Fibromyalgia: The Management of Chronic Widespread Pain

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Disclosure

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    - Research Grant
  - Pfizer
    - Speaking Honorarium

- This presentation discusses off label use of medications for chronic widespread pain
At the end of this presentation, the audience should be able to:

- List the diagnostic criteria and features of Fibromyalgia
- Investigate a patient for other causes of chronic widespread pain
- Discuss the evidence based recommendations for the treatment of Fibromyalgia
Expectation management is a key component in managing chronic widespread pain. Patient education is crucial. There is no cure for fibromyalgia.

Focus on functional restoration along with pain control.

Daily cardiovascular exercise is a staple of fibromyalgia management.

Fibromyalgia symptoms fluctuate in nature. Don’t chase fibromyalgia flares with short acting pain medications, especially opioids.

Patients with fibromyalgia can have other causes of pain that require definitive treatment. New pain complaints need to be addressed and investigated as necessary.
Medications should be introduced to patients with an explanation of how success of a treatment will be defined.

Medication titration should start low and go slow.

What works for one does not work for all. Treatment must be individualized to the patient.

A multidisciplinary program which involves medication titration, activity modification and psychological intervention is preferable to individual therapies.
Making the Diagnosis
Fibromyalgia is a syndrome of unknown etiology, characterized by diffuse musculoskeletal pain, widespread tenderness on palpation, fatigue and sleep disturbance.

It occurs in all ages, both sexes and all cultures, but occurs more frequently in:
- Women (3:1) (9:1)
- Patients between the ages of 35 – 60 years

In Canada:
- Fibromyalgia affects an estimated 4.9% of adult women and 1.6% of adult men

Emerging evidence of a genetic component of FM
- First degree relatives of patients with FM have an 8 fold greater risk of developing FM than the general population
- Twin studies suggest half the risk of developing chronic widespread pain is genetic and half is environmental
- Specific gene mutations may predispose individuals to FM including polymorphisms in the COMT enzyme, the serotonin receptor and transporter and the dopamine D4 receptor are potentially associated with FM

Environmental factors that may trigger the onset of FM
- Physical trauma or injury
- Infections (hepatitis C, Lyme disease)
- Psychological stressors

COMT = catechol-O-methyltransferase
Pathogenesis of Fibromyalgia

- Increased CSF levels of substance P (>3x) and the excitatory neurotransmitter glutamate in patients with fibromyalgia
- fMRI studies show a marked regional increase in cerebral blood flow following a painful stimulus in patients with FM compared to controls not suffering FM
- Deficit in the endogenous pain inhibitory systems noted in fibromyalgia patients


Pathogenesis of Fibromyalgia

- FM is a condition of global dysregulation of pain processing
- Central sensitization is one component
  - Mechanisms of central sensitization
    - Excitatory mechanisms
    - Inhibitory mechanisms

American College of Rheumatology (ACR) Classification Criteria

- History of widespread pain that has been present for at least 3 months (ALL of the following should be present):
  - Pain on both sides of the body
  - Pain above and below the waist
  - Axial skeletal pain
  - Pain in at least 11 of 18 tender point sites on digital palpation with an approximate force of 4 kg or pressure needed to turn the examiner’s thumbnail white
    - For a “positive” tender point, the subject must state that the palpation was painful

Illustration of Tender Points

- **Occiput** (2) - at the suboccipital muscle insertions
- **Low cervical** (2) - at the anterior aspects of the intertransverse spaces at C5-C7
- **Trapezius** (2) - at the midpoint of the upper border
- **Supraspinatus** (2) - at origins, above the scapula spine near the medial border
- **Second rib** (2) - upper lateral to the second costochondral junction
- **Lateral epicondyle** (2) - 2 cm distal to the epicondyles
- **Gluteal** (2) - in upper outer quadrants of buttocks in anterior fold of muscle
- **Greater trochanter** (2) - posterior to the trochanteric prominence
- **Knee** (2) - at the medial fat pad proximal to the joint line

Symptoms of Fibromyalgia

- Pain, fatigue, and sleep disturbance are present in at least 86% of patients*

* US data

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

- Symptoms have been present at a similar level for at least 3 months
- The patient does not have a disorder that would otherwise explain the pain
- Widespread pain index (WPI) and Symptom Severity (SS) scores either:
  - WPI $\geq 7$, SS $\geq 5$
  - WPI 3-6, SS $\geq 9$

Widespread Pain Index (WPI)

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

- Shoulder girdle, left
- Shoulder girdle, right
- Upper arm, left
- Upper arm, right
- Lower arm, left
- Lower arm, right
- Hip (buttock), left
- Hip (buttock) right
- Upper leg, left
- Upper leg, right
- Lower leg, left
- Lower leg, right
- Jaw, left
- Jaw, right
- Chest
- Abdomen
- Neck
- Upper back
- Lower back
- None of these areas

