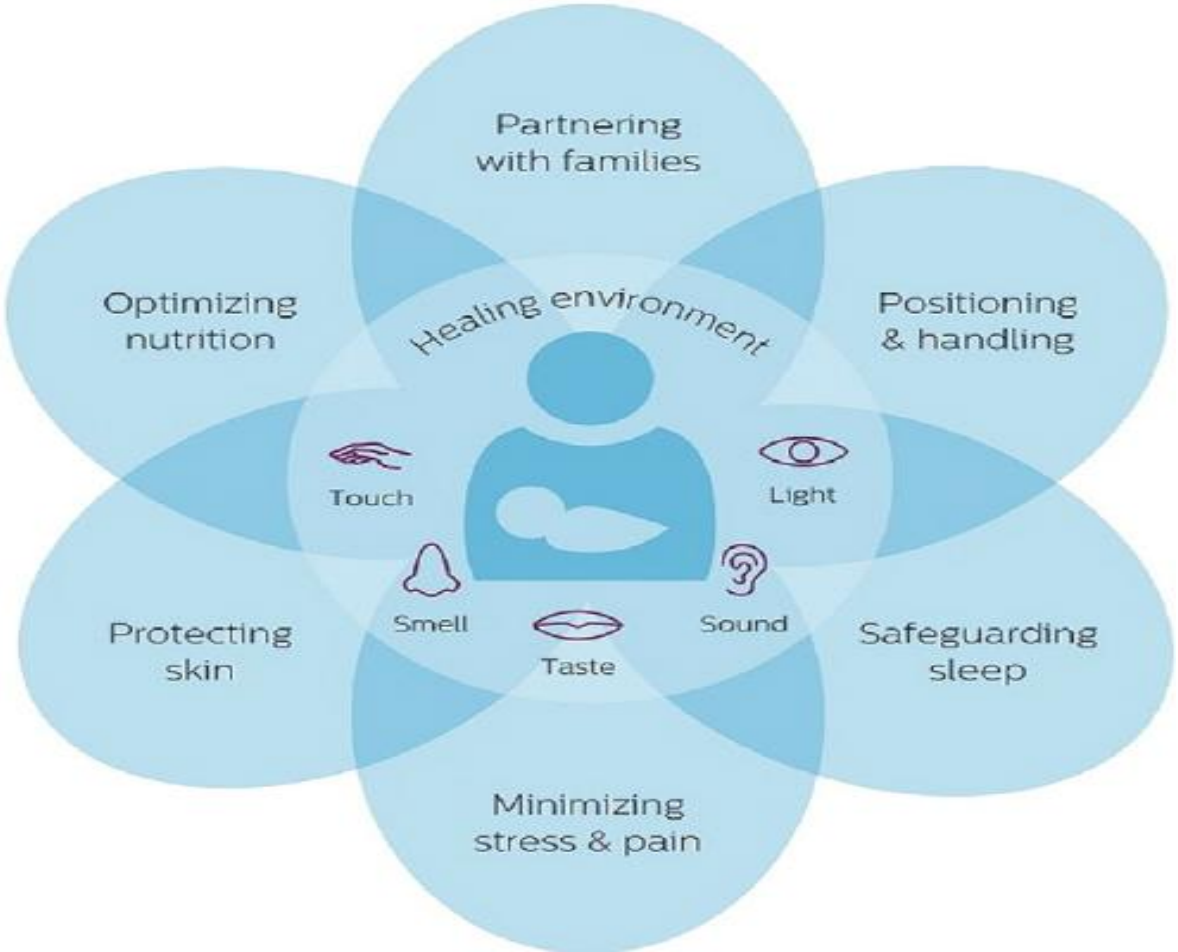
Objectives

1. Neonatal sensory pain system
2. Neonatal pain assessment tools
3. Neuroprotective strategy for prems: Minimizing pain and stress

Neuroprotective strategy in premature neonates

- The World Health Organisation (WHO) estimates that 15 million babies are born prematurely each year worldwide (WHO, 2015)
- Early intervention in premature babies is essential to promote their neurodevelopment, comfort, security and growth
- Seven neuroprotective core measures for family-centered developmental care of the premature neonate are: healing environment, partnering with families, positioning and handling, minimizing stress and pain, safeguarding sleep, protecting skin, and optimizing nutrition

Neonatal Integrative Developmental Care Model



Neonatal Integrative Developmental Care Model (Philips Mother and Child Care).

