MANAGEMENT

Goals of Treatment

Goals in Pain Management

- Involve the patient in the decision-making process
- Agree on realistic treatment goals before starting a treatment plan



Farrar JT et al. Pain 2001; 94(2):149-58; Gilron I et al. CMAJ 2006; 175(3):265-75.

Prognosis of Patients with Fibromyalgia

- Chronic condition, but improvement frequently seen in community practice, particularly when patients are diagnosed and treated early
 - Kennedy and Felson found 66% of 29 US patients followed in an academic rheumatology referral practice indicated some improvement over 10 years
 - After 2 years of treatment with a simple regimen, Australian patients with fibromyalgia:
 - 47% no longer fulfilled Smythe or ACR criteria for fibromyalgia
 - 24.2% of patients in remission

Fitzcharles MA et al. J Rheumatol 2003; 30(1(:154-9; Kennedy M, Felson DT. Arthritis Rheum 1996; 39(4):682-5.

Management of Fibromyalgia: Recommended Treatment Approach

- Multidisciplinary therapy individualized to patients' symptoms and presentation is recommended
- A combination of non-pharmacological and pharmacological therapies may benefit most patients

Non-pharmacological

- Aerobic exercise
- Cognitive behavioral therapy
- Patient education
- Strength training
- Acupuncture*
- Biofeedback*
- Balneotherapy*

Pharmacological

- Non-narcotic analgesics
- Analgesic antiepileptics
- Antidepressants
 - TCAs
 - SSRIs
 - SNRIs
- Muscle relaxants
- Other

*Limited evidence for efficacy exists

Balneotherapy: treatment of disease or health conditions by bathing

SNRI = serotonin-norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant Arnold LM *et al. Arthritis Rheum* 2007; 56(4):1336-44; Carville SF *et al. Ann Rheum Dis* 2008; 67(4):536-41; Clauw DJ, Crofford LJ. *Best Pract Res Clin Rheumatol* 2003; 17(4):685-70; Goldenberg DL *et al. JAMA* 2004; 292(19):2388-95; Mease P. *J Rheumatol* 2005; 32(Suppl 75):6-21.

Core Treatment of Fibromyalgia



Adapted from: Arnold LM. Arthritis Res Ther 2006; 8(4):212; Goldenberg DL et al. JAMA 2004; 292(19):2388-95.

Overview of Fibromyalgia Management

Develop treatment plan At follow-up visits Confirm fibromyalgia reflecting patient's evaluate: priorities and diagnosis • **Progress towards** preferences treatment goals • Physical activity Pharmacotherapy • Use of self-management Non-pharmacological techniques therapy Educate the patient • Medication efficacy and adverse effects Treatment of comorbid conditions Comorbidities • Adjustments to Identify other health care treatment plan providers who can work with Collaborate with patient Maintain focus on you to care for patient to prioritize individual progress over time treatment goals vs. daily ups Identify community resources and downs for self-management

Adapted from: Arnold LM et al. Mayo Clin Proc 2012; 87(5):488-96.

Multimodal Treatment of Fibromyalgia Based on Biopsychosocial Approach



Arnold LM et al. Mayo Clin Proc 2012; 87(5):488-96.

Fibromyalgia: Medication Is Just One Part of the Treatment Approach



DHEA = dehydroepiandrosterone; FDA = Food and Drug Administration; NSAID = non-steroidal anti-inflammatory drug Häuser W et *al. Arthritis Res Ther* 2014; 16(1):201; Fitzcharles MA *et al. Evid Based Complement Alternat Med* 2013; 2013:528952; Sumpton JE, Moulin DE. *Handb Clin Neurol* 2014; 119:513-27.

Non-pharmacological Treatment

Non-pharmacological Treatment of Fibromyalgia

Sleep hygiene	Physical activity	Cognitive behavioral therapy	Self- management support

Seek support from other health care professionals – nurses, social workers, occupational therapists, physiotherapists, psychologists, psychiatrists, etc.

