Pathogenesis and Treatment of Fibromyalgia Syndrome

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Fibromyalgia syndrome is a condition that, despite its common presentation in the general public, is fraught with controversy by virtue of its inherent lack of objective confirmation. Some practitioners even refute its existence, emphasizing the lack of confirmatory objective tests. In a recent volume of this journal, the diagnosis and clinical features of fibromyalgia were addressed by this author.[1] Since that publication, a group of experts has been in the process of modifying the 1990 American College of Rheumatology (ACR) criteria for fibromyalgia which relied on the presence of pain all over and of at least 11 to 18 painful tender points distributed in all four quadrants of the body.[2] New proposed 2010 ACR criteria for diagnosis of FMS will soon be published and will show predictive value for a diagnosis of FMS in weighing just symptom criteria with elimination of a fibromyalgia tender point count. Still this author would comment that a physical examination for fibromyalgia tender points should still be carried out.

Theories on etiopathogenesis of FMS

There are many proposed mechanisms and contributing factors to the development of FMS. Fibromyalgia embodies the biopsychosocial model with emerging physiologic and psychological factors being operative. It is recognized that there are both central (brain and spinal cord) and peripheral (nerves and soft tissue) mechanisms of pain operative in FMS.[3]

Central mechanisms

Central pain pathways appear to be stepped up or hypersensitized in FMS. Central sensitization denotes enhanced excitability of neurons in the dorsal horn of the spinal cord. This enhances the responses of large and small caliber primary afferent fibres. Central "wind up" of pain is related to prolonged stimulation of C fibers in the dorsal horn of the spinal cord. This leads to temporal summation of second pain.[4] The spinal gate theory has long been championed in chronic pain.[5] Neuroplasticity as well as brain mapping have been suggested. Hypothalamic pathways appear to be altered in fibromyalgia patients.[6] Alteration in neurotransmitters has been demonstrated on Position Emission Tomography (PET) and Single Photon Emission Tomography (SPECT) brain scans which are essentially used for research purposes.[7] It has been demonstrated that decreased levels of neurotransmitters including serotonin and noradrenaline, provide a mechanism of action of the SNRI anti depressant duloxetine (Cymbalta) in fFMS. [8, 9] This apparent overlap of some of the favoured neurobiologic changes of depression and fibromyalgia is noteworthy. Some practitioners suggest that fibromyalgia is really an affective spectrum disorder.[10] Alterations of dopaminergic pathways in the brain have also been proposed.[11] Referral patterns of pain, mapped in the homunculi of the brain, have been championed by Smythe as a mechanism in FMS.[12]

Peripheral mechanisms

The peripheral finding of painful tender points suggests that there is a peripheral mechanism of pain operative in FMS. This is termed "nocioceptive" pain. FMS patients appear to have a decreased pain threshold. Increased levels of substance P, and excitatory neurotransmitter have been found in the CSF of fibromyalgia sufferers. This central increase of substance P, in turn, leads to increased peripheral nerve pain or nocioceptive pain.[13, 14] An increase in nerve growth factor has also been demonstrated as a mechanism of up regulation of peripheral pain.

Psychosocial factors

Depression is common in fibromyalgia but it is unclear which comes first.[15] Depression and fibromyalgia have similar patterns of noradrenaline and serotonin alterations in the brain. Stress such as post traumatic stress disorder from a history of abuse such as physical or sexual abuse has been linked with a greater risk of FMS in adulthood.[16] Patients with FMS are often hypervigilant and pain focussed. Again, FMS embodies the biopsychosocial model of pain.[17] FMS fulfills many features of "Pain Disorder" under the umbrella of "Somatoform Disorders" in the Psychiatry DSM IV TR.[18]

Sleep disorder

Sleep disorder with a non restorative sleep pattern is an integral feature of fibromyalgia. This was reported in the 1970's in classic studies by Smythe and Muldofsky in Toronto.[19] Patients report not feeling well rested in the morning. Sleep deprivation of normal adults can induce FMS, although less readily in well conditioned individuals.[20] Sleep apnea should be considered, particularly in males with FMS.[21]

Physical trauma

The relationship between physical trauma and FMS is a debatable issue with some studies supporting such an association and some detracting from such a link.[22-24] This can be an issue to consider in presentations of patients following injurious events.

