Section A -Research paper

Pathophysiology and management of Acute Postoperative Pain in Pediatrics

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Abstract:

Although postoperative pain remains incompletely controlled in some settings, increased understanding of its mechanisms and the development of several therapeutic approaches have substantially improved pain control in past years. Advances in our understanding of the process of nociception have led to insight into gene-based pain therapy, the development of acute opioid-induced hyperalgesia, and persistent postsurgical pain. Use of specific analgesic techniques such as regional analgesia could improve patient outcomes.

Keywords: pain, analgesia, postoperative.

Introduction:

The International Association for the Study of Pain (IASP) defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage" **(1).** Such an expansive definition of pain emphasizes the subjective nature of pain and how psychosocial, developmental, ethnic, genetic, and cultural factors impact its experience. Defining pain in this manner gives explanation to the pain experienced by a fearful child waiting for intravenous cannulation however, pain can occur and exist in the absence of tissue damage. Furthermore, a caregiver is urged to address both the psychological and physical aspects of pain in order to effectively and reliably treat it **(2).**

Pain is a protective sensation that acts as an early warning system designed to minimize tissue damage, which is the positive aspect of pain. On the other end of the spectrum, negative characteristics have both an immediate impact on the well-being of a child and may result in long-term detrimental consequences. Nevertheless, latter results in prolonged stimulation and pathological alterations to the peripheral or central nervous system (CNS) is brought about by untreated or inadequately managed pain **(3).**

Children may suffer mild to severe pain from a vast array of encounters during the perioperative period. Most often, this type of

pain is characterized as somatic pain. It is described as acute, well localized and sharp in nature. Children also encounter episodes of visceral or neuropathic pain. Visceral pain is characterized as diffuse and aching, whereas neuropathic pain associated with nerve damage is burning in nature. Acute pain from minor and major procedures is associated with acute illness or an acute exacerbation of a chronic illness such as in sickle cell anemia **(4)**. In spite of the known presence of pain in children, epidemiological studies demonstrate the continued lack of adequate pain management in this population. Gaining an understanding of the pathophysiology of pain and how to apply age-appropriate pain assessment tools will help to create targeted pain treatment plans that promote the implementation of successful pain management strategies and improved pain control in children. **(5).**

Neuroscience of Pain

Transduction, transmission, modulation, and perception are processes that define pain. Pain is distinguished from nociception in that pain is a perception, while nociception is the biophysical process that encodes noxious stimuli that often, but not always, leads to the expression of pain. **(6).**

Several types of pain are produced by noxious mechanical, thermal, or chemical injury (nociceptive pain, inflammatory pain, and neuropathic pain), and whatever the type of pain, it passes through the following pathway. **(7).**

1) Specialized pain receptors, nociceptors, on the afferent somatosensory A-δ and C neurons transduce noxious stimuli into electrical activity. These encoded nociceptive signals are transmitted through sensory neurons traveling through the dorsal horn of the spinal cord.
2) Sensory neurons synapse on secondary neurons that cross the midline of the spinal cord and transmit the nociceptive signals, usually through specific ascending "pain tracts" that include the spinothalamic, spinomesencephalic, and spinoreticular tracts.
3) The signals from the periphery project into a "neuromatrix" that includes the thalamus, hypothalamus, anterior cingulate cortex, somatosensory cortex, brain stem, periaqueductal gray-matter (PAG), brain stem reticular nuclei, and locus ceruleus.

These tracts spread to a wide variety of sites in the brain that are involved with nociceptive processing (Fig. 1). **(8).** Signals reaching the somatosensory cortex are perceived as pain, on the other hand, other signals project into the midbrain and areas that are involved with the affective (emotional) components of pain. **(9).**

Pain modulation occurs through neuronal projections from the PAG area and the nucleus raphe magnus, which form descending pathways that inhibit or facilitate pain signals at lower levels of the central nervous system (CNS), including the substantia gelatinosa (the Rexed lamina II) **(10).**

Current research proved that the neuro-anatomic and neuroendocrine systems necessary to perceive pain are present by the 25th week of gestation, but the descending inhibitory systems are not completely developed until sometimes after birth. Tissue injury produces a neuroendocrine stress response and inflammatory immunologic changes that modulate pain. Local inflammatory reaction induced by mast cells, macrophages, and neutrophils produces leakage of plasma, increased capillary wall permeability, and the release of mediators like kinins, amines, arachidonic acid derivatives, tumor necrosis factor (TNF), purines, potassium ions, hydrogen ions, serotonin, primary afferent amines, proteases, and nerve growth factor.

