

Comorbidity of Chronic Pain & Depression and Its Treatment Outcome: A Review

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Abstract: Depression, according to WHO predicted to be ranked second only after ischemic heart disease by the year 2020. To make an accurate diagnosis of major depression in the setting of chronic pain is very difficult. Physical symptoms are common in depression, and, in fact, vague aches and pain are often the presenting symptoms of depression. These symptoms include chronic joint pain, limb pain, back pain, gastrointestinal problems, tiredness, sleep disturbances, psychomotor activity changes, and appetite changes. A high percentage of patients with depression who seek treatment in a primary care setting report only physical symptoms, which can make depression very difficult to diagnose. Neurotransmitters level also shows deep connection between pain and depression; as both are mediated by serotonin and norepinephrine, the monoamines. Remission largely depends upon recovery from all the pain symptoms otherwise it may be a cause of relapse.

Keywords: Depression, chronic pain, Neurotransmitters, serotonin, norepinephrine, Remission

I. Introduction

What is Chronic Pain?

The International Association for the Study of Pain defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage”.¹ Pain can be considered chronic when it persists for more than 1 month after anticipated tissue healing, or if it has been present for at least 3 of the previous 6 months.² Common causes are joint arthritis, degenerative disc disease, traumatic injuries and various types of headache. Chronic pain can also occur as part of a generalised pain syndrome, such as fibromyalgia. The emergence of chronic pain has been associated with a range of physical, psychological and social risk factors. These factors interact in complex and dynamic ways, often conceptualised within a biopsychosocial framework.³

Biology & Types of Pain:

There are generally two kinds of pain namely nociceptive pain & neuropathic pain. Nociceptive pain which is something caused by actual or threatened tissue damage. Neuropathic pain is caused by a lesion or disease involving the nervous system. It may have signs of an altered pain response such as allodynia, hyperalgesia and is treated with agents targeting the nervous system abnormality. Neuroplastic change is one possible explanation for the altered pain perception, persistence of pain beyond tissue healing, and resistance to commonly used analgesics that are frequently found in chronic pain. Poorly treated pain can lead to development of sensitization which is increased susceptibility to feel pain to subthreshold stimulus.⁴

There are three categories of sensory neurones, defined by their roles in the transduction of sensory information at the primary afferent terminal before its encoding and transmission to the spinal cord. The first type is myelinated: fast conducting and transduces low-intensity signals such as innocuous, mechanical stimulation of the skin A β fibres. The second type is unmyelinated: slow conducting and responds to high intensity activation by noxious heat, mechanical and chemical stimuli C fibres; these are also referred to as nociceptive sensory neurones nociceptors. The third type of sensory neurone has an intermediate conduction velocity, is myelinated, and also responds to high intensity activation A Ω fibres. Under normal circumstances, only C and A Ω fibres transmit nociceptive information, but recent research utilizing knock-out and transgenic models in combination with physiological, pharmacological and biochemical analyses, has implicated all three types of sensory neurone in chronic pain disorders.⁴

What is depression?

A major depressive disorder occurs without a history of a manic, mixed, or hypomanic episode. A major depressive episode must last at least 2 weeks, and typically a person with a diagnosis of a major depressive episode also experiences at least four symptoms from a list that includes changes in appetite and weight, changes in sleep and activity, lack of energy, feelings of guilt, problems thinking and making decisions, and recurring thoughts of death or suicide.⁵

Comorbidity of pain and depression:

An individual's response to chronic pain reflects characteristics of the pain and the person's thoughts and behaviour developed during the course of the illness, which are subject to positive and negative reinforcement.⁶ The link between pain and depression appears to be a shared neurologic pathway.⁷ Response to painful physical stimuli is moderated in the brain by serotonin and nor- epinephrine, which also affect mood. Patients with neurotransmitter dysregulation may have an imbalance of serotonin and norepinephrine, which may explain the connection between painful physical symptoms and depression. When a patient with depression complains that he or she is feeling physical pain, there may be a chemical reason. The pain response appears to have evolved towards a level of complexity that is related to the cognitive capacity of

the organism. The realization of pain is a multidimensional process involving physical, emotional and perceptual integration. The primary function of pain is to protect the organism from a potentially tissue-damaging stimulus via activation of spinal reflex withdrawal mechanisms. Ascending pain pathways and their supraspinal targets contribute towards two distinct, yet related, aspects of pain: (I) the sensory-discriminative aspect which involves the perception and detection of a noxious stimulus in terms of its intensity, location and duration, and (II) the affective-cognitive aspect which encapsulates the relationship between pain and mood, including pain memories, individual coping strategies, and the overall rationalization of the pain response. Imaging studies of the forebrain have revealed that noxious stimulation also activates neurones in the insular and anterior cingulate cortical areas, in addition to areas of the limbic system including the amygdala, hippocampus, and hypothalamus.^{8,9}

