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Review Article

Fibromyalgia and Sleep Disturbance: A Vicious Circle

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Abstract

Fibromyalgia is a chronic non-inflammatory and non-autoimmune diffuse pain syndrome affecting the musculoskeletal system. Traditionally, poor sleep quality has been linked as a feature of fibromyalgia that is a consequence of severe pain and depression. Many studies confirm the bidirectional roles of fibromyalgia and sleep disturbance, creating a vicious circle. More studies are needed to elucidate the exact pathophysiology of this condition and create new, more effective treatments as fibromyalgia can have a severe negative impact on social, mental, emotional and physical state of the patient.

Keywords: Fibromyalgia; Sleep disturbance; Alpha-delta sleep; Fibrositis

Abbreviations

FMS: Fibromyalgia Syndrome; ACR: American College of Rheumatology; WPI: Widespread Pain Index; SSS: Symptom Severity Scale; CNS: Central Nervous System; HPA: Hypothalamic-Pituitary-Adrenal

Introduction

Fibromyalgia, or Fibromyalgia Syndrome (FMS) is a chronic (>3 months) non-inflammatory and non-autoimmune diffuse pain syndrome affecting the musculoskeletal system. There is no clear etiology and is mostly a diagnosis of exclusion. There are characteristic tender points present on physical examination (Figure 1) and the patients often mention morning stiffness, non-restorative sleep, severe fatigue, low back pain, paresthesias, allodynia (pain from a normally non-painful stimulus) hyperalgesia (inappropriately intense pain from a normally painful stimulus), Raynaud's-like symptoms, depression and anxiety, making the clinician to think of a vague list of differentials. For many clinicians FMS remain a controversial condition [1]. Yet, with a prevalence of approx. 3% worldwide [2], FMS is one of the most common musculoskeletal conditions. The complaint of great significance except from musculoskeletal symptoms is the poor sleep quality which leads to further fatigue, anxiety and depression [3].

History

FMS is now a generally well-recognized clinical condition which causes chronic pain and disability if left untreated. In 1904, Gowers used the term "fibrositis" to describe patients suffering from non-specific regional musculoskeletal pain [4]. In 1972, Smythe described the characteristic generalized pattern of pain, along with a set of criteria that stimulated clinical interest and research [5]. The term "fibromyalgia" was first used in 1976 by Hench [6]. Until then, many terms have been used to describe the condition, such as interstitial myofibrositis [7], generalized tendomyopathy [8], psychogenic rheumatism [9], and many other. In 1990, the first American College of Rheumatology (ACR) criteria were published followed by the revised criteria in 2010 (Table 1) that excluded tender points, allowing less extensive pain, and giving importance to patient-reported somatic symptoms and cognitive difficulties. Note that the Symptom Severity Scale (SSS) includes the symptom "waking unrefreshed" which delineates the importance of sleep for FMS patients.

Epidemiology

The prevalence of FMS has been studied in many countries around the globe with varying results. Most studies used the 1990 ACR criteria. The global mean prevalence of FMS was 2.7%, ranging from 0.4% in Greece [10] to 9.3% in Tunisia [11]. There is a female to male preponderance with higher incidence in women over 50 years of age [12]. Furthermore, FMS is more prevalent in subjects with low

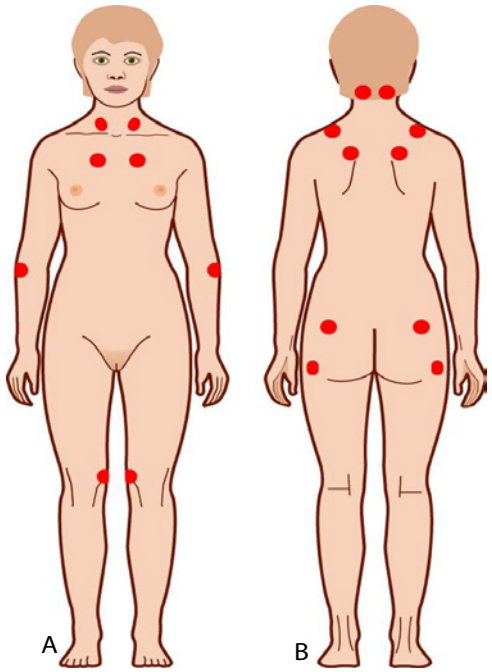

Figure 1: Location of the 18 (9 pairs) specific tender points in FMS patients (A) – *Low cervical*: anterior aspects of the intertransverse spaces at C5-C7; *Second rib*: second costochondral junctions; *Lateral epicondyle*: 2 cm distal to the epicondyles; *Knee*: medial fat pad proximal to the joint line; (B) – *Occiput*: suboccipital muscle insertions; *Trapezius*: midpoint of the upper border; *Supraspinatus*: above the medial border of the scapular spine; *Gluteal*: upper outer quadrants of buttocks; *Greater trochanter*: posterior to the trochanteric prominence.