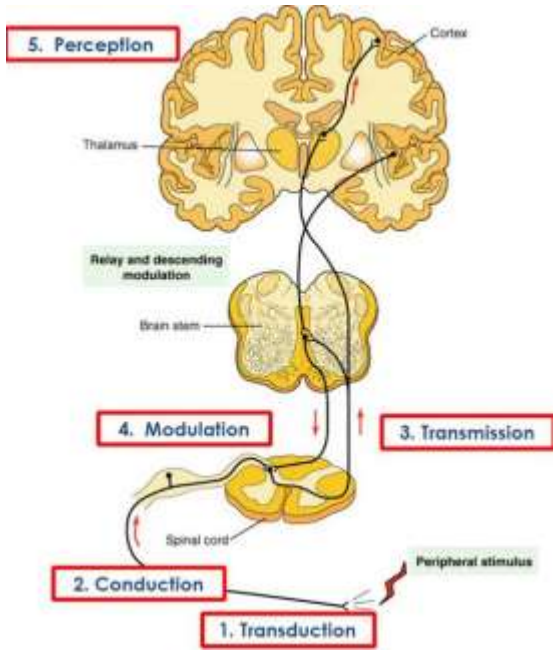

Figure (1): Overview of the basic nociceptive circuit **(11).**

This inflammatory reaction decreases the threshold for neuronal activation, and results in hyper-algesia, leading to chronic pain, moreover, the intracellular changes alter the properties of the pain neurons making pain cells to be more excitable and reactive to harmless stimuli, producing central sensitization or "wind-up". With central sensitization, pain becomes self-sustaining and very difficult to treat. Even non-noxious sensations can evoke pain if wind-up is present; examples of which are complex regional pain syndrome type 1 and allodynia **(12).**

➢ **Endogenous substances modulating nerve function:**

Peripheral activation of the nociceptors (transduction) is modulated by a number of chemical substances, which are produced or released when there is cellular damage (Tab. 1). These mediators influence the degree of nerve activity and, hence, the intensity of the pain sensation. Repeated stimulation typically causes sensitization of peripheral nerve fibers, causing lowering of pain thresholds and spontaneous pain, a mechanism that can be experienced as cutaneous hypersensitivity. **(13).**

Table (1): Selected chemical substances released with stimuli sufficient to cause tissue damage:

Substance	Source
Potassium	Damaged Cells
Serotonin	Platlets
Bradykinin	Plasma
Histamine	Mast Cells
Prostaglandins	Mast Cells
Leukotrienes	Damaged cells
Substance P	Primary nerve afferents

➢ Modulation of pain perception: (14)

There are many mechanisms that modulate pain perception: segmental inhibition, the endogenous opioid system, and the descending inhibitory nerve system.

❖ **Segmental inhibition**: The noxious impulse that crosses the synapse between the Ad and C nerve fibers and the cells in the dorsal horn of the spinal cord can be blocked by stimulation of inhibitory nerve in the spinal cord that result from stimulation of the Aß fibers (carry impulses from low-threshold mechano- receptors such as touch).

❖ **Endogenous opioid system**: Three compounds (Enkephalin, Endorphin, and Dynorphin) were found to bind to the opium receptors that are located in the peri-aqueductal gray matter, ventral medulla, and spinal cord.

❖ **Descending inhibitory system**: Certain brain-stem areas (periaqueductal gray-matter and rostral medulla) can control the ascent of noxious impulse to the brain, serotonin and noradrenaline are the main neuro-transmitters of this pathway.

