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Research Article

Primary Fibromyalgia Syndrome: Therapeutic Usefulness of Combined Pharmaceutical and Educational Approaches

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Abstract

Objective: Several pharmacological and non-pharmacological approaches have been adopted in Primary Fibromyalgia Syndrome but results have proved to be partial or unsatisfactory. The aim of our work is to verify, through a prospective, controlled, randomized study, the effectiveness in patients with Primary Fibromyalgia Syndrome of the standard pharmacological approach (Group A, 22 patients) compared to the adoption of the same pharmacological approach combined with an educational approach based on the Cognitive Behavioral Model over a three-month observation period (Group B, 24 patients).

Method: Fibromyalgia Impact Questionnaire and Visual Analogue Scale were mainly used to evaluate the results.

Results: Both indexes improved significantly since the first month of observation and at the end of the three months of study (FIQ: Group A: 78.6+0.4 *vs* 58.5+3.1, p=.0000; Group B: 78.4+0.2 *vs* 50.3+3.1, p=.0000. VAS: Group A: 9.5+0.2 *vs* 6.5+0.3, p=.0000; Group B: 9.7+0.2 *vs* 5.3+0.3, p=.0000). Furthermore, improvement was more rapid and intensive in the Group B in comparison to the group A. A Satisfaction Index used in the group B showed that this protocol was very appreciated for methodology, tutors competence and knowledge insights into the disease.

Conclusion: A combined therapeutic, pharmacological and educational approach might be a useful tool for the management of a complex and debilitating disease (especially on a personal, familiar, and social level) such as Primary Fibromyalgia Syndrome.

Keywords: Fibromyalgia; Therapy; Educational approach

Introduction

Primary Fibromyalgia Syndrome (PFS) is a complex clinical condition - of unknown etiology - marked by chronic, widespread musculo-skeletal pain, also affecting the relevant tendons and ligaments, which manifests in algogenic points (commonly known as "tender points") located in specific tendon and musculo-skeletal areas. It is also accompanied by a number of symptoms, among which the most frequent are fatigue, sleep disturbances, psycho-affective disorders, headaches, asthenia [1-4].

Lacking either biological or objective indicators which might stand for a medical "gold standard", the current diagnostic approach is still based on the American Rheumatology College (ARC)-1990 criteria, or "*pain in the 4 quadrants of the body and on the axial skeleton for at least 3 months, pain in at least 11 out of 18 specific tender points under finger pressure amounting to 4 kg/cm*^{2}" [5]. New diagnostic principles have been recently proposed based on the data of a special multicenter research trial. The latter range from well-known symptoms [such as chronic fatigue, early morning awakenings with ensuing feeling of inadequate rest] to cognitive and somatic symptoms which are part of the Widespread Pain Index (WPI) scale and Symptoms Severity Scale (SSS), in order to adopt a more objective clinical and diagnostic approach to the pathology [6,7]. Notably, the newly-proposed diagnostic criteria have not replaced the current ACR-1990 principles yet.

On a pathophysiological level, little is known about the causes triggering the disease, even though psychological, social, environmental, bio-mechanic, neurobiological and neuroendocrine factors have been considered [8-13].

On a therapeutic level, notwithstanding several pharmacological and non-pharmacological approaches have been adopted [14-23], results have essentially proved partial or unsatisfactory. The recent use of new drugs such as pregabalin, duloxetine, milnacipran and amitriptyline, initially regarded as first-line drugs in treating Primary Fibromyalgia Syndrome, has led to fairly modest and often contradictory outcomes [24-28].

