Fibromyalgia

Suraj Achar, MD, FAAFP

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Learning Objectives

1. Use validated criteria, symptom scores, and presence of chronic widespread pain with fatigue and sleep symptoms for diagnosis of fibromyalgia syndrome.

2. Evaluate patients with diagnosed fibromyalgia for comorbid conditions and treat or refer accordingly.

3. Follow an evidence-based, algorithm based on appropriate guidelines, for the pharmacologic management of chronic pain, including fibromyalgia.

4. Develop collaborative treatment to avoid opioids for fibromyalgia, taper off/refer opioid legacy patients, and use opioids appropriately for acute pain incidents.

Audience Engagement System

Step 1

Step 2

Step 3
Controversial!

• Pts look well
  • Miss Pennsylvania 2001 (fibromyalgia aware)
• NL Vital signs $ PE nl except TTP
• Laboratory and radiologic studies are nl
• Organic vs Psychosomatic?
• Research→ disorder of pain regulation form of CSS

History

• Defined first in France late 20th Century (Fibrositis)
• Discussed in Medical Literature 17th century
• Ancient Hx: Referenced in book of Job
• Now accepted
  • WHO
  • AMA
  • NIH
Fibromyalgia=CSS
(new lat., fibro-, fibrous tissue, Gk. myo-, muscle, Gk. algos-, pain)

• Is the name correct?
  • Muscle Disease? Φ pathologic or biochemical abnormality in muscle
  • Muscle pathology is secondary to pain and inactivity rather than primary in nature

Central Sensitivity Syndromes (CSS)

Dysregulation spectrum
Triad

- Pain
- Fatigue
- Sleep disturbance

Other common symptoms

- Cognitive
- Psychiatric
- Headache
- Paresthesia's

Other symptoms and disorders
- IBS, IC, Pelvic pain
Cognitive Disturbance: Majority “fibrofog”

- Attention and difficulty doing tasks that require rapid thought changes.
- Subjective cognitive deficits >> than changes on objective measures, either by brain imaging or validated instruments.

A meta-analysis of 23 case-control studies found significant cognitive impairment in FM patients compared with healthy controls that were explained in part by levels of pain and depression.

- Large effect sizes were found in learning/memory and attention/psychomotor speed ($g = 0.94$, $p = .013$; $g = 1.22$, $p < .001$, respectively).
- Medium effect sizes were reported in executive function and working memory ($g = 0.72$, $p < .001$; $g = 0.75$, $p < .001$, respectively).

Depression and anxiety scores were associated with the effect size of group differences in cognitive function ($p < .001$, 95% CI = 0.01–0.02).


Psychiatric symptoms

- Depression and/or anxiety are present in 30 to 50%
- Anxiety disorders, bipolar disorder, post traumatic stress disorder, and traits such as catastrophizing and alexithymia are more common.

Numbness, tingling, burning, or creeping/crawling sensations, especially in BL arms & legs

Detailed neurologic evaluation or formal electrophysiologic testing is usually unremarkable

Overview

• Prevalence/Genetics?
  • 3.4% women vs 0.5% men⁴
    • Europe > USA > China
  • Most common cause of generalized MSK pain in women 20-55
    • 40% of all pts referred to a Pain clinic
    • 15% Rheumatology clinics
    • 8% family medicine patients

Pathophysiology

**Research Findings**

- Fluoroquinolone Link?
- Neuroendocrine Axis?
  - Sleep encephalogram-abnormalities in deep sleep → Pain
  - Low HGH/IGF at night

**Misc**

- Elevated substance P in CSF
- Low serum Cortisol, serotonin in CNS
- Dopamine
- Skin biopsies → small fiber neuropathy

Pathophysiology?

- A single event “causes” FM?.
- Rather, many physical and/or emotional stressors may trigger or aggravate symptoms
  - Allergic reaction: Fluoroquinolone toxicity (FQAD)
    - 1.63 (95% CI: 1.41-1.87)
  - Lyme disease
  - Emotional or physical trauma

**References**

Genetics?

- 1° relatives of patients with FM
  - 8.5 times more likely
  - Familial aggregation of lowered thresholds for pressure-induced pain
- No candidate Gene so far?

Characteristic features and diagnostic evaluation for fibromyalgia

<table>
<thead>
<tr>
<th>History</th>
<th>PE</th>
<th>Labs NL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Widespread pain</td>
<td>TTP multiple sites</td>
<td>CRP/ESR</td>
</tr>
<tr>
<td>&gt;3 month</td>
<td>Absence of joint swelling, redness or passive loss of motion</td>
<td>CBC</td>
</tr>
<tr>
<td>Fatigue, sleep disturbance</td>
<td></td>
<td>( TSH, CPK if indicated)</td>
</tr>
<tr>
<td>Other symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>cognitive disturbances, headaches, bowel irritability</td>
<td></td>
</tr>
</tbody>
</table>
History of Dx

• 1st: ACR 11/18 TTP
• ACR 2010 (WPI/SSS)
• DX
  • ~15 physicians ~ 5 years
  • > 50% of cases are misdiagnosed
  • unnecessary surgery or costly Rx without benefit
  • Most patients “nothing is medically wrong” → imaginary.

