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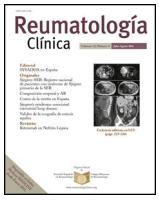

Special Article

Recommendations by the Spanish Society of Rheumatology on Fibromyalgia. Part 1: Diagnosis and treatment☆

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ABSTRACT

Objective: To prevent the impairment of fibromyalgia patients due to harmful actions in daily clinical practice that are potentially avoidable.
Methods: A multidisciplinary team identified the main areas of interest and carried out an analysis of scientific evidence and established recommendations based on the evidence and "formal evaluation" or "reasoned judgment" qualitative analysis techniques.
Results: A total of 39 recommendations address diagnosis, unsafe or ineffective treatment interventions and patient and healthcare workers' education. This part I shows the first 27 recommendations on the first 2 areas.
Conclusions: Establishing a diagnosis improves the patient's coping with the disease and reduces health-care costs. NSAIDs, strong opioids and benzodiazepines should be avoided due to side effects. There is no good evidence to justify the association of several drugs. There is also no good evidence to recommend any complementary medicine. Surgeries show a greater number of complications and a lower degree of patient satisfaction and therefore should be avoided if the surgical indication is not clearly established.

Recomendaciones SER sobre el manejo de los pacientes con fibromialgia. Parte I: diagnóstico y tratamiento

Palabras clave:
Fibromialgia
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RESUMEN

Objetivo: Evitar el deterioro de los pacientes con fibromialgia por actuaciones perjudiciales en la práctica clínica potencialmente evitables.

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Métodos: Un panel multidisciplinar de expertos identificó las áreas claves, analizó la evidencia científica y formuló las recomendaciones a partir de esta evidencia y de técnicas cualitativas de "evaluación formal" o "juicio razonado".
Resultados: Se han elaborado 39 recomendaciones sobre diagnóstico, tratamientos no eficaces ni seguros, educación del paciente y formación del profesional. En esta parte I se reflejan las 27 primeras, referidas a las 2 primeras áreas.
Conclusiones: Establecer el diagnóstico mejora el afrontamiento del paciente y reduce los costes sanitarios. Se deben evitar AINE, opioides mayores y benzodiacepinas por los efectos adversos. No existe una evidencia sólida que justifique la asociación de fármacos. Tampoco existe una buena evidencia para recomendar ningún tipo de terapia complementaria. Las cirugías muestran más complicaciones y un grado de satisfacción menor por el paciente por lo que deben evitarse si la indicación no está claramente establecida.

Introduction

Fibromyalgia (FM) is a disease characterised by generalised chronic pain that the patient locates in the musculoskeletal system. There are also other associated symptoms such as sleep disorders, fatigue disproportionate to activity performed, cognitive impairment, anxiety, or depression, which frequently accompany this disease and make it one with the poorest quality of life as perceived by the patient[1].

The concept of FM has greatly changed in recent decades, due to recent findings of several abnormalities in nervous system function at the level of cellular activation mechanisms, nerve pathway disturbances, cytokines, and neurotransmitters in these patients[2]. Once considered a medically unexplainable disease, knowledge about the pathophysiological and organic basis of FM is growing.

The prevalence of FM in our population is high, affecting 2.45% of the adult population, especially middle-aged women[3]. This high prevalence make the condition a major health problem, together with the fact that FM entails significant associated health costs in terms of direct health resource consumption and indirect costs from lost working days[4].

We now know several obstacles that hinder treatment and cloud the prognosis of the disease. The most obvious is how to make the diagnosis, which remains controversial among medical staff due, among other reasons, to the lack of adequate training for professionals in safely and confidently addressing the needs of this disease and its sufferers.

Moreover, there is no curative treatment for FM, and therefore optimal use must be made of all pharmacological and other measures to achieve the best possible control of the disease. In this sense, and because there are no curative treatments, a multitude of complementary therapies have proliferated around FM, many of which have no solid basis for their application in treating this disease. This situation can disorientate patients, who often do not know how to distinguish between the various therapies proposed to them, and this results in an increased risk of side effects and adverse economic consequences.

From the perspective of evidence-based medicine, several scientific societies have already made some recommendations on the treatment and management of FM with the aim of improving the situation of patients; one of the most recent is that published by EULAR[5]. A detailed comparative study of the main guidelines[6] shows that they generally coincide in their recommendations in the aspects for which there is sufficient scientific evidence, such as the use of amitriptyline, pregabalin, duloxetine, aerobic exercise, cognitive behavioural therapies and multidisciplinary therapies, all of which have the highest grades of recommendation.

