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FIBROMYALGIA – OFFERING EVIDENCE BASED TREATMENT

FIBROMIALGIA: TRATAMIENTO BASADO EN LA EVIDENCIA

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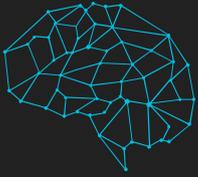
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ABSTRACT

Introduction: Fibromyalgia (FM) is a clinical condition characterized by chronic widespread pain, fatigue, non refreshing sleep, mood disturbance and cognitive impairment with accompanying functional disability. It's etiology and even it's existence as a clinical entity have been discussed over the last decades. The lack of understanding of it's physiopathology and the fact that, to this date, there is no strong effective treatment for it makes this discussion even more relevant for clinicians. We here try to revise some of the clinical relevant data available to this day.

Methods: This paper is a narrative revision which gathers information based on a PubMed database search from the last 6 years (2012-2018), in Portuguese or English, for clinical trials or reviews, on the term "Fibromyalgia treatment".

Results and discussion: Although there isn't a single strong intervention for FM patients, there is enough evidence suggesting that patient education on the symptoms, on the disease itself and on the realistic treatment goals can benefit these patients. Exercise is also evidence based and should be appropriately suggested. Classical and new Cognitive Behavioural Therapy (CBT) interventions should be seen as the corner stone of treatment in these patients, specially if having co-morbid affective disorders. Many drugs have been studied in the hopes of helping FM patients but few have evidence to support its recommendation.

Keywords: Fibromyalgia, pain, psychiatry, therapeutics, psychosomatic medicine.

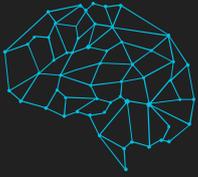
RESUMEN

Introducción: La fibromialgia (FM) es una condición clínica caracterizada por dolor crónico generalizado, fatiga, sueño no reparador, alteraciones del estado de ánimo y deterioro cognitivo con discapacidad asociada, en casos extremos. Su etiología, e incluso su existencia como entidad clínica, se han debatido en las últimas décadas. La falta de comprensión de su fisiopatología y el hecho de que, hasta la fecha, no exista un tratamiento suficientemente efectivo, convierte el debate en muy relevante para los clínicos.

Metodología: Este documento revisa información basada en una búsqueda en la base de datos de PubMed de los últimos 6 años (2012-2018), en portugués o inglés, para ensayos clínicos o revisiones, en los términos "Fibromyalgia Treatment".

Resultados y Discusión: Aunque no existe una sola intervención suficientemente sólida para pacientes con FM, gozamos de evidencias suficientes que sugieren que la educación del paciente sobre los síntomas, la enfermedad misma y los objetivos del tratamiento realistas pueden beneficiarlos. El ejercicio también se basa en la evidencia y debe sugerirse de manera apropiada. Las intervenciones clásicas y de segunda y tercera generación de la Terapia Cognitivo Conductual (TCC), deben considerarse la piedra angular del tratamiento en estos pacientes, especialmente si se asocian trastornos afectivos comorbidos. Muchos fármacos se han estudiado con la esperanza de ayudar a los pacientes con FM, pero pocos tienen evidencia para sostener su recomendación.

Palabras clave: Fibromialgia, dolor, psiquiatría, terapéutica, medicina psicosomática.



INTRODUCTION

Fibromyalgia (FM) is a medical clinical condition characterized by chronic widespread pain, fatigue, non refreshing sleep, mood disturbance and cognitive impairment (Macfarlane et al., 2017) with accompanying functional impairment and disability.

This condition shares many features, including familiar increased risk, with other chronic pain entities such as primary headaches, temporomandibular disorder, irritable bowel syndrome or interstitial cystitis.

In 1990, the American College of Rheumatology (ACR) set the research criteria which characterized FM as condition of pain and tenderness requiring at least 11 points of tenderness for the clinical diagnosis (F. Wolfe et al., 1990).

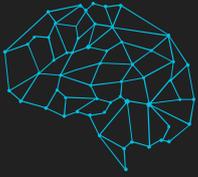
Although it can be seen at any age, its prevalence peaks between 40 and 60 years (Turk & Adams, 2016). Prevalence is higher in women (1,0 to 4,9%) than in men (0 to 2,9%) as shown in studies from Europe, USA and Canada (Bourgault et al., 2015). However, studies in clinical settings tend to show a higher disproportion with a 8:1 to 10:1 ratio (Macfarlane et al., 2017). Women are only 1.5 times more likely than men to experience Chronic Widespread Pain (CWP) but are 10 times more likely to have 11 or more tender points. This is probably one of the reasons for a much higher prevalence rate in women (Williams & Clauw, 2009). The tender point diagnostic criteria is also hypothesized to have raised the frequency of distressed patients as population base studies find that CWP is less associated with distress comparing with the 11 tender point criteria (Williams & Clauw, 2009). The fact that most of the early studies took place in tertiary care centres may also have increased the perception that a high proportion of these patients had psychiatric comorbidity (Williams & Clauw, 2009). In 2010, the American College of Rheumatology suggested a new set of criteria based on a Widespread Pain Index and a Somatic Symptoms Scale, thus trying to improve diagnosis accuracy and acknowledging that most diagnosis were made without a proper physical examination to examine tender points (Frederick Wolfe et al., 2010). These new proposed criteria emphasize the importance of symptoms in other domains rather than pain, including cognitive and somatic symptoms.

