Date: August 3, 2021

Clinical Protocol: Fibromyalgia and Chronic Pain in Related Disorders

PREAMBLE

- There is no cure for FM. Treatment strategies focus on symptoms relief and quality of life. Pharmacologic treatment mainly focuses on pain and sleep.
- The drugs are presented in the order (more or less) to try them
- The actual order of use will depend on prior treatment, patient preference, etc.
- Look for "two fors" (drugs that benefit two or more problems)
- Provide patient with information/dose adjustment handout
- Given the different mechanisms of action, patients often end up on 2 or more drugs
- Patients with ME/CFS may need to be titrated more slowly, and may not tolerate higher doses of medications
- It is expected that physicians would educate themselves about these drugs beyond the outline provided below

1. PATIENT EDUCATION

- Incorporated into multiple offerings (e.g., handouts, web-based resources)
  - FM Patient Resources
- Incorporated into group educational activities
- "Family and Friends" session
  - Check the website under the News and Events

2. PHYSICAL ACTIVITY

- The most important thing is to establish if your patient has coexisting ME/CFS. If so, exercise may not be an option. For those without ME/CFS exercise can help with sleep, pain, and mood
- However, even those without ME/CFS and associated post-exertional malaise need to pace themselves in order to avoid worsening their symptoms
- Exercise should be construed within the larger context of activity. Patients with low activity tolerances should use their limited energy to perform activities of daily living rather than formal exercise
- Offered in group setting with PT

3. SLEEP

- Sleep disturbance is a major component of FM and pain
- See Sleep Protocol for details

4. DIET

- Offered in a group setting with dietitian
- Many patients benefit from a low-inflammatory diet
- The major emphasis, however, is a healthy diet

5. ALTERNATIVE AND COMPLEMENTARY THERAPIES

- Offered in a group setting with our naturopath

- Some agents are crossing into mainstream medicine and may be worth trying:

5.1 Co-enzyme Q
- 200 mg TID

5.2 D-Ribose
- 5 g TID

5.3 Magnesium Malate
- 250 mg QID

5.4 Vitamin D
- 2000 IU daily

6. PSYCHOLOGICAL AND BEHAVIOURAL THERAPIES
- Incorporated into group sessions
- For patients waiting to get into our program, on-line courses are available

7. INTERVENTIONS

7.1 Trigger Point Injection, etc.
- Maneuvers that target muscular trigger points, lengthen muscle contractures, and release painful scars and other connective tissue restrictions
- For example:
  - Myofascial release
  - Trigger Point Injections
  - Nerve blocks
- Check availability in the community:
  - Change Pain Clinic: http://www.changepain.ca
  - Muscle MD Clinic: http://musclemd.ca
  - Myo Clinic (Victoria): http://www.myoclinic.ca
  - Other practitioners across the province

7.2 Acupressure
- Offered as part of our group activities.

8. MEDICATIONS

- Patients tend to be very sensitive to medications, so use the smallest dose available (even fractions of a tablet or consider compounding lower doses)
- Many of the medications help with sleep and therefore can cause daytime somnolence and brain fog (cognitive symptoms
  - We usually start with an evening/bedtime dose rather than a divided daily dose
  - We usually up-titrate the evening/bedtime dose to maximum before considering adding a daytime dose
  - We sometimes push the evening/bedtime dose higher rather than adding a daytime dose. For instance, the total daily dose of Lyrica can be given in the evening rather than BID with better tolerance and fewer side effects
- If patient is unsure whether or not medication is helping, a trial of tapering is warranted
  - Patient are more likely to notice when pain comes on rather than when it gets better

8.1 Tricyclics

- Used for pain and sleep
- Improves sleep architecture
- Not used during the day
- Watch for:
  - Dry mouth
  - Hangover effect
  - Blurred vision
  - Urinary retention
- May need to taper at higher doses when discontinuing
- May need to decrease sleep medication to prevent a hang-over effect

8.1 A Amitriptyline

- Start 5 mg 2 hrs before bed (or 12 hrs before getting up in the morning)
- Increase to 10 mg after 1 week
- Increase by 5 mg increments at 2-week intervals
- Increase to 70 mg as tolerated, depending on benefit & side effects
- Many patients cannot tolerate more than 20-30 mg and some even less

8.1 B Cyclobenzaprine

- Alternative to amitriptyline
- Also helps with muscle spasms
- Start 5 mg 2 hrs before bed (or 12 hrs before getting up in the morning)
- Increase by 5 mg increments at 2-week intervals
- Increase to 20 mg as tolerated, depending on benefit & side effects
- Not generally used during the day, but may be tried during the day in patients who tolerate the evening dose and have run out of oral medication options
- occasional patients may benefit from 3 divided doses
  - Increase by 5 mg increments at 2-week intervals
  - Maximum dose 20 mg TID with last dose taken 2 hours before bed

