

FIBROMYALGIA AND EHLERS-DANLOS SYNDROME Hypermobile (EDSh)

(Written in language for patients)

Fibromyalgia (FM) and Ehlers-Danlos Syndrome Hypermobile are two musculoskeletal diseases that present similar characteristics (1), making it difficult to differentiate between them. Mary Ann Fitzcharles (2), who is an authority on FM, reminds us that the mechanism of pain in FM is unknown and finds that there is a relationship between FM and EDSh. According to this doctor, there is growing evidence that at least a subgroup of patients with musculoskeletal pain or FM are hypermobile. Acasuso (3), in Spain, has written about new FM perspectives. According to him, there is a lack of agreement among researchers as to whether chronic fatigue, FM and other conditions can be said to be similar or even identical. It is very possible that many patients with FM are actually EDSh since this diagnosis is little known by doctors, not only in Chile, but in most countries. In my 30 years in the USA, I saw patients with Fibromyalgia every day and now I make this diagnosis very occasionally. Since my return to Chile, I have seen more than 4,000 cases of EDSh (now in 2023 about 9.000), with which we have acquired the necessary experience to safely diagnose this disease. In this article we will discuss the relationship between these two conditions.

WHAT IS FIBROMYALGIA?

FM is known to produce chronic fatigue and pain in the muscles and fibrous connective tissues, such as ligaments and tendons. It mainly affects the muscles and their unions with the bone. Although it also feels like a disease that affects joints. It can give joint pain (arthralgias), but it is not a true form of arthritis and does not cause inflammation of joints nor joint deformities. If a patient with FM or EDSh has red, hot joints, it means that he has two conditions, FM or EDSh and Gout, Rheumatoid Arthritis or Lupus, etc.

It is one of the most frequent causes of consultation in rheumatology (10 to 20% of patients in Chile) and exists in 4% of the US population.

FM is a chronic disease that gives musculoskeletal pain and in 66% of cases it is associated with Chronic Fatigue. The exact cause of the problem is unknown, but it is known that a combination of different factors can cause it, such as stressful situations, physical or emotional trauma, and hormonal changes. The pain is very variable, stress and cold produce greater stiffness of the joints and tendons, while exercise, deep sleep and heat relax, reducing pain.

In the past, there was no clinical evidence that this disease existed, the knowledge of the disease came only from the descriptions of the symptoms given by FM patients, for this reason, for a long time it was believed that FM did not exist as a condition or that it was not important. However, in recent years, more defined guidelines have been established to aid diagnosis. The American College of Rheumatology (ACR) created criteria for the diagnosis of Fibromyalgia in 1990 (4), but in reality, it is very vague and is based on a history of generalized pain that covers several parts of the body and on the presence of at least 11 of 18 painful points (figure 1). In addition, this criterion was not designed to be applied to individual patients, but for epidemiological studies. Because of this, more than half of the patients clinically diagnosed with FM do not meet this criterion. In addition, according to Clauw (5), 20% of arthritis have positive FM criteria. Crofford (6) studying the ACR FM criteria a decade after it was implemented, estimates that it did not capture the essence of the FM Syndrome, since it only considers pain and no other important symptoms such as fatigue, memory and sleep impairment, stress and depression.

WHAT IS EHLERS-DANLOS HYPERMOBILE (EDSh) ?

Joint Hypermobility Syndrome (JHS) is one of the classic Hereditary Disorders of Collagen Fiber (AHFC) (7), such as Ehlers-Danlos, Marfan and Osteogenesis Imperfecta, with which it shares many symptoms, although to a lesser degree.

In some people, hypermobility is accompanied by tissue weakness due to a hereditary alteration of collagen, which produces recurrent symptoms of both the musculoskeletal system (joint pain, bursitis, tendinitis, joint subluxations, back pain, etc.) and others. tissues: uterine or rectal prolapse, abdominal hernias, varicose veins, hemorrhoids, thin (transparent) skin with striae, capillary fragility and poor healing, mitral valve prolapse, myopia, drooping eyelids, etc.

Currently for many authors, the Ehlers-Danlos Hypermobile (EDSh) is the same and formerly called Joint Hypermobility Syndrome, (JHS). Some of these EDSh patients (15%) are tall, lanky young men (Marfanoid habitus). Due to the alteration of collagen, it is common for women with EDS to have light blue sclera and not white as normal, which in men is less frequent.

