Overview of

Fibromyalgia

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Fibromyalgia

- Fibromyalgia is a chronic centralised pain syndrome.
- Fibromyalgia is a disabling condition that encompasses musculoskeletal pain, fatigue, depression, and sleep disturbances.
- It can significantly worsen the patient's quality of life.

- There is no diagnostic laboratory test or imaging.
- It is characterised by chronic widespread pain for which no physical explanation can be given.

- There are accompanying symptoms, which may or may not be present in an individual and will usually vary over time.

- FM affects 2-5% of the population.
- There is a female:male incidence ratio of 2:1
- There is a waxing and waning pattern to the condition.
- There is scepticism in the medical profession as to the validity of the diagnosis.

Symptoms of fibromyalgia

- Pain – chronic (3 months +) widespread and unexplained (central symptom)
- Mood disturbance
- Cognitive impairment
- Fatigue
- Other associated conditions/symptoms

Other associated conditions/symptoms

- Irritable bowel syndrome
- Migraine
- Severe menstrual pain
- Lower urinary tract symptoms
- Facial and tempromandibular joint pain
- Somatic symptoms
- Sexual dysfunction (up to 97% of sufferers)

- In some individuals, fibromyalgia is triggered by a physical or psychological event or disorder; in others, it develops gradually with no precipitating cause.
- Although fibromyalgia can occur at any time of life, even in childhood, onset is usually in middle age, and the likelihood increases with age.
- A family history of fibromyalgia may play a part in the development of the disorder.

- The pathogenesis of fibromyalgic pain is multifactorial.
- There is no practical diagnostic test and imaging is only helpful to rule out underlying pathology.
- However in research studies, where more invasive testing and specialised imaging is available, physiological changes have been identified in fibromyalgia.

- The underlying problem in fibromyalgia is an enhancement of the neurophysiologic sensory response.
- This is evidenced by abnormal activity in pain centres in response to touch and heat, increased neuropeptides both peripherally in the nociceptors and centrally in the cerebrospinal fluid (notably Substance P) and is manifest in the allodynia experienced by fibromyalgia sufferers.

- The increased concentration of neuropeptides and other substances related to the excitation of the pain pathways in the CSF may be linked to the fatigue, mood disturbance and cognitive impairment seen in fibromyalgia.

- Patients with fibromyalgia often have other symptoms that could be considered as "visceral allodynia" e.g. irritable bowel, pelvic pain, lower urinary tract symptoms etc.
- These conditions could be considered as sensory attenuation based.

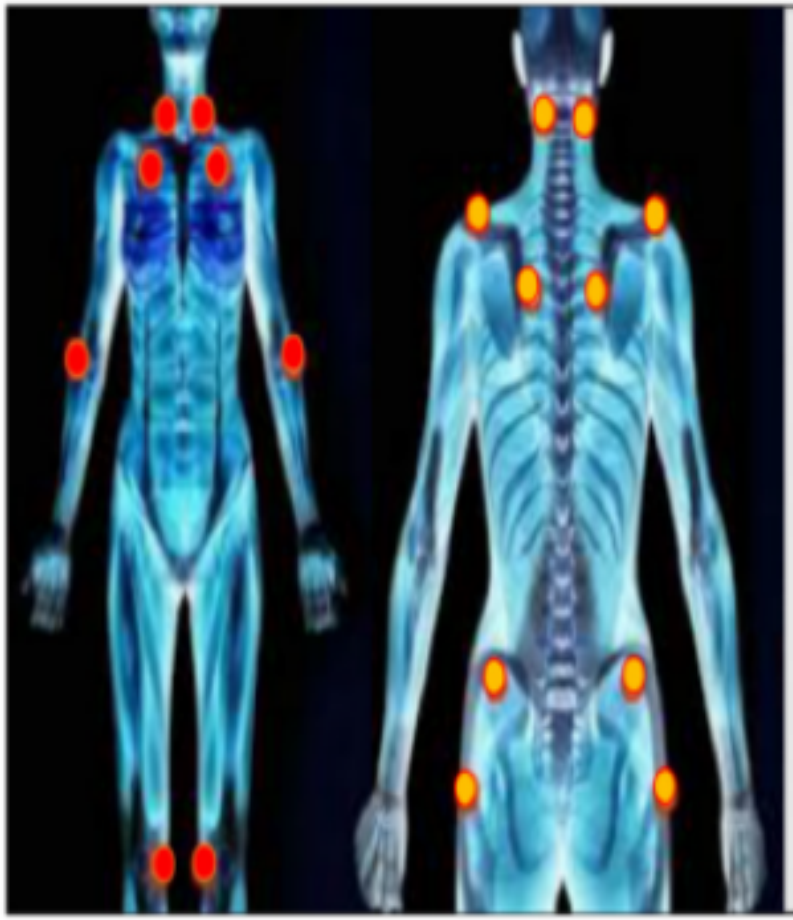
Making a diagnosis

- Fibromyalgia should be suspected in patients presenting with chronic (greater than 3 months), multifocal pain that cannot be explained by an obvious pathological process – e.g. inflammation, infection, degeneration or neoplasm.
- Once fibromyalgia is suspected simple laboratory tests should be performed to exclude conditions that can present in the same way as fibromyalgia.