8.1 C Nortriptyline

- Alternative to amitriptyline
- Useful in patients who have tried amitriptyline in the past and didn't tolerate it (usually because amitriptyline was started at too high a dose)
- Generally, less benefit for pain, but also fewer side effects
- Start 10 mg 2 hrs before bed (or 12 hrs before getting up in the morning)
- Increase by 10 mg increments at 2-week intervals
- Increase to 50-70 mg as tolerated, depending on benefit & side effects
- Most patients cannot tolerate more than 20-30 mg and some even less

8.2 Anticonvulsants

- Used for pain
- Also helps with sleep, anxiety, dysesthesia, and restless leg
- Topiramate also helps with migraines
- Start with evening dosing and add during day later
- Watch for:
  - Sedation (common)
  - Cognitive dysfunction
  - Weight gain (or weight loss with topiramate)

- Edema
- Not a good choice in obesity, metabolic syndrome, or fear of gaining weight
- Topiramate may be an alternative in these patients as it causes weight loss (used off-label as a diet drug in the US).
- Avoid abrupt withdrawal; need to taper
- Balance pain relief (benefit) with day time somnolence (side effect)
  - Start with evening dose rather than BID dosing
  - Titrate the evening dose to maximum before adding any during the day
  - Many patients don't tolerate daytime dosing
- Monitor weight

8.2 A Pregabalin (Lyrica)

- Expensive $$$ (not a Pharmacare benefit)
- Patient dosing schedule
  - Inform patients not to expect benefit until 100 mg (to prevent early discontinuation)
  - Titrate the evening dose to maximum before adding any during the day
  - Rather than splitting the dose BID, use more in the evening

AM	Evening	
	25 mg	
	50 mg	
	75 mg	
	100 mg	Patient review at 100 mg
	125 mg	
	150	
	175	
	200	
	225	
	250	
	275	
	300	
25	300 mg	
50	300 mg	
75	300 mg	
100	300 mg	
125	300 mg	
150	300 mg	
Physician review for higher doses / multidrug regimens Maximum dose 450 mg / day		

- Increase dose at 1 (or more) week intervals depending on side effects (dizziness and drowsiness are common)
- If unsure current dose is helping, trial of tapering warranted

8.2 B Gabapentin

- Alternative to pregabalin if cost is a factor (is a Pharmacare Benefit)
- Patient dosing schedule
  - Inform patients not to expect benefit until 600 mg (to prevent early discontinuation)
  - Titrate the evening dose to maximum before adding any during the day

AM	Afternoon	HS	
		100 mg	
		200 mg	
		300 mg	
		400 mg	
		500 mg	
		600 mg	Patient review at 600 mg
		700 mg	
		800 mg	
		900 mg	
100 mg		900 mg	
100 mg	100 mg	900 mg	
200 mg	100 mg	900 mg	
200 mg	200 mg	900 mg	
300 mg	200 mg	900 mg	
300 mg	300 mg	900 mg	
Physician review for higher doses Maximum dose 3600 mg / day			

- Increase dose at 1 (or more) week intervals depending on side effects (dizziness and drowsiness are common)
- If unsure current dose is helping, trial of tapering warranted

8.2 C Topiramate

- No specific evidence for fibromyalgia but clinical experience has found it to be helpful
- Strong evidence for other pain syndromes
- May be useful when gabapentinoids can't be used due to obesity, metabolic syndrome or fear of gaining weight
  - Used off-label as a weight loss drug in the US
- Also, useful if patient has migraines
- Watch for:
  - Drowsiness
  - Cognitive dysfunction
  - GI upset
  - Good water intake (prevent renal stones)
  - Weight loss
- Check blood work at baseline; 2 mo; 4 mo; 10 mo; 16 mo:
  - Lytes (metabolic acidosis)
  - Neutropenia
  - Elevated liver enzymes
- Patients who benefit but have daytime somnolence may do better with just night time dosing
- Patient dosing schedule
  - Inform patients not to expect benefit until 50 mg BID (to prevent early discontinuation)

AM	Evening	
	12.5 mg	
	25 mg	
	50 mg	
	50 mg	
	70 mg	
	100 mg	Patient review at 100 mg

AM	Evening	
	125 mg	
	150 mg	
	175 mg	
	200 mg	
25 mg	200 mg	
50 mg	200 mg	
75 mg	200 mg	
100 mg	200 mg	
125 mg	200 mg	
150 mg	200 mg	
175 mg	200 mg	
200 mg	200 mg	
		Maximum dose 200 mg BID