Count up the number of areas checked and enter your WPI score here: ______
(range 0 – 19)
### Symptom Severity Score (SS)

#### Symptom Severity Score – Part 2a.

<table>
<thead>
<tr>
<th>Fatigue</th>
<th>Waking un-refreshed</th>
<th>Cognitive symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 = No problem</td>
<td>0 = No problem</td>
<td>0 = No problem</td>
</tr>
<tr>
<td>1 = Slight or mild problems;</td>
<td>1 = Slight or mild problems;</td>
<td>1 = Slight or mild problems;</td>
</tr>
<tr>
<td>generally mild or intermittent</td>
<td>generally mild or intermittent</td>
<td>generally mild or intermittent</td>
</tr>
<tr>
<td>2 = Moderate; considerable</td>
<td>2 = Moderate; considerable</td>
<td>2 = Moderate; considerable</td>
</tr>
<tr>
<td>problems; often present and/or</td>
<td>problems; often present and/or at a</td>
<td>problems; often present and/or at a</td>
</tr>
<tr>
<td>at a moderate level</td>
<td>moderate level</td>
<td>moderate level</td>
</tr>
<tr>
<td>3 = Severe; pervasive,</td>
<td>3 = Severe; pervasive,</td>
<td>3 = Severe; pervasive,</td>
</tr>
<tr>
<td>continuous, life disturbing</td>
<td>continuous, life disturbing</td>
<td>continuous, life disturbing</td>
</tr>
<tr>
<td>problems</td>
<td>problems</td>
<td>problems</td>
</tr>
</tbody>
</table>

Tally your score for Part 2a and enter it here: ________
Symptom Severity Score (SS)

Symptom Severity Score – Part 2b.

- Muscle pain
- Irritable bowel syndrome
- Fatigue/tiredness
- Thinking/remembering problem
- Muscle weakness
- Headache
- Pain/cramps in abdomen
- Numbness/tingling
- Dizziness
- Insomnia
- Depression
- Constipation
- Pain in the upper abdomen
- Nausea

- Nervousness
- Chest pain
- Blurred vision
- Fever
- Diarrhea
- Dry mouth
- Itching
- Wheezing
- Raynauld’s
- Hives/welts
- Ringing in ears
- Vomiting
- Heartburn
- Oral ulcers

- Loss/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
- Bladderspasms

0 symptoms = score of 0
1 to 10 symptoms = score of 1
11 to 24 symptoms = score of 2
25 or more symptoms = score of 3

Add you SS 2a and SS 2b scores: ________
(range 0 – 12)
A patient satisfies diagnostic criteria for FM if the following 3 conditions are met:

- Symptoms have been present at a similar level for at least 3 months
- The patient does not have a disorder that would otherwise explain the pain
- Widespread pain index (WPI) and Symptom Severity (SS) scores either:
  - WPI ≥ 7, SS ≥ 5
  - WPI 3-6, SS ≥ 9
<table>
<thead>
<tr>
<th>Differential Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Addison Disease</td>
</tr>
<tr>
<td>Anxiety Disorder</td>
</tr>
<tr>
<td>Chronic Fatigue Syndrome</td>
</tr>
<tr>
<td>Conversion Disorder</td>
</tr>
<tr>
<td>Cushing Syndrome</td>
</tr>
<tr>
<td>Depression</td>
</tr>
<tr>
<td>Dysmenorrhea</td>
</tr>
<tr>
<td>Dysthymic Disorder</td>
</tr>
<tr>
<td>Endometriosis</td>
</tr>
<tr>
<td>Factitious Disorder</td>
</tr>
<tr>
<td>Growth Hormone Deficiency</td>
</tr>
<tr>
<td>Gynecologic Pain</td>
</tr>
<tr>
<td>Hashimoto Thyroiditis</td>
</tr>
<tr>
<td>Hemochromatosis</td>
</tr>
<tr>
<td>Hepatitis C</td>
</tr>
<tr>
<td>Hyperparathyroidism</td>
</tr>
<tr>
<td>Hypochondriasis</td>
</tr>
<tr>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>Insomnia</td>
</tr>
<tr>
<td>Interstitial Cystitis</td>
</tr>
<tr>
<td>Irritable Bowel Syndrome</td>
</tr>
<tr>
<td>Malingering</td>
</tr>
<tr>
<td>Migraine Headache</td>
</tr>
<tr>
<td>Mitral Valve Prolapse</td>
</tr>
<tr>
<td>Opioid Abuse</td>
</tr>
<tr>
<td>Panic Disorder</td>
</tr>
<tr>
<td>Personality Disorders</td>
</tr>
<tr>
<td>Polymyalgia Rheumatica</td>
</tr>
<tr>
<td>Polymyositis</td>
</tr>
<tr>
<td>Posttraumatic Stress Disorder</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
</tr>
<tr>
<td>Sjogren Syndrome</td>
</tr>
<tr>
<td>Systemic Lupus Erythematosus</td>
</tr>
<tr>
<td>Temporomandibular Joint Disorder</td>
</tr>
</tbody>
</table>
Investigations

