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LITERATURE REVIEW: PAIN AND PAIN MANAGEMENT

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ABSTRACT Pain is the most common symptom of disease, which accompanies us from an early age. It is a protective mechanism to which the body responds to harmful stimulus. The feeling of pain can be caused by irritation of pain receptors or nociceptors, which can be found in the skin, joints and many internal organs. Pain receptors are sensitive to mechanical, thermal or chemical stimuli. The operation of noxious stimulus to these receptors results in the processing into an electrical signal. This impulse is conducted by nerve fibres into the spinal cord and then to the brain. At this point, there is the realization that something hurts us. The goal of pain therapies is to relieve pain whenever possible: from nociception to the conscious experience as well as to decrease the emotional response to the unpleasant experience. Nociception should be treated even in unconscious patients who appear to be clinically unresponsive to pain to help prevent sensitization of pain pathways which can lead to chronic pain. Therefore, this review article aims to put in place a thorough understanding of major pain conditions that we experience—nociceptive, Physiology and treatment and management of pain.

KEYWORDS : pain, nociceptors, pain management

DEFINITION:

Pain is defined as follows by various associations

Task force on taxonomy of the International Association for the Study of Pain (IASP) defines that pain is "An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."

The North American Nursing Diagnosis Association defines that pain is a state, in which an individual experiences and reports severe discomfort or an uncomfortable sensation.

Medical dictionary by Farlex: Pain is defined as an unpleasant feeling that is conveyed to the brain by sensory neurons.

Fields et al. defines that "Pain is an unpleasant sensation localized to a part of the body. It is often described in terms of a penetrating or tissue-destructive process (e.g.: Stabbing, burning, twisting, tearing, and squeezing) and/or of a bodily or emotional reaction (e.g.: Terrifying, nauseating, and sickening)."

Monheim defines pain as: "An unpleasant emotional experience usually initiated by noxious stimulus and transmitted over a specialized neural network to the central nervous system where it is interpreted as such."

Bell et al defines: The subject's conscious perception of modulated nociceptive impulses that generate an unpleasant sensory and emotional experiences associated with actual or potential tissue damage.

McCaffery and Pasero offered a clinically useful definition as: "Pain is whatever the experiencing person says it does." [1]

EPIDEMIOLOGY

Pain indicates the severity and type of injury. According to World Health Organization (WHO) injury is the leading cause of death among men and women age 15 to 44 years and will be the third leading cause of death and disability in all ages in 2020[2]

According to the Institute of Medicine (IOM), approximately 100 million Americans suffer from chronic pain at an estimated annual cost of approximately 600 billion dollars.[3] As per the National Health and Nutrition Examination Survey indicate that 1 in 4 Americans have suffered pain which lasts for long time, 42% stated that it lasts more than 1 year.[4]

Multiple causes of neuropathic pain have been described and its incidence is increasing to the ageing global population, increased incidence of diabetes mellitus and improved survival from cancer after chemotherapy. An imbalances between excitatory and inhibitory somatosensory signaling, alterations in ion channels and variability in the way that pain messages are modulated in the central nervous system all have been implicated in neuropathic pain.[5]

CHARACTERISTICS OF ACUTE AND CHRONIC PAIN

Pain is classified majorly into two types acute- nociceptive pain (somatic/ visceral) and chronic pain (neuropathic/ functional) based on intensity. Acute pain is highly desirable, in this type patients are unusually insomniac and dependent and tolerable to medication. Among chronic pain patients chances of significant environmental/family issues are the major cause and they are commonly insomniac and commonly dependent and tolerable to medication hence depression is common.

Acute pain:

Acute pain was once defined simply in terms of duration. It is now viewed as a "complex, unpleasant experience with emotional and cognitive, as well as sensory, features that occur in response to tissue trauma[6]. Common sources of acute pain include trauma, surgery, labor, medical procedures, and acute disease states. Acute pain serves an important biological function, as it warns of the potential for or extent of injury. A host of protective reflexes (e.g., withdrawal of a damaged limb, muscle spasm, autonomic responses) often accompany it. However, the "stress hormone response" prompted by acute injury also can have adverse physiologic and emotional effects.[7] Symptoms includes a sharp or dull, burning, shock-like, tingling, shooting, radiating, fluctuating.

