Brazilian consensus on the treatment of fibromyalgia

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Received on 10/06/2009. Approved for publication on 11/24/2009. Roberto Ezequiel Heymann and Eduardo dos Santos Paiva received honorariums from Lilly, Janssen-Cilag, Boehringer, Apsen, and Pfizer for speeches and consulting services; Milton Helfenstein Junior received honorariums from Pfizer and Merck Sharp for speeches and consulting services; Daniel Feldman Pollak received honorariums from Lilly, Pfizer, and Merck Sharp; José Eduardo Martinez received honorariums from Sanofi Aventis, for speeches, and Pfizzer, for speeches and consulting services; José Roberto Provenza received honorariums from Roche, Bristol, Ache, and Pfizer to participate in clinical studies with new drugs at PUC-Campinas; Marcelo Cruz Rezende received honorariums from Lilly-Boehringer, to participate in symposiums, and from Pfizer, for speeches and to participate in sympostiums; Valério Valim Cristo received honorariums from Roche for presentations, conferences, or speeches, besides financing for studies, teaching organization, or to attend symposiums sponsored by Lilly, Genzyme, and Schering-Plough. The remaining authors declare the absence of conflicts of interest.

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INTRODUCTION

Fibromyalgia is one of the most frequent rheumatologic conditions, its main characteristic being diffuse and chronic muscle-skeletal pain.

In a study carried on in Brazil, in the city of Montes Claros, fibromyalgia was the second most common rheumatologic condition observed, after osteoarthritis. In this study a prevalence of 2.5% was observed in the population, the majority being females, from which 40.8% were between 35 and 44 years old.[1]

Besides the painful setting, these patients often complain of fatigue, sleep disturbances, morning stiffness, and paresthesia on the extremities, subjective edema sensations and cognitive disturbances. Association with other comorbidities is often found, contributing to the suffering and decline in quality of life of these patients. Among the most frequent comorbidities found, we can mention depression, anxiety, chronic fatigue syndrome, myofascial syndrome, irritable bowel syndrome and nonspecific urethral syndrome.[2]

These patients use more analgesic therapies and seek medical and diagnostic services more often than the normal population. Thus, it is not surprising that in the USA their annual costs are as high as U$9,573.00, representing expenses 3 to 5 times higher than the average population.[3] A considerable portion of these costs might be saved when the patient is properly diagnosed and treated, avoiding unnecessary complementary exams and medications useless for his/her treatment.[4]

Although fibromyalgia has been recognized as a disease long ago, it has only been seriously investigated in the last three decades. Little is known about its etiology and pathogenesis. Up to date, there are no treatments considered highly efficacious.

Fibromyalgia is a syndrome primarily investigated and treated by rheumatologists mainly because it involves a chronic condition of musculoskeletal pain, but often these patients require a multidisciplinary attendance aiming to reach a broad and complete approach of their symptoms and comorbidities.

In 2004 the Brazilian Society of Rheumatology published the first fibromyalgia guidelines, with the goal of guiding the diagnosis and treatment of this syndrome.[5]

The goal of the SBR 2006-2008 management in this work was not only to update the guidelines for treatment of fibromyalgia, but also to innovate, by bringing together specialists from other medical fields with knowledge about this syndrome to reach a consensus about its treatment.

METHODOLOGY

The themes reviewed here were divided among three categories: 1) Importance of the fibromyalgia diagnosis with general recommendations; 2) Pharmacological treatment; 3) Non-pharmacological therapeutic modalities. The degrees of recommendation and the levels of scientific evidence were taken from the Guidelines Project from the Brazilian Medical Association.[6]

The methodology was based on the BASCE System,[7] an organizational method developed by the consulting firm Axia. Bio with the goal of minimizing deviations and bias of the results, based in scientific criteria previously established in literature. The BASCE System proposes a systematic approach for the adaptation of guidelines and consensus generated in different scenarios, observing the answer to questions relevant to the local scenery, through the presentation of results in an explicit and transparent manner, so that the material generated has quality and local scientific validity through:

Broad and systematic search in the medical literature for guidelines and consensus regarding a particular disease; Structured evaluation (**A**) of them with participation of 4 or more local specialists who make the Selection of the material to be used, based in scores; Panel of Consensus and external review with another 8 or more local specialists; Structuring (**E**) of the material adapted to the local reality.

This process was divided into two phases.