Around 30% of EDSh patients have chronic fatigue (Dysautonomia) (8) due to arterial hypotension, secondary to weakness of the collagenous wall of the veins and an associated alteration of the autonomous nervous system (Sympathetic-Vaso-Vagal). This is more frequent in young people and in our study (8) of 1751 patients

with EDS_h, Dysautonomia was found in 80% of the women and in 60% of the men, younger than 30 years of age.

PAIN IN SED_h AND FM

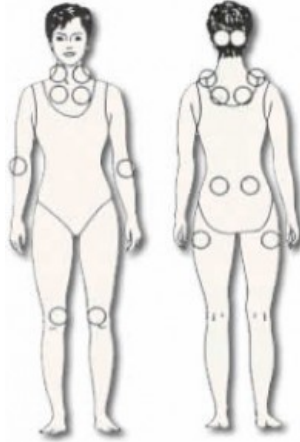
Pain is the most prominent symptom in both FM and EDS_h. Generally, it is felt throughout the body. It can start in one region, such as the neck and shoulders, and after a period of time it spreads. The pain is usually diffuse, recurrent, and migratory and does not follow anatomic patterns. It can be of the tendonitis type (enthesitis = inflammation of the tendon insertion site in the bone), bursitis or affect the joints (arthralgia) or muscles (myalgia). Some terms commonly used to describe the pain in FM are: burning, tingling, like fire, severe, terrible pain. It varies with the time of day, activity level, weather, sleep patterns, and stress or tension. Most people with FM describe their condition as having the flu, with persistent muscle pain; some people end up having very severe pain. The pain is sometimes worse with activity.

Both FM and EDS_h are characterized by arthralgia, myalgia, enthesitis, morning stiffness of the hands or generalized stiffness, diffuse swelling of the hands and feet, and chronic fatigue. When a general physical examination is done, people with FM or EDS_h are normal and appear healthy, however a more detailed examination of their muscles will reveal painful areas (figure 1). The presence of these tenderpoints suggests FM, although they can also be found in the EDS_h, so they are non-specific and depend on the pressure exerted by the examiner. The painful areas in FM and EDS_h are similar to the areas that hurt in other types of muscle and bone problems, such as tennis elbow and trochanteric bursitis (inflammation of the outer part of the hip). and tendon attachment sites, such as at the medial border of the scapula. It is necessary that rheumatologists (doctors specializing in arthritis and rheumatism) carry out a comprehensive examination and request the relevant tests to rule out other pathologies, such as rheumatoid arthritis, lupus, spondylus-arthropathies, etc.

Family history is also important since in EDS_h, due to its Autosomal Dominant inheritance, it affects 50% of the children. There is a certain familial tendency in FM, but it is not a hereditary disease. It is 8 times more frequent in the close relatives of the patient with FM than in the general population. Hypermobility has been described in a high number of patients diagnosed with FM. In a study by Gedalia (9), carried out in Israel of 338 children, from 9 to 15 years of age, 13% had joint hypermobility and 6% FM. Of the children with FM, 81% had hypermobility and 40% of those with

hypermobility had FM, demonstrating a strong association between the two diseases.

Figure 1. The dots in this figure indicate the different sites of the “trigger points”.



FATIGUE AND SLEEP INTERRUPTIONS.

About 90% of people with FM have moderate or severe fatigue, with a lack of energy, decreased resistance to exercise, or a kind of exhaustion, such as the flu or lack of rest. Many times, fatigue, is more of a problem than pain. Generally, people with this disease wake up tired after sleeping through the night. In EDSH, chronic fatigue is worse at noon and in the afternoon. They usually wake up well and get tired as the day progresses. I ask them “if their batteries run out” in the afternoon, or when walking slowly or standing for a long period. They are usually tired, sleepy (they yawn often) and have mood alterations. Frequently seen as depressed and labeled as anti-social, but it is because of low blood pressure, that they do not function well. Because of this, they are extremely cold, get dizzy and sometimes faint (which is rare). The interesting thing, is that it does not happen when they are busy, happy or doing their job or a hobby, but at the end of the day or when they are tired or bored. This condition called Dysautonomia can be confirmed with an exam called the Tilt Test. The patient is placed on a stretcher and tied, so that he does not move and the head of the stretcher is raised until it is at 80°, then blood pressure is taken every 10 minutes. Now in 2023 we do not recommend the use of the Tilt Test, because it can give false negative results, meaning that if negative, it does not rule out Dysautonomia. Another important reason, is that it can produce severe arrhythmias, such as cardiac arrest.

