PATHOPHYSIOLOGY OF CANCER RELATED PAIN: A BRIEF REPORT

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Abstract

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. Cancer related pain is still permanent, and is feared as problematic worldwide. Cancer pain management is the most problematic when found in patients who have a malignant tumor, and represents the most feared consequences for patients and their families. Cancer related pain management stays a challenge in cancer patients, their families, and oncology nurses due to lack of knowledge and assessment of pain which causes inadequate pain management. There is agreement among experts about the classification of pain into nociceptive, neuropathic, psychogenic, mixed, or idiopathic. This classification is found useful in assessment and therapeutic decision making. Nonetheless, it is now widely accepted that persistent pain may be sustained by different types of mechanisms and experts agree that clinical characteristics can be used to broadly divide pain syndromes into nociceptive, neuropathic, psychogenic, mixed, or idiopathic. Those involved with overlapping cancer related pain should be aware of the barrier of the realization that faces health care providers; thus, they need more studies to further understand the unique molecular mechanisms by which cancer produces sensitization and pain so that new pharmacological targets can be identified that will reduce or block tumor-evoked sensitization.

Key words: pain, cancer, nociceptive pain, neuropathic pain, psychogenic pain, idiopathic pain.

Introduction

What is Pain? What is the relationship between pain and cancer?

The International Association for the Study of Pain's proudly used definition states: "Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage." Cancer related pain is still permanent, and is feared as problematic worldwide. Cancer pain management is the most problematic when found in patients who have a malignant tumor, and represents the most feared consequences for patients and their families (Alexopulos, et al. 2010). Cancer related pain management remains a challenge in cancer patients, their families, and oncology nurses due to lack of knowledge and assessment of pain which causes inadequate pain management (Winslow, Seymour, & Clark, 2005). However, we found inadequate pain management in different settings, especially in vulnerable populations. (Sydney, Dy, Asch, Arash, Homayoon, Walling, et al. 2008).

The most common problem facing cancer patients is bone metastases from lung, prostate, and breast cancer; practically most of the breast cancer patients, and spinal cord compression patients needs emergency intervention and management (Stenseth, Bjornnes, Kaasa, et al, 2007). The prevalence of pain among cancer patients is high worldwide: 64% in patients with metastatic or terminal disease, 59% in patients on anticancer treatment and 33% in patients who had been cured of cancer (Everdingen, Rijke, Kessels, Schouten, Kleef, &Patijn, 2007).

According to the American pain society if the plan of pain management includes both pharmacological and non-pharmacological interventions, it is

considered effective. This is because oncology nurses perform holistic care and have sustained interaction with patients and their families throughout the continuum of cancer care (American Pain Society, 2005). Thus, it is important for health care providers to understand the updated knowledge on pathophysiology of cancer pain.

Pathophysiology of Pain

Pain is sustained by different types of mechanisms. There is agreement among experts about the classification of pain into nociceptive, neuropathic, psychogenic, mixed, or idiopathic. This classification is found useful in assessment and therapeutic decision making. Nonetheless, it is now widely accepted that persistent pain may be sustained by different types of mechanisms and experts agree that clinical characteristics can be used to broadly divide pain syndromes into nociceptive, neuropathic, psychogenic, mixed, or idiopathic. Although this classification is clearly an oversimplification, it has been found useful in assessment and therapeutic decision making.

Mechanisms of Nociceptive Pain

According to Willis (2007) nociceptive pain occurs as a result of the normal activation of the sensory system by noxious stimuli, a process that involves transduction, transmission, modulation and perception.Tissue injury activates afferent neurons (nociceptors), which have A-delta and C-fibers that respond to noxious stimuli and are found in skin, muscle, joints, and some visceral tissues. These fibers have specific receptors responsible for mechanical, chemical or thermal stimuli. Transduction is the process by which exposure to a sufficient stimulus produces depolarization of the peripheral nerve. Depolarization of the primary afferent involves a complex neurochemistry, in which substances produced by tissues, inflammatory cells and the neuron itself influence transduction. Once depolarization occurs, transmission of information proceeds proximally along the axon to the spinal cord and then on to higher centers (Schaible, 2007; Stein, et al, 2009). The transmission of these neural signals are from the site of transduction (periphery) to the spinal cord and brain (Apkarian, Bushnell, Treede, &Zubieta, 2005)

The neurochemistry of these processes involves many compounds, including endorphins, neurokinins, prostaglandins, biogenic amines, GABA, neurotensin, cannabinoids, purines, and many others. The endorphinergic pain modulatory pathways are characterized by multiple endogenous legends and different types of opioid receptors: mu, delta, and kappa. Endorphins are present in the periphery, on nerve endings, immune related cells and other tissues, and are widely distributed in the central nervous system (CNS). They are involved in many neuroregulatory processes apart from pain control, including the stress response and motor control systems.