The biopsychosocial model is crucial for understanding FM. Familial and genetic predisposition have been studied with an eight fold increased risk of developing FM in first degree relatives (Williams & Clauw, 2009) and several polymor-

phisms have been identified in genes related to monoamines transport (Williams & Clauw, 2009). Although still inconsistent and not clearly understood, dysfunction in hypothalamic-pituitary-adrenal axis and autonomic nervous system have been reported in FM patients. The presence of an environmental stressor/trigger, which can be a physical trauma, an infection, an hormonal alteration or a psychological/emotional stress, frequently one of interpersonal nature, is also known to be associated with FM (Williams & Clauw, 2009). All of these factors interact with psychological, cognitive and behavioural functioning to develop FM symptoms. To know these different etiological elements is essential to understanding FM and FM patients. We should also be aware of the relevance of central pain modulation to explain FM symptoms - central sensitization and defective pain modulation phenomena are crucial and seem to be altered by psychosocial factors (Bennett, 2016). The lack of diffuse noxious inhibitory control is linked to dysfunction in Serotonin and Noradrenergic activity while the endogenous opioidergic systems seem to remain intact or with increased activity - this could also explain why Serotonin Norepinephrine Reuptake Inhibitors (SNRI) can be helpful while Opiates don't.

The ultimate causes for the central sensitivity are still not known but factors such as genetic predisposition, deficiencies in neurotransmitter levels, biochemical changes in the body, endocrine dysfunction, psychological trauma and comorbid disorders seem to play a part in its development. The subjective experience of pain seems to correlate with one's cognitions, feelings and behaviours (Turk & Adams, 2016) and psychological factors such as catastrophizing and expectancy beliefs are thought to influence central sensitization. The fact that therapeutic interventions of a more global nature - CBT and central acting pharmacologic agents SNRI antidepressants - show better results than those interventions commonly used for pain secondary to damage or inflammation of peripheral tissues - Non-Steroidal Anti Inflammatory Drugs (NSAIDs), opioids, injections, surgery - highlights the relevance of central abnormalities in pain processing (Williams & Clauw, 2009).

The response to pain is influenced by the patients own characteristics, determining whether a patient can keep on doing daily tasks despite of the pain or avoiding them, anticipating exacerbation symptoms and assuming a "seek role". It has been stated that personality traits play a role in FM, pain perception and response (Hermoso et al., 2017). The response that these behaviours elicit in the patient's social



environment is crucial to modulate these thoughts and behaviours (Turk & Adams, 2016).

METHODS

This paper gathers information based on a search in the PubMed database from the last 6 years (2012-2018), in Portuguese or English, for clinical trials or reviews, on the terms "Fibromyalgia treatment".

RESULTS

OVERALL APPROACH

The evidence highlights the need for a multi step intervention on these subjects.

Being a medical condition we should start by an accurate diagnosis with clinical characterization of the symptoms and exclusion of other medical entities related to widespread pain and fatigue. Pain should be medically and pharmacologically addressed by the attending physician or a pain specialist – the evidence for symptom based analgesia goes beyond the scope of this paper.

A substantial proportion of these patients present with refractory or residual pain after these medical interventions. Every approach should begin with clear patient education on this disorder and the treatment goals. Exercise should also be considered as a first line intervention to be proposed for all patients.

Frequently these patients present co-morbid affective disorders and/or interpersonal conflicts which can benefit from a psychiatric intervention, both pharmacological and psychotherapeutic. Modern psychiatry has become somehow detached from pain as a mental state. The increasing importance of international classification systems for psychiatric entities and the intense search for a biological mechanism underlying pain has driven us away from the emotional, cognitive and psychosocial aspects of pain (González, 2017)

Traumatic experiences (physical and psychological) or significant life events should be searched for properly in order to better understand our patient and to explore a possible link with the symptoms presented through the body. Although it is not sufficient nor needed for FM to exist, a 97% increased risk for painful somatic syndromes in adulthood is linked to childhood abuse (González, 2017).

Psychotherapy should be provided, specially for those with psychiatric co-morbidity. Pharmacotherapy is largely used and many drugs have been studied in this field, the choice of which and when to use should be based on the clinical symptoms, response to other interventions and psychotherapy availability. Many other interventions have been studied as none of the above have had a substantial strength to respond to these patients needs.