- Increase dose at weekly (or more) intervals
- If unsure current dose is helping, trial of tapering warranted

8.3 SNRIs

- Used for pain
- Norepinephrine effect (i.e., pain modulation) occurs at higher doses
- Also helps with comorbid depression or anxiety, and some unexplained physical symptoms (but not fatigue)
- If patient is currently on SSRI, consider a trial of switching from SSRI to SNRI
  - Can switch from one day to the next
  - Use same relative dose of SNRI
  - E.g., If patient is on 50% of a maximum dose of an SSRI, switch to 50% of a maximum dose of SNRI
- Coming off SNRI more difficult than SSRI
  - Slower taper
- Tell patient to expect "transition" effects in the first 7-10 days
  - Otherwise patient will think these are side effects and discontinue drug
  - Patient may feel "off," anxious, not like themselves, etc.
- Watch for:
  - Agitation, insomnia
  - Dyspepsia, and other GI side effects
  - Sexual dysfunction
  - Suicidal ideation
- Monitor blood pressure

8.3 A Duloxetine (Cymbalta)

- Expensive $$$ (not a Pharmacare Benefit)
- Inform patient not to expect benefit for 4-6 weeks (prevent premature discontinuation)
- Start 30 mg daily (or q 2 days in drug sensitive patients; compounding of smaller doses is also an option)
- Increase to 60 mg daily after 3 weeks if tolerated
- Stay on 60 mg for at least 2 months before considering further dose increase
- Physician review for doses above 60 mg daily
- Above 60 mg go to BID dosing
- Can increase to 90-120 mg daily in select patients who benefit
  - Pain benefit (i.e., norepinephrine reuptake inhibition) occurs at higher doses)

8.3 B Venlafaxine XR

- Alternative to duloxetine if cost is a factor (is a Pharmacare Benefit)
- Can also be tried in patients who did not tolerate duloxetine
  - Venlafaxine XR comes in much smaller incremental doses
- Inform patient not to expect benefit for 4-6 weeks after reaching dose of 112.5 mg
  - Prevent premature discontinuation
- Start 37.5 mg daily
- Increase by 37.5 mg increments at q 2-week intervals
- Reassess after 112.5 mg daily
- Target dose 225 mg daily
  - Can increase to 300 mg daily in select patient who benefit
  - Pain benefit (i.e., norepinephrine reuptake inhibition) occurs at higher doses)

8.4 Cannabinoids

- Used for pain
- Also helpful for anxiety, nausea, appetite, and sleep
- Can assist with opioid tapering
- Can be used both as regular dosing and prn

8.4 A Nabilone (Cesamet)

- Expensive $$$ (is a Pharmacare Benefit)
  - Both 0.25 and 0.5 mg covered by Pharmacare
- Watch for:
  - Drowsiness
  - Cognitive dysfunction
  - Psychoactive side effects
  - Dizziness
  - Dry mouth
  - Weight gain
- Use with caution in patients with orthostatic intolerance:
  - POTS (Postural Orthostatic Tachycardia Syndrome)
  - NMH (Neurally Mediated Hypotension)

- Patient dosing schedule
  - Start with 0.25 mg in the evening or at bedtime
    - If patient feels too drowsy if taken earlier, can be taken at bedtime
  - Increase dose according to table
  - Titrate the evening dose to maximum before adding any during the day
  - Try adding prn doses during the day to see if patient tolerates it before adding regular daily dosing
  - Maximum 6 mg per day

AM	**Afternoon**	**Evening/Bedtime**	
		0.25 mg	
		0.5 mg	
		0.75 mg	
		1.0 mg	
		1.25 mg	
		1.5 mg	
		1.75 mg	
		2 mg	Patient review at 2 mg total/day
0.25 mg			
0.25 mg	0.25 mg		
0.5 mg	0.25 mg		
0.5 mg	0.5 mg		
0.75 mg	0.5 mg		
0.75 mg	0.75 mg		
1 mg	0.75 mg		
1 mg	1 mg		Patient review at 4 mg total/day
Increase dose at weekly (or more) intervals Physician review for doses above 4 mg per day Consider regular + prn dosing Maximum 6 mg daily (2 mg TID)			

8.5 Low Dose Naltrexone

- Used for pain
- Some patients report benefit with cognitive symptoms and fatigue
- Anti-opioid: Not to be used for patients on opioids
- May have beneficial effects on inflammation and gliopathy
- Inexpensive drug but needs to compounded
  - Cost of compounding $$
  - Not a Pharmacare benefit
  - Compounding not usually covered by drug benefit programs
- Few side effects at lower doses but watch for:
  - Insomnia
  - Vivid dreams
  - "Activation:" nervous energy
  - Headaches
  - Dizziness
  - GI sided effects
- Inform patients not to expect benefit until on 4 mg daily for 2 months (prevent early discontinuation)

