

## Chronic Pain: Myofascial Pain and Fibromyalgia

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Chronic pain is a common dilemma encountered in daily practice. However, optimal treatment of chronic pain is a clinical challenge, especially for patients with chronic myofascial pain (CMP) and fibromyalgia, known as fibromyalgia syndrome (FMS). CMP has also been termed myofascial pain syndrome, the usage of which is not recommended, because CMP is now recognized as a disease (see below). CMP is characterized by chronic pain caused by fascial constrictions and multiple regional trigger points. A fascia is a connective tissue surrounding muscles. A trigger point is a highly sensitive area within the muscle resulting from noxious stimuli and is painful to touch. Myofascial pain is extremely common, and everyone may develop a trigger point at some time in life. In the United States, an estimated 14.4% of the general population suffer from chronic musculoskeletal pain and 21-93% of patients with regional pain complaints of having CMP [1]. FMS is another medical condition characterized by chronic, widespread musculoskeletal pain accompanied by fatigue, sleep, memory and mood disturbances [2,3]. The term “fibromyalgia” derives from Latin, *fibro-*, meaning “fibrous tissues”, Greek *myo-*, “muscle”, and Greek *algos-*, “pain”, which means “muscle and connective tissue pain”. FMS is estimated to affect 2–4% of the population [4,5], with a female to male incidence ratio of approximately 9:1 [6]. In contrast, CMP affects men and women equally. Both CMP and FMS most often affect 30-60 years-old individuals. The cost in care for chronic musculoskeletal pain is high in developed countries [7]. The annual cost of chronic pain in the United States, including healthcare expenses, lost income, and lost productivity, is estimated more than \$100 billion [8].

CMP causes distinct, isolated or regional muscle pain, such as pain in the neck, shoulders, upper and lower back, usually unilateral or worse on one side of the body. The muscular pain is persistent, aching, and deep, ranging from mild discomfort to excruciating and “lightning-like” pain. It usually does not resolve on its own, even after typical, first-aid self-care such as ice, heat, and rest. A hallmark of CMP is the presence of trigger points. A trigger point is a small, hard knot that may be visible and felt under the skin. The knot itself can be painful, especially when poked. Trigger points typically form as a result of trauma to the tissue. Trigger points might be “active” or “latent”. An active trigger point is a sensitive area of extreme tenderness that usually lies within the skeletal muscle and is associated with local or regional pain. A latent trigger point is a dormant area that has the potential to act like a trigger point. A latent trigger point does not cause pain during normal activities, but is tender when touched and can be activated when the muscle is strained, fatigued, or injured. Studies have demonstrated that 25-54% of asymptomatic individuals have latent trigger points [1].

The cardinal symptoms of FMS are chronic widespread pain, fatigue, and allodynia, a condition of non-painful stimuli causing painful sensation. Other symptoms may include tingling, muscle spasm and weakness, morning stiffness, fatigue, anxiety, panic attacks, cognitive or memory impairment (“fibrofog”) [4,9], depression [2,10], functional bowel disturbances [11], feeling overwhelmed due to high levels of sensory input and chronic sleep disturbances [12]. Although FMS is generally accompanied with chronic widespread pain, the latter may be localized [13]. For the diagnosis of FMS, the American College of Rheumatology published official criteria in 1990, known as “the ACR 1990”, including 1) widespread pain for at least three months in three quadrants of the body, and 2) abnormal sensitivity to palpation

in at least 11 of 18 specific tender points. Notably, a tender point is different from a trigger point [14,15]. Guidelines for the diagnosis and management of fibromyalgia have been published in various countries [16-18].

CMP and FMS may coexist and share some common symptoms, including musculoskeletal pain, headaches and/or migraines, sleep disturbances, imbalance and/or dizziness, memory decline, unexplained sweating, worsening symptoms due to stress, changes or extremes in weather, and physical activity. However, the two conditions are distinct. FMS is pervasive with chronic generalized pain and hyperirritability. In contrast, CMP may affect many parts of the body but is limited to trigger points.

More recently, CMP is recognized as a disease rather than a syndrome because muscle trauma leads to malformations of neuromuscular junction, where the nerve cells connect to muscle cells. This suggests CMP is a neuromuscular disease. FMS is a syndrome due to central sensitization to the underlying nociceptive or neuropathic pain, or a combination of the two.

Distinction between CMP and FMS is crucial because their response to treatment and prognosis are different. Trigger points can be effectively manipulated. A growing body of evidence shows that chronic pain can influence the central nervous system (CNS) and cause central sensitization [13]. CMP, if untreated, may incite and exacerbate FMS. Early treatment of CMP may help prevent FMS. The term central sensitivity syndrome has emerged for FMS, CMP, and other conditions involving central sensitization.