Chronic pain: Chronic pain was once defined as pain that extends 3 or 6 months beyond onset or beyond the expected period of healing. However, new definitions differentiate chronic pain from acute pain based on more than just time.[8] Chronic pain is also defined as a persistent pain that "disrupts sleep and normal living, ceases to serve a protective function, and instead degrades health and functional capability."[9]

Chronic pain may be nociceptive, neuropathic, or both and caused by injury (e.g., trauma, surgery), malignant conditions, or a variety of chronic non-life-threatening conditions (e.g., arthritis, fibromyalgia, neuropathy). In some cases, chronic pain exists de novo with no apparent cause.[8]

DIVISION OF PAIN:

- **Anatomic pain** – may be physiological receptor-functional (protective) or pathological, as a result of local changes.
- **Physiological pain** – superficial pain, caused by irritation of the skin receptors, mucous membranes and cornea by a damaging factor.
- **Pathological pain** – caused by chronic irritation of pain receptors by pain mediators released from damaged tissues.
- **Deep pain** – is pathological, can be caused by blood vessels, bone and joint system, muscles or organ structure.
- **Vascular pain** – caused by stimulation of mechano- and chemo- pain receptors, located in the outer membrane of large arteries and veins. Stretching of the vascular vessels causes pulsating, tension headaches.
- **Bone and joint pain** – the source of pain is stimulation of the pain receptors of the joint capsule and periosteum.
- **Myalgia** – caused by irritation of the receptors in muscles and fascias by accumulated metabolites, when they are over-load and tired.
- **Organ pain** – include biliary and renal colic.
- Wired pain – arises as a result of direct stimulation of the nerve fibers or pathways. Includes neuralgia, causalgia, radicalgia and phantom pain.
- **Neuralgia** – applies to the trigeminal nerve, sciatic, femoral and lateral femoral cutaneous nerve.
- **Radicalgia** – exacerbated by coughing and radiating movements to the appropriate areas of the skin.
- **Causalgia** – neuralgia with an autonomic component, results from large nerve injuries, with many of the sympathetic nerves. Pains are burning with dystrophic changes – cyanosis, oedema, muscle atrophy
- **Convolutional pain** – the result of compression on the nerve plexus, caused by cancer or inflammatory changes in the neck, top of the lungs, lower pelvis.
- **Phantom pain** – occurs in patients after amputation and relates to pain in the amputated limb. Incidence of this pain explains the existence of chronic pain of embedded memory.[10,11,12]

Characteristics of pain:

1. Superficial pain	skin or underlying subcutaneous and mucous tissues	local throbbing, burning, or pricking. It may be associated with tenderness, allodynia (pain from a stimulus which normally does not provoke pain), or hyperalgesia
2. Visceral pain	internal organs such as the large intestine or pancreas	diffuse, dull, aching pain poorly localized associated with nausea and other autonomic symptoms
3. Deep somatic pain	skin, bone, joint, muscle, or connective tissue	dull and aching in nature localize Injury or disease of deep somatic structures produces the same response as does injury to the skin or viscera.

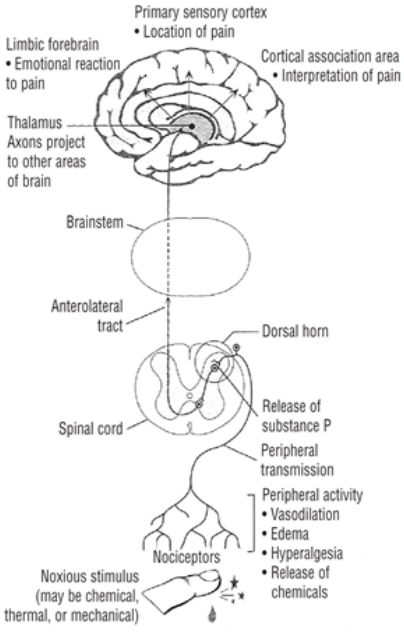

Fig: Physiology of pain perception

PHYSIOLOGY OF PAIN:

Pain is produced by processes that either damage, or are capable of damaging, the tissues. Such damaging stimuli are called "noxious" and are detected by specific sensory receptors called "nociceptors."[13] Nociceptors are identified as C-fibers and A-fibers. By definition, nociceptors respond selectively to noxious stimuli. These nociceptors are free nerve endings with cell bodies in the dorsal root ganglia and terminate in the superficial layers of the dorsal horn of the spinal cord. Here they relay messages by releasing neurotransmitters such as glutamate[14], substance P, and calcitonin gene related peptide (CGRP).[15] These "pain" neurotransmitters will result in the activation of the second-order neuron via their corresponding receptor. The second-order neuron crosses the spinal cord to the contralateral side and travels up the spino-thalamic tract until it reaches the thalamus. From there the third-order neuron is activated, traveling from the thalamus to the somato-sensory cortex, which allows for the perception of pain[16].

There may also be other manifestations of pain related to tissue injury including hyperalgesia, an exaggerated response to a noxious stimulus, and allodynia, the perception of pain from normally innocuous stimuli. Hyperalgesia and allodynia are the result of changes in either the peripheral or central nervous systems, referred to as peripheral or central sensitization, respectively.

