Lesson: Physiology of Pain

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About this Document

This document is a resource to the course: Core Measure 5 Minimizing Stress & Pain, Lesson: Physiology of Pain.

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Lesson: Physiology of Pain

Physiology of Pain

The fifth neuroprotective core measure of the Neonatal Integrative Developmental Care Model is “Minimizing Stress and Pain.” From the first moments after birth, the premature infant is subjected to noxious sounds, bright lights, stressful conditions and a multitude of painful procedures along with repetitive, non-nurturing handling and separation from mother during a period of rapid brain growth (Carbajal, et al., 2008; Stevens, et al., 2010; Johnston, et al., 2011). Seemingly typical handling and caregiving by the NICU staff such as bathing, weighing, and diaper changes are perceived as stress to the infant (Comaru & Miura, 2009; Liaw, Yang, Chang, & al., 2009). This altered sensory experience and untreated pain is inherently stressful and researchers have reported negative effects on both short-term and long-term consequences in the infant’s brain development. (Slater et al., 2010; Gaspardo et al., 2008, Bartocci, et al., 2006; Holsti et al., 2005; & Walker et al., 2009). Among all NICU experiences, acute pain is arguably the most physiologically disruptive and developmentally unexpected of all stimuli, though some clinicians do not consider it a risk factor for neurocognitive outcomes (Perlman, 2003).

Consequences of neonatal stress include increased energy expenditure, decreased healing and growth, impaired physiologic stability and altered brain development. NICU stressors and painful interventions may raise cortisol levels, limiting neuroplastic reorganization and therefore, learning and memory of motor skills. Infants that are exposed to repeated painful experiences can have negative short- and long-term consequences for brain organization during sensitive periods of development (Walker, 2014, Grunau, Tu, & Whitfield, 2010).

Perception of Pain

Not long ago health professionals believed that neonates, especially premature infants do not feel pain due to the immaturity of the central nervous system. This belief prevailed for decades with small and sick infants subjected to intense pain with no appropriate management. Unfortunately this belief prevails to date in some developing countries. This is despite the fact that over twenty years ago, researchers from Europe and the United States established that the anatomical, physiological and neurochemical structures which convey pain are well developed in neonates. Since, then there has been an explosion of research related to pain in premature infants and suggested interventions to ameliorate pain. Infants, even prematurely born infants, have the neurologic capacity to perceive pain at birth (Simons & Tibboel, 2006).

Premature infants spend much of their early days of life in an environment that is stressful and in many situations painful. Preterm infants all experience pain during their stay in the neonatal intensive care unit (NICU) as they are exposed to many diagnostic and therapeutic procedures that are necessary for their survival. Despite advances in neonatal pain assessment and management, non-pharmacologic and pharmacologic analgesic therapies continue to be underutilized to manage both acute and procedural pain (Carbajal, 2008). Untreated acute, recurrent or chronic pain related to disease or medical care may have significant and lifelong physiologic and psychological consequences (Walden, 2014). In order to effectively manage pain, a thorough pain assessment must be performed. The theory of nociception divides the pain system into three components: peripheral nervous system, spinal cord, and supraspinal/integrative level.
Peripheral Nervous System (Evans, 2001)

The peripheral nervous system is responsible for registering initial noxious stimuli; initiating local pain reactions through the release of biochemical mediators such as substance P and prostaglandins, which result in hyperalgia (increased sensitivity to painful stimuli), allodynia (pain caused by a stimulus that ordinarily does not cause pain), or dendritic sprouting or hyperinnervation (which results in hypersensitivity and a lower pain threshold that may persist into adulthood); and conducting nociceptive input to the spinal cord and central nervous system. Transmission of nociceptive impulses occurs along two types of afferent sensory fibers. A-delta fibers are thinly myelinated, rapid conducting fibers associated with acute pain or “first pain” (e.g., sharp, localized, pricking). C fibers are polymodal, unmyelinated, slow conducting fibers associated with aching, burning, throbbing, poorly localized chronic, or “second pain.” Nociceptive impulses are carried throughout both unmyelinated and thinly myelinated fibers, both in neonatal as well as the adult peripheral nervous system.

Spinal Cord (Evans, 2001)

The dorsal horns of the spinal cord integrate pain and other sensory stimuli and modulate pain perception. Afferent fiber neurotransmitters stimulate receptors in the dorsal horns, producing central sensitization (increased excitability of dorsal horn neurons that spreads to several adjacent segments of the spinal cord), “wind-up” (perceived increase in intensity or duration of painful stimuli), or secondary analgesia (hypersensitivity elicited by both painful and non-painful stimuli that extends to areas beyond the site of injury). Behavioral responses occur when the capabilities of neural mechanisms are exceeded by nerve impulses arriving in the dorsal horns (Melzack & Wall, 1965). Local spinal cord response to pain impulses from peripheral afferent fibers also stimulate efferent somatomotor neurons in the anterior horn and produces reflex withdrawal.

