Physiology of pain its clinical importance in medical field and management: Recent trends and brief review

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Abstract: Pain is a distressing feeling often caused by intense or damaging stimuli, such as various pathophysiological conditions, burning a body part, excess growth of an organ, growth of solid mass in organ or tissue pressing other organs of body or accidents. Because it is a complex, subjective phenomenon, defining pain has been a challenge. There are many ways to pain classifications. Basic format of treating dreaded pain of cancer to chronic pain is pharmacological as well as combing alternative mode of pain management techniques. If possible newer pain mechanisms and pharmacological agents are in research to provide better and effective pain control in both acute and chronic pain.

Keywords: Pain, mode of treatment, classification of pain, newer technique of pain management

INTRODUCTION:  
Pain is a distressing feeling often caused by intense or damaging stimuli, such as various pathophysiological conditions viz burning a body part, excess growth of an organ, growth of solid mass in organ or tissue pressing other organs of body or accidents. Because it is a complex subjective phenomenon, defining pain has been a challenge. According to International Association for the Study of Pain (IASP) pain is defined as "An unpleasant sensory or emotional experience associated with actual or potential tissue damage, or described in terms of such damage", is derived from a 1964 definition by Harold Merskey, and first published in 1979 by IASP in pain. Each individual learns the application of the word through experiences related to injury in early life. Pain was called by Sherrington “The physical adjunct of an imperative protective reflex” [3]. Pain motivates the individual to withdraw from damaging situations; it is considered one of the reflexes, to protect a damaged body part while it heals, and to avoid similar experiences in the future. Most pain resolves once the noxious stimulus is removed and the body has healed, but it may persist despite removal of the stimulus and apparent healing of the body. It is a major symptom in many medical conditions, and can interfere with a person's quality of life and general functioning. Psychological factors such as social support, excitement or distraction can significantly affect pain's intensity or unpleasantness [1].

CLASSIFICATION OF PAIN:  
Classifying pain is helpful in diagnosis, assessment and treatment of disease entity. There are many ways to classify pain and classifications may overlap. The common types of pain include:

1. Two major types of pain on the basis of time of perception of pain.  
a. Fast pain – It is felt within about 0.1 sec after pain stimulus is applied.  
b. Slow pain- It is felt only after one second or more after pain is applied.

2. Depends upon the duration of pain:  
a. acute pain: pain of less than 3 to 6 months duration  
b. Chronic pain: pain lasting for more than 3-6 months, or persisting beyond the course of an acute disease, or after tissue healing is complete.
C. acute-on-chronic pain: acute pain flare superimposed on underlying chronic pain [10].

3. Based on the intensity of pain, it can be also broadly categorized as: mild, moderate and severe:
   It is common to use a numeric scale to rate pain [10, 12].
   **Intensity where 0 = no pain and 10 is the worst pain imaginable:**
   a. Mild: <4/10  
   b. Moderate: 5/10 to 6/10  

4. Based on tissues it involves [1, 10].
   A. Nociceptive Pain: Pain is caused by stimulation of sensory nerve fibers tissue damage. It represents the normal response to noxious insult or injury of tissues.  
   **Eg:** Somatic: musculoskeletal (joint pain, myofascial pain), cutaneous; often well localized. Visceral: hollow organs and smooth muscle; usually referred as visceral pain.

B. Certain types of pain are referred to as **syndromes:**
   Myofascial pain syndrome refers to pain that is set off by trigger points located in the body's muscles egs; fibromyalgia .The pain experience may be an ache, a sharp stabbing, or a throbbing. Pain from tissue damage can be acute or it can be chronic, such as arthritis or chronic headaches and certain medical treatments, such as radiation for cancer, can cause tissue damage and pain.

C. Neuropathic pain: initiated or caused by a primary lesion or disease in the somatosensory nervous system. Sensory abnormalities range from deficits perceived as numbness to hypersensitivity (hyperalgesia or allodynia), and to paraesthesia’s such as tingling. Diabetic neuropathy, post-herpetic neuralgia, spinal cord injury pain, phantom limb (post-amputation) pain and post-stroke central pain [1, 2, 5, 10].

**d) Psychogenic pain:** Psychogenic pain most often has a physical origin either in tissue damage or nerve damage, but the pain caused by that damage is increased or prolonged by such factors as fear, depression, stress, or anxiety[11].