The aim of our work is to verify, through a prospective, controlled, randomized study, the effectiveness in patients with Primary Fibromyalgia Syndrome of the standard pharmacological approach-consisting in administering several drugs such as thiocolchicoside (a muscle relaxant centrally acting as a competitive $GABA_A$ and glycine receptor antagonist), paroxetine (an antidepressant of the selective serotonin reuptake inhibitor-SSRI-type), and lorazepam

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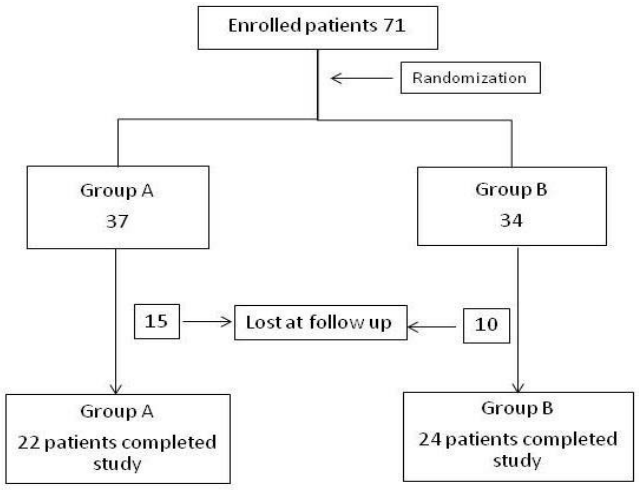

Figure 1: Flow chart of the study (see text for details).

(an intermediate-duration, benzodiazepine anxiolytic free of intermediate active metabolites) - compared to the adoption of the same pharmacological approach combined with an educational approach based on the Cognitive Behavioral Model [29-37], over a three-month observation period.

Patients and Methods

Patients

A number of 71 patients-67 females and 4 males-, aged between 26 and 67 years old, with a middle/high education, suffering from PFS as diagnosed according to ACR criteria-1990, previously admitted to the Clinic of Psychosomatic Medicine of the Internal Medicine Unit - were included in our study. The inclusion criteria were: age over 18 years old, Primary Fibromyalgia Syndrome as diagnosed is according to the criteria of the ARC-1990, acute intensity pain [score > 8] according to the Visual Analogue Scale (VAS) pain test. The exclusion criteria were: major psychiatric disorders, organ failure of any kind, acute and chronic inflammatory rheumatological diseases, autoimmune diseases, intake of drugs interfering with pain.

Methods

After anamnestic and clinical evaluation, all patients were administered the Visual Analogue Scale (VAS) pain test [38] and the Fibromyalgia Impact Questionnaire (FIQ) [39] either immediately and after 1, 2, and 3 months during treatment, in order to evaluate pain intensity and its global impact on the patient. The Fibromyalgia Impact Questionnaire (FIQ) is a reliable, validated self-assessment questionnaire that measures impact the disease in patients with PFS. FIQ contains scales for measuring Physical functioning, No days felt good, No workdays missed, Ability to do job, Pain, Fatigue, Tiredness, Stiffness, Anxiety, Depression.

After being divided into 2 groups, patients after simple randomization were administered one of the following treatment: Group A were administered tiocolchicoside (a 4 mg vial for 7 days monthly), paroxetina (a 20 mg tablet, ½ a tablet for 2 weeks and subsequently a tablet daily); lorazepam (a 1 mg tablet, ½ a tablet 3 times daily for 1 month, and subsequently ½ a tablet daily for 2 months); Group B were administered the same previous treatment along with a new educational approach based on the Cognitive Behavioral Model, consisting of 2 monthly meetings, each lasting 60 minutes, during which audio-visual supports were used to tackle the issues raised by the disease, an approach already used by our team in other areas with satisfactory results [40].

All patients were also introduced to the concept of "minimum effective dose" in relation to the molecules used [41], as suggested by our previous experiences that have shown the effectiveness of the drugs in terms of significant reduction of adverse events and addiction symptoms. The above mentioned concept also helps to stress the therapeutic importance of a conscious, involved and global commitment to the project (positive reinforcement, self-esteem increase), thus avoiding to just "empower" the drugs about possible improvements.

Patients were also prescribed to practice moderate physical exercise, consisting in a slow-pace walk (isotonic, aerobic exercise) in any location (e.g. at home, in the garden, on the street, in a square, in the countryside, ecc.), along with keeping a positive mental attitude while concentrating on the exercise, for 15 minutes twice a day and to be subsequently increased by 10 minutes per each month during the treatment [42-45]. Finally, Group B patients were also administered a Satisfaction Index Test, normally used by our research team in order to assess the educational program itself.

