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FIBROMYALGIA: FROM EPIDEMIOLOGY TO TREATMENT

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Abstract: The present study proposes to carry out an approach centered on Fibromyalgia, highlighting its clinic, diagnosis and treatment. For the selection of articles and documents, a search was used with the descriptors "Fibromyalgia", "Diagnosis", and "Signs and Symptoms". The databases used for consultation included UpToDate, Google Scholar, BIREME and DATASUS. Articles and national and international documents from health agencies available from 2005 to 2019 that supported this study were searched. With the aim of expanding knowledge on the subject, since the diagnosis, treatment and control of this rheumatic syndrome that significantly affects the quality of life of patients is of great relevance.
Keywords: Fibromyalgia, Rheumatic syndrome, Signs and symptoms, Treatment.

INTRODUCTION

Fibromyalgia is a chronic diffuse painful rheumatic pain syndrome involving tender points that worsen compression. In addition to the complaint of pain, some other symptoms, such as changes in concentration, headache, memory disorders, sleep disorders, paresthesia in the limbs, fatigue, gastrointestinal and genitourinary complaints may be present.

Although documented for a long time, most research related to fibromyalgia began only 4 decades ago. It was verified that the sum of genetic and environmental factors favor the development of the disease. It is clear that genetic predisposition is one of the most important factors, as these individuals generally have greater sensitivity to pain, less production or less availability of analgesic substances.

Thus, when these individuals are exposed to certain environmental factors, they may be sensitized to the disease. The anterior spinothalamic pathway communicates with several areas in the brainstem, changes in this pathway cause systemic symptoms since the brainstem is responsible for regulating sleep, memory, gastrointestinal and genitourinary systems, among others.

Another important factor is that the reduced levels of serotonin and dopamine due to the imbalance in neuromodulation at the CNS level are factors that predispose the individual to the development of depression.

EPIDEMIOLOGY

The proportion of individuals affected by Fibromyalgia is around 7 to 10 women for every 1 man, in general, the most affected age group is between 30-50 years old. In addition, this disease may be associated with other diseases such as systemic lupus erythematosus, rheumatoid arthritis and Sjogren's syndrome.

There are other less common diseases that need to be ruled out for the diagnosis of fibromyalgia, such as: inflammatory myopathies, hyperthyroidism, viral infections (HIV, hepatitis C) and osteomalacia. Another existing factor is that although it is not common, Fibromyalgia can also be triggered in children and the elderly.

Patients with fibromyalgia are at increased risk for somatic symptoms (67%), depression (55%), panic disorder (35%) and agoraphobia (30%). Furthermore, they have worse rates of pain, sleep quality and quality of life.

PATHOGENESIS

There is a relationship of genetic kinship in the development of this disease, as there are a number of genetic factors that together contribute to the development of greater susceptibility to pain, such as greater sensitivity to painful substances, less production or less availability of analgesic substances and receptors more readily activated.

However, there is the presence of environmental factors in the development of the disease, which cause sensitization causing

painful crises. There are studies that show that the two main causes of exacerbations are viral infections and physical trauma, which show the greater predisposition of some individuals to pain.

The anterior spinothalamic pathway communicates with various areas in the brainstem such as the amygdala and raphe nuclei, these areas are responsible for memory and concentration. Thus, as there is an illness in the pathways that communicate with the brainstem, changes occur in sleep, memory, concentration. In addition, there is a disturbance in neuromodulation by serotonin and dopamine, so there may be a tendency to depression and fatigue due to a delay in the noradrenergic and cortisolic response.

Fibromyalgia is the arm of the central sensitization syndrome, which occurs due to the imbalance between substances such as dopamine, serotonin, noradrenaline, glutamate and substance P in the central nervous system, which is the region that regulates the circadian cycle, peristalsis, among others. Due to this, symptoms such as functional dyspepsia, interstitial cystitis, chronic dysmenorrhea and irritable bowel syndrome may occur.

There are receptors in the CNS that modulate the release of neurotransmitters and neuropeptides such as serotonin, cholecystokinin, acetylcholine, GABA, substance P and dopamine. The function of these substances with sensory transmission, regulation of autonomic functions and pain regulation has been proven.

Substance P is a neuromodulator present in type C, non-myelinated nerve fibers. In the presence of nociceptive stimuli, C fibers release some neurons from the posterior horn of the spinal cord. Based on these aspects, any alteration in its production or degradation can result in defective pain perception.

In the meantime, elevated levels of substance P and reduced serotonin in CSF demonstrate that there are imbalances, since substance P modulates the afferent pathways that are responsible for carrying the painful stimulus and serotonin is present in the pain inhibition process. Thus, low serotonin levels have a reduced analgesic effect.

CLINICAL MANIFESTATIONS

Fibromyalgia (FM) is a complex clinical condition, characterized by the occurrence of diffuse pain, tender points sensitive to palpation and absence of joint or muscle inflammatory processes. Thus, the clinical picture of this syndrome is usually heterogeneous. In this bias, the central symptom, present in all patients, is diffuse and chronic pain, involving both the axial and peripheral skeletons.