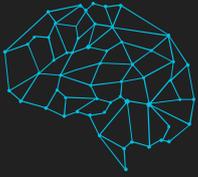
The connection established between the patient and its physician is crucial for treatment adherence, sense of patient's empowerment and clinical outcome. So it is important for physicians to be aware that this is a clinical valid medical problem and to validate patient's complaints while providing patient education on Fibromyalgia.

PATIENT EDUCATION

It is crucial to educate these patients on the nature of this disorder. Their continuous search for "something wrong" with them prevents them from being engaged in ameliorating their symptoms and increasing their functionality (Bennett, 2016). Explaining the biopsychosocial model for FM – the relevance of genetics and psychosocial factors contributing to predisposition, triggering and perpetuation of FM symptoms, opens the patient to a new approach on this disease (Macfarlane et al., 2017). Also, knowing the planned treatment strategy and the expected outcome is important and should be addressed early on.

EXERCISE

Exercise (aerobic and strengthening exercises such as walking or swimming) is the only strong for therapy based recommendation in European League Against Rheumatism guidelines (Macfarlane et al., 2017) as it reduces FM symptoms and improves physical functioning (Fernandes, Jennings, Nery Cabral, Pirozzi Buosi, & Natour, 2016). Exercise adherence seems to be related to self efficacy and belief about the benefit of the regime (Fernandes et al., 2016). Using Motivational Enhancement Therapy seems to improve pain, functional status and exercise engagement (Fernandes et al., 2016). A randomized control trial of seventy-five female patients showed no differences between swimming or walking on pain reduction, functional capacity and quality of life (Fernandes et al., 2016) with both interventions showing reduced pain, reduced analgesic usage and overall quality of life improvement (Fernandes et al., 2016). A recent Cochrane



revision on the available evidence favours aerobic exercise in improving Health-Related Quality of Life, physical function and pain intensity (Bidonde et al., 2017).

PSYCHOTHERAPY

According to the evidence gathered, **Cognitive Behavioural Therapy (CBT)** is presented as the most cost effective treatment for FM in adults - versus FDA approved pharmacotherapy (Luciano et al., 2014) but is not always satisfactory (Kathrin Bernardy, Füber, Köllner, & Häuser, 2010) and should be constructed over a biopsychosocial model. The patient, the disease and the environment must be taken into place in order to restructure unhealthy thinking and push towards behavioural changes for a better functioning (Turk & Adams, 2016). Removing myths about the disorder – “I am crazy” or “I caused this and I’m faking the symptoms for my own benefit” – are a very important part of this approach. Explaining that there is a difference between hurt (the pain the patient experiences chronically) and harm (the pain caused by an injury) can help the patient understand that, to some extent, he will have to live with the pain as our goal is to alleviate it and not to cure it.

Pain and sleep quality have a bidirectional link, so CBT interventions aiming to improve sleep can be beneficial for FM patients.

These patients frequently overestimate their capability to perform physical activity. By making them try exercise they can gain insight of this discrepancy and increase their exercise routines (Turk & Adams, 2016). Using CBT can help us focus on these gains rather than the disease and set realistic goals. Practical behavioural changes can help patients know how to better pace and increase activity.

Cognitive approaches on the role of stress on symptom development, improving communication with others and assertiveness training can be a part of CBT strategies on FM patients (Bennett, 2016). FM patients often show some resistance in acknowledging the link between stress and their physical symptoms. Working on gaining this insight, on the ability to change the modifiable stressors and to accept and cope with those which can't be altered is of great importance (Turk & Adams, 2016). Also, relaxation techniques seem to be beneficial as they improve patient's awareness of self control over pain (Turk & Adams, 2016).

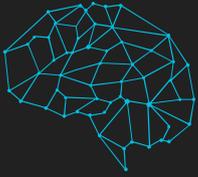
CBT is stated as a weak for on EULAR with studies showing reduced pain and disability with sustained long term results, although the quality of the individual trials was

generally considered poor (Macfarlane et al., 2017). CBT is especially relevant for those with mood disorders or poor coping strategies (Macfarlane et al., 2017) and it shows superior results in cognitive and affective domains. There is still conflicting evidence about it's efficacy in reducing pain with some studies supporting it (K. Bernardy, Klose, Welsch, & Häuser, 2018) while others state it does not help in this domain (Macfarlane et al., 2017).

Mindfulness Based Stress Reduction (MBSR) has growing evidence to support its use in these patients as it seems to improve symptom severity, perceived stress, depressive symptoms and sleep disturbance (Cash et al., 2015). So far it lacks evidence in improving pain, physical functioning and fatigue (Cash et al., 2015). Interestingly the improvement seems to be dependent of the time spent in house practicing rather than sessions attendance (Cash et al., 2015). It is hypothesized to work by improving the patients perceived control of the symptoms and increasing present-moment focus leading to lesser concerns about past stressors and future concerns over the disease (Cash et al., 2015).