PAIN

Misconceptions about Neonatal Pain

1. The pain pathways in neonates are unmyelinated or otherwise immature and cannot transmit painful stimuli to the brain.
2. There is no alternative for verbal self-report, which remains the "gold standard" for conveying a subjective experience like pain.
3. Pain perception is located only in the cortex, and thalamocortical connections must be fully developed in order to allow pain perception.
4. The human infant does not have the psychological context in order to identify any experiences as painful and this does not develop until two years or later.
5. New-born infants are at greater risk for developing the adverse effects of analgesic or sedative agents, or these drugs have adverse long-term effects on brain development and behaviour.

Neonatal sensory pain system

- By the middle of the second trimester, the human fetus has a highly differentiated and functional sensory system.
- This system appears to transmit different sensory modalities, like pain, touch, or vibration, which are mediated by very different pathways and loci of sensory processing in the mature adult nervous system.
- Neonatal responses to pain, include autonomic (e.g., increases in heart rate, blood pressure), hormonal (e.g., cortisol and catecholamine responses), and behavioural changes (e.g., facial grimace).
- These responses form the basis of the many pain assessment tools used to evaluate acute pain in the neonate

Neonatal brain response to pain

- Increased cortical activation in the somatosensory areas of the brain in response to painful stimuli (e.g. heel stick or venepuncture): preterm infants
- Term infants less than seven days old, functional magnetic resonance imaging (fMRI) studies identified brain activation in 18 of the 20 brain regions typically activated in healthy adults following noxious stimulation.
- These results demonstrate that sensory and affective components of pain are active in infants and suggest that the infant pain experience closely resembles that of adults

Effects of pain in the neonate

1. Altered pain pathways and thresholds
2. Altered programming of stress system
3. Impaired neurobehavioral outcomes, including cognitive, memory, and behavioural deficits
4. Altered neuronal and synaptic organization
5. Lower IQs
6. Alter the structure and function of the developing brain in preterm infants i.e. reduction of white and subcortical gray matter structures during maturation

These deficits may persist into adolescence and adulthood

(Beauchamp et al., 2008;Grunau, Holsti, & Peters, 2006; Grunau et al., 2009;Hermann, Hohmeister, Demirakca, Zohsel, & Flor,2006).

Effects of inadequately treated pain

- Altered pain response:
  - Several studies have reported that exposure to repetitive pain in early life may lead to greater risk of developing increased pain sensitivity and/or chronic pain syndromes during their subsequent lifespan
  - Infants exposed to circumcision pain at birth experienced greater pain at immunization four to six months later

- Neuro developmental outcomes:
  - Frequency of exposure to neonatal pain-related stress has been correlated with subsequent impairments in cognitive development, altered neurocognitive processing, decreased cortical thickness, and dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis

Pain in Neonates

- Exposure to repeated neonatal pain-related stress may lead to poorer cognitive, motor, and behavioural neuro-development in infants and children born very preterm

- Neonatal pain and stress can lead to anxiety like behaviours during adulthood

Types of neonatal pain

1. Acute or physiological pain – Occurs from skin-breaking procedures or tissue injury caused by diagnostic or therapeutic interventions. Infants admitted to the neonatal intensive care unit (NICU) repeatedly experience acute pain from an average of 12 to 16 invasive procedures each day.

2. Established pain – Occurs following surgery, localized inflammatory conditions (e.g., abscess or thrombophlebitis), or birth-related trauma.

3. Prolonged or chronic pain – Results from severe diseases such as necrotizing enterocolitis (NEC) or meningitis, or rare conditions such as scalded skin syndrome or Harlequin syndrome

Assessment of neonatal pain: Uptodate

Symptoms and signs of Pain in a neonate

- 1. Behavioural: Grimacing, Crying
- 2. Physiological: heart rate, respiratory rate and oxygen saturations
- 3. Hormonal: rise in catecholamine and cortisol level
- There may be challenges in pain assessment in SELECTED POPULATIONS:
  - Preterm or critically ill infants
  - Persistent or prolonged pain
  - Mechanically ventilated
  - Neurologically impaired including neurologic blockade