- Inflammatory rheumatic conditions
  - Early rheumatoid arthritis
  - Polymyalgia rheumatic
  - Giant cell arteritis
  - Systemic vasculitis
  - Inflammatory spondyloarthritis
  - Systemic lupus erythematosus
  - Myositis
- Hypothyroidism
- Depression
- Neuropathies (tend to be more localised)
- Multiple sclerosis (tend to have motor and sensory defects)
- Vitamin d deficiency

Laboratory tests should be tailored to the patient's symptoms, however if a diagnosis of fibromyalgia is suspected the following would be considered a baseline set of investigations:-

- Full blood count
- Erythrocyte sedimentation rate
- C-reactive protein
- Thyroid function
- Creatine kinase



OCCIPUT (2 points) – at the suboccipital muscle insertions

LOW CERVICAL (2 points) – at the anterior aspects of the intertransverse spaces at C5-C7

TRAPEZIUM (2 points) – at the midpoint of the upper border

SUPRASPINATUS (2 points) – at origins, above the scapula spine near the medial border

SECOND RIB (2 points) – upper lateral to the second costochondral junction

LATERAL EPICONDYLE (2 points) – 2 cm distal to the epincondyles

GLUTEAL (2 points) – in upper outer quadrants of buttocks in anterior fold of muscle

GREATER TROCHANTER (2 points) – posterior to the trochanteric prominence

KNEE (2 points) – at the medial fat pad proximal to the joint line

2010 criteria

Fibromyalgia Diagnostic Criteria

1) WPI: note the number areas in which the patient has had pain over the last week. In how many areas has the patient had pain? Score will be between 0 and 19.

Put a Check to indicate a painful region.

☐ Shoulder, Lt. ☐ Shoulder, Rt. ☐ Hip, Lt. ☐ Hip, Rt.	☐ Upper Leg, Lt. ☐ Upper Leg, Rt. ☐ Lower Leg, Lt. ☐ Lower Leg, Rt.	☐ Lower Back ☐ Upper Back ☐ Neck
☐ Upper Arm, Lt. ☐ Upper Arm, Rt. ☐ Lower Arm, Lt. ☐ Lower Arm, Rt.	☐ Jaw, Lt. ☐ Jaw, Rt. ☐ Chest ☐ Abdomen	☐ No pain in any of these areas

2010 criteria

2) SS scale score:

___ Fatigue

___ Waking unrefreshed

___ Cognitive symptoms

For the each of the 3 symptoms above, indicate the level of severity over the past week using the following scale:
0 = no problem
1 = slight or mild problems, generally mild or intermittent
2 = moderate, considerable problems, often present and/or at a moderate level
3 = severe: pervasive, continuous, life-disturbing problems

___ Considering somatic symptoms in general, indicate whether the patient has:*
0 = no symptoms
1 = few symptoms
2 = a moderate number of symptoms
3 = a great deal of symptoms

The SS scale score is the sum of the severity of the 3 symptoms (fatigue, waking unrefreshed, cognitive symptoms) plus the extent (severity) of somatic symptoms in general. The final score is between 0 and 12.

___ SS Scale Score

Criteria

A patient satisfies diagnostic criteria for fibromyalgia if the following 3 conditions are met:
1) Widespread pain index (WPI) ≥7 and symptom severity (SS) scale score ≥5 or WPI 3–6 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.

** Somatic symptoms that might be considered: muscle pain, irritable bowel syndrome, fatigue/tiredness, thinking or remembering problem, muscle weakness, headache, pain/cramps in the abdomen, numbness/tingling, dizziness, insomnia, depression, constipation, pain in the upper abdomen, nausea, nervousness, chest pain, blurred vision, fever, diarrhea, dry mouth, itching, wheezing, Raynaud's phenomenon, hives/welts, ringing in ears, vomiting, heartburn, oral ulcers, loss of/change in taste, seizures, dry eyes, shortness of breath, loss of appetite, rash, sun sensitivity, hearing difficulties, easy bruising, hair loss, frequent urination, painful urination, and bladder spasms.*

2010 criteria

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

1) Widespread pain index (WPI) 7 and symptom severity (SS) scale score 5 or WPI 3–6 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.