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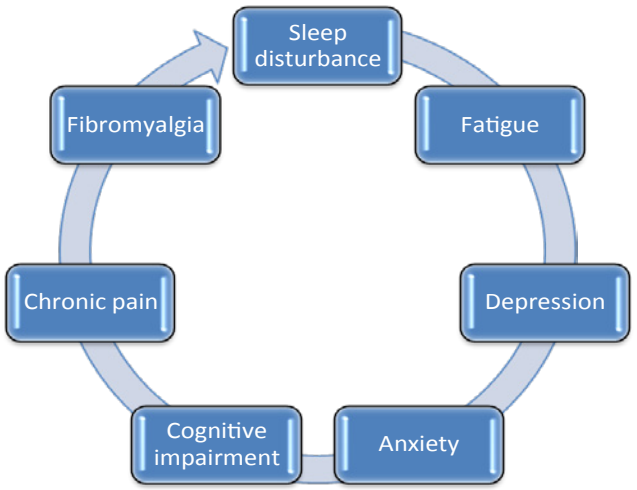

Figure 2: The vicious circle of sleep disturbance and FMS.

education level, low socioeconomic status [13], living in rural areas [14].

Pathophysiology of Fibromyalgia

Although the pathogenesis of FMS is not clear, abnormal pain processing seems to have a key role in pathophysiology. Current hypotheses center on atypical sensory processing in the Central Nervous System (CNS) but some components of the peripheral and autonomic nervous system are involved [15]. Central sensitization is the key term that describes various dysfunctions of the CNS involving ascending and descending neural pathways. Through central sensitization, patients with FMS experience the characteristic tenderness, manifested as allodynia and hyperalgesia, by lowered pain-pressure threshold [16]. Another interesting concept is the role of oxidative stress in FMS.

Sleep disturbance is one of the most interesting factors that could trigger FMS. There are many authors that support the theory that non-restorative sleep triggers or augments FMS symptomatology and others supporting the theory that FMS could be the reason of poor quality sleep. The truth could lie somewhere in between, creating a vicious circle of poor sleep quality due to FMS and non-restorative sleep augmenting the symptomatology of patients suffering from FMS. There are studies that show the prevalence of sleep abnormalities exceeding 90% of subjects with FMS [17]. Common complaints include restless leg syndrome-like disorders, frequent awakenings and daytime somnolence [18]. Examining the sleep architecture, the sleep disturbance associated with FMS, is termed alpha-delta sleep. Alpha-waves (8-13Hz) correspond to quite wakefulness with closed eyes, whereas, as deeper sleep is reached, the frequency of brain waves slows, so that delta-waves (<4Hz) account for >50% of brain wave activity. It is delta-wave sleep that is responsible for restful and restorative sleep. Alpha-delta sleep, is characterized by disruption of delta-wave sleep by frequent alpha-wave intrusion resulting in significantly reduced restorative sleep [19]. Although this sleep pattern is not specific for FMS and other pathologies could be the underlying cause such as emotional stress and sleep apnea syndrome [20,21], alpha-delta sleep pattern is clinically associated with non-restorative sleep.

Table 1: 2010 Fibromyalgia Diagnostic Criteria (ACR).

1.	WPI ≥7 and SSS score ≥5 or WPI 3-6 and SSS score ≥9
2.	Symptoms have been present at a similar level for at least 3 months
3.	The patient does not have a disorder that would otherwise explain the pain

Finally, the genetic component of the disease must not be forgotten. There is evidence for a role of polymorphisms of genes in the serotoninergic, dopaminergic, and catecholaminergic systems in the etiology of FMS.

Sleep Studies and FMS

As mentioned above, patients suffering from FMS report sleep problems (>90%) such as difficulty falling asleep, difficulty falling back to sleep after waking up during nocturnal sleep, and unrefreshing sleep [3,17,22]. There are studies in healthy volunteers that suggest FMS-like symptoms when sleep disruption occurs. Symptoms like musculoskeletal pain and decrease in pain threshold, mood disturbances, marked daytime fatigue, cognitive impairment and depression were common, suggesting that poor sleep quality could be the trigger for FMS [23,24,25]. Two interesting studies tried to find out if poor sleep quality predisposes individuals to the development of FMS. A large Norwegian study found out that 2.6% who did not have musculoskeletal pain or physical disability at the time of recruitment developed fibromyalgia over a 10-year period showing the strong relationship between sleep disturbance and FMS [26]. Another UK population-based epidemiological study with individuals aged >50 years, found out that 7.7% who reported no pain at baseline, developed widespread pain [27]. Sleep disturbance is also a common symptom of patients with depression, anxiety and fatigue but depression, anxiety and fatigue are also common problems in patients with FMS. Studies show that there is a bidirectional relationship of the aforementioned problems making the hypothesis of sleep disturbance and FMS even stronger [28,29].

Discussion & Conclusion

The diagnosis of FMS is often delayed by 2-3 years [30] and patients suffer the consequences of the condition feeling most of the time helpless, consuming valuable time of their lives trying to figure out what is the problem with them, consuming healthcare resources visiting different doctors and at the time of the correct diagnosis they are already in a chronic pain state. Fibromyalgia can have a negative impact on social, mental, emotional, physical and occupational wellbeing. Better quality sleep and pain control in FMS patients suggest that the development of treatments in that direction could prove more effective in the management of FMS. The vicious circle of sleep disturbance and FMS (Figure 2) must be elucidated by more studies targeting to FMS symptomatology relief by sleep modifications or new, more effective treatments.

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