Modulation of nociceptive transmission occurs through the release of metenkephalin from local interneurons as well as dopamine, norepinephrine, and serotonin from descending inhibitory axons. Preterm infants, however, have limited ability to modulate pain. Dopamine and norepinephrine are not available to modulate pain before 36 – 40 weeks gestation, and serotonin is not released until approximately 6 – 8 weeks after birth (Walden & Jorgenson, 2014).

Supraspinal/Integrative Level (Evans 2001)

Supraspinal areas (thalamus, cerebral cortex) integrate and process pain information; which modifies the cascade of neurochemical events triggered by nociception. Supraspinal centers are also involved in memory and learning from nociceptive experiences and produce systematic responses to pain including cardiovascular, respiratory, hormonal, metabolic, and immune adaptations and alterations.

This basic understanding of pain has been expanded to recognize that pain also has a response component. This component actually changes the nervous system and the way in which it responds to pain (Anand, 2000; Anand, Steve(n(s, & McGrath, 2007; Bartocci, et al., 2006).

Responses to painful stimuli can be demonstrated in nociceptive pathways from the periphery to the cortex in neonates, although the degree and nature of response change with age. Peripheral pain receptors (nociceptors) respond to mechanical, thermal and chemical stimuli following birth, and peripheral sensitization or primary hyperalgesia (reduced threshold and enhanced response to previously painful stimuli) develops within areas of tissue injury (Fitzgerald & Walker, 2009).
Significance of Pain Response in Neonates

Preterm infants are extremely vulnerable to pain. Decreased ability to attenuate pain may allow even relatively benign procedures to be perceived as painful, especially when occurring just after handling or another painful experience (Taylor, 2010). Painful procedures are not uncommon during an infant's stay in the NICU. Studies indicate that an infant delivered between 27-31 weeks gestation could possibly endure 134 painful procedures during the first two weeks of life with 10% of the youngest and most frail infants receiving more than 300 painful procedures (Stevens, Johnston, Franck et al., 1999).

Effects of repetitive pain

Repetitive, unrelieved pain can lead to serious and adverse consequences for neonates. Short-term consequences of painful procedures include decreased oxygen saturations and increased heart rates that place increased demands on the cardiorespiratory system. Additionally, pain can cause elevation in the intracranial pressure, increasing risk for intraventricular hemorrhage (IVH) in preterm neonates.

Immediate consequences of severe or repetitive painful experiences in the NICU may include:

- Physiologic instability
- Medical complications
- Sleep disturbances
- Feeding problems
- Poor self-regulation

Painful procedures may result in heightened pain sensitivity to routine handling as well as delayed recovery from noxious and routine caregiving procedures (Walden 2014). Doesburg et al. (2013), identified abnormal patterns of cortex-wide activity, critical windows for pain exposure and development of visual-perceptual abilities, and also established that recurrent neonatal pain was a risk factor for impaired neurocognitive outcomes.

Repetitive or prolonged pain has been implicated in enhanced neuronal cell death in the immature brain, with concerns for future neurodevelopmental outcome. Their conclusions included linking neonatal pain with visual-perceptual abilities and the development of thalamocortical connections in 7–8-year old extremely low gestational age (ELGA) children.

Pain response

Because premature infants cannot manifest pain as well mature infants due to lack of inhibitory control they may be at an increased risk for negative brain alterations in both structure and function (Brummelte, et al., 2012). Persistent changes in sensory processing were found in children 8–12 years following neonatal intensive care and the degree of change was more marked in those who also required surgery during the neonatal period (Hermann et al., 2006; Hohmeister, 2009; Walker, et al., 2009). Studies have documented and postulated several neurodevelopmental consequences such as learning and behavioral difficulties observed in later infancy and childhood and reduced brain white matter (Walker et al., 2009).

Pain produces a range of physiological and behavioral responses in neonates that can be utilized in clinical assessment tools to quantify pain severity and evaluate analgesic efficacy (Walker, 2014).
Physiology of Pain

Although pain scores have typically been used to evaluate the effects of pain-relief interventions, sleep structure has been documented as a more objective measure for prolonged effects of pain and its management (Axelin, et al 2010). The adverse impact of inadequate analgesia/anesthesia on acute morbidity following neonatal surgery has long been recognized (Walker, 2013). Changing levels of neural activity can alter the normal development of the central nervous system (CNS). As a result, there is increasing awareness of the need to not only reduce acute behavioral responses to neonatal pain, but also to protect from persistent sensitization of pain pathways and potential damaging effects of excess activity on brain development.

**Neuroprotective interventions**

Clinicians should provide preterm infants with neuroprotective interventions to not only relieve pain, but to also minimize stress (Altimier & Phillips, 2013; Liaw, et al, 2013). Minimizing stress in preterm infants may have many neurologic benefits such as reducing the likelihood of programming abnormal stress responsiveness. This may help preserve existing neuroplastic capacity (Pitcher, Schneider, Drysdale, Ridding, & Owens, 2011).

Infants have demonstrated markedly improved outcomes when the stress of environmental overstimulation is reduced. As we continue striving to improve morbidity and mortality rates, we are challenged to enhance neuroprotective strategies for these vulnerable infants.