Management

The management of fibromyalgia has 4 main components:-

- Patient education
- Physical therapy
- Psychological therapy/support
- Drug treatment

Psychological therapy/support

- CBT
- Try to stay positive
- Not to focus on the pain
- Catastrophising and stopping moving are poor prognostic indicators

Drug treatment

- Drug treatment should be tailored to the patient and the choice of medication should take in to account the additional symptoms affecting the patient.

Pharmacologic Therapy

- Patients with fibromyalgia have difficulty tolerating regular doses of most medications and supplements. They are sensitive to medications, and often experience adverse effects. To avoid those problems, use the lowest dose available or perhaps one half to one quarter of the lowest recommended dose.

- The US Food and Drug Administration (FDA) has approved three drugs for use in fibromyalgia: pregabalin (Lyrica), duloxetine (Cymbalta), and milnacipran (Savella). Pregabalin is used to reduce pain and improve sleep. The antidepressants duloxetine and milnacipran, which are used to relieve pain, fatigue, and sleep problems, are generally prescribed at lower doses than for treatment of depression.

- Other anticonvulsants and antidepressants are often used off-label to treat fibromyalgia and there is evidence that many can decrease pain sensitivity. In particular, tricyclic antidepressants (TCAs) have proven benefit but anticholinergic side effects often limit their use.

- Antianxiety agents are often used in combination with antidepressants and anticonvulsant drugs (both of which also have efficacy for anxiety and insomnia) and include benzodiazepines; alprazolam, temazepam, clonazepam, buspirone, trazodone.

- Antidepressants, Low-dose TCAs have proved to have short-term efficacy for pain control, improved sleep, and improved sense of well-being in patients with fibromyalgia.
- First-generation selective serotonin reuptake inhibitors (SSRIs), including fluoxetine (Prozac) and paroxetine (Paxil, Pexeva), improve symptoms in fibromyalgia but the high doses required often cause adverse effects that are poorly tolerated.

- A meta analysis published in 2011 estimated treatment differences vs. placebo, separately, for duloxetine, fluoxetine, gabapentin, milnacipran, pramipexole, pregabalin, either of two tricyclic antidepressants, and tramadol plus paracetamol
- The analysis examined pain response and did not report on other symptoms. The response was measured as a 30% reduction and a 50% reduction in reported pain from baseline

- when compared with placebo, statistically significant pain responses (improvement of 30% and 50%) were observed for patients treated with duloxetine, milnacipran 200 mg/day, pregabalin 300 or 450 mg/day, and tramadol plus paracetamol. Treatment with fluoxetine, gabapentin, or milnacipran 100 mg/day resulted in significant findings for the 30% improvement in pain response.

- All eight active treatments displayed evidence suggesting improvement over placebo in the treatment of pain in patients suffering from fibromyalgia.
- Seven of the eight regimens had increased discontinuation due to side effects when compared to placebo (the exception being fluoxetine).

- Another meta-analysis has documented that amitriptyline, growth hormone and sodium oxybate demonstrated significant effects on at least two of the core symptom domains of FM.
- Amitriptyline was found to have exhibited significant effects on three symptom domains: pain, sleep disturbance and fatigue, whereas growth hormone exhibited significant effect on pain and function.
- Pain was relieved by most treatments studied, but only growth hormone demonstrated a large effect size for pain.
- The rationale for using growth hormone is based on the fact that human growth production occurs mainly with aerobic exercise and slow wave sleep.

- Both of these are in low in FM. This has been confirmed in FM where production of growth hormone and levels of insulin-like growth factor-1 are low .
- Fluoxetine showed no effect at normal dosages and a medium effect size in quadruple the antidepressant dosage.
- Duloxetine, milnacipran, pregabalin and sodium oxybate showed small effects on pain, whereas citalopram showed no effect on pain.
- None of the pharmacologic treatments showed a large effect on sleep disturbance: amitriptyline, sodium oxybate and pregabalin showed medium effect sizes, whereas all other treatments with available data, except for milnacipran, showed small effects.
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- Among the remaining four domains (fatigue, affective symptoms, functional deficit, cognitive impairment), effects, if present at all, were typically small.
- The only large effect was shown by growth hormone for functional deficit and the only medium effect size was associated with amitriptyline and sodium oxybate on fatigue.

- https://www.uspharmacist.com/article/treatment-approaches-for-fibromyalgia
- https://emedicine.medscape.com/article/329838-treatment#d17

Farias *et al. Advances in Rheumatology* (2020) 60:35
https://doi.org/10.1186/s42358-020-00137-5

Advances in Rheumatology

RESEARCH Open Access

Comparing the efficacy and safety of duloxetine and amitriptyline in the treatment of fibromyalgia: overview of systematic reviews

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EJP
European Journal of Pain

REVIEW ARTICLE

More ubiquitous effects from non-pharmacologic than from pharmacologic treatments for fibromyalgia syndrome: A meta-analysis examining six core symptoms

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