DIAGNOSTIC TEST FOR PAIN:

Type	Definition	Potential Uses
Screening laboratory tests	Includes CBC, chemistry profile (e.g., electrolytes, liver enzymes, BUN, creatinine), urinalysis, ESR	Screen for illnesses, organ dysfunction
Disease-specific laboratory tests Imaging studies	Includes autoantibodies, sickle cell test	Autoimmune disorders, SCD
Diagnostic procedures	Includes lumbar puncture, thoracentesis, paracentesis, biopsy	Detection of various illnesses

Electrodiagnostic tests • EMG • NCS	Include EMG (direct examination of skeletal muscle via needle electrodes) and NCS (examination of conduction along peripheral sensory and motor nerves or plexuses)	Detection of myopathies, some neuropathies, MS
Diagnostic nerve block	Nerve block (injection of a local anesthetic to determine the source/ mechanism of the pain)	Multiple uses, including: Identification of structures responsible for the pain (e.g., sacroiliac or facet joint blocks) Differentiation between types of pain

DIFFERENT MEASURES FOR DIAGNOSING PAIN (Pain Assessment Scales)

Pain assessment mnemonics	Adult	Pediatrics
OPQRST QISS TAPED SOCRATES Video	Numerical Rating Scale (NRS) Visual Analog Scale (VAS) Defense and Veterans Pain Rating Scale (DVPRS) Adult Non-Verbal Pain Scale (NVPS) Assessment of Discomfort in Dementia (ADD) Behavioral Pain Scale (BPS) Critical-Care Observation Tool (CPOT)	Neonatal Pain, Agitation, and Sedation Scale (N-PASS) Neonatal/Infant Pain Scale (NIPS) Neonatal Facial Coding System (NFCS) CRIES Faces, Legs, Activity, Cry and Consolability (FLACC) Revised-FLACC Non Communicating Childrens Pain Checklist (NCCPC-R) Childrens Hospital of Eastern Ontario Pain Scale (CHEOPS) Wong-Baker Faces scale, Oucher Numerical Rating Scale (NRS) Visual Analog Scale (VAS)[17]

TREATMENT OF PAIN

As the transmission of pain involves many different receptors within the peripheral and central nervous system, multimodal analgesia is best employed to optimize pain control and limit side effects. Common drugs used in pain management include the following.

Anti-inflammatory [24]:

non-steroidal anti-inflammatory drugs (NSAIDs) reduce the synthesis of prostaglandins, potent sensitizers of primary afferent nociceptors, by inhibiting cyclooxygenase which is a key enzyme in the inflammatory cascade. The risk of gastrointestinal and other side effects with NSAIDs often prevent their use, particularly in the elderly. Common examples include salicylates, ibuprofen (Advil®), naproxen (Aleve®), and ketorolac (Toradol®)

Opioids [25]:

Opioids act both presynaptically and postsynaptically to produce an analgesic effect. Presynaptically, opioids block calcium channels on nociceptive afferent nerves to inhibit release of neurotransmitters such as substance P and glutamate which contribute to nociception. Postsynaptically, opioids open potassium channels which hyperpolarize cell membranes, increasing the required action potential to generate nociceptive transmission. The mu, kappa and delta opioid receptors mediate analgesia spinally and supraspinally. Common examples of mild opioids include codeine, oxycodone, and hydrocodone.

Antidepressants [26]:

are the mainstay of pharmacological management of neuropathic pain. Tricyclic antidepressants vprevent reuptake of endogenous serotonin and noradrenaline within the central nervous system, increasing the activity of the descending inhibitory pain pathways. Anti-cholinergic side effects predominate, with dry mouth and drowsiness. Examples include amitriptyline (Elavil®), nortriptyline (Aventyl®), and desipramine (Norpramin®). There is also evidence for the use of duloxetine, a serotonin and noradrenaline reuptake inhibitor (SNRI) in painful diabetic neuropathy.

Anticonvulsants [27]:

Examples include carbamazepine (Tegretol®), gabapentin (Neurontin®), Material protected by copyright and pregabilin (Lyrica®). this group of drugs act either by the blockade of sodium or voltage-gated calcium channels in nerve fibres, reducing excitability of neurons. These drugs may be effective in the management of chronic pain, although frequently cause adverse effects including ataxia, sedation and nausea.

Anesthetics [27]:

Anesthetics can be used for epidurals or nerve blocks to assist with acute or chronic pain. These are temporary, and may be effective up to three or four months. Risks and benefits must be evaluated prior to performing a block. lidocaine 5% plaster is indicated for post-herpetic neuralgia, and is also used for localized neuropathic pain (e.g. scar pain).