Guided imagery (GI) is a psychophysiological process in which a person imagines and experiences, an internal reality in the absence of external stimuli. It can be used to alter one's physiological processes, mental states or behaviours. Previous studies of GI in FM patients show conflicting evidence to support its use. The most recent data (Verkaik 2013) shows there isn't an effect on pain intensity in patients with FM. EULAR recommends it as *weak for* because there is still a lack of better and bigger studies.

Acceptance and Commitment Therapy is being studied as a possible approach to ameliorate clinical outcomes in these patients. ACT is a CBT based technique, it aims to improve thoughts on how to accept the experience of pain and disability by means of greater psychological flexibility and cognitive *disfusion* (the patient learns to step back from thoughts). Some studies have tried to evaluate its efficacy in chronic pain (McCracken, Sato, & Taylor, 2013), although more robust evidence needs to be set, the Randomized Clinical Trials (RCTs) showed improvement in disability and Depression in these patients. Acceptance of pain and emotional functioning aren't clearly stated as improving with ACT as further studies need to address these domains (McCracken et al., 2013). Pain intensity and physical quality of life don't seem to be improved by these approach but pain related functioning can be addressed using ACT (Wicksell et al., 2013).



Brief psychodynamic psychotherapy failed to prove superiority versus treatment as usual (patient education and pharmacotherapy) in patients with FM and Depression (Scheidt et al., 2013) but some studies support **Brief Interpersonal Psychotherapy** for multisomatofom conditions (Sattel et al., 2012)

As previously discussed in this paper, in clinical settings it seems rather important the type and quality of the doctor (or therapist) / patient relationship for a good outcome so this is something every physician should be aware when treating these patients.

PHARMACOTHERAPY

Being a relatively new field of studies and having unsatisfying response rates, the recommendations of different entities show some differences. Food and Drug Administration (FDA) approves the use of **pregabalin** (2007), **duloxetine** (2009) and **milnacipran** (2009); **Sodium Oxybate** was not approved as it raised concern over the potential for abuse and misuse. European League Against Rheumatism (EULAR) supports the use of **pregabalin, milnacipran, amitriptyline, cyclobenzaprine** and **tramadol**. The European Medicine Agency (EMA) has not approved any drug for this purpose, Health Canada has approved **duloxetine** and **pregabalin** and the Department of Health of the Australian Government has only approved **milnacipran**.

Although it's still not clear how much do antidepressants help these patients, the 2012 Canadian Guidelines include all antidepressants as potential drugs for the management of Fibromyalgia.

Two basic principals should base pharmacotherapy in these patients: start on low doses and always reassess the need for continuation (Macfarlane et al., 2017) and also separate treatment for continuous pain, based on pain modulators, and incidental pain which can be addressed intermittently with classical analgesics (Macfarlane et al., 2017). FM diagnosed patients receive a greater number of different drugs and for a longer period of time comparing to FM fulfilling criteria patients who haven't received this diagnosis before (Rivera & Vallejo, 2016). Also, a significant positive correlation was found between the number of somatic symptoms and the number of drugs consumed (Rivera & Vallejo, 2016).

Pregabalin improves pain, has only a very small effect on fatigue (Macfarlane et al., 2017), a small effect on sleep disturbances (Macfarlane et al., 2017) but has failed to

improve Depression (Calandre, Rico-Villademoros, & Slim, 2017). Although stated by EULAR as a *weak for* there is growing evidence to support its use in high dosages (Davis et al., 2018).

Amitriptyline improves pain, fatigue and sleep disturbances but has failed to improve depression (probably due to low doses used in clinical trials) (Calandre et al., 2017) It is considered by EULAR as *Weak for*, at low dose (Macfarlane et al., 2017).

Duloxetine improves pain, sleep and depression but with no strong action in fatigue (Calandre et al., 2017). Dosages of 20-30 mg/day seem to have no significant effect, but there were no differences between doses of 60 to 120 mg/day, suggesting optimal dosage around 60 mg/day (Macfarlane et al., 2017). Considered *weak for* on EULAR Guidelines.

Milnacipran acts on pain but shows little to no effect on depression and sleep disturbances. It may decrease frequency of pain up to 30% and patients show an overall sense of improvement (Welsch, Üçeyler, Klose, Walitt, & Häuser, 2018). It improves fatigue (better than duloxetine) although with a nonsubstantial effect size (Calandre et al., 2017). Also stated as *weak for* on EULAR.

SSRIs on FM patients improves pain and depression with a small effect size, they improve sleep with a nonsubstantial effect size and have no effect on fatigue (Macfarlane et al., 2017). A recent Cochrane review showed they are not better than placebo in FM patients (Ablin & Häuser, 2016) being a *weak against* in EULAR Guidelines.