➢ Protective function of pain:

Local release of chemicals such as substance P causes vasodilation, swelling and release of histamine from the mast cells that further increase vasodilation. This complex chemical signaling protects the injured area by producing behaviors that keep that area away from stimuli. Promotion of healing and protection against infection are aided by the increased blood flow and inflammation. **(15)**

➢ Adverse Pathophysiological effects of acute postoperative pain:

❖ Acute pain and the injury response:

Acute postoperative pain after inguinal hernia repair surgeries in pediatrics can activate a neuro-humoral and an immune response to injury (Fig. 2), and the injury responses have a major influence on acute pain mechanisms, so acute postoperative pain and injury of various types are inter-related and if it was severe and prolonged, the injury response becomes counter-productive and can have adverse effects on outcome. **(16).**

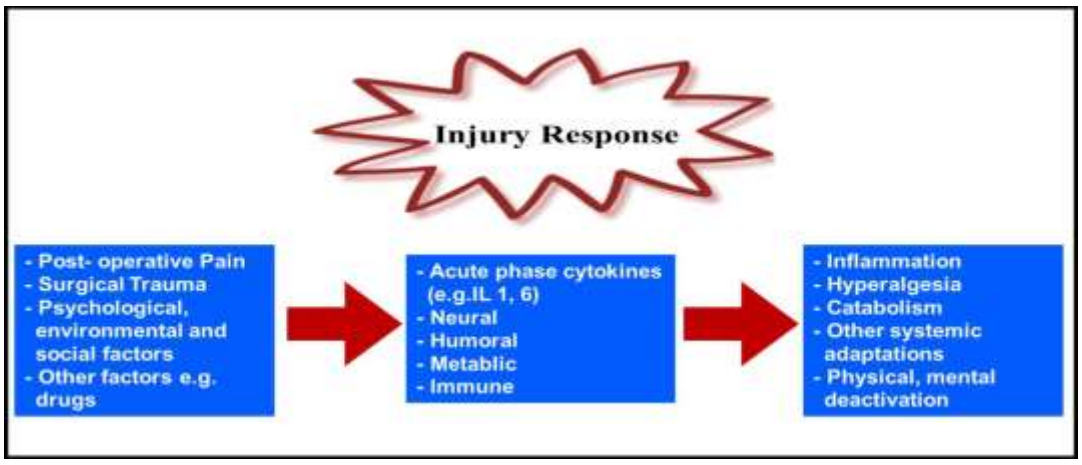

Figure (2): The post-operative injury response (17).

❖ Acute-phase response

The cytokine cascade activated in response to surgical trauma consists of a complex biochemical network with diverse effects on the injured host. Whereas elements of the immune system are stimulated to an excessive degree following major surgery, other functions such as that of cell-mediated immunity are dramatically paralyzed. Cytokines are immune mediators that direct the inflammatory response to sites of injury and infection and are essential for wound healing. An exaggerated production of proinflammatory cytokines from the primary site of injury, however, can manifest systemically as hemodynamic instability or metabolic derangements. Proinflammatory cytokine production in the intraoperative and early postoperative periods is initiated by macrophages and monocytes at the initial site of injury as part of the acute-phase response. These cytokines include tumor necrosis factor and interleukin 1 which are primarily responsible for the non-hepatic manifestations of the acute-phase response, including fever and tachycardia. In turn, TNF and IL-1stimulate the production and release of other cytokines, including IL-6. Interleukin 6 primarily regulates the hepatic component of the acute-phase response resulting in the generation of acute-phase proteins, including C-reactive proteins. Circulating levels of several other acute-phase proteins, including serum amyloid A,7 pro calcitonin,8 C3 complement, and haptaglobin, have also been shown to increase after traumatic insult, providing further evidence of a systemic host response**(18).**

