POSTOPERATIVE PAIN MANAGEMENT IN ORTHOPEDIC SURGERY

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Abstract

The routine use of peripheral nerve blocks and wound infiltration with long-acting local anesthetics as an adjuvant to local, regional and general anesthetic techniques can improve postoperative pain management after a wide variety of surgical procedures. multimodal analgesia which is achieved by combining different analgesics that act by different mechanisms and at different sites in the nervous system, resulting in additive or synergistic analgesia with lowered adverse effects of sole administration of individual analgesics,is needed for acute postoperative pain management due to adverse effects of opioid analgesics, which can impede recovery; yet, the literature on multimodal analgesia often shows variable degrees of success, even with studies utilizing the same adjuvant medication.

Key word: physiology of pain- pharmacological analgesia- regional anesthesia- orthopedic surgery.

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Introduction

Postoperative pain management is critical for optimal care of orthopedic surgery patients. Orthopedic procedures can cause severe intra-operative and post-operative pain. It is important to achieve optimal post-operative pain control since this will facilitate more rapid achievement of functional outcomes. Opioids, administered intramuscularly, as epidurals, or IV as patient-controlled analgesia, are effective for severe pain. Adjunctive therapy and preemptive analgesia such as nerve blocks, and methods of delivery such as infusion pumps, may be used after total knee arthroplasty and anterior cruciate ligament (ACL) reconstruction.

Oral opioids are effective for moderate to severe pain, and tramadol, with efficacy comparable to morphine but with fewer severe side effects, is selected for moderate to moderately severe pain. Opioid-sparing NSAIDs, such as ketorolac, and COX-2-specific NSAIDS have been used in pain management of hip, knee, and ACL procedures. An individualized regimen of appropriate analgesics, combined with nonpharmacologic treatments such as physical therapy or cryotherapy and patient education, can aid orthopedic surgery patients' recovery.

Chapter 1
PHYSIOLOGY OF PAIN

1.1.Definition

Pain is defined by the International Association for the Study of Pain (IASP) as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage."

[1] Thus pain has objective, physiologic sensory aspects as well as subjective emotional and psychological components.[2]

The term **"nociception"** (Latin – noci = harm or injury) is used only to describe the neural response to traumatic or noxious stimuli.[3]

1.2.Peripheral Transmission:

Peripheral transmission of pain consists of production of electrical signals at the pain nerve endings (**Transduction)** followed by propagation of those signals through the peripheral nervous system **(Transmission)**.

1.2.1.Transduction:

The primary sensory structure that accomplishes transduction is the nociceptor. Most nociceptors are free nerve endings that sense heat, mechanical and chemical tissue damage. Several types are described:

1)***Mechanoreceptors***, respond to pinch and pinprick,

2)***Silent nociceptors***, which respond only in the presence of inflammation.

3) ***polymodal mechanoheat nociceptors***. The last are most prevalent and respond to excessive pressure, extremes of temperatures (>42 ^{o}C and < 18 ^{o}C), and algogens (pain producing substances).

Polymodal nociceptors are slow to adapt to strong pressure and display heat sensitization.[4,5,6]

Recently, vanilloid receptor-1 (VR-1) was isolated from the sensory neurons. Vanillins are a group of compounds, including capsaicins that cause pain. The VR1 receptors not only respond to pain but also to protons and to temperatures >43 ^{o}C. Another receptor, VRL-1, which responds to temperatures above 50 ^{o}C but not to capsaicin, has been isolated from C fibers.[7]

1.2.2.Transmission:

Pain impulses are transmitted by two fiber systems. The presence of two pain pathways explains the existence of two components of pain:

A) Fast, sharp and well localized sensation (*first pain*) which is conducted by **Aδ fibers**. [8]

b) A duller slower onset and often poorly localized sensation (*second pain*) which is conducted by **C fibers**.[9]

Aδ fibers are myelinated, 2 – 5 μm in diameter and conduct at rates of 12 – 30 m/s, whereas **C fibers** are unmyelinated, 0.4 – 1.2 μm in diameter and conduct at rates of 0.5 to 2 m/s.