NON PHARMACOLOGICAL MANAGEMENT OF PAIN

Pain is a condition of neurological abnormality) Pain is a case of neurological condition with various causes associated with its occurrence. In certain pain conditions it cannot be treated completely hence can be managed to avoid further complications by following non pharmacological therapy along with pharmacological therapy. Regular Bed rest, Bracing, Manipulation and mobilization, Traction, Exercise, Education, Psychological intervention, Therapeutic modalities- transcutaneous nerve stimulation, electrical stimulation, ultrasound, superficial, Cryotherapy may be beneficial in pain management.[18]

Bed rest:

prolonged bed rest shows its effect in patients with neck and low back pain and also it shows its effects on bone, connective tissue, muscle, and psychosocial well-being. Taking bed rest less than 48 hours shows its significance in muscle spasm. Based on patient severity and site of pain the spacing(period) rest is considered.

Bracing:

in patients with soft tissue injury cervical collar shows response not more than 48 -72hours after injury as per many literature survey, lumbar bracing shows its importance in workplace to prevent low back injury and it has a role to prevent re-injury. In lumbar bracing persons a proper spine mechanics with lifting and bending activities should be followed to avoid further injuries.

The efficacy of lumbar bracing as a means to prevent low back injury in the work place. In addition, lumbar bracing appears to not enhance dynamic lifting capacity, nor improve lumbosacral biomechanics. In fact, lumbar supports have not

afforded more protection than a proper lift without the support. There may be a role after injury for the use of lumbar braces to prevent re-injury. This role has not clearly been established in the medical literature and probably is helpful as a proprioceptive reminder to use proper spine mechanics with lifting and bending activities.

Manipulation and Mobilization:

Many literature survey reveals that this kind of management is beneficial in one who suffers with neck pain and associated disorders. Massage and mobilization therapy shows a significant improvement in cervical movements. The Agency for Health Care Policy and Research (AHCPR) guidelines provide a manual to treat low back pain. No proper literature to guide that mobilization in the treatment of patients with acute low back pain, have been found to be effective.

Traction:

Cervical traction beneficial in radiculopathy and localized neck pain in individual patients with cervicogenic pain and spondylosis.[19] Lumbar traction has been preferred in patients with lumbar disc problems and no evidence to treat low back pain.

TENS:

Transcutaneous electrical nerve stimulation (TENS) is a non-invasive peripheral stimulation technique used to relieve pain. According to publication of Melzack and Wall's "Pain Mechanisms: A New Theory". They suggested that electrical stimuli could be used to activate large diameter peripheral afferents in order to inhibit central transmission of noxious information. The main techniques are: Conventional TENS (low-intensity, high-frequency) Acupuncture-like TENS (high-intensity, low-frequency) Intense TENS (high-intensity, high-frequency)

TENS shows its more beneficence in combination with pharmacotherapy instead of single use. A Systematic reviews on TENS reported a negative outcome in postoperative pain and labour pain. On Cochrane review reported that high frequency TENS shows a positive response in reducing pain associated with primary dysmenorrhea. RCTs suggest that TENS may be beneficial for acute orofacial pain, painful dental procedures, fractured ribs, acute lower back pain, angina, localized muscle pain, post-herpetic neuralgia, trigeminal neuralgia, phantom limb and stump pain, diabetic neuropathies and entrapment neuropathies, radiculopathies (cervical, thoracic and lumbar). TENS may also be beneficial for cancer and cancer related pain. Cochrane reviews on chronic low back pain, rheumatoid arthritis and mechanical neck disorders, post stroke shoulder pain and chronic recurrent headache.[20]

Ultrasound:

It is a type of therapeutic modalities in clinical practice for the treatment of musculoskeletal disorders such as pain, muscle spasm, joint contracture, and tissue injury. Morishita K et al demonstrated that therapeutic ultrasound is an effective treatment method when it applied with other therapeutic methods.[21,22]

Superficial heat:

It is used in the treatment of increased muscle tension and pain crises. Effects include vasodilation, increased blood flow, elimination of metabolic waste, reduction of nerve pain conduction, joint stiffness and muscle relaxation. It has various techniques like hot water bag, electrical pad, compress, silica gel pad etc. A study conducted by Nozaki et al used silica pads for masseter for twice a week and patient benefited by increased twisting force in Duchene muscular dystrophy. A similar studies by different authors at different body parts shows a positive response. Furlan RMM etal, concluded that moist heat technique was beneficial in TMD and thermal stimulus for a period of 5 – 30min, superficial heat for 20 min.[23]

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