The precise etiologies of CMP and FMS are not fully understood. It is commonly accepted that CMP may be caused by prior muscle injury [19]. CMP may subsequently develop into FMS manifesting widespread chronic pain and allodynia. The pathogenesis of FMS is likely due to a central sensitivity mechanism resulting from neuro-chemical imbalances. Activation of inflammatory pathway in the brain may cause aberrant pain processing [3,13]. Central sensitization occurs due to the presence of a lower threshold for pain and hyperactivity of pain-sensitive nerve cells in the spinal cord or brain. Importantly, neuroendocrine disruption such as growth hormone, insulin-like growth factor-1, cortisol, prolactin, androgens, leptin, and neuropeptide Y may also play a role [20-26], although disagreement exists [27-30] and administration of growth hormone in patients failed to show significant improvement [31]. These chronic neuroendocrine disruptive changes may activate hypothalamic corticotrophin-releasing hormone neurons, disrupt normal function

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of the pituitary-adrenal axis, and cause an increased stimulation of hypothalamic somatostatin secretion, which in turn could inhibit the secretion of other hormones [32]. Alterations in neuroendocrine and neurotransmitters may alter exercise-induced analgesic response [33] and potentiate nociceptive system causing allodynia [34,35]. Genetic predisposition also plays a role in the development of CMP and FMS [36]. For example, apolipoprotein E4 (Apo E4) genotype and selected environmental exposures (e.g. motor vehicle accidents) increases the risk of FMS [37]. Indeed, genetic polymorphisms of serotonergic [38], dopaminergic [39] and catecholaminergic[40] systems have been shown in FMS, though not specific as they are also seen in other disorders, including chronic fatigue syndrome [41], irritable bowel syndrome [42], and depression [43], which all are common comorbidities of FMS. Individuals with the 5-HT<sub>2A</sub> receptor 102T/C polymorphism have been shown at increased risk of developing FMS [44]. A high aggregation of fibromyalgia in families was demonstrated [45]. Using self-reporting of chronic widespread pain (CWP) as a surrogate marker for fibromyalgia, the Swedish Twin Registry reports monozygotic twins with CWP have a 15%, and Dizygotic 7%, increased chance of having CWP [46,47]. However, the mode of inheritance is most probably polygenic [36].

Although no specific lab tests confirm a diagnosis of CMP and FMS, tests do help identify predisposing risk factors. Current treatment for CMP includes pharmacological and non-pharmacological approaches. Pharmacological treatment includes non-steroidal anti-inflammatory drugs, tricyclic antidepressants, muscle relaxants, and anticonvulsants. Non-pharmacological treatment includes physical therapy, massage, stretching, heat, and ultrasound. Acupuncture and needle injection with or without medications into a trigger point can help relieve pain.

In this issue of JPMR, there are two articles related to the chronic pain. Dhadwal et al. present their clinical retrospective study on the efficacy of lidocaine trigger point injection (LTPI) in alleviating CMP. Of the 24 patients in the study who answered questionnaires after having received LTPI, 22 reported a significant pain relief (92%,  $P < 0.0001$ ). The pain level on a scale of 1-10 was  $8.9 \pm 0.4$  ( $\pm$  SE) prior to treatment and  $2.7 \pm 0.5$  after treatment, showing a significant pain reduction (70%,  $P < 0.0001$ ); which lasted for  $26 \pm 5$  days post injection. Dhadwal et al. conclude that LTPI appears to be an effective and tolerable adjunct treatment modality for CMP. Although several limitations in their study such as the small number of subjects, lack of a control group, and no discussion of the mechanism of LTPI in alleviating CMP, Dhadwal et al. provided additional evidence that peripheral manipulation by LTPI relieves CMP, which warrants further evaluation. In another article, Malemud reviewed recent literature regarding the mechanism accounting for the chronic pain in FMS. Low levels of serotonin and norepinephrine in the peripheral circulation appear to correlate with chronic pain. Increasing and/or maintaining higher levels of these neurotransmitters through inhibition of selective-serotonin or serotonin/norepinephrine (SSRI/SNRI) reuptake may form the pharmacological basis of treating chronic pain in FMS. However, previous studies showed that circulating levels of epinephrine and norepinephrine may be low, normal or high in FMS [48,49] and clinically not all FMS patients respond well to SSRI or SNRI therapy. Nevertheless, more studies are needed to explore the pathogenesis and the central sensitization mechanism of CMP and FMS to establish effective treatment for these entities.

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