**Pain of inflammatory origin:**
   Pain of inflammatory origin is the result of activation and sensitization of the nociceptive pain pathway by a variety of mediators released at a site of tissue inflammation. The mediators that have been implicated as key players are pro-inflammatory cytokines such as IL-1-alpha, IL-1-beta, IL-6 and TNF-alpha, chemokines, reactive oxygen species, vasoactive amines, lipids, ATP, acid and other factors released by infiltrating leukocytes, vascular endothelial cells, or tissue resident mast cells. Egs: appendicitis, rheumatoid arthritis, inflammatory bowel disease, and herpes zoster. Nerves function like electric cables transmitting signals, including pain signals, to and fro the brain. Damage to nerves can interfere with the way those signals are transmitted and cause pain signals that are abnormal. For egs; feeling of burning sensation even though no heat is being applied to the area that burns. Certain chemotherapy drugs, strokes, HIV infection, damage to CNS and peripheral nerves may cause nerve damage. Complex regional pain syndrome is a chronic pain syndrome that can follow a serious injury. It's described as persistent burning. Certain abnormalities such as abnormal sweating, changes in skin colour or swelling may be noticed in the area of the pain. Diabetic peripheral neuropathic pain comes from nerve damage in the feet, legs, hands, or arms caused by diabetes. Individuals with diabetic neuropathy experience various kinds of pain including burning, stabbing, and tingling. Shingles and postherpetic neuralgia: Shingles is a localized infection caused by the same virus that causes chickenpox. The rash and associated pain, which can be debilitating, occurs on one side of the body along the path of a nerve. Post-herpetic neuralgia is a common complication in which the pain from shingles lasts more than a month. Trigeminal neuralgia is condition causes pain as a result of inflammation of a facial nerve. The pain is described as intense and lightning like, and it can occur in the lips, scalp, forehead, eye, nose, gums, cheek, and chin on one side of the face. The pain can be set off by touching a trigger area or by slight motion [9, 14].

**In pain-pathways [2, 3, 10]:** There are three components of pain pathway - 1 A first order neurone (cell body in dorsal root ganglion) which transmits pain from peripheral receptor to a second-order neurone in the dorsal horn of the spinal cord, which axon crosses the midline to ascend as lateral spinothalamic tract to the thalamus where a third-order neurone projects to the post central gyrus (via the internal capsule). Even all pain receptors are free nerve ending, they use two separate pathways-dual pain pathway in spinal cord and brain stem, mainly corresponds two type of pain. In neo-spinothalamic tract for fast pain and paleo-spinothalamic tract for slow chronic pain. From periphery mechanical and acute thermal pain are transmitted by myelinated A-delta fibers. They terminate in lamina I of dorsal horns and excite second order neurons of neo-spinothalamic tract. These second order neurons cross opposite side of cord, then most of the fibers terminate in ventro-basal complex of thalamus, from thalamus third order neuron terminate in basal area of brain and somatosensory area. The paleo-spinothalamic pathway is much older system and transmits pain from the peripheral slow- chronic type C.
Pain fibers. Peripheral fibers terminate in the spinal cord almost entirely in lamina 2 and 3 of dorsal horns, also called substantia gelatinosa, from here fibers go to lamina 5, then cross to opposite side of the cord, and then upward to brain in anterolateral pathway. Pain fibers of spinothalamic pathway terminate widely to brain stem, only 1/10-1/4 fibers pass all the way to thalamus, hypothalamus and some basal regions of the brain. These fibers does not go to higher level, this is the reason slow chronic pain is poorly localized. Neurotransmitter for fast pain is glutamate, having duration of action only a few milli-seconds, and for slow pain is substance P, which is released slowly and gives more lagging sensation. The degree of reaction to painful stimuli varies from individual to individual, mainly because of existence of pain suppression (analgesia) system in CNS. Gate control hypothesis was given by Melzack and Wall in 1965 to explain spinal pain suppression system. Analgesia systems are predominantly noradrenergic, serotonergic and opioid inhibitory system.