- Complete blood count and differential
- Basic electrolytes, liver function and renal function tests
- Vitamin B12
- Urinalysis
- TSH
- Creatinine phosphokinase (CPK)
- Erythrocyte sedimentation rate (ESR)
- Antinuclear antibodies: A low-titer ANA is common in the general population and may be of no clinical significance if diagnostic features of SLE or related autoimmune disorders are absent.
- Rheumatoid factor: A positive result for rheumatoid factor does not support a diagnosis of RA in the absence of objective evidence of characteristic joint inflammation.
Summary

- FM is a common disease of middle age with a female-to-male ratio between 3:1 and 9:1
- Simple investigations and history will exclude other rheumatologic or psychiatric conditions
- The four cardinal symptoms of FM include: fatigue, widespread pain, sleep disturbance and cognitive slowing
- The diagnostic criteria has changed from tender point examination to the widespread pain index and symptom severity score
“Selling” the Diagnosis
Some tips on providing the diagnosis

- Be specific about the diagnosis
- Be positive about the diagnosis
- Reassure patients that FM is not progressive and that symptoms remain stable over time
- Promote and encourage patient self-efficacy around the disease but…
- Set realistic expectations
- Emphasize no cure but improved control of symptoms usually possible
- Active treatments generally superior to passive treatments
Diagnosis of fibromyalgia improves health satisfaction

- Prospective, community comparison of fibromyalgia patients in Canada that revealed significantly improved scores 36 months post-diagnosis on a 5-point Likert scale of self-reported health satisfaction

*Statistically significant versus baseline (Confidence Interval -1.2, -0.4).

Health Economic Consequences Related to the Diagnosis of Fibromyalgia

Tests and imaging

Referrals

GP visits

Drugs

UK figures

Summary

- Expectation management is key in providing the diagnosis of fibromyalgia
- Being specific and positive about the diagnosis improves health outcomes and reduces costs
- The natural history of FM is variable, a significant numbers of patients will improve
- Emphasize no cure but improved control of symptoms usually possible
- Use Internet and written resources and other members of a multi-disciplinary team to educate patients
Treatment of Fibromyalgia
Recommended Treatment Approach

- Multi-disciplinary therapy individualized to patients’ symptoms and presentation is recommended
- A combination of non-pharmacological and pharmacological therapies may benefit most patients

Non-pharmacological Treatments

- Strong evidence supports aerobic exercise and cognitive behavioral therapy
- Moderate evidence supports massage, muscle strength training, acupuncture and spa therapy (balneotherapy)
- Limited evidence supports spinal manipulation, movement/body awareness, vitamins, herbs and dietary modification

Choice of Medical Therapy in Fibromyalgia
Medical management of fibromyalgia

- Don’t set unrealistic goals; target functional improvement
- Important to manage patient’s expectations
- Keep the patient involved in treatment decisions
- Balance efficacy with side effects
- Avoid rapid dose escalation: start low, go slow!
# Best-evidence medication options

(Alphabetical order)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism of action</th>
<th>Evidence for efficacy</th>
<th>Major target symptom</th>
<th>Off/on-label indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline (nortriptyline, doxepin)</td>
<td>TCA (NE &gt; 5HT)</td>
<td>Good short-term</td>
<td>Sleep, pain, anxiety</td>
<td>Off</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Poor long-term</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclobenzaprine</td>
<td>Muscle relaxant (NE)</td>
<td>High</td>
<td>Sleep, Pain</td>
<td>Off</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>SNRI</td>
<td>High</td>
<td>Pain, sleep, depression</td>
<td>On</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>(\alpha-2\delta) binding: (\downarrow) (Ca^{2+})</td>
<td>Moderate</td>
<td>Pain, sleep, anxiety</td>
<td>Off</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>(\alpha-2\delta) binding: (\downarrow) (Ca^{2+})</td>
<td>High</td>
<td>Pain, sleep, anxiety</td>
<td>On</td>
</tr>
<tr>
<td>Tramadol</td>
<td>Opioid agonist SNRI</td>
<td>High</td>
<td>Pain</td>
<td>Off</td>
</tr>
</tbody>
</table>

**Abbreviations:** GABA, \(\gamma\)-aminobutyric acid; NE, norepinephrine; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant
## Some-evidence medication options