Both fiber groups end in the dorsal horn of the spinal cord. **Aδ fibers** terminate predominantly on neurons in laminas I and V, whereas the dorsal root **C fibers** terminate in laminas I and II. The synaptic junctions between these first order neurons and the dorsal horn cells in the spinal cord are sites of considerable plasticity. For this reason the dorsal horn has been called a gate, where pain impulses can be "gated" i.e., modified.[10]

Second-order neurons are either nociceptive-specific or wide dynamic range (WDR) neurons.

Nociceptive-specific neurons serve only noxious stimuli and are arranged somatotopically in lamina I and have a discrete somatic receptive field; they are normally silent and respond only to high threshold noxious stimuli. [11]

WDR neurons receive both noxious and non-noxious afferent input from **Aβ, Aδ** and **C fibers**. Differentiation between noxious and innocuous stimuli occurs by a higher frequency of WDR neuron discharge to noxious stimuli. WDR neurons are most abundant in lamina V.[12]

1.3.Central Transmission:

Central transmission includes **transmission and perception** whereby the electrical signals are transmitted from the spinal cord to the brain. Even though the transmission occurs from the peripheral receptor to the brain as one continuous process, for convenience we have divided this into peripheral and central transmission.

1.3.1.Transmission:

The axons of most of the second order neurons cross the midline at the anterior commisure to the contralateral side of the spinal cord to ascend as ***the Spinothalamic tract*** ending in the thalamus, reticular formation, nucleus raphe magnus and the periaqueductal gray.

This ascending tract can be divided into lateral and medial:

a) The lateral spinothalamic (**neospinothalamic**) tract projects mainly to the ventral posterolateral nucleus of the thalamus and carries discriminative aspects of pain, such as location, intensity, and duration.[13]

b) The medial spinothalamic (**paleospinothalamic**) tract projects to the medial thalamus and is responsible for mediating the autonomic and unpleasant emotional perception of pain.[14]

1.3.2.Perception:

The third order neurons are located in the thalamus and project to somatosensory areas II and I in the post-central gyrus and superior wall of the sylvian fissure.

Perception and discrete localization of pain take place in these cortical areas. Some fibers project to the anterior cingulated gyrus and are likely to mediate the suffering and emotional components of pain.[15]

1.4.Modulation:

Modulation of pain occurs peripherally at the nociceptor, in the spinal cord, or in supraspinal structures. This modulation can either inhibit or facilitate pain.

1.4.1.Peripheral modulation:

Nociceptors and their neurons display sensitization following repeated stimulation. Sensitization of nociceptors results in a decrease in threshold, an increase in frequency response, a decrease in response latency and spontaneous firing even after cessation of the stimulus (after discharges).

This primary hyperalgesia is mediated by release of algogens like histamine, bradykinin, PGE2 and leukotrienes from damaged tissues.

Secondary hyperalgesia or neurogenic inflammation is manifested by the triple response of flare, local edema and sensitization to noxious stimuli. It is primarily due to antidromic release of substance P (sP) from collateral axons of primary afferent neurons. Substance P degranulates histamine and serotonin, vasodilates blood vessels, causes tissue edema and induces formation of leukotrienes.[16]

1.4.2.Central modulation:

This can either facilitate or inhibit pain.

A) The Facilitatory mechanisms are:

i) Windup and sensitization of second order neurons.

ii) Receptive field expansion

iii) Hyper excitability of flexion responses.

Neurochemical mediators of central sensitization include sP, CGRP, VIP, cholecystokinin, angiotensin, galanin, L-glutamate and L-aspartate.

These substances trigger changes in membrane excitability by interacting with G-protein coupled receptors, activating intracellular second messengers, which in turn phosphorylate substrate proteins.

A common pathway leads to increased intracellular calcium concentration. For example glutamate and aspartate activate the NMDA receptor. Stimulation of ionotropic NMDA receptors causes intraneuronal elevation of $Ca2^{+}$, which stimulates nitric oxide synthase (NOS) and the production of nitric oxide (NO). NO as a gaseous molecule diffuses out from the neuron and by action on guanylyl

cyclase, NO stimulates the formation of cGMP in neighboring neurons. Depending on the expression of cGMP-controlled ion channels in target neurons, NO may be excitatory or inhibitory. NO has been implicated in the development of hyperexcitability, resulting in hyperalgesia or allodynia, by increasing nociceptive transmitters at their central terminals.[17]

B) Inhibitory mechanisms can be either Segmental or Supraspinal.

i) Segmental inhibition consists of activation of large afferent fibers subserving epicritic sensation inhibitory WDR neuron and spinothalamic activity. Glycine and γ-amino butyric acid (GABA) are amino acids that function as inhibitory neurotransmitters.