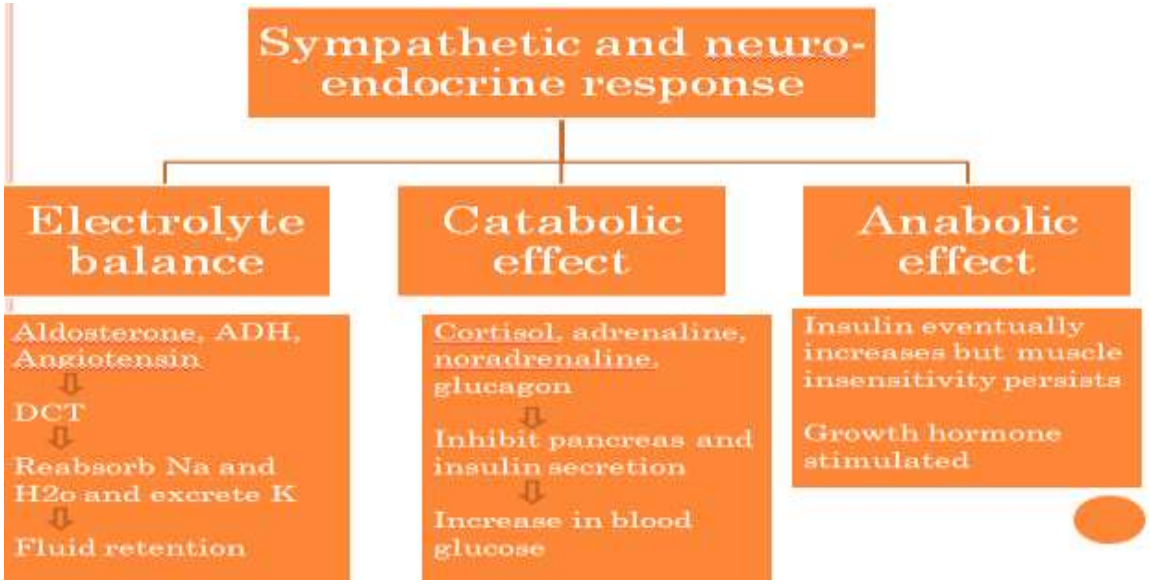

Fig (3): Metabolic and endocrine responses to injury. **(19)**

Influence of Anesthetic and Analgesic techniques on outcome after surgery:

Postoperative symptoms and complications can be prevented by a suitable choice of anesthetic and analgesic techniques for specific procedures. The aim of analgesic protocols is not only to reduce pain intensity but also to decrease the incidence of side-effects from analgesic agents and to improve patient comfort. Moreover, adequate pain control is a prerequisite for the use of rehabilitation programs to accelerate recovery from surgery. Thus, combining opioid and/or non-opioid analgesics with regional analgesic techniques not only improves analgesic efficacy but also reduces opioid demand and side-effects such as nausea and vomiting,sedation, and prolongation of postoperative ileus. **(20).**

Good pain control after surgery is important to prevent negative outcomes such as tachycardia, hypertension, myocardial ischemia, decrease in alveolar ventilation, and poor wound healing. Exacerbations of acute pain can lead to neural sensitization and release of mediators both peripherally and centrally. Advances in the knowledge of molecular mechanisms have led to the development of multimodal analgesia and new pharmaceutical products to treat postoperative pain. Indeed, regional versus systemic analgesia decreases postoperative pulmonary complications, and this impact is greater following abdominal surgery. **(21)**.

Assessment of Postoperative Pain in Pediatrics:

Assessment of pain and its impact on the patient is the most important first step in managing pain. The distinction between measurement and assessment in pain research has not always been clarified. Measurement refers to the application of some metric to a specific element; usually intensity of pain, However assessment is much broader, as it measures the impact of different factors on the experience of pain. These factors might include the affective response to noxious stimuli, the role of family style on the perception of pain, the impact on families of having a child in pain, and the meaning of pain to the child and to the family. **(22).**

Multiple pain assessment instruments or measures exist. However, choosing the correct age-appropriate and suitable instrument is difficult because many patients are non-verbal or are not cognitively aware. Knowledge of the properties and limitations of available assessment tools provides a means of choosing the correct one. **(23).**

➢ **Pain assessment tools may be classified as: (24)**

1.Self-report (i.e. visual analog or verbal numeric scales).