TREATMENT. MEDICINES

Anti-inflammatory drugs that are used to treat arthritis and other rheumatic conditions, have no major effect on FM or EDSH. However, modest doses of aspirin, ibuprofen, and acetaminophen (Tylenol) can help many people by decreasing pain and stiffness. Analgesics such as Nefersil and narcotics such as Tramadol are used to relieve pain and in special cases Gabapentin (neuropathic pain). Tranquilizers and muscle relaxants are also helpful. Cortisone derivatives are not effective and should be avoided, as they can have significant side effects.

In both FM and EDSH, steroid injections with Novocain reduce pain in trigger points and enthesitis areas, in addition to treating tendinitis and bursitis. Occasionally TENS units or Acupuncture are used to treat chronic pain. In cases resistant to treatment, a comprehensive plan can be attempted by a medical team of specialists, in a Pain Clinic.

Medications that promote deeper sleep and muscle relaxation can help many people with FM. Examples of these include: Amitriptyline (Elavil), Cyclobenzaprine (Flexeril, Tensodox) and other related medicines, such as Fluoxetine and Sertraline. Although these medications are used to treat depression, they are used in very small doses and only at bedtime, for people with FM. Therefore, they are not specifically used as antidepressants or tranquilizers in the treatment of FM, but rather to relieve pain and improve sleep. These drugs are also useful in the treatment of EDSH.

Although many people sleep better and have less discomfort when taking the hypnotics (Zolpiden), tranquilizers, or narcotics mentioned above, the level of improvement varies greatly from person to person. In addition, the medications can have side effects such as daytime sleepiness, constipation, dry mouth, and increased appetite. These side effects are rarely severe, but they can be bothersome and may also limit the use of these medications. For this reason, you may need to try a number of different medicines and adjust the dosage according to your doctor. When there is osteoarthritis associated with EDSH, even if it is initial, Glucosamine alone or with Chondroitin Sulfate is added (although its effectiveness is not yet proven), to reduce the progression of osteoarthritis, which appears earlier and is more severe in EDSH patients. Nowadays, we do densitometry in all patients with EDSH, since it is common for them to present low Bone Mineral Density (Osteopenia) and even Osteoporosis, even in adolescence and in both sexes. We have found (8) Osteopenia or Osteoporosis in 10% of men and women with EDSH, under 30 years

of age. If it exists, it must be treated and falls must be avoided, due to the danger of fractures.

What really improves the quality of life of patients with EDSH is the treatment of Dysautonomia, which is treated with general measures and medications. It is necessary to raise blood pressure, which is the cause of the problem, so you have to drink 2 to 3 liters of fluids a day, eat more salt (if there is no arterial hypertension), wear elastic socks or stockings, do not walk slowly, nor stand for long periods without moving. If these measures are not enough, your doctor may add medications such as Fludrocortisone (Florinef) or Midodrine (Gutron). Another very useful medication is Epinephrine (Effortil), which is no longer found in Chile. It is quite possible that Chronic Fatigue in FM is the same as Dysautonomia, since many patients with FM and fatigue have a positive Tilt Test, which is an indicator of fatigue secondary to low blood pressure.

In EDSH we started prescribing Folic Acid (FA) in 2005, as it has been shown to improve collagen bonds in bone and therefore it is possible (our theory) that it may be useful in the treatment of EDSH. It has also been shown to be useful for memory, osteoporosis, and improvement of collagen in arteries and veins. The best known, is its effect in preventing neural tube defects and other congenital malformations, when used in the periconceptional period. We recommend Magnesium which is useful to avoid muscle pain and cramps. It is also used in case of mitral valve prolapse. Lately it has been seen that vitamin D helps muscle tone. Vitamins C and B-12 are also useful in the treatment of collagen disorders.

EXERCISE AND PHYSICAL THERAPY

Two of the principles on which the treatment of FM and EDSH are based are:

- .- Stretch and mobilize stiff sore muscles, especially upon awakening and after a period of inactivity.

Modify the way you work or perform your daily tasks, trying to conserve energy and reduce pain.

- .- Improve cardiovascular conditioning and general physical condition.

You may hesitate to exercise, especially if you are in pain or feel tired. However, you can start a program with low-impact aerobics such as brisk walking, bicycling,

swimming, or water aerobics and get very good results. The exercises have an analgesic and antidepressant effect and contribute to increasing the patient's sense of general well-being and control over the disease. Yoga, Pilates, Tai Chi, cycling and swimming are very beneficial for these patients. Exercise regularly by starting slowly and gradually increasing to improve your fitness level.