It has been estimated that over 50% of patients suffering from chronic pain also express clinically diagnosable symptoms of depression.¹⁰ However, chronic pain, like depression, is not a single disease. In medical terms, it has a definition that spans a broad spectrum of pathophysiological and psychological aetiologies. In general, it can be categorized into four classes based on its origins: (i) undiagnosed medical or surgical disease, (ii) psychiatric disorder, (iii) neurologic lesion (e.g. multiple sclerosis), or (iv) somatic lesion (cancer, back pain, headache, HIV, rheumatoid arthritis). Treatment of chronic pain presents a difficult challenge, since it may require a multidisciplinary approach including pharmacotherapy, cognitive therapy, psychotherapy and neurosurgery. Given the diverse origins of chronic pain, controversy surrounds the relationship it bears to the depression with which it is often coexpressed. Five major hypotheses have been proposed: (i) the 'antecedent hypothesis', in which depression precedes the development of chronic pain, (ii) the 'consequence hypothesis', in which depression is a consequence of the chronic pain, (iii) the 'scar hypothesis', in which episodes of depression occurring before the onset of chronic pain predispose the patient to a depressive episode after the onset of pain, (iv) the 'cognitive mediation' hypothesis, in which psychological factors such as poor coping strategies are considered to mediate the reciprocal interactions between chronic pain and depression, and (v) the 'independent hypothesis', in which depression and chronic pain are considered to share some common pathogenic mechanisms but remain distinct diseases without causal interaction.¹¹ A recent meta-analysis, controlled on several levels to address each of the five current hypotheses of coexpression of depression and chronic pain, confirmed that depression was more common in chronic pain patients than in healthy controls, and indicated that depression was a consequence of the presence of chronic pain, not a predisposing factor.¹⁰

Treatment and Outcome:

Treatment of depression with symptoms of chronic pain always needs for the complete remission of pain symptoms or otherwise it becomes a cause of relapse. To rate the outcome there are several scales both clinician and self-rated version questionnaires. The most commonly used scales for measuring the symptoms of depression have been the Hamilton Rating Scale for Depression (HAM-D)¹² and the Montgomery Asberg Depression Rating Scale (MADRS)¹³. These 2 scales have traditionally been used in clinical trials for the express purpose of showing initial drug-placebo separation, but they are long and difficult to use in routine clinical practice. Neither scale includes all 9 DSM-IV criteria for major depressive disorder. Additionally, the parameters used to define remission on both the HAM-D and the MADRS are too inclusive. At a score of ≤ 7 on the HAM-D or ≤ 10 on the MADRS, which are often considered to indicate remission, patients may have shown improvement but are still clearly symptomatic. In addition, due to the demanding nature of these 2 rating scales, the chance they will be frequently used in primary care practices is small. There are several other rating scales to choose from, however. A 16-item scale, the Quick Inventory of Depressive Symptomatology (QIDS)¹⁴, that includes all 9 DSM-IV depression criteria. The advantage of QIDS is that it has a clinician-rated version QIDS-C and a self-rated version QIDS-SR. The psychometrics have been established enough to say that a score of 5 on the QIDS-SR can be defined as remission.

II. Conclusion

Depression and pain are frequently comorbid. To make a diagnosis of major depression is difficult in the setting of chronic pain. In fact, research has shown that physical symptom improvement was correlated with the improvement of other depression symptoms, which suggests that the patient's ability to achieve depression remission may be directly related to the reduction of painful physical symptoms.¹⁵ A treatment regimen that does not address pain symptoms and only focuses on core emotional symptoms could result in an incomplete remission and a poor treatment prognosis for the patient. So, it is necessary to choose efficacious therapeutic agents that promote the elimination of both the core symptoms and associated pain symptoms of depression to ensure remission and a return to full social functioning and to prevent relapse.

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