2.Behavioral (i.e. graded behavioral activities such as crying or change in limb activity).

3. Physiological parameters such as scoring heart rate and blood pressure.

4.Biochemical (i.e. neuro-endocrine responses are targeted).

5. Neuro-physiological (i.e. electromyogram (EMG), near-infrared spectroscopy (NIRS), and electroencephalogram (EEG)).
6. Multidimensional Pain Assessment Physiologic pain measures in conjunction with carefully applied behavioral scales have proven to be the best tools for measuring pain in this group. Multi-dimensional assessments are more accurate than single parameters. Composite pain measures use more than one parameter in assessing pain experience. Measures for older children often include self-report in addition to behavioral or physiologic indicators.

➢ **Good pain measurement tools must have: (25)**

1. To be valid, pain measure must measure a specific aspect of a child's pain (e.g., intensity) so that changes in a child's pain rating represent a meaningful and proportional change in the child's pain experience.
2. To be reliable, the measure must provide truthful and consistent pain ratings that do not change over time.
3. The measure must be free from response bias, that is, an instrument that will not direct the respondent to a particular answer.
4. In addition, the pain measure should be practical. If the measurement is too cumbersome, it will not be functional.
5. Finally, it is important to note that a pain scale is one tool of several ones that facilitates clinical decision making. It should not be used in isolation to assign a specific intervention to a predetermined score.

Assessments that use multiple measures (behavioral and physiologic) and that assess different aspects of the pain experience (e.g. intensity, location, pattern, and meaning) may result in more accurate evaluation of children's pain experiences. (Multidimensional Pain Assessment **(26).**

One of the challenges of pediatric pain management is the assessment and treatment of pain in preverbal children and patients with neurologic or cognitive impairment who cannot communicate their experience of pain**(27).**

Pain assessment is most accurate when the child can describe its location, nature, and severity. With appropriate words and tools, children over 3 years of age can reliably communicate their pain and may be able to relate their pain to a number or face on a scale. **(28).**

In children under 3 years, one must rely on a combination of behavioral clues and physiologic signs. Many of these signs are also seen in conditions other than pain, such as parental separation, hunger, fear, and anxiety. Thus misinterpretation is common. Parents can often determine whether their child is in pain by learning specific behaviors in their child that distinguish pain from distress or anxiety. **(29).**

Piaget described four developmental stages of childhood. During the initial sensorimotor stage (up to approximately2 years of age), children have little or no

understanding of pain and no language ability. During this stage, we rely on behaviors (posture, activity, crying, feeding, sleeping, etc.) and physiologic signs (e.g., tachycardia, hypertension, diaphoresis, and oxyhemoglobin saturation) to determine the severity of an infant's pain. **(30)**

We primarily rely on five different types of pain scales that are used in different age groups. For the neonatal population2 (up to approximately3 months of age), we use the Neonatal Infant Pain Scale (Table 2). It is primarily used to assess pain associated with medical procedures and includes assessment of facial expression, severity of crying, breathing patterns, movement of arms and legs, and state of arousal. (**30)**

Table (2): Neonatal Infant Pain Scale. **(30).**

Parameters	0 point	1 point	2 point
Facial expression	Relaxed	Grimace	-
Cry	No cry	Whimper	Vigorous crying
Breathing pattern	Relaxed	Change in breathing	-
Arms	Relaxed	Flexed/extended	-
Legs	Relaxed	Flexed/extended	-
State of Arousal	Sleeping/ Awake	Fussy	-

Pain level: 0–2 points = No pain, 3–4 points = Moderate pain, >4 points = Severe pain

The CRIES score is also used in infants and uses five parameters: severity of crying, oxygen requirement, increased heart rate and blood pressure, facial expression, and degree of sleeplessness, each of which are graded from zero to two; this gives a total between zero and 10 A score over four indicates that additional analgesics are required **(31).**