Some tips for exercising are:

- Gently stretch your muscles until you feel tension and hold there for a few seconds. If you prolong it, you may have cramps.
- Move your joints to the maximum normal range and in all possible directions.

Physical therapy can also help you if the following techniques are used:

- Treatments with heat and cold. Heat is used to reduce muscle contracture and cold to decrease pain.
- Massage
- Massage pool or jacuzzi
- Ultrasound
- Electrical stimulation to help control pain.
- Proper use of joints and conservation of energy.

In addition, you can consult with physiatrists and kinesiologists to design specific exercise programs to improve posture, flexibility, and fitness. In treating EDS patients it is necessary that the kinesiologist is familiar with the treatment of this condition, otherwise the results are sometimes counterproductive. These patients should avoid forceful extension of lax joints, especially fingers, wrists, and knees.

LIVING WITH FM OR WITH SEDh

Frequently, people with these diseases get many laboratory tests and see many different specialists in their search for answers. For this reason, they may feel

frustrated and fearful, which can increase the pain. Repeatedly, they are told that they do not have a real condition, because they look healthy and their lab tests come back normal. It is possible that there are doubts on the part of your family and friends, as well as on the part of your doctors about your discomfort. This situation can make them feel isolated, guilty, angry or depressed.

You and your family need to understand that FM and EDSH are chronic fatigue-causing conditions, and that the pain is real, and can sometimes be severe and disabling. These diseases are not life-threatening and are not disfiguring diseases, but should be treated as chronic diseases. Although your symptoms vary, the overall condition tends to improve over time. Having an accurate diagnosis and the excellent response to treatment of Dysautonomia improve the quality of life of these patients.

Many times, just knowing that FM and EDSH are not progressive or disfiguring diseases, allows people to stop having additional expensive medical tests and develop a more positive attitude towards their condition.

Some relaxation techniques that help manage the symptoms of FM and EDSH are:

- Meditation or prayer.
- Creation of visual images.
- Progressive muscle relaxation.
- Yoga.

In addition, you can examine sleep patterns to avoid factors that interfere with your rest, such as caffeine and alcohol. The more you learn about your condition and take an active role in finding the best means to lessen your symptoms, the better the results will be for you.

Currently there are support groups such as the Fibromyalgia Corporation of Chile (+56-2-2688-4726). In 2005 we created the Chilean Hypermobile Support Group. (See www.reumatologia-dr-bravo.cl). Knowing that you are not alone can be a great support for the patient.

Some people with FM or EDSH have very severe symptoms so they cannot function well at work or socially. These people require more attention through programs that often employ occupational therapists, social workers, specialized nurses, mental health professionals, physical rehabilitation counselors, and specialists in sleep and chronic pain treatment.

IN SUMMARY

FM and EDSH are the cause of recurrent and chronic pain. They are diseases that alter the quality of life and in which the pain comes and goes on a recurring basis. For example, pain and fatigue levels in some people are often as high as in Rheumatoid Arthritis. Because FM and EDSH can interfere with normal aspects of a person's life, careful planning of a treatment program is essential. It starts with the correct diagnosis and a detailed explanation of these conditions.

With proper therapy, most people with FM or EDSH improve and are able to manage their complaints. In most cases it is possible to improve your quality of life. However, a better understanding of the causes and aggravating factors of these conditions are necessary for early diagnosis, better treatment and perhaps even to develop prevention of these diseases.

For me, after seeing patients with FM daily in the United States for 30 years and more than 1,500 patients with EDSH in Chile in the last 10 years (now, more than 9.000 in 2023, in the last 20 years), I think that EDS includes all the symptoms of Fibromyalgia and also has a broader picture, because it also produces tissue damage due to the alteration of collagen tissue (early varicose veins, hernias, prolapse, spontaneous rupture of the lung, etc.). It is for this reason that I believe that Fibromyalgia is part of EDSH. This disease is hereditary and has a much more precise diagnostic criteria (Brighton Criterion) (13) than the ACR (American College of Rheumatology) criteria for FM. In addition, patients with EDSH have a characteristic phenotype (physical features), which we have discovered and published (15,16), which in some cases allows them to be identified with the naked eye, something that does not occur with FM. From the above, I believe that EDSH is the Fibromyalgia of the 21st Century (17), which is probably just a matter of names. Perhaps a good name would be Hypermobility Syndrome and Fibromyalgia (Hypermobility/Fibromyalgia Syndrome) or Ehlers-Danlos/Fibromyalgia Syndrome.

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