Phase I: Preparation of the questions that would be decided by the consensus group

For that purpose a bibliographic search was done in guideline databases, metanalysis and systematic reviews about fibromyalgia.

The literature search at the Pubmed portal was done with the following search strategy: ("fibromyalgia"[MeSH Terms] OR "fibromyalgia"[All Fields]) AND systematic [sb] AND (("1"[PDAT]: "2008/06/13"[PDAT]) AND (English[lang] OR Spanish[lang] OR Portuguese[lang])). One hundred and nine papers were found, of which 24 were shown to be publications that matched the search goals and, later on, were captured in their complete format and text (*full text*). Fifteen papers were selected, in its majority metanalysis, and also guidelines.[8-22]

At Cochrane Library, the term *"fibromyalgia"* yielded one paper in the session of complete metanalysis.[23] In the part of protocols, two unfinished projects were identified.

In the NICE (National Institute of Clinical Excellence) and OASIS portals typing of the word "*fibromyalgia"* did not result in any articles. In the DARE portal, two relevant abstracts of systematic reviews were found. In the *National Guideline*

Clearinghouse, the search for "*fibromyalgia*" has shown 17 items, four being guidelines of interest.[9,24,26]

A group of six rheumatology specialists, considered fibromyalgia scholars and researchers (Group I), by indication from the Brazilian Rheumatology Society, evaluated the guidelines obtained in the research project using a tool adequate for this type of score.[27] Incorporation of international guidelines in the local discussion was evaluated based on the criteria established by the AGREE Collaboration (Appraisal of Guidelines Research and Evaluation), which allow evaluation and comparison among different guidelines, supporting, thus, the utilization of the best criteria found in each guideline. AGREE is a generic tool, applicable to any pathology, including the following: diagnostic aspects, promotion of health, treatment and other interventions.

The methodology proposed by AGREE evaluates the quality of the statement as well as the quality of some aspects intrinsic to the recommendations, divided in six domains: Extent and purpose (Global Objective of the orientation norm); involvement of the parties (representation of all interested parties and potential users), rigidity of the development (the process of evidence collection used and the formulation of recommendations); clarity and presentation e (Language and format), applicability (application of the recommendations in terms of organization, behavior and costs) and editorial independence (exemption of the recommendations and acknowledgements of conflicts of interest).

Based on this method of evaluation, the guidelines that reached a percentage equal or higher than 51% in all domains were chosen.[8,25,26] These selected guidelines served as basis for the preparation of an initial questionnaire for the development of the consensus. This initial questionnaire was then evaluated and modified by the members of Group I. Other metanalysis and systematic reviews that did not go through the AGREE method were also evaluated by the Group I specialists, who decided for or against their incorporation in the list of recommendations to be questioned.

The Group I specialists were alerted that the recommendations should be prepared according to their degree of recommendation and applicability in Brazil.

Once the preparation of this questionnaire was concluded by Group I, we move onto the next phase of the project, that is, the voting of these recommendations.

Phase II: Voting

Phase II consisted in a meeting among physicians of several specialties who study and treat fibromyalgia, with the purpose of voting for or against the statements made by Group I. These statements reproduce the findings obtained in the studies consulted in the first phase. In order to do that, Group II was formed by joining Group I members with specialists selected by their respective medical associations, taking into consideration their experience and recognition in the treatment of the disease in question. Group II was, therefore, composed by 30 specialists coming from the following societies: Brazilian Rheumatology Society, Brazilian Society for the Study of Pain, Brazilian Medical Clinic Society, Brazilian Orthopedics and Trauma Society, Brazilian Academy of Neurology and Brazilian Association of Physical Medicine and Rehabilitation.

Voting of the elaborated statements was electronic, and the participants were not identified individually, only the group results being displayed. At the time of voting all specialists were alerted that the recommendations should be evaluated according to the degree of recommendation and applicability in Brazil.

All recommendations were voted as YES or NO, and, according to the BASCE methodology,[7] and only those that had a voting of YES or NO equal or higher than 70% within the group were considered consensual. The statements that did not obtain consensus in the first voting were material for argumentations between a favorable and an opposing specialist. At the end of this debate a new voting took place. The questions that did not reach the established percentage after the second round of voting were considered as not reaching consensus and, therefore, were not included in the recommendations of this Brazilian Consensus.

This way, the practices recommended here were those that obtained at least 70% consensus and the non-recommended were those where at least 70% of the specialists agreed in not recommending. The ones that did not reach consensus were those where there was not a minimum of 70% agreement for or against them.