Arnold LM et al. Mayo Clin Proc 2012; 87(5):488-96.

Alternative Medicine/Chiropractic Treatments for Fibromyalgia

- 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

Non-pharmacologic Treatments with Demonstrated Efficacy Currently in Use

Cognitive Behavioral Therapy

- Positive effects on coping with and control over pain
 - Not proven to improve pain
- Proven to improve physical function
- Should be done by a trained professional





Aerobic and Strengthening Exercises

- Reduce pain, increase self-efficacy,
 - improve quality of life and reduce depression
- Low-to-moderate intensity, 2–5 times/week

Patient Education

 Conflicting evidence but some studies have shown improvements in pain, sleep, fatigue and quality of life



Brosseau L et al. Phys Ther 2008; 88(7):857-71; Brosseau L et al. Phys Ther 2008; 88(7):873-86; Goldenberg DL et al. JAMA 2004; 292(19):2388-95...

Non-pharmacologic Interventions to Improve Sleep in Fibromyalgia

- 1. Avoid stimulants
- 2. Go to bed and rise at regular times
- 3. Avoid napping through day
- 4. Exercise regularly, particularly in the afternoon
- 5. Use the bed only for sleep and sex
- 6. Relax before bed
- 7. Printed information on sleep for patients



What is helpful for fatigue?

- Improvement of sleep hygiene
- Avoid napping through the day
- Moderate physical activity
- Pacing
- Realistic goal setting
- Healthy eating
- Avoid stimulants
- Cognitive behavioral therapy
- Some medications may improve fatigue

Lera S et al. J Psychosom Res 2009; 67(5):433-41; Rossy LA et al. Ann Behav Med 1999; 21(2):180-91; Williams DA. Best Pract Res Clin Rheumatol 2003; 17(4):649-65.

Physical Activity and Fibromyalgia

Benefits

- Stimulates release of endorphins and enkephalins within 30 minutes
- These bind to opioid receptors, reducing pain by an action on both ascending and descending neural pathways

Recommendations for Fibromyalgia

Type of Exercise

- Try to include different types in one session (*e.g.*, aerobic, strengthening, stretching)
- Patient preference and availability should guide selection

Intensity

- Start low, go slow
- Gradually increase to reach moderate intensity level

Cognitive Behavioral Therapy in Fibromyalgia

Technique

Learn to identify emotions that influence cognitive and affective components of pain (anxiety, helplessness, depression)

Employ active cognitive, problem-solving and distraction/relaxation techniques to modify emotions

Develop active strategies targeting well-being and control

Thieme K, Turk DC. Reumatismo 2012; 64(4):275-85.

IASP: Non-pharmacological Treatment of Fibromyalgia

- Exercise
- Cognitive behavioral therapy
- Multimodal treatment programs
- Balneotherapy
- Homeopathy
- Mild infrared hyperthermia
- Acupuncture

Non-pharmacological Treatment of Fibromyalgia: APS Guidelines



Non-pharmacological Treatment of Fibromyalgia: Canadian Guidelines

- Self-management strategies with active patient participation and interventions that improve self-efficacy should be an integral component of the therapeutic plan for the management of fibromyalgia
- Persons with fibromyalgia should participate in a graduated exercise program of their choosing
- **Cognitive behavioral therapy** even for a short time is useful and can help reduce fear of pain and fear of activity
- There is currently insufficient evidence to support the recommendation of complementary and alternative medicine treatments for the management of fibromyalgia

Non-pharmacological Treatment of Fibromyalgia: Brazilian Consensus

Recommended	Not Recommended
 Cognitive behavioral therapy 	Biofeedback
• Exercise	Chiropractic manipulation
 Musculoskeletal exercises ≥2x/week 	Hypnotherapy
Individualized aerobic	Homeopathic treatment
exercise programs	Therapeutic massage
 Individualized stretching programs 	 Global postural reeducation
 Muscular strengthening programs 	Pilates
Physical therapy	
 Psychotherapeutic support 	
Rehabilitation	
Relaxation	