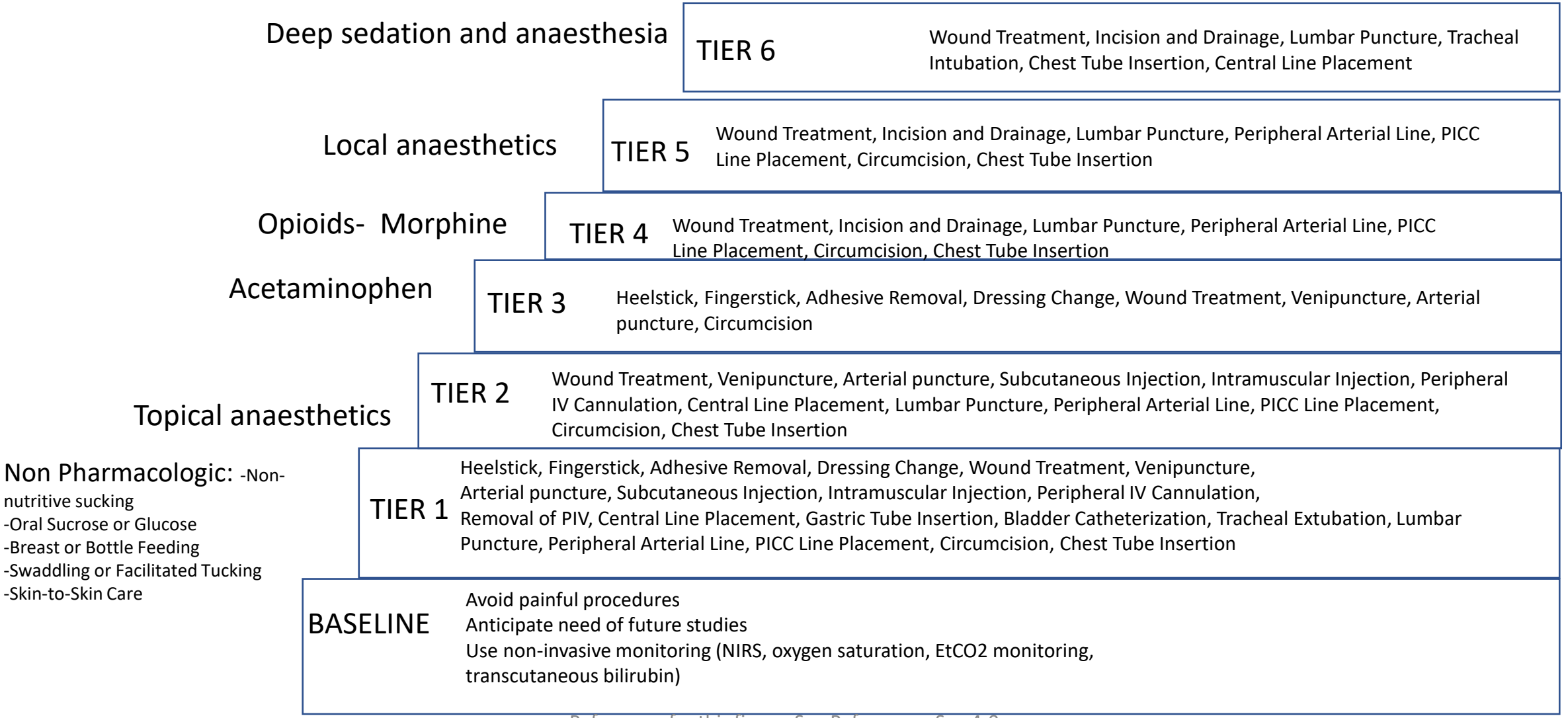
Pain assessment tools

- PIPP (premature infant pain profile): Heart rate, oxygen saturation, facial actions
- NIPS (neonatal infant pain score): Facial expression, crying, breathing patterns, arm and leg movements, arousal
- NFCS (neonatal facial coding system): Facial actions
- N-PASS (neonatal pain, agitation and sedation scale): Crying, irritability, facial expression, extremity tone, vital signs
- CRIES (cry, requires oxygen, increased vital signs, expression, sleeplessness)
- COMFORT scale
- DAN (Douleur Aigue¨ du Nouveau-ne´): Facial expression, limb movements, vocal expression

Approach to pain in a neonate

- Routinely assess the infant for detection of acute and/or prolonged pain.
- Reduce the number of painful procedures and unnecessary noxious stimuli.
- Prevent/reduce acute pain by providing pre-emptive analgesia for any anticipated painful procedure. This includes a combination of nonpharmacological methods and pharmacologic therapy.
- Anticipate and treat postoperative pain following surgery.
- Avoid, ameliorate, or limit the duration of prolonged continuous pain/stress.
- Monitor patient responses to analgesic intervention using validated assessment tools. Provide additional analgesia if needed.