Approach to treatment of FMS

General considerations

The therapeutic approach to FMS is multimodal (Table 1). Diagnosis and education of the patient along with validation and reassurance are first in order. The ruling out of a more sinister condition should be of solace to the patient. Yet, despite the benign nature of FMS, some patients catastrophize upon learning of this diagnosis. The physician should be supportive but should not enable the patient or promote disability. Treatment involves cooperation between the patient and the physician; the patient must participate in his/her therapy. The goal is to intercept pain pathways by various means. These fall into non pharmacologic and pharmacologic interventions.

Non-Pharmacologic therapy

Cognitive behavioural therapy

Cognitive behavioural therapy (CBT), which is a means of encouraging positive thought patterns, has been shown to be efficacious in FMS.[25] This can be offered by a psychiatrist or psychologist, but admittedly such services can be hard to access. Branches of the arthritis society in some locations may offer group programs for fibromyalgia self-management and there are also books and on line programs for self administered cognitive therapy.

Excercise: just do it!

Aerobic exercise to improve conditioning is important in FMS.[26] A supervised low impact type exercise program with power walking or use of a stationary exercise machine, or water exercise are optimal and can be built upon in a slow graded fashion culminating in independent exercise by

Table 2

Treatment of FMS

Step 1: Diagnosis, education

Step 2: Non pharmacologic methods
A. Cognitive Behavioural Therapy (CBT) and counselling
B. Actve aerobic excercise

Step 3: Pharmacologic methods:
A. Simple analgesics:
- acetaminophen, sometimes NSAIDs, topical treatments

B. Opiate analgesic:
- avoid opiate narcotics but can consider tramadol

C. Treatment of sleep disorder:
- Tricyclics such as amitriptylene, nortriptylene and cycobenzaprine
- can consider zopliclone or trazodone;
- avoid benzodiazepines

D. Antidepressant meds:
- Duloxetine
- other SNRI's or SSRI's

E. Nerve modulating drugs:
- Gabapentin
- Pregabalin

These various steps do not necessarily have to be introduced in this order and can be introduced in parallel with one another.

the patient. Attaining one`s target heart rate for 20 to 40 minutes at least three days a week is ideal. However, even shorter bouts of exercise in small segments through out the day, which total 30 minutes in a given day, may be beneficial for FMS patients. Excercise has to be taken on with a slow but sure approach.

Pharmacologic therapy:

Analgesics: As far as pharmacologic therapy, acetaminophen can be tried but is often inadequate in these patients. Anti inflammatories have a role if there is felt to be a concomitant articular problem or if a seronegative spondyloarthropathy, such as ankylosing spondyltis, is suspected.[27] Topical analgesic creams can be tried, but often the patient`s pain is too diffuse and generalized for topical therapy. Opiate analgesics should be avoided as the chronicity of FMS means that habituation is a likelihood. However, many practitioners introduce tramadol and this drug has been included in recommended therapies for FMS by the European Union League Against Rheumatism. Consensus on treatment of fibromyalgia syndrome.[28]

Treatment of sleep disorder with tricycclics

Treatment of the sleep disorder is important and begins with good sleep hygiene. Diagnosis and treatment of sleep apnea is also important. Pharmacologic treatment with low dose tricyclics such as amitryptilene (Elavil), nortryptilene (Aventyl) or cyclobenzaprine (Flexeril) is indicated.[29,30] Trazadone (Desyrel) is chosen by some physicians for sleep disorders. One of the benefits of this group of drugs is that they are non-habituating. It is useful to introduce these drugs in a low dose a few hours before bedtime to avoid a hangover effect.