Pain rehabilitation: [2, 3, 10, 16] a pain rehabilitation model can be applied to the entire spectrum of pain conditions, from acute musculoskeletal injuries, to sub - acute and recurrent injuries aggravated by poor ergonomics and / or physical impairments , to more complex chronic pain conditions where interplay of biologic, psychological and social influences and beliefs. The basic pharmacological drugs used to treat pain are divided under two categories narcotics and NSAIDS drugs [13, 15]. Most dread pain and diseases of chronic pain symptoms are treated as such eg s cancer pain, neuralgic pain etc. Most cancer pain can be managed using conventional strategies. Most important is to keep the patient informed about their disease and on other side in managing the pain. Positive attitude that the pain will be controlled goes half way towards controlling the pain. The strategy of combining different modes of analgesia is more fruitful. In addition well-known established treatments, such as non-narcotic drugs (acetaminophen, aspirin and ibuprofen) and narcotic medications (morphine and methadone), several newer methods are being used to treat chronic pain, with varying degrees of success. If the patient is in severe pain, this must be addressed immediately the drug of choice is morphine and other synthetic opioids. One such treatment uses a transcutaneous electrical nerve stimulation (TENS) device, which delivers a small electrical current to the skin surrounding the painful area(s).

It is well accepted mode of treatment in the M.P.D.S (Myo- facial pain dysfunction syndrome) and to some extent of success in the treatment of tempro-mandibular pain dysfunction syndrome (TMDS). It is considered safe overall and the effectiveness of TENS in treating chronic pain is still under debate, but it has helped some patients. While not exactly a new technique, the use of marijuana (also known as cannabis) for medical purposes such as chronic pain relief is partially successful and not widely recommended due to CNS depression as major side effect [6]. It acts on cannabinoid receptors. The long-term benefits of marijuana on chronic pain remain unknown due to the lack of scientific research. [10]Spinal cord stimulation (SCS) involves implanting a small device beneath the skin that creates small electrical impulses near the base of the spine. It is also called as "pain pacemaker". This SCS device can now work via remote control, which allows the patient to adjust the level of the electrical signals in response to increasing or decreasing pain. The effectiveness of spinal cord stimulation is still under study and implantation of these expensive devices requires extensive testing of individuals with specific types of pain to maximize the potential of success. Not unlike an SCS device, a "pain pump" or "drug pump" is a device implanted beneath the skin but this unit actually delivers medication directly to the fluid surrounding the spinal cord. Use of a pain pump is not widespread because of the expense involved, but for certain patients, these devices have proven effective because the amount of medication needed is lower, which can reduce the negative side effects experienced with other drug-delivery techniques.

Unconventional treatments for chronic pain have grown significantly in the past two decades due to the growing acceptance of non-conventional medical methods, such as herbal supplements, yoga, meditation, etc. These various processes are collectively referred to as CAM or complementary and alternative medicine. Briefly, a complementary technique will be used along with other pain-control treatments, while an alternative method is used in lieu of another type of treatment.

The list of CAM treatment types is long; few eg s are but includes massage therapy, acupuncture, hypnosis, magnetic therapy, tai chi, and herbal or dietary supplements. While some of these processes and products might lack significant scientific research to prove their effectiveness, it is important to remember two things. First, some of the treatments now used in conventional medicine, such as chiropractic care and herbal supplements, existed outside of mainstream medicine for a long time. More importantly, many people suffering from chronic pain have found some degree of relief. Virtual reality (VR) has been used to manage pain and distress associated with a wide variety
of known painful medical procedures. In clinical settings and experimental studies, participants immersed in VR experience reduced levels of pain, general distress/unpleasantness and report a desire to use VR again during painful medical procedures. Investigators hypothesize that VR acts as a non-pharmacologic form of analgesia by exerting an array of emotional affective, emotion-based cognitive and attention processes on the body's intricate pain modulation system. While the exact neurobiological mechanisms behind VR's action remain unclear, investigations are currently underway to examine the complex interplay of cortical activity associated with immersive VR. Recently, new applications, including VR, have been developed to augment evidenced-based interventions, such as hypnosis and biofeedback, for the treatment of chronic pain [8]. There is a broad spectrum of therapeutic physical agents available for to aid in the management of both acute and chronic pain conditions eg; thermotherapy, hot packs, fluid therapy, electrical heating pad, cryotherapy, light therapy, ultrasound, laser, etc [10].

CONCLUSION:

In confronting the bewildering complexity of pain pathways, treating the chronic pain and chronic pain syndromes of unknown etiology are still puzzling and challenging to the medical sciences. Above all newer techniques of pain management technique and pharmacological agent without much adverse effect are matter of research.

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