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism of action</th>
<th>Evidence for efficacy</th>
<th>Major target symptom</th>
<th>Off/on-label indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atypical antipsychotics</td>
<td>Dopamine</td>
<td>Limited case studies, add-on therapy</td>
<td>Sleep</td>
<td>Off</td>
</tr>
<tr>
<td>Cannabinoids</td>
<td>CB 1 receptor agonist</td>
<td>Good for pain, sleep and anxiety</td>
<td>Pain, Sleep, Anxiety</td>
<td>Off</td>
</tr>
<tr>
<td>Pramipexole</td>
<td>Dopamine agonist</td>
<td>Some – limited population studied</td>
<td>Fatigue, Pain</td>
<td>Off</td>
</tr>
<tr>
<td>Sertraline</td>
<td>SSRI</td>
<td>Compared versus PT</td>
<td>Pain, Depression</td>
<td>Off</td>
</tr>
<tr>
<td>Topical therapies (lidocaine, diclofenac, doxepin)</td>
<td>Local analgesia</td>
<td>Low</td>
<td>Pain</td>
<td>Off</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>SNRI &gt; SSRI</td>
<td>Moderate in pain, limited FM study</td>
<td>Pain, depression, anxiety</td>
<td>Off</td>
</tr>
</tbody>
</table>
# No-evidence medication options

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism of action</th>
<th>Rationale for use</th>
<th>Concern for use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepines*</td>
<td>GABA increase</td>
<td>Muscle relaxant</td>
<td>Addiction, Side effects</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Prostaglandin inhibition</td>
<td>Analgesia</td>
<td>NSAID-related side effects</td>
</tr>
<tr>
<td>Opioids</td>
<td>Opioid receptor agonists</td>
<td>Analgesia</td>
<td>Addiction, Side effects</td>
</tr>
<tr>
<td>Psychostimulants (dextroamphetamine, methylphenidate)</td>
<td>NE Dopamine</td>
<td>Fatigue</td>
<td>Diversion, Abuse</td>
</tr>
<tr>
<td>Zopiclone</td>
<td>GABA</td>
<td>Sleep</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: NSAID, nonsteroidal anti-inflammatory drug

* Single double-blind study of alprazolam plus ibuprofen showing evidence.
Polypharmacy

- Is often necessary for symptom control
- May exacerbate or cause some of the target symptoms of FM (cognitive impairment, sleep disturbance, fatigue)
- Be aware of drug interactions (serotonin syndrome for example)
Summary

- Pain is the most common symptom of FM
- Set realistic treatment goals and expectations
- Use non pharmacologic treatments first
- Use medical therapies that target the most troublesome symptoms and have evidence for efficacy in FM
- Start low, go slow – reassure
- Use polypharmacy with care
- Balance medication side effects and risk with optimizing function
- Avoid opioids
Managing Associated Symptoms
Managing Fatigue

- Improvement of sleep hygiene
- Moderate physical activity
- Pacing
- Realistic goal setting
- Healthy eating
- Cognitive behavioral therapy (CBT)
Managing Fatigue

There are no generally accepted, on-label medications that improve the fatigue associated with FM.

Physical activity is the only non-pharmacologic strategy proven to reduce fatigue.
Improving Sleep

- Rule out secondary causes of sleep disorders
- Consider lifestyle modification as a first step to manage sleep problems
  1. Avoid stimulants
  2. Regular time to bed and to rise
  3. Avoid napping through day
  4. Regular AM exercise
  5. Bed is for sleep and sex
  6. Relaxation exercise before bed
- Use medical therapies that target sleep when it is prevalent disabling symptom
Mood Disorders in Fibromyalgia

- At time of diagnosis, approximately 20–40% of individuals with fibromyalgia have an identifiable current mood disorder (e.g., depression or anxiety)
  - lifetime prevalence of depression: 74%
  - lifetime prevalence of anxiety disorder: 60%
- Fibromyalgia is common, depression is common. They frequently occur together but are separate disorders
- Use an interdisciplinary team and multimodal therapies to help treat FM and comorbid depression
- Therapies which may treat both include cognitive behavior therapy and antidepressants with analgesic properties
Incomplete Treatment Response in Fibromyalgia
Currently, there is no currently validated acceptable tool for assessing response to treatment.

Consider evaluation of patients with FM in these dimensions:

- Pain
- Sleep
- Fatigue
- Functionality (physical and psychological)
- Mood
Functional improvement versus symptom remission

- Symptomatic remission is resolution of all symptoms associated with the condition
- Functional improvement is improvement of symptoms to the point where patients can maximize function (vocational, interpersonal, social)
Expectation management is a key component in managing chronic widespread pain. Patient education is crucial. There is no cure for fibromyalgia.

- Focus on functional restoration along with pain control.
- Daily cardiovascular exercise is a staple of fibromyalgia management.
- Fibromyalgia symptoms fluctuate in nature. Don’t chase fibromyalgia flares with short acting pain medications, especially opioids.
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Questions?