Diagnosis: (ACR) in 1990

- Widespread pain in all four quadrants of the body
- Duration ≥ 3 months

- TTP > 11 of the 18 specified tender points (only consistent PE finding)
  • 4sec → 4kg of force (blanch thumbnail)
Problems with tender point examinations

- Only ~ 85% S/S (other rheumatic diseases?)
- Not intended for use in clinical practice.
- Focused on specific TP locations despite the evidence that FM is a central pain disorder.
- Impossible to standardize & not performed, even by rheumatologists.
- Neglected multiple somatic symptoms of FM.

2010 ACR preliminary diagnostic criteria

New Dx instruments

**WPI**
Measure of the # of painful body regions from a defined list of 19 areas.

**SSS**
Estimate of fatigue, waking unrefreshed, & cognitive symptoms, and the # of somatic symptoms in general.

ACR 2011 modification:
Self administered

1990 → 2010, or the 2011 modified FM criteria ↓ estimates of the prevalence by fourfold

1990, 2010 ~ 1.5%  →  2011 = 5.4%

Modified criteria identified >men & more influenced by somatic symptoms than by pain

WPI: Check each area you have felt pain in over the past week

<table>
<thead>
<tr>
<th>L, R</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Shoulder Girdle</td>
<td>Chest</td>
</tr>
<tr>
<td>Lower arm</td>
<td>Abdomen</td>
</tr>
<tr>
<td>Hip (buttock)</td>
<td>Neck</td>
</tr>
<tr>
<td>Upper leg</td>
<td>Upper back</td>
</tr>
<tr>
<td>Lower leg</td>
<td>Lower back</td>
</tr>
<tr>
<td>Jaw</td>
<td>None of these areas</td>
</tr>
</tbody>
</table>

Symptom Severity Score (Part 2a)

Fatigue

- 0. No problems
- 1. Mild: It comes and goes.
- 2. Moderate: You usually have or feel it.

Waking unrefreshed (still tired)

- 0. No problems
- 1. Mild: It comes and goes.
- 2. Moderate: You usually have or feel it.

Thinking problems/cognitive symptoms

- 0. No problems
- 1. Mild: It comes and goes.
- 2. Moderate: You usually have or feel it.
### Symptom Severity Score (Part 2b)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Nervousness</th>
<th>Loss/change in taste</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue/tiredness</td>
<td>Chest pain</td>
<td>Seizures</td>
</tr>
<tr>
<td>Thinking or remembering problems</td>
<td>Fever</td>
<td>Shortness of breath</td>
</tr>
<tr>
<td>Muscle weakness</td>
<td>Diarrhea</td>
<td>Loss of appetite</td>
</tr>
<tr>
<td>Headache</td>
<td>Dry mouth</td>
<td>Rash</td>
</tr>
<tr>
<td>Pain/cramps in abdomen</td>
<td>Itching</td>
<td>Sun sensitivity</td>
</tr>
<tr>
<td>Numbness/tingling</td>
<td>Wheezing</td>
<td>Hearing difficulties</td>
</tr>
<tr>
<td>Dizziness</td>
<td>Raynaud's</td>
<td>Easy bruising</td>
</tr>
<tr>
<td>Insomnia</td>
<td>Hives/welts</td>
<td>Hair loss</td>
</tr>
<tr>
<td>Depression</td>
<td>Ringing in ears</td>
<td>Frequent urinations</td>
</tr>
<tr>
<td>Constipation</td>
<td>Vomiting</td>
<td>Painful urination</td>
</tr>
<tr>
<td>Pain in upper abdomen</td>
<td>Heartburn</td>
<td>Bladder spasms</td>
</tr>
<tr>
<td>Nausea</td>
<td>Oral ulcers</td>
<td></td>
</tr>
</tbody>
</table>

### Scoring WPI/SSS

- **WPI 0-19**
- **SSS 2a 0-9**
- **SSS 2b**
  - 0 = 0
  - 1-10 = 1
  - 11-24 = 2
  - >24 = 3
- **SSS = 2a + 2b**

- **+ Fibromyalgia**
  - 1a: WPI ≥7 and SS ≥5
  - 1b WPI 3-6 & SSS ≥9
  - Duration > 3 months
  - No other disorder explains the pain
Poll Question 1

What labs should be ordered initially?