IMAO were evaluated as *weak against* with non convincing efficacy data and life threatening interactions being reported (Macfarlane et al., 2017).

Sodium oxybate is not recommend and even rejected by regulatory agencies (FDA and EMA) despite some initial promising results in FM.

Cyclobenzaprine improves sleep disturbances and pain but not fatigue or depression (Welsch, Üçeyler, Klose, Walitt, & Häuser, 2018) while showing a high rate of side effects and dropouts (Macfarlane et al., 2017).

Tramadol, as well as tramadol+acetaminofeno, acts only on pain – effects on sleep, depression and fatigue were not expected and therefore not studied (Calandre et al., 2017). *Weak for* on EULAR.

NSAID (nonsteroidal anti-inflammatory drugs) were considered *weak against* as there is no evidence of their benefit in these patients (Macfarlane et al., 2017).



Despite not finding any reviews, the EULAR committee stated a *strong against* evaluation on the use of **strong opioids** and **corticosteroids** in FM patients for the lack of evidence and the known side effects/risks of these drugs (Macfarlane et al., 2017).

Growth hormone was evaluated as strong against in EULAR recommendations based on concerns on safety and scarce effect on pain. A small study with 12 patients showed decreased muscle pain, stiffness and fatigue and increased libido using **transdermal testosterone gel** (White et al., 2015) but further studies need to take place to strengthen these data.

Despite improvement in sleep and fatigue, **benzodiazepines and Z-drugs** (zolpidem and zopiclone) are not recommended as they failed to improve other FM symptoms and raise concerns for their tolerance and abuse potential (Ablin & Häuser, 2016).

Many other drugs have had at least one Randomized Clinical Trial: **Gabapentin, Trazodone, Tropicsetron** and **Dolasetron** (5HT₃ antagonists), **Quetiapine, Nabilone** (synthetic cannabinoid agonist of the CB₁ receptor), **Naltrexone** (opioid antagonist), **Pramipexole** (a D₃/D₃ dopaminergic agonist), **Moclobemide** and **Pirlindole** (two reversible MAO-A antagonist), **Memantine** (an NMDA receptor antagonist) and **Melatonin** (the pineal hormone). From all of the above, only Gabapentin showed some efficacy for the management of Fibromyalgia (Calandre et al., 2017), but, despite being similar to **Pregabalin, Gabapentin** hasn't been studied so extensively and has no formal indication for FM treatment to this date.

There have been few studies trying to analyse effects on cognitive impairment in FM – so far, **Milnacipran** shows a significant but nonsubstantial effect size and **Duloxetine** a small effect size (Calandre et al., 2017).

If we consider FM as a multidomain condition (pain, fatigue, sleep disturbance, cognitive impairment) we can see that none of the approved drugs strongly addresses all of them, with **Amitriptyline** being the broader one. This raises the possibility of a drug combination but there are still few trials on this option.

Many of the studies in this field try to establish evidence based pharmacologic possibilities for a common and difficult to treat condition. There is very scarce evidence comparing the effects of these drugs. **Duloxetine** seems to be superior to **Pregabalin** in amelioration of pain but **Pregabalin** was better than **Duloxetine** in addressing sleep disturbances (Calandre et al., 2017).

The drug selection should be based on the most disturbing symptom for the individual patient – **Duloxetine** for depression; **Pregabalin, Amitriptyline** or **Cyclobenzaprine** for sleep disturbances and **Milnacipran** or **Amitriptyline** for fatigue (Calandre et al., 2017).

OTHER INTERVENTIONS

Multimodal interventions should be considered for those with severe disability.

Combining programs with exercise, education and CBT approaches seem to be beneficial for patients (Martins et al., 2014) with longer interventions showing better outcomes in reducing pain (Saral, Sindel, Esmaeilzadeh, Sertel-Berk, & Oral, 2016). Recommend by EULAR as a *weak for*.

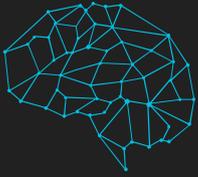
Occipital nerve stimulation is not recommended at the time because of potential complications, invasiveness and cost of the procedure despite some reports of pain reduction (Ablin & Häuser, 2016), improved sleep, mood, fatigue and quality of life as it can alter pain processing (Plazier, Ost, Stassijns, De Ridder, & Vanneste, 2015).

Lidocaine infusion shows controversial evidence with trials lacking strength to support its use in FM patients. Although it seems to diminish pain, it is an expensive and time consuming procedure which needs to take place in a clinic with resuscitation and hemodynamic monitoring capacities (Ablin & Häuser, 2016).