As documentation, the consensus meeting was filmed and also documented through electronic vote.

CAPTURE OF RESOURCES

The Brazilian Rheumatology Society hired the services of the company Axia.Bio for capture of resources, technical conduction of the consensus and structuring of the meetings of the Brazilian Consensus for the treatment of fibromyalgia.

The resources for the realization of this consensus were obtained from the laboratories Mantecorp Chemical and Pharmaceutical Industry, Ltd. (*Mantecorp Indústria Química e Farmacêutica Ltda.*), **Janssen-Cilag** Pharmaceutical Ltd.

(*Janssen-Cilag Farmacêutica Ltda*.), Apsen Pharmaceutical *(Apsen Farmacêutica*) and Pfizer Laboratories Ltd. (*Laboratórios Pfizer Ltda.*). Each of these companies contributed with an equal amount, equivalent to ¼ of the costs. The capture of resources was a responsibility of the company Axia.Bio, who contacted and met with representatives in charge of these companies. The name of the specialists involved in this work was kept confidential, and any contact between these companies and the physicians participating in the consensus was forbidden. This way we could guarantee the lack of bias in our results.

RESULTS

Seventy four questions were voted, and consensus was reached in 68 (92%) of these. Only 6 (8%) questions did not obtain consensus.

Diagnosis and general recommendations

Fibromyalgia must be recognized as a complex and heterogeneous health condition in which there is a disturbance in the processing of pain associated with other secondary characteristics (degree of recommendation D, level of evidence IV).[8]

The diagnosis of fibromyalgia is exclusively clinical and eventual subsidiary exams might be requested only for differential diagnosis (degree of recommendation D) (Group I). The diagnosis must be confirmed at the beginning of the treatment so that we can clarify to the patient what is true and what is false (degree of recommendation D).[25] The patient education is a critical factor for the ideal control of fibromyalgia (degree of recommendation B).[25] As part of the initial treatment, we must provide the patients basic information about fibromyalgia and its treatment options, educating them about pain control and self-control programs (degree of recommendation A).[25]

A complete understanding of fibromyalgia demands a broad evaluation of pain, function and psycho-social context (degree of recommendation D, level of evidence IV).[8] Besides pain, it is important to evaluate the seriousness of the other symptoms like fatigue, sleep disturbances, mood disturbances, cognition disturbances, and the impact of these on the quality of life of the patient (degree of recommendation D).[25] There was consensus that fibromyalgia does not justify work exclusion (degree of recommendation D) (Group I-SBR).

The strategy for the ideal treatment of fibromyalgia demands a multidisciplinary approach with a combination of non-pharmacological and pharmacological treatment modalities. The treatment must be worked out, in discussion with the patient, according to the intensity of his/her pain, functionality and its characteristics, (degree of recommendation A),[8,25] being important also to take into consideration his/her bio-psycho-social questions, (degree of recommendation D) (Group I-SBR) and cultural questions (degree of recommendation D).[26]

Chronic pain is a persistent health condition that modifies one's life. The goal is the control, not the elimination (degree of recommendation D).[26]

Drug treatment

Among the tricyclic compounds, **amitriptyline** and the muscle relaxant cyclobenzaprine reduce pain and often improve the functional capacity, being, thus, recommended for the treatment of fibromyalgia (degree of recommendation A, level of evidence Ib).[8] **Nortriptyline** was recommended by the group for the treatment of fibromyalgia, as opposed to imipramine and clomipramine which were not recommended (degree of recommendation D) (Group I SBR).

Among the selective serotonin reuptake inhibitors there was a consensus that fluoxetine also reduces pain and often improves the functional capacity, being also recommended for the treatment of fibromyalgia (degree of recommendation A, level of evidence Ib).[8] The use of serotonin reuptake inhibitors like fluoxetine, in combination with tricyclics, is also recommended for the treatment of fibromyalgia (degree of recommendation B).[25] The isolated use of other serotonin reuptake inhibitors like sertraline, paroxetine, citalopram and escitalopram, was not recommended (degree of recommendation D) (Group I SBR).

Among the anti-depressives that block serotonin and noradrenalin reuptake, duloxetine and milnacipran were recommended for reducing pain and often improving the functional capacity of patients with fibromyalgia (degree of recommendation A, level of evidence Ib).[8] There was no consensus as to the utilization of venlafaxine in patients with fibromyalgia (degree of recommendation D) (Group I SBR).