A. CRP/ESR, CBC
B. TSH and Cortisol
C. CBC, RF & ANA
D. Vitamin D level

Potential tests to consider?
(controversial not cost effective)

- TSH
- 25-Hydroxy vitamin D level: Low levels can cause muscle pain and tenderness.
- Vitamin B-12 level: Very low levels can cause pain and fatigue?
- Iron studies
  - Iron deficiency is common. May cause or worsen fatigue, poor sleep, and depressive symptoms.
  - RLS $\Rightarrow$ > 20% transferrin saturation Ferritin > 50 ng/mL.
- Magnesium: Low levels $\Rightarrow$ muscle spasms > 2 mEq/L
Other self report questionnaires

- Modified Health Assessment Questionnaire
- Fibromyalgia Impact Questionnaire
- Checklist of current symptoms
- Scales for helplessness and cognitive performance
- The Physician Health Questionnaire–9 for depression
- The Generalized Anxiety Disorder–7 questionnaire for anxiety
- The Mood Disorder Questionnaire to screen for bipolar disease

Goals: Reduce symptoms

- Chronic widespread pain
- Fatigue
- Insomnia
- Cognitive dysfunction
Poll Question 2

Which should you recommend first?

A. Herbal supplements
B. Weight lifting
C. Running 3 miles, 5 days a week
D. Acupuncture
E. Walking around the block
Prescribed exercise in people with fibromyalgia: parallel group randomized controlled trial

- Selwyn C M Richards and David L Scott
  BMJ 2002; 325: 185

- Exercise type:
  - Treadmill and cycle ergometry

- Exercise duration
  - 6 minutes x 2 class/week
  - 25 minutes x 2/class/week

- Intensity
  - sweat while able to talk comfortably

Results: Intention to treat
Exercise group vs. relaxation group

<table>
<thead>
<tr>
<th>Category</th>
<th>Improvement at 3 months</th>
<th>1 year follow up:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improvement at 3 months</td>
<td>35% vs 18%</td>
<td>(%) who fulfill criteria for fibromyalgia</td>
</tr>
<tr>
<td>Reductions in tender point counts</td>
<td>4.2 v 2.0</td>
<td>31/69 v 44/67</td>
</tr>
<tr>
<td>Scores: fibromyalgia impact questionnaire</td>
<td>4.0 v 0.6</td>
<td>2.0 v 0.6</td>
</tr>
</tbody>
</table>
2017 update on exercise

Cochrane systematic review found moderate-quality evidence that aerobic exercise improves health-related quality of life and low-quality evidence that aerobic exercise decreases pain and improves physical function.

European League Against Rheumatism (EULAR) report found that the only "strong" therapy recommendation was exercise.


Strength and flexibility?

Evidence of benefit from strength training in some small trials:
- reduced pain severity with comparable results to those of an aerobic exercise program
- improved exhaustion in fibromyalgia subjects

A systematic review found that water exercises and swimming lessened pain and improved function in patients with fibromyalgia.

Tai Chi

  - 66 pts, 1 hour BIW
  - Control: wellness education & stretching
  - FIQ scores: baseline/12weeks
    - 63/35 vs 68/59

Poll Question 3

Which of the following is not FDA approved for Fibromyalgia?

A. Amitriptyline  
B. Duloxetine  
C. Pregabalin  
D. Minacirpan
Poll Question 4

Which of the following is true?

A. The majority of patients experience a substantial improvement with the FDA approved antidepressants (amitriptyline, duloxetine and milnacipran)
B. Systematic reviews and meta-analyses conclude that low dose amitriptyline should be the first agent used in FM
C. Evidence suggests that the best dose of cyclobenzaprine should be 1-4mg
D. Pregabalin may be preferred in patients with depression


A randomized, double-blind crossover trial of fluoxetine and amitriptyline in the treatment of fibromyalgia.

- Fluoxetine 20mg/day & amitriptyline 25mg/day
  - 30% improvement alone
  - 50% improvement together
- Julius Axelrod→Nobel
- Are You Ready to be Happy?
  No matter what things in life upset you, there is a Prozac-Pez Dispenser for you
Polypharmacy are there risks?

- JAMA 1997
  - 36 y/o man
  - Recurrent major depression
- Rx: Amitryptyline 150mg/day & Fluoxetine 40mg/day
- What happened?
  - Cytochrome P450 enzyme CYP2D6

Combination therapy?

- SSRI/SNRI am + TCA pm
- SNRI (duloxetine) am with anticonvulsant (pregabalin) pm
- > compliance combination therapy or monotherapy?