Non-pharmacological Treatment of Fibromyalgia: EULAR Guidelines



Non-pharmacological Treatment of Fibromyalgia: AMWF Guidelines

Recommended

- Acupuncture
- Biofeedback
- Cognitive behavioral therapy
- Functional training
- Meditative movement therapies

- Multicomponent therapy
- Patient and psychological education
- Strength training

Not Recommended

- Chiropractic
- Cold therapy
- Homeopathy
- Laser
- Magnetic field therapy
- Massage

- Mindfulness-based stress reduction as sole treatment
- Reiki
- Therapeutic writing
- Transcranial direct
 current stimulation

No Positive or Negative Recommendation

- Elimination diet, vegetarian diet or therapeutic fasting
- Exercise therapy
- Foot reflexology massage therapy
- Full body heat treatment

- Lymphatic drainage
- Osteopathy
- Physiotherapy
- Ultrasound/electrotherapy

AMWF = Association of the Scientific Medical Societies in Germany

Arnold B et al. Schmerz 2012; 26(3):287-90; Eich W et al. Schmerz 2012; 26(3):268-75; Köllner V et al. Schmerz 2012; 26(3):291-6; Langhorst J et al. Schmerz 2012; 26(3):311-7; Winkelmann A et al. Schmerz 2012; 26(3):276-86.

Non-pharmacological Treatment of Fibromyalgia: Hong Kong MPNP Recommendations

- Cognitive behavioral therapy
- Lifestyle changes:
 - Balanced diet
 - Meditation/relaxation techniques
 - Sleep hygiene
- Physical therapy:
 - Exercise (aerobic exercise, strength training)
 - Hydrotherapy or aquatherapy
 - Occupational/physiotherapy
- Trigger point injection

MPNP = Multidisciplinary Panel on Neuropathic Pain

The Multidisciplinary Panel on Neuropathic Pain. *Recommendations for the Management of Fibromyalgia*. Available at: http://www.mims.com/Hongkong/pub/topic/Medical%20Progress/2011-01/Recommendations%20for%20the%20Management%20of%20Fibromyalgia. Accessed: August 30, 2013.

Pharmacological Treatment

Central Sensitization Produces Abnormal Pain Signaling



Adapted from: Campbell JN, Meyer RA. *Neuron* 2006; 52(1):77-92; Gottschalk A, Smith DS. *Am Fam Physician* 2001; 63(10)1979-86; Henriksson KG. *J Rehabil Med* 2003; 41(Suppl):89-94; Larson AA *et al. Pain* 2000; 87(2):201-11; Marchand S. *Rheum Dis Clin North Am* 2008; 34(2):285-309; Rao SG. *Rheum Dis Clin North Am* 2002; 28(2):235-59; Staud R. *Arthritis Res Ther* 2006; 8(3):208-14; Staud R, Rodriguez ME. *Nat Clin Pract Rheumatol* 2006; 2(2):90-8; Vaerøy H *et al. Pain* 1988; 32(1):21-6; Woolf CJ *et al. Ann Intern Med* 2004; 140(6):441-51.

Loss of Inhibitory Control: Disinhibition



Attal N, Bouhassira D. Acta Neurol Scand 1999; 173:12-24; Doubell TP et al. In: Wall PD, Melzack R (eds). Textbook of Pain. 4th ed. Harcourt Publishers Limited; Edinburgh, UK: 1999; Woolf CJ, Mannion RJ. Lancet 1999; 353(9168):1959-64.

How $\alpha_2 \delta$ Ligands Decrease Pain Sensitivity



Note: gabapentin and pregabalin are $\alpha_2 \delta$ ligands Bauer CS *et al. J Neurosci* 2009; 29(13):4076-88.