In general, patients have difficulty indicating the topography of the pain, many times referring to peri-articular sites, without specifying whether the origin is muscle, bone or joint. The character of the pain is quite variable, and may be burning, stabbing, heaviness or the "tiredness type".

In view of the above, with regard to the presentation of pain, a portion of the patients refer that the pain is initially more localized in a certain region, especially in the cervical spine, involving or not the trapezius, other times starting as a cervicobrachialgia or as a cervicodorsalgia. Another part of the patients claims that the pain was diffuse, affecting segments of the spine, upper and lower limbs.

It is common to report worsening pain due to cold, humidity, climate change, emotional tension or physical exertion. Furthermore, symptoms that may be associated with pain are non-restorative sleep and fatigue, present in the vast majority of patients.

Another symptom that is usually present is the "feeling", referred to by the patient, of edema, particularly in the hands, forearms and trapezius, which is not observed by

the examiner and is not related to any inflammatory process. In addition to these musculoskeletal manifestations, many suffer from complain of symptoms unrelated to the locomotor system.

Among this variety of complaints, headache, dizziness, tinnitus, atypical chest pain, palpitation, abdominal pain, constipation, diarrhea, dyspepsia, premenstrual tension, urinary urgency, difficulty concentrating, paresthesias that do not respect the dermatomal distribution, and memory loss stand out.

It is also worth mentioning that about 30% to 50% of patients have depression. The sleep disorder mentioned above is present in almost 100% of patients with fibromyalgia and has varied characteristics. Among them are the difficulty in inducing sleep and night awakenings, making it difficult to establish a restorative sleep. Sleep disorders lead to consequences such as cognitive deficits, morning tiredness and greater chances of triggering psychiatric disorders, which are often associated with fibromyalgia. Anxiety, mood and behavior changes, irritability or other psychological disorders accompany about 1/3 of these patients, although the psychopathological model does not justify the presence of fibromyalgia.

DIAGNOSIS

The diagnosis is clinical, based on a set of subjective symptoms, being suspected in cases of chronic pain for at least three months with no other identified cause. The pain is characteristically widespread, and is usually accompanied by moderate to severe sleep disturbances or fatigue, also lasting at least three months. Other symptoms may also be associated.

Various classification criteria for fibromyalgia (FM), such as the ACR 2010 preliminary diagnostic criteria (2010 criteria) for FM and the AAPT diagnostic criteria for FM, were developed and tested to provide homogeneity across patient populations for clinical studies, and especially useful for tracking the severity of symptoms over time.

AMERICAN COLLEGE OF RHEUMATOLOGY PRELIMINARY DIAGNOSTIC CRITERIA FOR FIBROMYALGIA AND MEASUREMENT OF SYMPTOM SEVERITY:

CRITERION:

A patient meets the diagnostic criteria for fibromyalgia if the following 3 conditions are met:

1) Widespread Pain Index (WPI) ≥7 and Symptom Severity Scale (SS) score ≥5 or WPI 3 to 6 and SS scale 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.

VERIFICATION:

1) WPI

Note the number of areas where the patient has had pain in the last week. In how many areas did the patient feel pain? The score will be between 0 and 19:

- Neck
- Mandible, left
- Jawbone, right
- shoulder girdle, left
- shoulder girdle, right
- upper arm, left
- upper arm, right
- lower arm, left
- lower arm, right
- Chest
- abdomen
- Upper back
- lower back
- Hip (buttock, trochanter), left

- Hip (buttock, trochanter), right
- Upper leg, left
- Upper leg, right
- Lower leg, left
- Lower leg, right

2) SS scale score:

For each of the 3 symptoms below, please indicate the level of severity over the past week using the following scale:

0 = no problem

1 = mild or mild problems, usually mild or intermittent

2 = moderate, considerable problems, often present and/or at a moderate level

3 = Severe, pervasive, ongoing, life-disturbing problems

- Fatigue (0 to 3)
- Waking up without rest (0 to 3)
- Cognitive symptoms (0 to 3)

How many of the following has the patient had in the past 6 months?

- Pain or cramps in the lower abdomen
- Depression
- Headache

The SS scale score is the sum of the severity of the 3 symptoms (fatigue, awakening unrefreshed, cognitive symptoms) plus the number of discriminated symptoms present. The final score is between 0 and 12.

Often, fibromyalgia can be associated with other preconditions, such as: irritable bowel syndrome, depression, panic syndrome and others. Since, the concomitance of fibromyalgia with these underlying pathologies, they aggravate the symptoms and are predictors of: one per pain index, sleep quality and quality of life. In addition, it is a factor that makes the diagnosis difficult. In these cases, laboratory tests can be used to rule out pathologies that may present similar symptoms.

Remembering that the diagnosis of Fibromyalgia is completely clinical and there is no laboratory marker or imaging exam characteristic of this pathology.

Furthermore, the SBR does not recommend the use of polysomnography to assess sleep disorders in the diagnosis of fibromyalgia and there is no scientific evidence that supports the benefit of using thermography for the diagnosis of fibromyalgia.