Vitamin D supplementation is being studied enthusiastically in many fields of Medicine. Some studies seem to show it improves pain in FM patients but the results are still short and too controversial to recommend its use (Wepner et al., 2014).

Hyperbaric oxygen therapy seems to have an anti-nociceptive effect via activation of endogenous opioids and inhibition of the inflammation response, showing promising results in FM patients, but carries several risks of oxygen toxicity and other side effects so further studies are needed before it can become a recommended procedure in these patients (Ablin & Häuser, 2016).

Transcranial Magnetic Stimulation (TMS) may modulate mood and show overall improvement in FM patients despite only marginal effects on pain (Ablin & Häuser, 2016), however, bigger and better studies still need to take place to establish TMS as a therapeutic option. **Transcranial Direct Currents Stimulation (TDCS)** over the primary motor cortex seem to improve pain in FM patients but there are still few studies on this subject to support its generalized use.



Acupuncture is stated by EULAR has having a *weak for* recommendation based on several studies showing improvement in pain reduction although also stating issues regarding the lack of understanding of its active mechanism and lack of consistency when compared with sham acupuncture (Goldie & Hogg, 2016).

Biofeedback is a *weak against* on EULAR with some results showing pain intensity reductions but lacking good quality studies to support its use (Ablin & Häuser, 2016).

Hydrotherapy/spa therapy has shown improvement in pain maintained in the long term therefore being recommended as a *weak for* on EULAR ((Macfarlane et al., 2017).

Hypnotherapy shows controversial results between trials which is why it is a *weak against* for EULAR. **Meditative movement** (qigong, yoga or a combination) is still being studied but seems to bring benefits in sleep and fatigue being recommend by EULAR as a *weak for*. In the same manner, Tai Ji Quan has some preliminary promising evidence improving fatigue, quality of life, disability, pain, sleep and anxiety but needs stronger studies to support it (Maddali Bongji et al., 2016).

CONCLUSIONS AND DISCUSSION

Fibromyalgia is a complex entity sampling the interesting field of psychosomatics and bringing psychological and somatic pain together. Its understanding requires a vision of the patient as a whole in order to plan a multimodal and stepwise treatment to ameliorate the patient's symptoms and improve its functioning.

Patient education on the disease and its treatment should be the starting point. CBT based interventions (classical or more recent therapies) can help these patients in the affective domains of the disease but also in an overall manner in improving quality of life.

Many pharmacologic strategies have been studied. Some drugs have been approved to be used in these patients – Milnacipran, Duloxetine, Amytriptiline, Pregabaline. Their use should be tailored to patients needs and tolerance.

To these date, the interventions known show limited response so these patients should be treated by psychiatrists with experience in Psychosomatics. The use of multimodal interventions has been proved to be beneficial, so multidisciplinary teams are of major importance in this field. Being the basis of psychiatric practice, doctor-patient therapeutic relationship is critical in any intervention for Fibromyalgia

patients as these interventions may be frustrating and tense.

In the years to come more and better clinical studies are expected to bring better resources in the psychological and also in the pharmacological intervention.

DECLARATION OF AUTHORSHIP, GOOD PRACTICES AND ASSIGNMENT OF RIGHTS

This study had no financing of any kind nor have the researchers involved in it. Author Mário Santos was responsible for data gathering and writing of the essay while author Lúcia Ribeiro was responsible for editing and reviewing its content. The authors declare the absence of potential conflicts of interest.

Declaration of authorship, good practices and assignment of rights

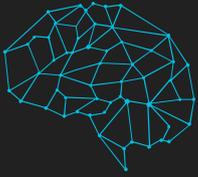
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REFERENCES

1. Ablin, J. N., & Häuser, W. (2016). Fibromyalgia syndrome: Novel therapeutic targets. *Pain Management*, 6(4), 371–381. <https://doi.org/10.2217/pmt-2016-0007>
2. Bennett, R. M. (2016). Pain management in fibromyalgia. *Pain Management*, 6(4), 313–316. <https://doi.org/10.2217/pmt-2016-0026>
3. Bernardy, K., Klose, P., Welsch, P., & Häuser, W. (2018). Efficacy, acceptability and safety of cognitive behavioural therapies in fibromyalgia syndrome—A systematic review and meta-analysis of randomized controlled trials. *European Journal of Pain* (London, England), 22(2), 242–260. <https://doi.org/10.1002/ejp.1121>
4. Bernardy, Kathrin, Füßer, N., Köllner, V., & Häuser, W. (2010). Efficacy of cognitive-behavioral therapies in fibromyalgia syndrome—A systematic review and metaanalysis of randomized controlled trials. *The Journal of Rheumatology*, 37(10), 1991–2005. <https://doi.org/10.3899/jrheum.100104>
5. Bidonde, J., Busch, A. J., Schachter, C. L., Overend, T. J., Kim, S. Y., Góes, S. M., ... Foulds, H. J. (2017). Aerobic exercise training for adults with fibromyalgia. *The Cochrane Database of Systematic Reviews*, 2017(6). <https://doi.org/10.1002/14651858.CD012700>
6. Bourgault, P., Lacasse, A., Marchand, S., Courtemanche-Harel, R., Charest, J., Gaumond, I., ... Choinière, M. (2015). Multicomponent Interdisciplinary Group