$\alpha_2\delta$ Ligands Bind to $\alpha_2\delta$ Subunit of Voltage-Gated Calcium Channels



Arikkath J, Campbell KP. Curr Opin Neurobio 2003; 13(3):298-307; Catterall WA. J Bioenerg Biomembr 1996; 28(3):219-30; Gee NS et al. Biol Chem 1996; 271(10):5768-76..

$\alpha_2 \delta$ Ligands Reduce Calcium Influx in Depolarized Human Neocortex Synaptosomes



Concentration (µM)

$\alpha_2 \delta$ Ligands Modulate Calcium Channel Trafficking



- $\alpha_2 \delta$ ligands reduce trafficking of voltage-gated calcium channel complexes to cell surface *in vitro*
- $\alpha_2 \delta$ ligands prevent nerve-injury induced up-regulation of $\alpha_2 \delta$ in the dorsal horn

BCH = 2-(-)-endoamino-bicycloheptene-2-carboxylic acid; ER = endoplasmic reticulum; GBP = gabapentin Bauer CS *et al. Neurosci* 2009; 29(13):4076-88; Hendrich J *et al. Proc Natl Acad Sci U S A* 2008; 105(9):3628-33.

Adverse Effects of $\alpha_2\delta$ Ligands

System	Adverse effects
Digestive system	Dry mouth
CNS	Dizziness, somnolence
Other	Asthenia, headache, peripheral edema, weight gain

 $\alpha_2 \delta$ ligands include gabapentin and pregabalin CNS = central nervous system Attal N, Finnerup NB. *Pain Clinical Updates* 2010; 18(9):1-8.

How Antidepressants Modulate Pain



Suggested Mechanisms of Analgesic Action of Antidepressants

Mechanism of Action	Site of Action	TCA	SNRI
Reuptake inhibition	Serotonin Noradrenaline	+ +	+ +
Receptor antagonism	α-adrenergic NMDA	+ +	- (+) milncipran
Blocking or activation of ion channels	Sodium channel blocker Calcium channel blocker Potassium channel activator	+ + +	(+) venlafaxine/ - duloxetine ? ?
Increasing receptor function	GABA _B receptor	+ amitripline/ desipramine	?
Opioid receptor binding/ opioid-mediated effect	Mu- and delta-opioid receptor	(+)	(+) venlafaxine
Decreasing inflammation	Decrease of PGE2 production decrease of TNFα production		

GABA = γ-aminobutyric acid; NDMA = N-methyl-D-aspartate; PGE = prostaglandin E; SNRI = serotonin-norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant; TNF = tumor necrosis factor Verdu B *et al.* Drugs 2008; 68(18):2611-32.

Adverse Effects of Antidepressants

System	TCAs	SNRIS
Digestive system	Constipation, dry mouth, urinary retention	Constipation, diarrhea, dry mouth, nausea, reduced appetite
CNS	Cognitive disorders, dizziness, drowsiness, sedation	Dizziness, somnolence
Cardiovascular	Orthostatic hypotension, palpitations	Hypertension
Other	Blurred vision, falls, gait disturbance, sweating	Elevated liver enzymes, elevated plasma glucose, sweating

CNS = central nervous system; TCA = tricyclic antidepressant; SNRI = serotonin-norepinephrine reuptake inhibitor Attal N, Finnerup NB. Pain Clinical Updates 2010; 18(9):1-8.

IASP: Pharmacological Treatment for Fibromyalgia



IASP = International Association for the Study of Pain Sommer C. *Pain Clin Updates* 2010; 18(4):1-4.

Pharmacological Treatment of Fibromyalgia: APS Guidelines



APS = American Pain Society; SNRI = serotonin norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant Goldenberg D *et al. JAMA* 2004; 292(19):2388-95.

Pharmacological Treatment of Fibromyalgia: Canadian Guidelines



SNRI = serotonin norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant Fitzcharles MA *et al. Pain Res Manag* 2013; 18(3):119-26.