However, certain actions are still often taking place in the FM patient's environment that need to be detected; these being the main reason it has not been possible to achieve the best possible situation for these patients.

SER's aim in undertaking this systematic literature review is to identify common actions in clinical practice that may be detrimental to the FM patient and to establish a series of recommendations to prevent these patients' situation from deteriorating.

Methodology

Design

We used a qualitative synthesis of the scientific evidence and consensus techniques that captures the agreement of experts based on their clinical experience and the scientific evidence[7].

Phases of the process

We took the following steps in drafting this document:

1 *Creation of the working group*. A multidisciplinary working group was formed consisting of 5 rheumatologists who are members of the SER, a family doctor, a psychologist, a psychiatrist, a nurse, and a patient with FM. The rheumatologists were chosen through an open call to all SER members. The Committee on Clinical Practice Guidelines (CPG) and SER Recommendations assessed the curriculum vitae of all applicants according to objective criteria of their contribution to the knowledge of FM, mainly through participation in publications in journals of impact in the last 5 years.

Each of the participants was endorsed by their society to participate in this document. The clinical and methodological aspects were coordinated, respectively, by one of the rheumatologists, as principal investigator (PI), and a methodology specialist, who is a technician from the Research Unit (RU) of the SER.

2 *Identification of key areas*. All members of the working group were involved in structuring the document and establishing the contents and key aspects. First, the clinical research questions that could have the most impact in providing information on the management of FM were identified. It was then determined which of these needed to be answered by formulating a patient, intervention, comparison, outcome (PICO) question. The setting, perspective, intervention, comparison, evaluation (SPICE) format was also used to identify qualitative evidence to provide information from the "patient perspective". The methodology to follow in the process of drafting the recommendations was also defined.
3 *Literature search*. A literature search was carried out in the following databases: Pubmed (MEDLINE), EMBASE (Elsevier), Cochrane

Library (Wiley Online), Cinhal (EBSCOhost) and PsycInfo. The searches were closed with dates of July 2019. A later search update was carried out in April 2020. The process was completed with a manual search of references and conference posters and abstracts considered of interest by the reviewers and experts.

4 *Analysis and synthesis of the scientific evidence*. Several rheumatologists from the SER evidence review group and methodologists from the RU were in charge of systematically reviewing the available scientific evidence. The overall level of scientific evidence was assessed using the Scottish Intercollegiate Guidelines Network levels of evidence[7] for the PICO questions (Appendix B Annex 1, Supplementary data) and the GRADE-CERQual (Confidence in the Evidence from Reviews of Qualitative research)[8] approach for qualitative evidence from the SPICE questions (Appendix B Annex 2, Supplementary data). *Formulation of the recommendations*. After the critical reading, the PI and members of the expert group proceeded to formulate specific recommendations based on the scientific evidence. In the case of quantitative evidence, this was based on "formal evaluation" or "reasoned judgement", summarising the evidence for each of the clinical questions beforehand. The quality, quantity and consistency of the scientific evidence, the generality of the results, their applicability and their clinical impact were also considered. The Scottish Intercollegiate Guidelines Network system[7] (Appendix Annex 1, Supplementary data) was used to grade the recommendations. Again, the GRADE-CERQual[8] approach was used for the evidence from qualitative research (Appendix B Annex 2, Supplementary data). The recommendations are divided into four main areas: diagnosis and prognosis of FM, ineffective and unsafe therapeutic interventions, FM patient education and information, and training of FM professionals.

5 *External review*. At the end of the previous phase, a final draft of the document was prepared and sent for independent external review to professionals selected for their knowledge of FM to increase the external validity of the document and ensure the accuracy of the recommendations.

6 *Public exposure*. This draft was then put through a process of public exposure to SER members and different interest groups (pharmaceutical industry, other scientific societies, and patient associations) to gather their assessment and scientific argumentation of the methodology or recommendations.

7 *Scientific societies*. The scientific societies involved in drafting this guideline, represented by members of the drafting group, are the Spanish Society of Rheumatology (SER), the Spanish Society of Primary Care Physicians (SEMERGEN), the Spanish Society of Clinical and Health Psychology (SEPCyS), the General Council of Official Nursing Associations of Spain (CGE), and the Spanish Society of Fibromyalgia and Chronic Fatigue (SEFIFAC).