Opioid drugs mimic the action of endogenous opioid ligands. Most of the drugs used for pain are full mu receptor agonists. Other pain modulating systems, such as those that use monoamines (serotonin, norepinephrine and dopamine), histamine, acetylcholine, cannabinoids, growth factors and other compounds, are targets for nontraditional analgesics, such as specific antidepressants and anticonvulsants (Apkarian, Bushnell, Treede , & Zubieta, 2005).

Nociceptive pain can be acute (short-lived) or chronic (long-lived), and may primarily involve injury to somatic or visceral tissues. Pain that is inferred to be related to ongoing activation of nociceptors that innervate somatic structures, such as bone, joint, muscle and connective tissues, is termed “somatic pain”. This pain is described as aching, squeezing, stabbing, or throbbing. Arthritis and metastatic bone pain are examples of somatic pain.

Pain arising from stimulation of afferent receptors in the viscera is referred to as visceral pain. Visceral pain caused by obstruction of hollow viscous is poorly localized and is often described as cramping and gnawing, with a daily pattern of varying intensity. When organ capsules or other structures such as myocardium, are involved, however, the pain usually is well localized and described as sharp, stabbing or throbbing, descriptors similar to those associated with somatic pain (Apkarian, Bushnell, Treede, & Zubieta, 2005).

The neurogenic inflammation involves the release from nerve endings of compounds such as substance P, serotonin, histamine, acetylcholine, and bradykinin. These substances activate and sensitize other nociceptors. Prostaglandins produced by injured tissues also may enhance the nociceptive response to inflammation by lowering the threshold to noxious stimulation.(Apkarian, Bushnell, Treede, & Zubieta, 2005).

Mechanisms of Neuropathic Pain

Neuropathic pain is due to direct injury or dysfunction of the peripheral or central nervous system. These changes may be caused by injury to either neural or non-neural tissues (Jarvis & Boyce-Rustay, 2009). The neuropathic pain is described as an uncomfortable sensation such as burning, shock-like or tingling (Truini &Cruccu, 2006). Injury to a peripheral nerve axon can result in abnormal nerve morphology. The damaged axon may grow multiple nerve sprouts, some of which form neuromas. The severe sprouts, including those forming neuromas, can generate spontaneous activity, which peaks in intensity several weeks after injury. These areas of increased sensitivity are associated with a change in sodium receptor concentration, and other molecular processes, and also can occur at sites of demyelization or nerve fiber injury not associated with the severing of axons (Jarvis & Boyce-Rustay, 2009). Some alterations in morphology and function result

in peripheral sensitization, which may be related to a lower threshold for signaling or an expansion in receptive fields. In contrast to the still poor understanding of the mechanisms of peripherally generated neuropathic pain, there is almost no information about the processes that induce or sustain centrally generated pain syndromes. Functional neuroimaging has demonstrated the extraordinary neuroplasticity of the brain in the setting of a neuropathic pain, such as phantom pain, but the mechanisms responsible are unknown (Bingel & Tracey, 2008).

Mechanisms of Psychological and Idiopathic Pain

The experience of persistent pain appears to induce disturbances in mood (reactive depression or anxiety), impaired coping, which in turn, appears to worsen pain. This phenomenon is known generically as “psychogenic” pain and is subject to the specific diagnoses coded under the Soma to form Disorders in the Diagnostic and Statistical Manual of the American Psychiatric Association (American Psychiatric Association, 2000). It is very important that patients who have acute or persistent pain without a known physical source not be inappropriately labeled. This may lead to inadequate assessment in the future and therapeutic decisions that are inappropriately skewed; unfortunately, it also leads to stigmatization of the patient and the potential for greater suffering. When reasonable inferences about the sustaining pathophysiology of a pain syndrome cannot be made, and there is no positive evidence that the etiology is psychiatric, it is best to label the pain as idiopathic.

Summary and Conclusion

From the point of view, of overlapping cancer related pain we should be aware of the barriers that face health care providers; thus, there is a need for more studies to further understand the unique molecular mechanisms by which cancer produces sensitization and pain so that new pharmacological targets can be identified that will reduce or block tumor-evoked sensitization.

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