A tiered approach to analgesia in neonate



References for this figure: See References: See 4-9

Pharmacologic analgesia

- Opioids: morphine, fentanyl
- Acetaminophen
- Local anaesthetics: lidocaine/prilocaine 5% cream (EMLA) and tetracaine 4% gel (Ametop)

Morphine

- Both analgesia and sedation
- Wide therapeutic window
- Attenuates physiologic stress responses
- Used for post-op pain/trauma/intubation
- May improve ventilator synchrony and sedation but in ventilated preterm studies show little or no benefit over placebo
- Increased duration of ventilation
- Delay in attaining full feeds
- Hypotension

Non pharmacologic analgesia

- Underlying mechanisms:

1. Gate control theory which proposes that stimuli or interventions traveling the ascending pathways to the brain may inhibit nociceptive signals or transmission, reducing the amount of pain the infant is exposed to.

2. Release of endomorphins and oxytocin

Non pharmacologic analgesia

1. Kangaroo Mother Care: effective for treatment of a single painful procedure and repeated painful procedure.

- Facilitates preterm infants' behavioural and physical responses to return to the baseline phase **more quickly** than incubator care after repeated painful procedures.

2. Oral Sucrose

- A meta-analysis suggested there is an increase effect of sucrose when given two minutes prior to the painful procedure. A calming effect lasts up to five to seven minutes with this procedure (Stevens et al., 2008).

3. Breastfeeding
4. Facilitated Tucking/ Swaddling
5. Pacifier
6. Non-nutritive sucking (NNS)
7. Sensorial saturation (use of touch, massage, voice, and smell)

Non pharmacologic analgesia

- There is a role for combination of non pharmacological therapy
- Also combinations of pharmacological and non pharmacological therapies can alleviate pain

Oral sucrose

- Proven to be safe and effective for reducing procedural pain from various painful events: heel lance, venepuncture, nasogastric tube insertion, and eye examination. (acute, episodic pain)
- Oral: 20–30 % solution
- Multiple doses are more effective than single
- Causes endogenous opioid release, through an unknown mechanism
  - Reduces PIPP score and duration of crying in neonates
  - Dampened physiologic responses for heart rate, oxygen saturation, or vagal tone
  - Reduced facial expressions specific for pain
- Unclear - the required dose of sucrose needed for optimal efficacy (doses range between 0.012 and 0.12 g)

  - the safety in neonates who are of VLBW, unstable, and/or ventilated.

Breastfeeding/ breast milk

- Superior alternative to oral sucrose or glucose for pain control in infants
- Benefits:
    - maternal proximity and ventral skin-to-skin contact, which increase beta endorphin and oxytocin levels in newborns, and the effects of sugars, fats, and other nutrients in breast milk combined with nutritive sucking to reduce pain and divert the infant's attention away from the painful stimulus.
- Supplemental breast milk is a reasonable option for providing neonatal analgesia, but less effective than breastfeeding or sucrose/glucose

Breastfeeding/ breast milk

- Advantage for one-time painful procedures
- Neonates who were breastfed during heel stick procedures and venepunctures showed a significant decrease in the variability of physiologic response as compared to swaddling, holding by mother, placebo, pacifier use, or oral sucrose
- Reduce PIPP score

Kangaroo care

- There is conclusive evidence to recommend KC as an intervention for reducing pain reactivity and improving regulation of pain-related distress in preterm infants
  - Lower scores on the PIPP
  - Lower salivary cortisol
  - Reduced HR variability (HRV)
  - Decreased crying time

Facilitated Tucking

- Positioning infants with extremities flexed and close to the trunk with blanket rolls in a restricted mode.
  - Reductions on pain assessment scores
  - Shorter mean sleep disruption time and less crying time.

- In term and preterm infants, facilitated tucking or swaddling is more effective than no intervention in reducing pain responses to invasive procedures (eg, endotracheal suctioning and heel stick)

Swaddling

- involves wrapping an infant in a blanket with minimal restraint; limbs are flexed, and hands are accessible for exploration
- Less effective in relieving repeated heel stick pain than sucrose, but in combination with sucrose it had additive effects
- Reduced pain scores during tracheal suctioning in preterm neonates
- More effective than either placebo, oral glucose, or oxycodone therapy
- Tight swaddling has been associated with an increased risk of developmental dysplasia of the hip

Non Nutritive sucking

- Placing a pacifier in an infant’s mouth to promote sucking behaviour without providing breast milk or formula for nutrition.
- Effective in decreasing length of hospital stay in preterm infants, to facilitate the transition to bottle feeding, and to decrease pain during circumcision in newborns.
- Efficacy of NNS in reducing pain in preterm infants has not been sufficiently documented.
  - stimulates orotactile and mechanoreceptors in the mouth, thus modulating transmission or processing of nociception by the endogenous nonopioid system

Non nutritive sucking

- Infants offered pacifiers had lower increases in heart rate and decreased crying in response to painful stimuli compared with those who received no intervention , swaddling alone, rocking alone , or sensory stimulation.
- Oral sucrose and breastfeeding is preferred to NNS.