Structure

The document includes the recommendations made, subdivided into the different areas mentioned above.

Additional information

The complete recommendations document and patient information is available on the SER website.

Results

The recommendations total 39 and address four main areas: diagnosis and prognosis, ineffective and unsafe therapeutic interventions, patient education and professional training. This document presents the first 27, referring to the areas of diagnosis and pharmacological, complementary and alternative, or surgical interventions that have not shown efficacy/effectiveness or safety (Table 1).

Diagnosis and prognosis of FM

Does a diagnosis improve the prognosis in people with suspected fibromyalgia?

Recommendation 1: It is recommended that clinicians make a diagnosis of fibromyalgia in all patients they attend with chronic pain associated with other manifestations suggestive of fibromyalgia (Recommendation grade D).

Recommendation 2: It is also recommended that a diagnosis of fibromyalgia be made in all patients who meet ACR 1990/2010 criteria, to reduce hospital admissions, medical visits, referrals to rheumatology, use of NSAIDs and other non-indicated drugs, and unnecessary diagnostic tests (Recommendation grade √).

Recommendation 3: A diagnosis of fibromyalgia should not be avoided on the grounds that this worsens the clinical situation of patients in the long term (Recommendation grade D).

Recommendation 4: The patient's concerns and expectations in relation to the disease should be analysed with them, with the aim of improving their quality of life, mood, legitimising the symptoms they present, to achieve greater self-esteem and self-confidence in the working and socio-familial environment; and to correct misconceptions to prevent them fearing that they are suffering from another type of disease. (Strong recommendation in favour).

Recommendation 5: Clinicians should bear in mind that because a patient has been diagnosed with fibromyalgia does not necessarily mean that every new symptom they experience should be considered part of fibromyalgia (Strong recommendation in favour).

The diagnosis of FM remains controversial. For some authors[9], patients with FM are not helped by the diagnosis, as they can become candidates for "victimisation". According to these authors, most symptoms remain stable over time, pain increases and some aspects of quality of life improve, suggesting that patients cope better with symptoms without the need for a diagnosis.

For other authors[10], people diagnosed with FM enter the health system and easily become victims of medical iatrogenesis.

FM is the main cause of chronic generalised pain, and its prevalence is more than 12% of all consultations in rheumatology clinics[11]. The rate in our population is 2.45%[3], and it is the second most frequent diagnosis after low back pain and degenerative pathology, depending on the patient's age[12].

Given the high prevalence of the disease, it is important to know whether making the diagnosis has any negative effects or, rather, helps to improve quality of life and reduce the overall impact on the patient and the social and healthcare setting.

The scientific evidence comes from studies with two types of design. Seven quantitative studies (experimental, quasi-experimental and descriptive)[13–19] were identified of the effect of the diagnosis as an intervention and 12 qualitative studies (interviews and focus groups with patients)[20–31] that investigate the impact of the diagnosis from the perspective of the patients themselves. Finally, we identified studies that do not meet the inclusion criteria, but may provide additional information on other aspects of the diagnosis[32–34].

The results obtained in these studies address four different areas: effect of the diagnosis on health status; use of health resources and costs; impact on quality of life; and health relationships. Full information on the results obtained from the evidence review is available on the SER website.

The different studies show a high degree of consistency as to the benefits of establishing the diagnosis of FM in relation to most of the variables analysed.

Table 1
SER recommendations on the management of patients with fibromyalgia (part I).