DIFFERENTIAL DIAGNOSES:

- **Rheumatoid arthritis, Sjögren's syndrome, and systemic lupus erythematosus**: They may present with generalized arthralgias, myalgias and fatigue, and like FM more often affect younger women, however, features of RA, such as multiple joint swelling, or of SLE, such as facial rash and multisystem inflammation, do not occur in FM.
- **Spondyloarthritis:** They may present with pain and axial skeletal stiffness similar to that of FM and may be misdiagnosed as FM, however, spinal motion in FM is usually normal, and there are characteristic imaging and radiological features of ankylosing spondylitis and other forms of spondyloarthritis that are not observed in FM.
- **Polymyalgia rheumatica:** These patients tend to be older at onset and to have more generalized stiffness than severe, generalized pain. An elevated erythrocyte sedimentation rate (ESR) OR C-reactive protein (CRP) is present in the vast majority of cases, but is normal in patients with FM. In addition, they respond well to modest doses of glucocorticoids.
- **Osteoarthritis:** the person feels localized joint pain, restricted to the affected joints, and generalized joint and periarticular pain not present in osteoarthritis (OA)

TREATMENT

The treatment of Fibromyalgia reduces the main manifestations of this disorder, using both non-pharmacological measures and drug therapy. It must be individualized and have the support of a multidisciplinary team.

Treatment aims at relieving pain, improving sleep quality, maintaining or restoring emotional balance, improving physical conditioning and fatigue, and specific treatment of associated disorders. Initially, educate and inform the patient and their family members, providing them with as much information as possible about the syndrome and assuring them that their symptoms are real. The patient's attitude is a determining factor in the evolution of the disease.

PHARMACOLOGICAL TREATMENT

The pharmacological treatment of fibromyalgia can be applied in monotherapy or in combination with drugs, including antidepressants, muscle relaxants, anticonvulsants, cannabinoids, opioids, N-methyl D-Aspartate antagonists, melatoninergic agonists, peptidergic substances, among others.

TRICYCLIC ANTIDEPRESSANTS

These drugs act by altering the metabolism of serotonin and noradrenaline, and in peripheral nociceptors and mechanical receptors, promoting peripheral and central analgesia, enhancing the analgesic effect of endogenous opioids, increasing the duration of phase 4 of n-REM sleep, improving the disorders of sleep and reducing mood swings in these patients.

Amitriptyline 12.5–50mg, usually administered 2 to 4 hours before bedtime, improves fatigue, pain and sleep in these patients. Cyclobenzaprine, a tricyclic agent with a structure similar to that of amitriptyline, is a drug that does not have antidepressant effects and is used as a myorelaxant. Doses of 10 to 30 mg, taken 2 to 4 hours before bedtime, are significantly effective in relieving most fibromyalgia symptoms. The efficacy and tolerability of amitriptyline and cyclobenzaprine in the treatment of fibromyalgia can be considered similar.

SELECTIVE SEROTONIN REUPTAKE BLOCKERS

Selective serotonin reuptake blockers, especially fluoxetine, can be used in the syndrome. Fluoxetine, when used in conjunction with a tricyclic derivative, can amplify the action of the latter in pain relief, sleep and overall well-being. It must be administered in the morning in doses between 10 and 40 mg.

BENZODIAZEPINES

Alprazolam in doses between 0.5 and 3 mg increases the effectiveness of the therapeutic response when associated with non-steroidal anti-inflammatory drugs (NSAIDs). Benzodiazepines must not be routinely used in patients with fibromyalgia due to the onset of dependence, and when used, they must be weaned correctly.

ANALGESICS

Paracetamol and dipyrone are alternatives for analgesia, as adjuvant treatment. The use of tramadol hydrochloride associated with paracetamol contributes to the improvement of pain in patients with fibromyalgia.

NON-PHARMACOLOGICAL TREATMENT

Fibromyalgia is a pathology that involves neuropsychological, organic and social aspects, therefore, the non-pharmacological approach is parallel to the use of drugs due to the possibility of remission of the active phase of the disease.

According to Pereira et al (2021), the use of acupuncture proved to be effective in reducing pain in patients with Fibromyalgia, increasing the connection to endogenous antinociceptive-opioid systems and μ-opioid receptors (MORs), in addition to reducing symptoms that are associated with illness such as insomnia and depression. Concomitant to this, measures such as physical exercise and cognitive-behavioral therapy were effective in reducing symptoms.

In cognitive-behavioral therapy, the performance of the biofeedback model, which aims at the body-mind connection, proved to be a suggestion for improvement and control of pain and mood, lasting for up to 6 months.

This way, the therapy aims to modify the levels of activity and healthy behavior, to achieve a change in behavior and finally generate a lower intensity of pain. In this line of reasoning, according to Busch AJ (2011), the use of physical activity programs promotes endogenous analgesia, collaborating with a sense of well-being, improving pain training and physical function.

According to Efrati et al (2015), hyperbaric oxygen therapy improves the quality of life of patients with chronic fibromyalgia due to the reduction of neuroplasty and reduction of abnormal brain activity in areas that are related to pain.

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