Moclobemide, an anti-depressive MAO inhibitor, was recommended for the treatment of fibromyalgia for reducing pain and often improving the functional capacity of patients with fibromyalgia (degree of recommendation A, level of evidence Ib).[8]

There was no consensus as to the utilization of trazodone in patients with fibromyalgia (degree of recommendation D) (Group I SBR).

The dose of all anti-depressives must be individualized and any concomitant mood change must be treated (degree of recommendation D).[25]

The anti-Parkinson medication pramipexole was also recommended for the treatment of fibromyalgia to reduce pain (degree of recommendation A, level of evidence Ib),[8] being specially indicated in the presence of sleep disturbances and restless legs syndrome (degree of recommendation A).[25]

Simple analgesics and light opioids might be also considered for the treatment of fibromyalgia, as opposed to the potent opioids, which were not recommended (degree of recommendation D, level of evidence IV),[8] Tramadol was recommended for treating pain in fibromyalgia (degree of recommendation A, level of evidence Ib).[8] Its association with paracetamol was considered effective in the treatment of fibromyalgia (degree of recommendation B).[25]

Tropisetron was also recommended for treating pain in fibromyalgia (degree of recommendation A, level of evidence Ib).[8]

Among neuromodulating drugs, gabapentine (degree of recommendation A),[22] and pregabaline were recommended. This last one was considered efficacious in reducing pain in patients with fibromyalgia (degree of recommendation A, level of evidence Ib).[8] On the other hand, topiramate was not recommended (degree of recommendation D) (Group I SBR).

Corticosteroids should not be used (degree of recommendation D, level of evidence IV).[8] Non-steroidal anti-inflammatory drugs must not be used as first line medication in patients with fibromyalgia (degree of recommendation A).[25]

Zoplicone and zolpidem were recommended for the treatment of sleep disturbances in fibromyalgia (degree of recommendation D) (Group I SBR).

Clonazepam, tinazidine and alprazolam were not recommended for use in fibromyalgia (degree of recommendation D) (Group I SBR).

Non-medical treatment

Patients with fibromyalgia must be advised to undertake musculoskeletal exercises at least twice a week (degree of recommendation B),[25] Individualized programs of aerobic exercises might be beneficial to some patients (degree of recommendation C, level of evidence IIb),[8] who must be advised to undertake moderately intense aerobic exercises (60-75% maximum cardiac frequency age-adjusted ([210 minus the patient's age]) twice or three times a week (degree of recommendation A),[25] reaching the point of light resistance, not the pain threshold, avoiding this way the pain induced by the exercise. This is particularly important in the subgroup of individuals with articular hypermobility (degree of evidence B),[25] The exercise program must start at a level below the patient's aerobic capacity and progress in frequency, duration or intensity as soon as his/her conditioning level and strength increase. The progression of exercises must be slow and gradual (degree of recommendation D)[25] and patients should be encouraged to maintain continuity to retain the gains induced by the exercises (degree of recommendation B).[25]

Individualized stretching programs (degree of recommendation D) (Group I SBR) or muscular strengthening ones might also be beneficial to some patients with fibromyalgia (degree of recommendation C, level of evidence IIb).[8]

Other therapies like rehabilitation and physical therapy or relaxation might be used in the treatment of fibromyalgia, depending on the necessities of each patient (degree of recommendation C, level of evidence IIb)[8].

Cognitive-behavioral therapy is beneficial to some patients with fibromyalgia (degree of recommendation D, level of evidence IV).[8] Psychotherapeutic support might be also, used in the treatment of fibromyalgia, depending on the necessities of each patient (degree of recommendation C, level of evidence IIb).[8]

There was no consensus on the indication of treatments with clinical support as balneotherapy (degree of recommendation A)[25] or acupuncture (degree of recommendation C).[25]

There was consensus in not recommending hypnotherapy, biofeedback, chiropractic manipulation and therapeutic massage for pain release in fibromyalgia (degree of recommendation B).[25]

Other therapies like Pilates, GPR/RPG (global postural re-education) and homeopathic treatment were not recommended for the treatment of fibromyalgia (degree of recommendation D) (Group I There is no scientific evidence that alternative therapies like teas, orthomolecular therapies, crystals, chromotherapy and Bach floral remedies, among others, are efficacious (degree of recommendation D) (Group I SBR). There is also no scientific evidence that infiltrations of painful points in fibromyalgia are efficacious (degree of recommendation D) (Group I SBR).

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