Neurotransmitter modulating drugs

Pregabalin (Lyrica) has been found efficacious in numerous controlled trials in which it has been shown to improve the pain of FMS.[31-33] It has been approved and cited by the Health Protection Board (HPB) in Canada and the analogous FDA in the US as a drug for treatment of fibromyalgia syndrome. Despite the name pregabalin, this agent does not act on the gamma-aminobutyric acid (GABA) receptors, nor does gabapentin. These agents act on the calcium channels of the central nervous system. Decreasing the flow of calcium by these agents leads to inhibition of various neurostransmitters including glutamate and substance P. Gradual introduction of pregabalin starting with 25 mg at night and working up every week by 25 mg increments, as tolerated towards a dose of 75 to 150 mg b.i.d. or so is suggested. The maximum dose would be 450 mg a day but this is not attained in most patients. It may offer benefits even if one does not get to the aforementioned target dose. Pregabalin can also help the sleep disorder of FMS.[34] Dizziness from this drug

Table 2

The author's 10 pearls of wisdom in dealing with patients with fibromyalgia

1. Try to limit visits to one complaint at a time
2. Do not let the patient keep dwelling on their pain description and other somatic complaints
3. Be supportive and reassuring, but do not become an enabler
4. Avoid excessive appointments and over medicalizing
5. Do not assume everything is ascribable to FMS (*eg*, rule out cardiac cause of chest pain)
6. There are effective treatment modalities but ultimately the patient has to live to his/her symptoms
7. Do not promote disability if it can be avoided
8. If you have access to a multidisciplinary pain clinic and cognitive behavioural therapy, consider this as it is hard to help the patient in isolation from other caregivers[36]
9. Remain positive and proactive and acknowledge your limitations
10. Realize what you can and can not do.

may limit its use but this side-effect generally wears off 1 to 2 weeks after each dose increment.

Gabapentin (Neurontin) is another neuroleptic drug has been shown to be efficacious in FMS but is not accepted by the HPB at this point for FMS.[33] It also modulates calcium channels in the central nervous system as its purported mechanism of action. Again beginning with lower dosages is important with gradual titration upward as need be. Just starting at 100 mg to 300 mg at night can be a good starting point.

Antidepressant therapy

It is important to treat depression or anxiety which often co exist with FMS. Duloxetine (Cymbala), an anti depressant with both serotonin and noradrenaline re-uptake inhibition (SNRI) has been shown to be efficacious for the pain of FMS at a dose of 30 mg to 60 mg a day.[9] It can also serve to ameliorate the depression. Other anti depressants can be used including the Selective Serotonin Reuptake Inhibitors SSRI`s or other SNRI`s but duloxetine is the one which is specifically studied and targeted for FMS pain.[35] Often patients with FMS do not tolerate medications well and this can limit the success of pharmacologic interventions.

Naturopathic therapy

Naturopathic therapy is outside of the expertise of this writer.

Disability and Fibromyalgia

Fibromyalgia imposes a huge disability burden and it should be thought through before placing patients on long-term disability as they tend not to get back to the workplace. Patients with FMS may need to pace themselves. Long term disability policies are often all or none and not conducive to part time work. This is a challenging issue for the treating physician.

Conclusion

Some physicians continue to challenge the concept of fibromyalgia and suggest we have created a problem by acknowledging this disorder and enabling disability behaviour by the patient. Yet, over and over again, patients present in a manner consistent with FMS. To be nihilitistic about FMS does not serve the patient well, in view of this author. Fibromyalgia remains a syndrome which challenges the patient and caregiver alike. For some pearls of wisdom, which will hopefully support the physician in dealing with FMS patients please refer to Table 2. A confident, proactive approach always focussing on the positive can be of great value to you and your patient with FMS.

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For references, please contact **cme@sta.ca**

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