	GR
Diagnosis and prognosis of FM	
Recommendation 1: It is recommended that clinicians make a diagnosis of fibromyalgia in all patients they attend with chronic pain associated with other manifestations suggestive of fibromyalgia.	D
Recommendation 2: It is also recommended that a diagnosis of fibromyalgia be made in all patients who meet ACR 1990/2010 criteria, to reduce hospital admissions, medical visits, referrals to rheumatology, use of NSAIDs and other non-prescribed drugs, and unnecessary diagnostic tests.	√
Recommendation 3: A diagnosis of fibromyalgia should not be avoided on the grounds that it will worsen the patients' clinical situation in the long term.	*D*
Recommendation 4: The patient's concerns and expectations in relation to the disease should be analysed with them, with the aim of improving their quality of life, mood, legitimising the symptoms they present, to achieve greater self-esteem and self-confidence in the working and socio-familial environment; and to correct misconceptions to prevent them fearing that they are suffering from another type of disease.	*Strong*
Recommendation 5: Clinicians should bear in mind that because a patient has been diagnosed with fibromyalgia does not necessarily mean that every new symptom they experience should be considered part of fibromyalgia.	*Strong*
Therapeutic interventions that are neither effective nor safe	
Pharmacological treatment	
Recommendation 6: There are insufficient studies to recommend the use of non-steroidal anti-inflammatory drugs (NSAIDs) for the treatment of pain in adult patients with fibromyalgia.	*A*
Recommendation 7: the drafting group does not recommend the use of major opioids for the treatment of pain in patients with fibromyalgia, due to insufficient evidence of their effectiveness and possible risk of adverse effects.	√
Recommendation 8: no pharmacological combination can be recommended or discouraged in the treatment of adult patients with fibromyalgia, as there is insufficient evidence on their efficacy and safety.	*C*
Recommendation 9: The use of anticonvulsants such as lacosamide or lamotrigine to reduce pain is not recommended due to lack of efficacy.	B
There is no evidence of the effectiveness of other antiepileptic drugs such as carbamazepine, clonazepam, phenytoin or valproate, or the existing evidence on their effectiveness is insufficient to make a recommendation for or against.	√
Recommendation 10: The drafting group does not recommend chronic use of benzodiazepines or z-drugs in patients with fibromyalgia due to a lack of evidence on their effectiveness and the possible risk of addiction and other adverse effects.	√
Complementary alternative medicine (CAM)	
Recommendation 11: although statistically significant results on the efficacy of transcranial electrical stimulation or transcranial magnetic stimulation have been observed in some studies, the drafting group considers that as these techniques are of limited clinical relevance, they cannot be recommended in the treatment of patients with fibromyalgia.	B
Recommendation 12: There is insufficient evidence to recommend the use of TENS in the treatment of fibromyalgia until trials of methodological quality demonstrate its efficacy.	B
Recommendation 13: More studies are needed that assess the efficacy of cannabinoids (nabilone) in improving pain and quality of life to recommend their use in patients with fibromyalgia.	√
Recommendation 14: Although in some studies it appears that nabilone may be more effective than amitriptyline in improving sleep quality, it is not recommended for use in patients with fibromyalgia due to a higher frequency of adverse effects	√
Recommendation 15: Homeopathy, chiropractic, osteopathy, and manipulations are not recommended in the treatment of fibromyalgia, due to the lack of studies confirming the efficacy and safety of these techniques	√
Recommendation 16: There is insufficient evidence to recommend pulsed electromagnetic therapy in the treatment of fibromyalgia	B
Recommendation 17: there is insufficient evidence to recommend relaxation monotherapy in the treatment of fibromyalgia, due to the limited benefit obtained in the improvement of pain and quality of life	D
Recommendation 18: although results of short-term improvement in certain clinical variables have been observed in some studies with therapeutic massage, as they are so few and of doubtful clinical significance, its use in the treatment of patients with fibromyalgia cannot be recommended	B
Recommendation 19: There is insufficient evidence to recommend the use of Reiki or touch therapy in the treatment of patients with fibromyalgia	B
Recommendation 20: Dry needling is not recommended in patients with fibromyalgia, due to the lack of evidence and the possibility of frequent side effects	√
Recommendation 21: there is insufficient evidence to recommend hyperbaric oxygen or ozone therapy	√
Surgical interventions	
Recommendation 22: In patients with fibromyalgia with a well-established indication for total knee arthroplasty, it is recommended that the intervention be performed. However, they should be monitored postoperatively given the possibility of a greater number of medical and surgical complications.	D
Recommendation 23: It is not recommended that arthroscopic or subacromial shoulder decompression surgery in patients with FM be discouraged a priori. However, given the possibility of poorer recovery and patient satisfaction following the surgery, the indication should be closely reviewed, alternatives sought, and the patient informed.	C
Recommendation 24: It is recommended that indications for spinal arthrodesis surgery in patients with fibromyalgia be carefully assessed for the possibility of postoperative medical complications.	C
Recommendation 25: Careful assessment of postoperative opioid use is recommended in fibromyalgia patients undergoing any type of surgery.	D
Recommendation 26: In women undergoing breast cancer surgery, preoperative assessment for fibromyalgia is recommended to predict postoperative neuropathic pain.	D
Recommendation 27: The drafting group of this document recommends preoperative assessment for fibromyalgia in people with chronic pain who are to undergo any type of surgery, given the possibility of a greater number of complications and higher opioid use in the postoperative period.	√

FM: fibromyalgia; GR: grade of recommendation (Appendix B see Annex 1 and Annex 2, Supplementary data).