- There are theoretical reasons to take it at bedtime but side effects (especially insomnia and vivid dreams are more common)
  - Can start with nighttime dose and switch to AM if side effects occur
- Use one of the 2 regimens below
  - FM patient can usually start at 1 mg: Regimen 1
  - ME/CFS patients are more sensitive and should start at 0.5 mg: Regimen 2
- Target (max) dose: 4.5 mg daily as tolerated
  - Give new script for 4.5 mg dose
- The optimal dose of naltrexone is unknown – studies were done using 4.5 mg
  - Responders may benefit from a trial of incrementally increasing the dose up to 9 mg per day and in some cases 12 mg per day

Regimen 1 - FM:

- Give patient 2 prescriptions: 1 mg and 4.5 mg
- Start with 1 mg qhs or qAM
- Increase dose according to table below
- Many patients will need to increase the dose more slowly
- Use 1 mg capsules until you get to 4 mg

HS or AM	
1 mg daily	For 1 week
2 mg daily	For 1 week
3 mg daily	For 1 week
4 mg daily	For 1 week
4.5 mg daily	Stay on this dose for at least 1 month
Follow up with clinic to assess continued use	

Regimen 2 – ME/CFS or FM patients very sensitive to medications:

- Start with 0.5 mg qhs or qAM
- Increase dose by 0.5 mg every 2 weeks
- Many patients will need to increase the dose more slowly
- Patients may or may not get to the target dose of 4.5 mg
- Patients should stay at the same dose (stop increasing) if they get side effects
- Prescribe 0.5 mg capsules to start
  - Give a script for 2 mg capsules so that patient doesn't need to take too many capsules at once when they got to this dose (also reduces cost of compounding)
  - When final dose is established, can be prescribed as single capsule

HS or AM	
0.5 mg daily	For 2 week
1 mg daily	For 2 week
1.5 mg daily	For 2 week
2 mg daily	For 2 week (switch to large capsule)
2.5 mg daily	For 2 week
3 mg daily	For 2 week
3.5 mg daily	For 2 week
4 mg daily	For 2 week
4.5 mg daily	For 2 week (prescribe as single capsule)

8.6 NSAIDs

- No evidence of efficacy in fibromyalgia
- May benefit patients with "peripheral pain generators" (e.g., OA, back pain, etc.)
  - I.e., Secondary pain drivers
- Best used for short periods or prn
- Long term use associated with GI, renal, and cardiac side effects
- E.g., diclofenac 25-75 mg TID
- May need to provide gastro-protection
  - Addition of PPI
    - e.g., pantoprazole 40 mg daily
  - Combination drugs
    - e.g., Arthrotec (diclofenac + misoprostol)
      - Expensive $$$; not covered
    - e.g., Vimovo (naproxen + esomeprazole)
      - Expensive $$$; not covered
- Toradol may be helpful in acute severe flares

8.7 Opioids

- Avoid opioids in these patient populations
  - Opioid induced hyperalgesia more common
  - No evidence of efficacy for stronger opioids
- Tramadol (with or without acetaminophen) may be helpful in refractory cases
- Try to get patients off opioids if other meds have not been tried
  - See Opioid Taper and Discontinuation protocol
- Opioids are not prescribed by CCDP (except for tramadol)

8.7 A Tramadol

- Expensive $$$ (not a Pharmacare benefit)
- Tramadol 50-100 mg q6h prn; max 400 mg / day
- Tramacet (Acetaminophen 325 mg and Tramadol 37.5 mg)
  - 1-2 tabs q6h prn
  - max 8 tablets / day

9. ASSESS AND TREAT COEXISTING CENTRAL SENSITIVITY SYNDROMES

- May require referral out
- Central Sensitivity Syndromes include:
  - IBS
  - Migraine
  - Tension Type Headaches
  - POTS
  - Multiple Chemical Sensitivities
  - Interstitial Cystitis
  - Pelvic Pain Syndromes
  - Irritable Larynx Syndrome
  - Restless Leg Syndrome
  - Non-cardiac Chest Pain
  - Temporomandibular Disorders
  - Myofascial Pain Syndrome
  - Central Abdominal Pain Syndrome
  - PTSD

10. ASSESS AND TREAT FOR COEXISTING ANXIETY AND MOOD DISORDERS

- Referral to psychiatrist for selected patients

Patient Resources:
http://www.bcwomens.ca/health-info/living-with-illness/fibromyalgia