Table (3): The CRIES Scale **(21).**

CRIES SCALE FOR POSTOPERATIVE PAIN			
	0	1	2
Crying	No	High-pitched	Inconsolable
Requires SpO_2 >95%	No	F_IO_2<30%	F_IO_2<30%
Increased vital signs	Heart rate and blood pressure equal to or less than preoperative values	Less than 20% of preoperative values	Greater than 20% of preoperative values
Expression	None	Grimace	Grimace/grunt
Sleeplessness	No	Awakens frequently	Awake

The second Piaget developmental stage is the preoperational stage (approximately 2 to 7 years), in which children acquire some language ability and can localize pain, differentiate "a little" and "a lot," and can use simple terms to describe their pain such as "boo-boo," "ouch," "hurt," and "ow-ee." For this age group, we commonly use the Wong-Baker FACES scale or the FLACC scale This FACES scale has recently been updated to include more realistic facial expressions. Mature children in this stage may be able to use patient-controlled analgesia **(30)**

➢ **FACES scale: (32)**

Figure (4): FACES scale **(32)**

➢ **FLACC scale:**

The FLACC scale or Face, Legs, Activity, Cry, and Consolability scale is one of the most commonly and widely used behavioral observation pain scales to assess pain for children between the ages of 2 months and 7 years or individuals that are unable to communicate their pain. The level of response for each observation is given a numerical value rating from "0" to "2," with "0" being the most comfortable with no pain and "2" being the most painful, which results in a total score between "0" and "10."

Table (4): FLACC scale **(33)**.

Category	Scoring		
	0	1	2
Face	No expression or smile.	Occasional grimace/frown, withdrawn or disinterested.	Frequent/constant quivering chin, clenched jaw.
Leg	Normal position or relaxed	Uneasy, restless, tense	Kicking or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid or jerking
Cry	No cry	Moans or whimpers, occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content and relaxed	Reassured by occasional touching, hugging or being talked to, distractible	Difficult to console or comfort

The FLACC scale has also been found to be accurate for use with adults in intensive-care units (ICU) who are unable to speak due to intubation. The FLACC scale offered the same evaluation of pain as did the Checklist of Nonverbal Pain Indicators scale which is used in ICUs.

Instructions

❖ **Patients who are awake:**

o Observe for at least 2-5 minutes.

o Observe legs and body uncovered.

o Reposition patient or observe activity; assess body for tenseness and tone.

o Initiate consoling interventions if needed.

❖ **Patients who are asleep:**

o Observe for at least 5 minutes or longer.

o Observe body and legs uncovered.

o If possible reposition the patient.

o Touch the body and assess for tenseness and tone.

Each category is scored on the 0-2 scale which results in a total score of 0-10.

❖ **Assessment of FLACC Pain Score:**

o 0 = Relaxed and comfortable.

o 1-3 = Mild discomfort.

o 4-6 = Moderate pain.

o 7-10 = Severe discomfort/pain,

Also commonly used is the Revised-FLACC (rFLACC) scale, which is a modification of the FLACC scale aimed to better evaluate pain in pediatric patients with cognitive impairments, in addition to those who are unable to report their pain score because of age or have difficulty with oratory or motor skills. As such, rFLACC was modified to include several additionalbehavioral descriptors, including: verbal outbursts, tremors, increased spasticity, jerking movements, and respiratory pattern changes, such as breath holding or grunting **(34).**