However, in terms of consumption of healthcare resources, the reviewed publications show some inconsistency between them with two opposing tendencies. Annemans[15] in the United Kingdom and Lamotte[16], in France extrapolating from Annemans' data, state that the diagnosis reduces expenditure, albeit minimally. In contrast, White[17] and Berger[18] in the USA, state that the diagnosis leads to a considerable increase in resource and drug expenditure. The studies have different follow-up times which could explain this lack of consistency, and are conducted in different health systems which could also explain some differences. Furthermore, the studies do not use control groups or the group they use is of patients with established FM; in other words,

they do not use a control group without an established diagnosis.

The drafting group considers that diagnosing FM can be applied easily in our healthcare system without any increase in human or financial resources. Due to their training and knowledge, making diagnosing FM is within the reach of any rheumatologist, and the possibility of generalising it to PC doctors and other specialties is feasible with basic training in the most relevant aspects of this disease.

For the patient, having a diagnosis means greater security in the knowledge that their clinical manifestations are due to a recognised disease. This enables them to know the appropriate therapeutic resources to improve their situation and to cope with their disease in the best conditions possible.

Diagnosing FM means that the patient stops looking for explanations for their symptoms and as a result tends to reduce the number of visits to specialists and the amount of healthcare resources used. This would reduce the overall impact of the disease by reflecting its reality.

Therapeutic interventions that are neither effective nor safe

Pharmacological treatment

Which pharmacological interventions and/or combinations of benzodiazepines, non-steroidal anti-inflammatory drugs (NSAIDs), Z-drugs, anticonvulsants, tramadol, and major opioids have not shown efficacy/effectiveness and safety in the treatment of fibromyalgia?

Recommendation 6: There are insufficient studies to recommend the use of non-steroidal anti-inflammatory drugs (NSAIDs) for the treatment of pain in adult patients with fibromyalgia (Grade A recommendation).

Recommendation 7: The drafting group does not recommend the use of major opioids to treat pain in patients with fibromyalgia due to insufficient evidence of their effectiveness and the possible risk of adverse effects (Recommendation grade √).

Recommendation 8: No pharmacological combination can be recommended or discouraged in the treatment of adult patients with fibromyalgia, in the absence of sufficient evidence on their efficacy and safety (Recommendation grade C).

Recommendation 9: The use of anticonvulsants such as lacosamide or lamotrigine to reduce pain is not recommended due to lack of efficacy (Recommendation grade B).

There is no evidence of the effectiveness of other antiepileptic drugs such as carbamazepine, clonazepam, phenytoin or valproate, or the existing evidence on their effectiveness is insufficient to make a recommendation for or against (Recommendation grade √).

Recommendation 10: The drafting group does not recommend the chronic use of benzodiazepines or Z-drugs in patients with fibromyalgia due to lack of evidence on effectiveness and the possible risk of addiction and other adverse effects (Recommendation grade √).

The data on pharmacological treatment in patients with FM show poor results[35], with 33% improvement in the severity of the variables analysed in only a third of patients[36].

Antidepressants such as tricyclics and serotonin and norepinephrine reuptake inhibitors, gabapentinoids such as pregabalin and gabapentin, and analgesics such as tramadol at low doses have shown efficacy in randomised clinical trials; these are the drugs recommended by the scientific societies[5].

However, other drugs for which there is no solid evidence of efficacy in FM are frequently added, making combined drug treatment with more than three drugs a reality in 30% of patients[37], and 40% of patients are using five or more drugs (polymedication)[38].

NSAIDs are very commonly used in patients with FM, in more than 40%[39]. Their use should be rationed due to potential adverse gastrointestinal, renal, and cardiovascular effects[40].