### Dual Reuptake Inhibitors

<table>
<thead>
<tr>
<th>Drug</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duloxetine, Minacipran</td>
<td>• Similar efficacy as pregabalin</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>• (limited data???)</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>• Pts not tolerant to amitriptyline</td>
</tr>
<tr>
<td></td>
<td>• ↓pain by 30%</td>
</tr>
<tr>
<td></td>
<td>• 60mg -120mg/day</td>
</tr>
<tr>
<td></td>
<td>• 6month data</td>
</tr>
<tr>
<td></td>
<td>• Benefit noted in 1st three months</td>
</tr>
<tr>
<td></td>
<td>• Continues &gt;1 year</td>
</tr>
<tr>
<td></td>
<td>• SE: nausea, headache, dry mouth</td>
</tr>
</tbody>
</table>

### Poll Question 5

Should we ever use traditional opioids to treat pain from Fibromyalgia?

A. Yes  
B. No
Oxycodone for neuropathic pain and fibromyalgia in adults
Cochrane Database Syst Rev. 2014

- RCT’s (double blind), Intention to treat, >200 participants
- NNH= 4.3
- No convincing, unbiased evidence suggests that oxycodone (as oxycodone CR) is of value
  - diabetic neuropathy
  - postherpetic neuralgia
  - other neuropathic pain conditions
  - Fibromyalgia
- Department of Clinical Geratology, Oxford University Hospitals NHS Trust
- AAN: 2014 position paper: COAT therapy risks> benefits

Tramadol

**Pharmacology**
- monoaminergic vs opioid?

**The development of tolerance and dependence**
- Uncommon
- Abuse liability?
- NNTs of 3.4 (95% CI, 2.3 to 6.4).

**Schedule?**
- August 18th 2014

**Dosing**
- 25-400mg/day

**SE:**
- seizures?
- Pts with addiction
Acupuncture?

- A 2013 systematic review and meta-analysis
  - 395 patients/0 randomized trials
  - Improvement in pain and stiffness
  - Sham Rx works as well in pain, fatigue, sleep, or global well-being
  - Electro > regular
Injection therapies and other modalities?

Brain Neuromodulation

- Positive results
  - transcranial direct current stimulation (tDCS)
  - Transcranial magnetic stimulation (TMS)
- Mixed results
  - Occipital and C2 nerve stimulation
  - transcutaneous electrical nerve stimulation (TENS)

Pharmacologic Rx with Limited/Mixed Data

- **Naltrexone**
  
  |  | Pilot data ➔ satisfaction & mood, no improvement with sleep/fatigue |

- **Memantine**
  
  |  | Improved pain & pain thresholds (NMDA) receptor antagonist available for Rx dementia dementia. |

- **Pramipexole**
  
  |  | Improved pain however studied on opioids? |

- **Quetiapine**
  
  |  | (Seroquel) dual diagnoses of both fibromyalgia and major depressive disorder |

- **GH**
  
  |  | 1 small RCT ➔ improved with low IGF Expense is prohibitive |

- **Canabinoids**
  
  |  | Systematic review of Nabilone no better than placebo? |

- **Creatinine**
  
  |  | Muscle strength no other improvement |

- **Vit D**
  
  |  | Improved mood, pain and quality of life scores |

**Rx in Children**

- Pharmacotherapy is generally not indicated or recommended.
- Psychotherapy, exercise, relaxation techniques, and education
- 12 week RCT
  - **Exercise**
  - Qigong
Complications of fibromyalgia

- Extreme allodynia with high levels of distress
- Opioid or alcohol dependence
- Marked functional impairment
- Severe depression and anxiety
- Obesity and physical deconditioning
- Metabolic syndrome

Prognosis?

- 10 outpatient visits/year & 1 hospitalization every 3 years.
- Pain & disability → Metabolic syndrome
- 15-44% disability
- 1/3 modify work to keep job
- 10 x suicide, 6x cirrhosis, 3x CVD

Practice Recommendations

- Use WPI and SSS to evaluate and monitor
- 1st line and strongest Rx = exercise → monitor with technology
- Avoid opioids & benzodiazepines
- Low dose amitriptyline 10mg to 25mg may be a good first choice

Summary

Common: Dx WPI/SSS self report

Pathophysiology --> Dysregulation

Significant effects
- QOL
- Disability
- Co-morbidities
Summary:
sachar@ucsd.edu

Best management
- SE’s
- Exercise
- HEP → PT
- Medications
  - Avoid Opioids
  - TCA/SNRI/Anticonvulsants
  - CBT!
- Alternative Rx
  - (Tai Chi/Yoga)
  - Accupuncture
  - Neuromodulation

Pt education

Arthritis Foundation
MedlinePlus Health → US National Library of Medicine
American College of Rheumatology
National Fibromyalgia & Chronic Pain Association
The American Fibromyalgia Syndrome Association
FamilyDoctor.org: AAFP
  - “Be sure to take all medicines according to your doctor’s instructions”
Questions