Pathophysiology of Pain

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“Why so much pain and suffering in this world?” “What a pain he or she is!” The word pain is used in various contexts. Most often it is linked to emotions of grief, sorrow and suffering. The word “pain” comes from the Latin word “poena” meaning a fine, a penalty. “Pain as the fifth vital sign” has been introduced by the American Pain Society in 1996. According to the International Association for the Study of Pain (IASP) it is defined as “Pain is an unpleasant sensory and emotional experience arising from actual or potential tissue damage.”

It is a sensation that can range from mild, localized discomfort to agony. Pain has both physical and emotional components. The physical part of pain results from nerve stimulation. Pain may be contained to a discrete area, as in an injury, or it can be more diffuse, as in disorders like fibromyalgia. Pain is also a term specifically used to denote a painful uterine contraction occurring in childbirth known as labour pains.

With this background, it is necessary to have the basic understanding of the neuroanatomy and physiology of pain to tackle it in a reasonable way in the era of evidence-based medicine.

Hence, I am sure all the readers of this issue will recollect their 1st MBBS days as a medical student, when all of us have been trained in physiology of pain. Lets go into flash-back and recollect a few of those aspects.

Types of Pain, its Receptors And Stimuli

Most of the body ailments cause pain. The ability to diagnose different clinical conditions depends on a clinician’s knowledge of different types of pain. Pain is a protective mechanism. It occurs when tissues are damaged and there is a natural reaction from the individual to remove pain stimulus. The pain receptors are free nerve endings. They are present in superficial layers of skin, periosteum, arterial walls, joint surfaces, falx cerebri and the tentorium. The pain receptors are stimulated by mechanical, thermal and chemical stimuli. Physiologically pain has been classified into 2 types: fast pain and slow pain. Fast pain is felt within 0.1 sec. It is also described as sharp, acute, electric or pricking pain. It is commonly felt in superficial tissues, seldom in deeper tissues. Fast pain pathway is stimulated by mechanical or thermal pain stimuli and carried by Aδ fibers at velocities between 6 and 30 m/sec. Sharp pain makes the person aware of the damaging influence and react immediately to remove himself or herself from the stimulus. Slow pain is also called burning, aching, throbbing, gnawing, nauseating or chronic pain. It is present in skin as well as deep tissues. The slow pain pathway is mainly stimulated by chemical stimuli (but also by mechanical and thermal) and carried by type C fibers at velocities between 0.5 and 2 m/sec. Chemicals like bradykinin, serotonin, histamine, potassium ions, acids, acetylcholine and proteolytic enzymes are responsible to generate pain. Prostaglandins and substance P enhance the sensitivity of the nerve endings without directly exciting them. The pain receptors are non-adapting and hence differ from other receptors of sensations. They have the unique property of hyperalgesia. The factors causing pain are heat, lactic acidosis resulting from tissue ischemia, tissue contusion, bacterial infection; muscle spasm due to stimulation of mechanical receptors directly and indirectly by compression of blood vessels thereby causing ischaemia.

Pain Pathways

On entering the spinal cord from dorsal spinal roots, the pain fibers terminate on relay neurons in dorsal horns. Further, they are carried to the brain by the neospinothalamic tract or the paleospinothalamic tract.
Aδ fibers transmit mainly mechanical and thermal pain, terminate in the dorsal horns, cross over to the opposite side of the cord and continue upwards to the brain as anterolateral columns. Most fibers terminate in the ventrobasal or posterior nuclei of the thalamus; few fibers terminate in the reticular areas. Signals are also sent to the somatosensory cortex. Glutamate is the neurotransmitter secreted in the spinal cord at Aδ fibers (Figure 1).

The Paleospinothalamic tract

The C fibers which carry slow pain terminate in the substantia gelatinosa of dorsal horns in spinal cord. They also cross over to the opposite side and continue as anterolateral ascending tracts. The paleospinothalamic tract terminates in brain stem in one of the following areas:

1. Reticular nuclei of medulla, pons and mesencephalon.
2. Tectal area of mesencephalon deep. 10-25% of the fibers pass to the thalamus.
3. Periaqueductal gray region surrounding the aqueduct of Sylvius.

The signals are relayed into the intralaminar and ventrolateral nuclei of thalamus, hypothalamus and basal regions of brain. The pain carried by slow chronic pathway is poorly localised. Substance P is the neurotransmitter concerned with slow pain (Figure 2).

Higher Centres for Pain

Reticular formation, thalamus and lower brain centres cause conscious perception of pain. But the cerebral cortex is responsible for interpreting the quality of pain. The pain signals have a strong effect on the arousal system which explains the disturbed sleep or insomnia in a person experiencing pain.
Analgesia System

The pain threshold varies from person to person and the reaction to pain is highly variable. There is a natural inbuilt system of the brain to suppress input of pain signals called analgesia system. The analgesia system is diagrammatically represented in Figure 3.

The neurotransmitters released by the analgesia system are enkephalin and serotonin. Enkephalins inhibit pre and post synaptic C fibers and Aβ fibers when they synapse in dorsal horns, thus blocking the pain signals at initial entry into the spinal cord. Activation of the analgesia system by nervous signals entering the periaqueductal gray and periventricular areas or inactivation of pain pathways by analgesics almost totally suppress the pain signals entering through the peripheral nerves.

The large type Aβ sensory fibres responsible for carrying touch sensation can depress transmission of pain signals from the same area. Hence, when stimulated simultaneously, there is suppression of pain. This is the rationale and the basis of pain relief by applying liniments, massage, acupuncture and acupressure.

Visceral pain and Concept of Referred Pain

The viscera in the different parts of the body also have pain receptors. The visceral pain differs from the surface pain. The visceral pain in the thorax and abdominal cavity is transmitted through the C fibers. The visceral pain fibers synapse in the spinal cord on same second order neurons that receive pain signals from the skin fibers. Hence pain in the remote or deep seated organs is experienced in the skin which have a common embryological dermatomal origin. This is called as referred pain. The stimuli for visceral pain also include ischaemia, smooth muscle spasm, excess distension of hollow organs, action of proteolytic enzymes and stretching of surrounding connective tissue.

Coming back to the present day from our flash-back, this special issue of JAPI “Understanding Pain-The 5th Vital Sign” discusses elaborately the ways of assessing pain, managing acute and chronic pain. There are also practical tips on evaluation of the back pain and the various interventions necessary for pain management. At times, it may be challenging to all the clinicians when the pain in psychogenic in nature; hence the differential diagnosis and treatment of psychogenic pain disorder has been discussed in this special issue. Managing pain is a team-work and hence beyond the patient and the clinician, the paramedics particularly the physiotherapist has a major role to play. The issue has been well written by a series of authors well known in their fields for the management of pain. I am quiet confident that this special issue on pain would act as a ‘Bible’ for all the practitioners and the resident doctors of various specialities in making our patients free from pain i.e “Aah se Aha tak!”

References