The use of opioids for the treatment of chronic non-cancer pain has increased dramatically in recent decades[41]. Major opioids, i.e., more potent than tramadol, are used by 27% of these patients[42]. Therefore, the possibility of side effects and significant interactions with other drugs is not negligible and could aggravate the clinical manifestations of the disease. Thus, for example, in patients with FM who are major opioid users, it has been shown that only discontinuing opioids results in an improvement in the clinical manifestations[41].

The drugs most frequently used by FM patients include NSAIDs, benzodiazepines, Z-drugs, some anticonvulsants, and major opioids. The most used drugs, or combinations of drugs, that have not demonstrated efficacy or safety in these patients need to be assessed.

The evidence found for this question was limited. Only one SR was found that evaluates the efficacy and safety of NSAIDs, another SR that evaluates anticonvulsants, another that evaluates pharmacological combinations, and finally one that evaluates oxycodone[43–57]. Studies were found that do not meet the inclusion criteria, but may provide additional information on other aspects of the diagnosis[5,45].

Full information on the results obtained from the evidence review is available on the SER website (Appendix B Table 2, Additional material).

It is particularly important to detect drugs, or drug combinations that are not effective for FM, as the side effects of many drugs aggravate the clinical manifestations of the disease itself.

Thus, the evidence found on the ineffectiveness of NSAIDs in the treatment of pain in patients with FM should lead to their being discontinued. Although there is insufficient evidence to advise for or against the use of the major opioids in the treatment of FM, the drafting group considers that they should not be used due to the serious adverse effects described with this type of drug.

The drafting group considers that it is always important to avoid polymedication in any patient, but even more so in patients with FM as these patients are very often polymedicated.

Complementary alternative medicine

Which complementary alternative medicine (CAM) interventions have not shown efficacy/effectiveness and safety in the treatment of fibromyalgia?

Recommendation 11: although statistically significant results on the efficacy of transcranial electrical stimulation or transcranial magnetic stimulation have been observed in some studies, the drafting group considers that as these techniques are of limited clinical relevance, they cannot be recommended in the treatment of patients with fibromyalgia (Recommendation grade B).

Recommendation 12: There is insufficient evidence to recommend the use of TENS in the treatment of fibromyalgia until trials of methodological quality demonstrate its efficacy (Recommendation grade B).

Recommendation 13: More studies are needed that assess the efficacy of cannabinoids (nabilone) in improving pain and quality of life to recommend their use in patients with fibromyalgia (Recommendation grade √).

Recommendation 14: Although in some studies it appears that nabilone may be more effective than amitriptyline in improving sleep quality, it is not recommended for use in patients with

fibromyalgia due to a higher frequency of adverse effects (Recommendation grade √).

Recommendation 15: Homeopathy, chiropractic, osteopathy, and manipulations are not recommended in the treatment of fibromyalgia, due to the lack of studies confirming the efficacy and safety of these techniques (Recommendation grade √).

Recommendation 16: There is insufficient evidence to recommend pulsed electromagnetic therapy in the treatment of fibromyalgia (Recommendation grade B).

Recommendation 17: there is insufficient evidence to recommend relaxation monotherapy in the treatment of fibromyalgia, due to the limited benefit obtained in the improvement of pain and quality of life (Recommendation grade D).

Recommendation 18: although results of short-term improvement in certain clinical variables have been observed in some studies with therapeutic massage, as they are so few and of doubtful clinical significance, its use in the treatment of patients with fibromyalgia cannot be recommended (Recommendation grade B).

Recommendation 19: There is insufficient evidence to recommend the use of Reiki or touch therapy in the treatment of patients with fibromyalgia (Recommendation grade B).

Recommendation 20: Dry needling is not recommended in patients with fibromyalgia, due to the lack of evidence and the possibility of frequent side effects (Recommendation grade √).

Recommendation 21: there is insufficient evidence to recommend hyperbaric oxygen or ozone therapy (Recommendation grade √).

The limited efficacy and adverse effects of drugs limit their use, and therefore patients with FM often resort to CAM therapies. In this regard, Perry[58] reports that 90% of patients have used some form of CAM for symptom control. CAM is defined as "... diagnosis, treatment, and/or prevention which complements mainstream medicine by contributing to a common whole, satisfying a demand not met by orthodoxy, or diversifying the conceptual frameworks of medicine"[58].