Pharmacological Treatment of Fibromyalgia: Brazilian Consensus

Recommended

- $\alpha_2 \delta$ ligands: gabapentin, pregabalin
- Anti-Parkinson medication: pramipexole
- MAOI antidepressants: moclobemide
- Non-benzodiazepine hypnotics: zopiclone, zolpidem
- SNRIs: duloxetine, milnacipran
- SSRIs: fluoxetine
- TCAs: amitriptyline, cyclobenzaprine, nortriptyline
- Tropisetron
- Weak opioids: tramadol

Not Recommended

- Benzodiazepines: clonazepam, alprazolam
- Corticosteroids
- nsNSAIDs/coxibs
- SSRIs: citalopram, escitalopram, paroxetine, sertraline
- Strong opioids
- TCAs: clomipramine, imipramine
- Tinazidine
- Topiramate

Coxib = COX-2-selective inhibitor; MAOI = monoamine oxidase inhibitor; nsNSAID = non-selective non-steroidal anti-inflammatory drug; SNRI = serotonin norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant Heymann RE *et al. Rev Bras Reumatol* 2010; 50(1):56-66.

Pharmacological Treatment of Fibromyalgia: EULAR Guidelines

Recommended

- $\alpha_2 \delta$ ligands (pregabalin)
- Antidepressants (amitriptyline, fluoxetine, duloxetine, milnacipran, moclobemide, pirlindole)
- Pramipexole
- Tramadol
- Tropisetron

May be considered

- Simple analgesics (acetaminophen)
- Other weak opioids

Not recommended

- Corticosteroids
- Strong opioids

EULAR = European League Against Rheumatism Carville SF *et al. Ann Rheum Dis* 2008; 67(4):536-41.

Pharmacological Treatment of Fibromyalgia: AMWF Guidelines

Recommended

- Amitriptyline
- Duloxetine, with comorbid depression or anxiety
- Pregabalin
- SSRIs (fluoxetine, paroxetine), with comorbid depression

Not Recommended

- Anxiolytics
- Cannabinoids
- Dopamine agonists
- Flupirtine
- Hormones
- Hypnotics
- Ketamine
- Local anesthetics
- Milnacipran

- MAOIs
- Sodium oxybate
- Neuroleptics
- Non-steroidal antirheumatics
- Muscle relaxants
- Strong opioids
- Tropesitron
- Virostatics

No Positive or Negative Recommendation

- Acetaminophen
- Metamizole
- Weak opioids

AMWF = Association of the Scientific Medical Societies in Germany; MAOI = monoamine oxidase inhibitor; SSRI = selective serotonin reuptake inhibitor Sommer C *et al. Schmerz* 2012; 26(3):297-310. Pharmacological Treatment of Fibromyalgia: Hong Kong MPNP Recommendations

- α2δ ligands (gabapentin, pregabalin)
- SNRIs (duloxetine, milnacipran)
- TCAs (amitriptyline, cyclobenzaprine)
- Tramadol

MPNP = Multidisciplinary Panel on Neuropathic Pain; SNRI = serotonin norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant The Multidisciplinary Panel on Neuropathic Pain. *Recommendations for the Management of Fibromyalgia*. Available at: <u>http://www.mims.com/Hongkong/pub/topic/Medical%20Progress/2011-</u> 01/Recommendations%20for%20the%20Management%20of%20Fibromyalgia. Accessed: August 30, 2013.

Non-adherence to Medication in Fibromyalgia

Non-adherence to medication	n (%)*
Did you forget to take your medication?	31 (24.4)
Were you careless at times about taking your medication?	26 (20.5)
When you felt better, did you sometimes stop taking your medication?	25 (19.7)
If you felt worse when you took your medication, did you sometimes stop taking your medication?	25 (19.7)
Endorsement of at least one item	60 (47.2)

***127 women were surveyed** Sewitch MJ *et al. Rheumatology (Oxford)* 2004; 43(5):648-54.

Strategies to Improve Adherence

- Simplify regimen
- Impart knowledge
- Modify patient beliefs and human behavior
- Provide communication and trust
- Leave the bias
- Evaluate adherence

Simplifying Medication Regimen

- If possible, adjust regimen to minimize:
 - Number of pills taken
 - Number of doses per day
 - Special requirements (e.g, bedtime dosing, avoiding taking medication with food, etc.)