Segmental inhibition appears to be mediated by $GABA_b$ receptor activity, which increases K^+ conductance across the cell membrane.

Ii) Supraspinal inhibition occurs whereby several supraspinal structures send fibers down the spinal cord to inhibit pain at the level of the dorsal horn.

These include periaqueductal gray, reticular formation, and nucleus raphe magnus (NRM). Axons from these structures act pre-synaptically on the primary afferent neurons and post-synaptically on second-order neurons (or interneurons). These inhibitory pathways utilize monoamines, such as noradrenaline and serotonin, as neurotransmitters and terminate on nociceptive neurons in the spinal cord as well as on spinal inhibitory interneurons which store and release opioids. Noradrenaline mediates this action through α_2 receptors. The endogenous opiate system act via enkephalins and β-endorphins. These mainly act presynaptically whereas the exogenous opiates act postsynaptically.[18,19]

1.5.Reflex responses:

Somatic and visceral pain fibers are fully integrated with the skeletal motor and sympathetic systems in the spinal cord, brain stem and higher centers. These synapses are responsible for reflex muscle activity that is associated with pain.

In a similar fashion reflex sympathetic activation causes the release of catecholamines, locally and from the adrenal medulla. This increases heart rate and blood pressure with a consequent increase in myocardial work, increased metabolic rate and oxygen consumption. Gastrointestinal tone is decreased leading to delayed gastric emptying.

Pain also causes an increase in the secretion of catabolic hormones and decreased secretion of anabolic hormones.

The metabolic responses to pain include hyperglycemia due to gluconeogenesis and decreases in insulin secretion or action increased protein metabolism and increased lipolysis.

The respiratory responses could be either hyperventilation due to stimulation of respiratory center or hypoventilation due to splinting and reflex muscle spasm. The diencephalic and cortical responses may include anxiety and fear. Pain stimulates psychological mechanisms with deleterious emotional effects.[20]

1.6.Conclusion:

Understanding pain physiology is very important in countering it. From what is known it is clear that pain recognition involves transduction, transmission, modulation and perception. The signal is modulated at various levels before perceived. Various transmitters, facilitators and inhibitors are involved. Body responds to painful stimuli, which may be helpful or counter-productive. Better knowledge helps not only in artificial modulation of pain but also to suppress the harmful reflex responses.

Chapter 2
PHARMACOLOGICAL ANALGESIA

2.1.Introduction:

Adequacy of postoperative pain control is one of the most important factors in determining when a patient can be safely discharged from a surgical facility and has a major influence on the patient's ability to resume their normal activities of daily living.[21]

Perioperative analgesia has traditionally been provided by opioid analgesics. However, extensive use of opioids is associated with a variety of perioperative side effects [*e.g.*, ventilatory depression, drowsiness and sedation, postoperative nausea and vomiting (PONV), pruritus, urinary retention, ileus, constipation] that can delay hospital discharge.[22]

Intraoperative use of large bolus doses or continuous infusions of potent opioid analgesics may actually increase postoperative pain as a result of their rapid elimination and/or the development of acute tolerance.

In addition, it has been suggested by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) that excessive use of postoperative opioid analgesics leads to decreased patient satisfaction. Partial opioid agonists (*e.g*, tramadol) are also associated with increased side effects (*e.g.*, nausea, vomiting, ileus) and patient dissatisfaction compared to both opioid [23] and non-opioid analgesics.

Therefore, anesthesiologists and surgeons are increasingly turning to non-opioid analgesic techniques as adjuvants for managing pain during the perioperative period to minimize the adverse effects of analgesic medications.

Multimodal or "balanced" analgesic techniques involving the use of smaller doses of opioids in combination with non-opioid analgesic drugs [*e.g.*, local anesthetics, ketamine, acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs)] are becoming increasingly popular approaches to preventing pain after surgery and facilitating the recovery process.[24,25,26] (***Table 1***)