Previous SRs have established the CAM interventions that have been shown to be effective in the treatment of FM[59]. The current aim is to update the search for available evidence to assess the safety of CAM interventions and to establish those that are not effective or efficacious.

The evidence identified for the wide range of existing treatments categorised as complementary and alternative medicine has been divided into the following groups: 1) non-invasive brain stimulation; 2) transcutaneous stimulation; 3) cannabis; 4) homeopathy; 5) chiropractic and osteopathy; 6) electromagnetic therapy; 7) relaxation/training; 8) massage; 9) energy therapies; 10) dry needling; and 11) ozone therapy/hyperbaric oxygen[60–98]. Studies were found that do not meet the inclusion criteria, but they may provide additional information on other aspects of the diagnosis[99–102].

Full information on the results of the evidence review is available on the SER website.

The drafting group considers that within the CAM interventions assessed, those related to non-invasive brain stimulation have the most consistent results. However, in both electrical stimulation and magnetic stimulation, there is significant heterogeneity in the methodology for applying the interventions.

The work on TENS is less consistent. In general, the studies have major risks of bias and small sample sizes, and the results show that TENS is not effective for pain if compared to no treatment, but is effective compared to physical activity, superficial heat, hydrotherapy, or SAMe.

The evaluation of cannabinoids focused on nabilone and shows quite consistent results on pain relief and sleep, but not on mood. There is also considerable consistency regarding the low safety of nabilone, showing significant side effects.

The studies on homeopathy, chiropractic and osteopathy are very heterogeneous and with small sample sizes, and therefore no conclusions could be drawn.

Regarding relaxation methods, massage or energy therapies, the SRs identified include only one RCT on the subject and vary greatly in methodology and in the evaluation of the results.

The drafting group considers that the results of the studies of the various CAM interventions assessed do not mean they should be applied directly in our public health system as no clear efficacy has been demonstrated. They are more likely to be used in the field of private medicine, although this in turn encourages a greater risk of professional intrusion in the treatment of patients with FM.

The CAM interventions studied have an acceptable safety role, except for nabilone and chiropractic. This facilitates their use, even if there is no evidence of their efficacy.

The analysis in this review supports professionals who care for FM patients in advising or discouraging certain CAM interventions, based on efficacy, safety, and cost-effectiveness.

Surgical interventions

Which surgical interventions have not shown efficacy/effectiveness or safety in the treatment of fibromyalgia?

Recommendation 22: In patients with fibromyalgia with a well-established indication for total knee arthroplasty, it is recommended that the intervention be performed. However, they should be monitored postoperatively given the possibility of a greater number of medical and surgical complications (Recommendation grade D).

Recommendation 23: It is not recommended that arthroscopic or subacromial shoulder decompression surgery in patients with FM be discouraged a priori. However, given the possibility of poorer recovery and patient satisfaction following the surgery, the indication should be closely reviewed, alternatives sought, and the patient informed (Recommendation grade C).

Recommendation 24: It is recommended that indications for spinal arthrodesis surgery in patients with fibromyalgia be carefully assessed for the possibility of postoperative medical complications (Recommendation grade C).

Recommendation 25: Careful assessment of postoperative opioid use is recommended in fibromyalgia patients undergoing any type of surgery (Recommendation grade D).

Recommendation 26: In women undergoing breast cancer surgery, preoperative assessment for fibromyalgia is recommended to predict postoperative neuropathic pain (Recommendation grade D).

Recommendation 27: The drafting group of this document recommends preoperative assessment for fibromyalgia in people with chronic pain who are to undergo any type of surgery, given the possibility of a greater number of complications and higher opioid use in the postoperative period (Recommendation grade √).

FM is known to affect pain processing mechanisms in the nociceptive system[103], is associated with high analgesic consumption[104], and has increased comorbidities[105] coexisting with other musculoskeletal or visceral diseases[106], which may contribute to pain. Patients with FM often require surgical intervention with the risk of unsatisfactory outcomes that may be different to those of people without FM.

The aim of this SR is to evaluate the safety and efficacy of surgery in musculoskeletal and visceral processes when FM is an associated comorbidity.

The scientific evidence found on the indication for surgical interventions in patients with FM comes solely from observational studies[107–123]. Studies were found that do not meet the inclusion criteria, but may provide additional information on other aspects of the diagnosis[124–127].