- Intervention for Self-Management of Fibromyalgia: A Mixed-Methods Randomized Controlled Trial. *PLOS ONE*, 10(5), e0126324. <https://doi.org/10.1371/journal.pone.0126324>
7. Calandre, E. P., Rico-Villademoros, F., & Slim, M. (2017). Pharmacological treatment of fibromyalgia: Is the glass half empty or half full? *Pain Management*, 7(1), 5–10. <https://doi.org/10.2217/pmt-2016-0044>
 8. Cash, E., Salmon, P., Weissbecker, I., Rebholz, W. N., Bayley-Veloso, R., Zimmaro, L. A., ... Sefhton, S. E. (2015). Mindfulness Meditation Alleviates Fibromyalgia Symptoms in Women: Results of a Randomized Clinical Trial. *Annals of Behavioral Medicine*, 49(3), 319–330. <https://doi.org/10.1007/s12160-014-9665-0>
 9. Davis, F., Gostine, M., Roberts, B. A., Risko, R., Cappelleri, J. C., & Sadosky, A. (2018). Interpreting the Effectiveness of Opioids and Pregabalin for Pain Severity, Pain Interference, and Fatigue in Fibromyalgia Patients. *Pain Practice: The Official Journal of World Institute of Pain*, 18(5), 611–624. <https://doi.org/10.1111/papr.12651>
 10. Fernandes, G., Jennings, F., Nery Cabral, M. V., Pirozzi Buosi, A. L., & Natour, J. (2016). Swimming Improves Pain and Functional Capacity of Patients With Fibromyalgia: A Randomized Controlled Trial. *Archives of Physical Medicine and Rehabilitation*, 97(8), 1269–1275. <https://doi.org/10.1016/j.apmr.2016.01.026>
 11. Goldie, L., & Hogg, K. (2016). BET 2: Acupuncture and fibromyalgia: Table 2. *Emergency Medicine Journal*, 33(10), 743–744. <https://doi.org/10.1136/emermed-2016-206204.2>
 12. González, P. A. M. (2017). PSQUIATRÍA Y DOLOR CRÓNICO. 11.
 13. Hermoso, B., García-Fontanals, A., García-Blanco, S., García-Fructuoso, F., Gutiérrez, T., López-Ruiz, M., ... Deus, J. (2017). DE DOLOR EN FIBROMIALGIA: UN ESTUDIO PILOTO DE CASOS Y CONTROLES. 11.
 14. Luciano, J. V., D'Amico, F., Cerdà-Lafont, M., Peñarrubia-María, M. T., Knapp, M., Cuesta-Vargas, A. I., ... García-Campayo, J. (2014). Cost-utility of cognitive behavioral therapy versus U.S. Food and Drug Administration recommended drugs and usual care in the treatment of patients with fibromyalgia: An economic evaluation alongside a 6-month randomized controlled trial. *Arthritis Research & Therapy*, 16(5). <https://doi.org/10.1186/s13075-014-0451-y>
 15. Macfarlane, G. J., Kronisch, C., Dean, L. E., Atzeni, F., Häuser, W., Fluß, E., ... Jones, G. T. (2017). EULAR revised recommendations for the management of fibromyalgia. *Annals of the Rheumatic Diseases*, 76(2), 318–328. <https://doi.org/10.1136/annrheumdis-2016-209724>
 16. Maddali Bongio, S., Paoletti, G., Calà, M., Del Rosso, A., El Aoufy, K., & Mikhaylova, S. (2016). Efficacy of rehabilitation with Tai Ji Quan in an Italian cohort of patients with Fibromyalgia Syndrome. *Complementary Therapies in Clinical Practice*, 24, 109–115. <https://doi.org/10.1016/j.ctcp.2016.05.010>
 17. Martins, M. R. I., Gritti, C. C., Junior, R. dos S., Araújo, M. C. L. de, Dias, L. C., Foss, M. H. D. A., ... Rocha, C. E. D. A. (2014). Randomized controlled trial of a therapeutic intervention group in patients with fibromyalgia syndrome. *Revista Brasileira de Reumatologia (English Edition)*, 54(3), 179–184. <https://doi.org/10.1016/j.rbre.2013.10.002>
 18. McCracken, L. M., Sato, A., & Taylor, G. J. (2013). A Trial of a Brief Group-Based Form of Acceptance and Commitment Therapy (ACT) for Chronic Pain in General Practice: Pilot Outcome and Process Results. *The Journal of Pain*, 14(11), 1398–1406. <https://doi.org/10.1016/j.jpain.2013.06.011>