- Recommend all medications be taken at the same time of day (if possible)
- Link taking medication to daily activities, such as brushing teeth or eating
- Encourage use of adherence aids such as medication organizers and alarms

American College of Preventive Medicine. *Medication Adherence Clinical Reference*. Available at: <u>http://www.acpm.org/?MedAdherTT_ClinRef</u>. Accessed: October 8, 2013; van Dulmen S *et al. BMC Health Serv Res* 2008; 8:47.

Imparting Knowledge

- Provide clear, concise instructions (written and verbal) for each prescription
- Be sure to provide information at a level the patient can understand
- Involve family members if possible
- Provide handouts and/or reliable websites for patients to access information on their condition
- Provide concrete advice on how to cope with medication costs

Modifying Patient Beliefs and Behaviors: Motivational Interviewing Technique

Techniques

- Express empathy
- Develop discrepancy
- Roll with resistance
- Support self efficacy

Examples

- "It's normal to worry about medication side effects"
- "You obviously care about your health; how do you think not taking your pills is affecting it?"
- "I understand that you have a lot of other things besides taking pills to worry about"
- "It sounds like you have made impressive efforts to work your new medication into your daily routine"

Bisono A *et al.* In: O'Donoghue WT, Levensky ER (eds). *Promoting Treatment Adherence:* A *Practical Handbook for Health Care Providers.* SAGE Publications, Inc.; London, UK: 2006.

Providing Communication and Trust: Communication Tips

- Be an active listener
 - Focus on the patient
 - Nod and smile to show you understand
- Make eye contact





- Be aware of your own body language
 - Face the patient
 - Keep arms uncrossed
 - Remove hands from pockets
- Recognize and interpret non-verbal cues

McDonough RP, Bennett MS. *Am J Pharm Educ* 2006; 70(3):58; Srnka QM, Ryan MR. *Am Pharm* 1993; NS33(9):43-6.

Leaving the Bias



American College of Preventive Medicine. *Medication Adherence Clinical Reference*. Available at: <u>http://www.acpm.org/?MedAdherTT_ClinRef</u>. Accessed: October 8, 2013.

Evaluating Adherence: 4-Step Strategy for Detecting Non-adherence



Hahn S, Budenz DL. Adv Stud Ophthalmol 2008; 5(2):44-9.

Conviction and Confidence: A Model for Successful Interventions

- Patient conviction (i.e., sense of the patient's personal, emotional recognition of the benefits of changing a behavior)
 - "Is increasing your physical activity a priority for you?"
 - Increase conviction by getting patients to articulate benefits of change
- Patient confidence (i.e., sense of the patient's ability to modify a behavior)
 - "If you did decide to become physically active, how confident are you that you would be able to follow though?"
 - Increase confidence by identifying barriers to change and helping patients overcome those barriers by identifying their own solutions

Conviction – Confidence Model



Adapted from: Keller VF, White KM. J Clin Outcomes Manage.1997; 4(6):33-6;

Miller WR, Rollnick S. Motivational Interviewing: Preparing People to Change Addictive Behavior. Guilford Press; New York, NY: 1991.

Summary

Management: Summary

- Set realistic treatment goals and manage patient expectations
- Incorporate both pharmacological and non-pharmacological strategies
- Use non-pharmacological treatments first
- Use medical therapies that target pain and have evidence for efficacy in fibromyalgia as first-line pharmacotherapy
 - Balance medication side effects and risk with optimizing function
 - Chose medications that target the most troublesome symptoms
 - Start low, go slow reassure patients