The results obtained were organised into two different main areas: efficacy and safety. Full information on the results obtained from the review of the evidence is available on the SER website.

The different studies in patients with FM are highly consistent in the similarity of surgical outcomes with patients without FM. However, they are also significantly consistent in that the degree of patient satisfaction after surgery is lower and that the number of complications, both medical and surgical, is higher in patients with FM.

The drafting group considers that surgeons can easily apply the recommendations made in this document to our healthcare system, as only the possibility that the patient has an associated FM should be considered before surgery is performed. Although the focus here was work related to musculoskeletal surgery, the drafting group believes it is highly likely that these recommendations can be generalised to any surgical procedure.

The most relevant aspect of these recommendations is that their application may result in fewer postoperative complications. This would therefore also reduce the economic costs associated with surgery.

For the drafting group, it is important to emphasise that the aim of these recommendations is to ensure that indications for surgery are always correctly established in a patient with FM for them to benefit from the surgery and avoid unnecessary post-surgical complications.

Conclusions

Because there are no curative or highly effective treatments for patients with FM, therapeutic resources must be fully optimised to achieve the best possible situation for the patient. There are systematic reviews on the most useful therapeutic modalities for the treatment of FM and recommendations made by several scientific societies for the optimal management of this disease[5,6].

However, it is essential to detect other frequent actions in clinical practice that may be detrimental to the situation of patients with FM. In other words, knowing what needs to be done is just as important as knowing what is being done but is detrimental to the patient. This has been the main objective of this systematic review and the recommendations in this paper.

One of the first conclusions drawn from this review is the importance of making the diagnosis of FM. Contrary to the beliefs of some doctors, who consider that the diagnosis aggravates the situation of the patient and the health system itself[10], our systematic literature review shows the opposite: the patient improves with the diagnosis, feels more confident to face their illness and this results in less pressure on the health system with a reduction in economic costs.

In relation to treatment, some drugs that have not been shown to be effective and are harmful in the long term should be dispensed with, such as major opioids, benzodiazepines and NSAIDs, frequently used for the treatment of patients with FM[104]. Although the strength of the recommendation is at expert group level, the review group considers that recent data on the toxicity of major opioids and benzodiazepines advise against their use[128]. We also found no solid evidence to justify the use of benzodiazepines in the treatment of FM[128].

We found no solid evidence either to justify the frequent combination of several drugs to treat these patients. Polymedication is very common among patients with FM and is known to generally aggravate the situation of any patient due to multiple adverse effects and frequent drug interactions[37]. It is important to take this aspect into account and only to use the drugs that show clinical improvement.

In terms of recommending treatments based on alternative or complementary medicine, there is no solid evidence to recommend any type of treatment. However, most of these therapeutic modalities do not have serious side effects and can be agreed with the patient if they feel there is any benefit to be gained.

Patients with FM undergo more surgery compared to any other type of rheumatological disease[129]. However, our review showed that patients with FM have more medical and surgical complications after surgery, consume more healthcare resources, require more postoperative medication, and have a higher degree of dissatisfaction with the operation. However, long-term functional outcomes are similar to those of other patients without the disease and surgery should not be discouraged if the surgical indication is clearly established.

Agenda for future research

After the systematic review of current scientific evidence for the management of patients with FM, undertaken to draft these recommendations, the expert panel considers that there are many aspects to be included in an agenda for future research; these include the following, among others:

- Studies are needed that address the mechanisms of action of analgesics, NSAIDs and major opioids on central pain in FM patients.
- More randomised, double-blinded, placebo-controlled clinical trials are needed that assess the efficacy and safety of new pharmacological treatments, in monotherapy and combination therapy, in the treatment of patients with FM.
- Prospective studies are needed to confirm an increase in post-mastectomy neuropathic pain in FM patients to help propose preventive measures.
- Prospective studies are needed to examine whether the FM population who undergo knee or hip replacement represent a risk factor for the development of long-term severe chronic joint pain.
- Prospective studies are needed to determine whether the presence of FM can alter the outcome of spinal arthrodesis surgery.

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Conflict of interests

Javier Rivera Redondo has received funding from Pfizer for his participation in courses/congresses; fees from Jansen, Novartis, Pfizer, Roche, Sanofi and UCB for presentations, and has received financial support from Italfarmaco for consultancy for pharmaceutical companies and other technologies.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.reuma.2021.02.004.

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