 19. Plazier, M., Ost, J., Stassjins, G., De Ridder, D., & Vanneste, S. (2015). C2 Nerve Field Stimulation for the Treatment of Fibromyalgia: A Prospective, Double-blind, Randomized, Controlled Cross-over Study. *Brain Stimulation*, 8(4), 751–757. <https://doi.org/10.1016/j.brs.2015.03.002>
 20. Rivera, J., & Vallejo, M. A. (2016). Fibromyalgia is associated to receiving chronic medications beyond appropriateness: A cross-sectional study. *Rheumatology International*, 36(12), 1691–1699. <https://doi.org/10.1007/s00296-016-3568-2>
 21. Saral, I., Sindel, D., Esmaeilzadeh, S., Sertel-Berk, H. O., & Oral, A. (2016). The effects of long- and short-term interdisciplinary treatment approaches in women with fibromyalgia: A randomized controlled trial. *Rheumatology International*, 36(10), 1379–1389. <https://doi.org/10.1007/s00296-016-3473-8>
 22. Sattel, H., Lahmann, C., Gündel, H., Guthrie, E., Kruse, J., Noll-Hussong, M., ... Henningsen, P. (2012). Brief psychodynamic interpersonal psychotherapy for patients with multisomatoform disorder: Randomised controlled trial. *The British Journal of Psychiatry: The Journal of Mental Science*, 200(1), 60–67. <https://doi.org/10.1192/bjp.bp.111.093526>
 23. Scheidt, C. E., Waller, E., Endorf, K., Schmidt, S., König, R., Zeeck, A., ... Lacour, M. (2013). Is brief psychodynamic psychotherapy in primary fibromyalgia syndrome with concurrent depression an effective treatment? A randomized controlled trial. *General Hospital Psychiatry*, 35(2), 160–167. <https://doi.org/10.1016/j.genhosppsych.2012.10.013>
 24. Turk, D. C., & Adams, L. M. (2016). Using a biopsychosocial perspective in the treatment of fibromyalgia patients. *Pain Management*, 6(4), 357–369. <https://doi.org/10.2217/pmt-2016-0003>
 25. Welsch, P., Üçeyler, N., Klose, P., Walitt, B., & Häuser, W. (2018). Serotonin and noradrenaline reuptake inhibitors (SNRIs) for fibromyalgia. *The Cochrane Database of Systematic Reviews*, 2, CD010292. <https://doi.org/10.1002/14651858.CD010292.pub2>
 26. Wepner, F., Scheuer, R., Schuetz-Wieser, B., Machacek, P., Pieler-Bruha, E., Cross, H. S., ... Friedrich, M. (2014). Effects of vitamin D on patients with fibromyalgia syndrome: A randomized placebo-controlled trial. *Pain*, 155(2), 261–268. <https://doi.org/10.1016/j.pain.2013.10.002>
 27. White, H. D., Brown, L. A. J., Gyurik, R. J., Manganiello, P. D., Robinson, T. D., Hallock, L. S., ... Yeo, K.-T. J. (2015). Treatment of pain in fibromyalgia patients with testosterone gel: Pharmacokinetics and clinical response. *International Immunopharmacology*, 27(2), 249–256. <https://doi.org/10.1016/j.intimp.2015.05.016>
 28. Wicksell, R. K., Kemani, M., Jensen, K., Kosek, E., Kadetoff, D., Sorjonen, K., ... Olsson, G. L. (2013). Acceptance and commitment therapy for fibromyalgia: A randomized controlled trial: ACT for fibromyalgia: A randomized controlled trial. *European Journal of Pain*, 17(4), 599–611. <https://doi.org/10.1002/j.1532-2149.2012.00224.x>
 29. Williams, D. A., & Clauw, D. J. (2009). Understanding Fibromyalgia: Lessons from the Broader Pain Research Community. *The Journal of Pain*, 10(8), 777–791. <https://doi.org/10.1016/j.jpain.2009.06.001>
 30. Wolfe, F., Smythe, H. A., Yunus, M. B., Bennett, R. M., Bombardier, C., Goldenberg, D. L., ... Clark, P. (1990). The American College of Rheumatology 1990 Criteria for the Classification of Fibromyalgia. Report of the Multicenter Criteria Committee. *Arthritis and Rheumatism*, 33(2), 160–172.
 31. Wolfe, Frederick, Clauw, D. J., Fitzcharles, M.-A., Goldenberg, D. L., Katz, R. S., Mease, P., ... Yunus, M. B. (2010). The American College of Rheumatology Preliminary Diagnostic Criteria for Fibromyalgia and Measurement of Symptom Severity. *Arthritis Care & Research*, 62(5), 600–610. <https://doi.org/10.1002/acr.20140>