Table (5): The revised FLACC SCALE **(34).**

(REVISED) FLACC Scale SCORING			
Categories	**0**	**1**	**2**
Face	No particular expression or smile.	Occasional grimace or frown, withdrawn, disinterested, **Sad, appears worried.**	Frequent to constant quivering chin, clenched jaw, **distressed looking face, expression of fright/ panic.**
Legs	Normal position or relaxed; **usual tone and motion to limbs.**	Uneasy, restless, tense, **occasional tremors.**	Kicking, or legs drawn up, **marked increase in spasticity, constant tremors, jerking.**
Activity	Lying quietly, normal position, moves easily, **regular, rhythmic respirations.**	Squirming, shifting back and forth, tense, **tense/guarded movements, mildly agitated, shallow/ splinting respirations, intermittent sighs**	Arched, rigid or jerking, **severe agitation, head banging, shivering, breath holding, gasping, severe splinting.**
Cry	No cry (awake or asleep)	Moans or whimpers: occasional complaint, **occasional verbal outbursts, constant grunting**	Crying steadily, screams or sobs, frequent complaints, **repeated outbursts, constant grunting.**
Consolability	Content, relaxed	Reassured by occasional touching, hugging, or being talked to: distractible	Difficult to console or comfort, **pushing caregiver away, resisting care or comfort measures.**

Each of the five categories (**F**) Face; (**L**) Legs; (**A**) Activity; (**C**) Cry; (**C**) Consolability is scored from 0-2, which results in a total score between zero and ten.

During Piaget's concrete operations stage (approximately8 to 12 years), children think logically and can be taught methods of cognitive and behavioral pain control such as distraction, relaxation, guided imagery, and hypnosis. They can relate details about their pain such as how the pain varies with activity or time of day. For children in this age range, we use FACES, or a simple verbal numeric 11-point scale0–10) on which 0 represents no pain and 10 represents the worst pain imaginable. Patient-controlled analgesia is often used during this developmental stage. **(30)**

In the final stage of child development, Piaget's formal operations stage, abstract thought is possible. Adolescents can more precisely characterize their pain with adjectives like burning, stinging, throbbing, or stabbing. They can articulate subtle changes in severity of pain with different treatments. For this age group, we can use numeric pain scores and patient-controlled analgesia. A variety of nonpharmacologic techniques can be used as adjuncts to control pain, including imagery, hypnosis, distraction, relaxation, and biofeedback**(30).**

Management of Pediatric Pain

➢ Pre-emptive and preventive analgesia: (35)

❖ Pre-emptive analgesia: defined as treatment that starts before surgery and prevents the establishment of central sensitization caused by incisional and inflammatory injuries (covers the period of surgery and the initial post-operative period). **(35)**

❖ Preventive analgesia: is an approach that aims to minimize sensitization by perioperative noxious stimuli including those arising preoperatively, intraoperatively, and postoperatively. The reduced pain and/or analgesic consumption that is observed after the duration of action of the target drug ensures that the preventive effect is not simply an analgesic effect. **(36).**

Indeed, Tissue injury initiates processes that lead to the transition from acute to chronic pain that include:

o Excito-toxic destruction of normally anti-nociceptive inhibitory neurons in the dorsal horn.

o Glial reaction.

o Afferent-maintained central sensitization.

o Switch of GABAergic inter-neurons in the dorsal horn from being normally anti-nociceptive to pro-nociceptive inter-neurons **(5).**

It is well documented that although general anesthesia may attenuate synaptic transmission of afferent injury discharge from the periphery to the spinal cord and brain, it does not completely block it. Moreover, systemic opioids may not provide a sufficiently effective blockade of the neuro-transmission of spinal nociceptive neurons to prevent central sensitization. **(37).**

The idea that surgical incision is the trigger of central sensitization has been broadened to include the sensitizing effects of preoperative noxious inputs and pain, also other noxious stimuli include intraoperative stimuli, postoperative peripheral and central inflammatory mediators and ectopic neural activity **(37).**

Recent meta-analysis provides support for pre-emptive epidural analgesia. The efficacy of different pre-emptive analgesic interventions (epidural analgesia, local anesthetic wound infiltration, systemic opioids, and systemic NSAIDs) was analyzed in relation to different analgesic outcomes. Improvements were found in all outcomes, but the most effective was epidural analgesia **(38).**

Another study demonstrated a clear preventive effect on the development of residual pain up to 1 year after surgery with continuous peri-operative epidural analgesia (**39).**

➢ Pain prevention by non-pharmacologic interventions:

Pain prevention is an important first step in controlling pain. Both non-pharmacologic and pharmacologic treatment have proven efficacy in children. The importance of the psychological state and complexity of a children's personality and their psychosocial background cannot be

overlooked. It is known that the social and psychological composition of the children and their family dynamics influence pain sensitivity and therapeutic efficiency in multiple ways **(40).**

Also, memories of previous pain experiences and socialization around painful events all influence subsequent reactions to pain. The increasing trend toward the use of multimodal and interdisciplinary approaches to pain management in children has provided more tools to effectively treat and possibly preempt pain **(41).**

An example of these tools are the non-pharmacologic interventions like cognitive and behavioral techniques that include mind-body therapies such as play therapy, hypnosis, distraction. Other therapies such as acupuncture, acupressure, and massage are classified as manipulative therapies **(42**).

It is important to ensure that any therapy is age appropriate and not contraindicated based on the child's medical condition, cultural, or religious beliefs. Remember that these therapies are employed as adjuncts and may not relieve all pain by themselves.**(25).**

➢ **Post-operative Pain Management in Infants and Children:**

Prevention of pain whenever possible, using multi-modal analgesia, has been shown to work well for nearly all cases and can be adapted for day cases, major cases, the critically ill child, or the very young. Many acute pain services use techniques of concurrent or co-analgesia based on four classes of analgesics, namely local anesthetics, opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), and acetaminophen (paracetamol) **(43).**

In particular, a local/regional analgesic technique should be used in all cases unless there is a specific contra-indication. Also, the opioidsparing effects of local anesthetics, NSAIDs, and acetaminophen are useful **(44).**

Systemic Analgesia:

Commonly used medications for postop pain control include opioids, NSAIDs and/or acetaminophen, steroids, gabapentin or pregabalin, IV ketamine, and IV lidocaine. Oral administration of opioid medication is preferable over the intravenous route. Intramuscular medications are discouraged. However, during circumstances in which parenteral route of medication administration is needed (ex, risk of aspiration, ileus), intravenous patient-controlled analgesia (PCA) is recommended. With PCA analgesia, avoid a basal infusion of opioid medication in opioid-naïve patients **(45).**

The addition of acetaminophen or NSAIDs is associated with reduced opioid consumption and better pain control than using opioids alone. Gabapentin or pregabalin are recommended for administration preoperatively, especially in opioid-tolerant patients, as they have been shown to reduce opioid requirements. Due to its extensive side effect profile, ketamine is only for major surgeries, in highly opioid-tolerant patients, or opioid intolerant patients. Intraoperative IV lidocaine infusions have associations with a shorter

duration of ileus and better analgesic control compared to placebo **(46).**

Local, Intra-articular, or Topical Techniques:

Peripheral nerve blocks, intra-articular anesthetic injections, anesthetic wound infiltration, and topic anesthetics can be used to help with site-specific pain control. These methods are not in routine use. Their administration should be considered based on beneficial evidence **(47).**

Regional anesthetic techniques:

A local anesthetic with or without the addition of IV opioid medication is an option for fascial plane block, site-specific regional anesthetic injections, or in some cases epidural injections depending on the type of procedure performed. An anesthesiologist typically performs these techniques under ultrasound guidance. The use of continuous IV medication (in drip form) is preferable to single-injection techniques in cases where the duration of postoperative pain is prolonged. Intrapleural analgesia is not recommended for pain control as there is little evidence to suggest benefit, and high systemic absorption within the pleural space increases the risk of drug toxicity**(47).**

Neuraxial anesthetic techniques:

Typically involves an epidural injection with local anesthetic with or without the addition of IV opioid medication. May also include the intrathecal (spinal) injection of opioid medicines. Epidural analgesia may be given as a continuous infusion or as patient-controlled analgesia. These techniques are for routine use in major thoracic and abdominal procedures, cesarean sections, and hip or lower extremity surgeries. They are especially beneficial in patients at risk for cardiac or pulmonary complications, or prolonged ileus (**20).**

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