Sensorial saturation

- Sensorial saturation results from multi-modal sensory inputs (eg, touch, massage, taste, voice, and smell) during a painful procedure

- Several reports have shown greater pain reduction in infants who received a combination of sensorial saturation (eg, radiant warmth or exposure to familiar scent) and oral sucrose during painful procedures compared with oral sucrose alone

Massage Therapy

- Form of systematic tactile and kinesthetics stimulation that has been noted to enhance the infant's developmental outcomes, lower serum cortisol levels, shorten hospital stay, and enhance weight gain.

- There is insufficient evidence to support the use of massage in reducing pain in preterm infants

Rocking

- Results in vestibular stimulation.
  - Maternal has been reported to decrease pain responses in full-term neonates
  - Using waterbeds in preterm neonates has been found to promote quiet state and growth and to reduce apnoea
  - Rocking as an intervention to decrease pain in preterm infants lacks evidence and is based on traditional practices

Emerging modalities

Reduce pain responses and increase physiological stability during neonatal pain

- Music
- Therapeutic touch
- Using a radiant warmer or localized warming
- Osteopathic manipulation and medical acupuncture

References

- 1. Effect of repeated Kangaroo Mother Care on repeated procedural pain in preterm infants: A randomized controlled trial Haixia Gao a, Guihua Xu
- 2. Improving pain management in neonates exposed to intravenous insertions: A quality improvement initiative* Angelica M. Lagunas
- 3. Pain Interventions in Premature Infants: What Is Conclusive Evidence and What Is Not
- 4. Lago P, Garetti E, Merazzi D, et al. Guidelines for procedural pain in the newborn. Acta Paediatr (Oslo, Norway: 1992). 2009;98(6):932–9. doi:10.1111/j.1651-2227.2009.01291.x. A foundational systematic review of procedural pain prevention and treatment of NICU neonatal patients.
- 5. Anand KJ, Aranda JV, Berde CB, et al. Summary proceedings from the neonatal pain-control group. Pediatrics. 2006;117(3 Pt 2):S9–22.Bueno M, Yamada J, Harrison D, et al. A systematic review and meta-analyses of nonsucrose sweet solutions for pain relief in neonates. Pain Res Manag. 2013;18(3):153–61.

References

- 6. Taddio A, Shah V, Hancock R, et al. Effectiveness of sucrose analgesia in newborns undergoing painful medical procedures. CMAJ. 2008;179:37. Chermont AG, Falcao LF, de Souza Silva EH, de Cassia Xavier Balda R, Guinsburg R. Skin-to-skin contact and/or oral 25% dextrose for procedural pain relief for term newborn infants. Pediatrics. 2009;124:e1101–7.
- 7. Taddio A, Ohlsson A, Einarson TR, et al. A systematic review of lidocaine-prilocaine cream (EMLA) in the treatment of acute pain in neonates. Pediatrics. 1998;101:E1.
- 8. Kaur G, Gupta P, Kumar A. A randomized trial of eutectic mixture of local anesthetics during lumbar puncture in newborns. Arch Pediatr Adolesc Med. 2003;157:1065.
- 9.US Food and Drug Administration. FDA drug safety communication: reports of a rare, but serious and potentially fatal adverse effect with the use of over-the-counter (OTC) benzocaine gels and liquids applies to the gums or mouth.

References

- 10. A Guide to Pain Assessment and Management in the Neonate Norina Witt1 ; Seth Coynor1; Christopher Edwards2,3; Hans Bradshaw
- 11. Uptodate: Assessment of neonatal pain
- 12. Effect of early procedural pain experience on subsequent pain responses among premature infants Atef El-Sayed Donia a, Omar Atef Tolba
- 13. Prevention and treatment of neonatal pain: Uptodate
- 14. The consequences of pain in early life: injury-induced plasticity in developing pain pathways

ASANTE

•