The study was approved by the Ethical Committee of the Medical Faculty at Bari University. This study received informed consent from all patients.

Statistical analysis

All the variables studied were subjected to a statistical analysis. For the quantitative variables, we calculated the mean values and SD; for the qualitative variables, we calculated frequencies and percentages. For the statistical analysis of the mean values between T0 and T1, we used the independent-samples t-test or the Mann-Whitney U-test for independent samples. Variations along the period of observation within each group were tested by one-way analysis of variance. Chi-square test with Fisher test correction for small numbers was used for comparison among percentages. The significance value was set at P less than 0.05. For statistical processing, we used the data processing program statistical package for social science, version 20.0 (IBM Corporation, Armonk, New York, USA).

Results

After randomization, no differences for age and level of education were found between group A and B of enrolled patients (Figure 1).

Out of 71 patients enrolled, 19 of them, specifically 11 (9 females and 2 males) belonging to Group A and 8 females belonging to Group B, did not show up at the first monthly check, or called in to inform that they had suspended or unilaterally altered the treatment for various reasons (no symptom improvement, increase in pain, doctor's orders). Out of remaining 52 patients, 4 females belonging to Group A and 2 females belonging to Group B did not show up at the scheduled check after the second month without further explanation. Finally, 46 patients completed the study, 22 belonging to Group A and 24 to Group B.

In both groups, the score of FIQ and of VAS reduced significantly

Table 1: Fibromyalgia Impact Questionnaire: total score at time 0 and after 1, 2 and 3 months of therapy (M±SD) (A = patients of group A, n= 22; B= patients of group B, n= 24).

	Time 0	1m	2m	3m	p
Group A (n=22)	78.6±0.4	75.7±0.9	68.1±1.2	58.5±3.1	Time 0 <.00001 vs all
Group B (n=24)	78.4±0.2	74.9±0.4	52.1±3.9	50.3±3.1	Time 0 <.00001 vs all
p	0.02	0.0002	0.000001	0.000001	

Table 2: Fibromyalgia Impact Questionnaire: score of the item Anxiety at time 0 and after 1, 2 and 3 months of therapy (M±SD) (A = patients of group A, n= 22; B= patients of group B, n= 24).

	Time 0	1m	2m	3m	p
Group A (n=22)	8.2±0.8	8.1±1.1	7.2±0.8	7.04±0.6	Time 1m <.00001 vs 2m and 3m
Group B (n=24)	8.4±0.8	7.5±0.7	7.0±0.8	6.9±0.6	Time 0 <.0001 vs 1m and <.00001 vs 2m and 3m
p	n.s.	0.01	n.s.	n.s.	

Table 3: Fibromyalgia Impact Questionnaire: score of the item Depression at time 0 and after 1, 2 and 3 months of therapy (M±SD) (A = patients of group A, n= 22; B= patients of group B, n= 24).

	Time 0	1m	2m	3m	p
Group A (n=22)	7.2±1.1	7.2±1.0	6.9±0.9	6.6±0.6	Time 0 <.003 vs 2m and 3m
Group B (n=24)	7.3±0.9	7.1±0.7	6.6±0.6	6.2±0.7	Time 0 <.004 vs 2m and <.00004 vs 3m
p	n.s.	n.s.	n.s.	0.02	

Table 4: Visual Analogue Scale: total score at time 0 and after 1, 2 and 3 months of therapy (M±SD) (A = patients of group A, n= 22; B= patients of group B, n= 24).

	Time 0	1m	2m	3m	p
Group A (n=22)	9.5±0.2	9.0±0.2	7.8±0.3	6.5±0.3	Time 0 <.00001 vs all
Group B (n=24)	9.7±0.2	8.5±0.2	6.4±0.2	5.3±0.3	Time 0 <.00001 vs all
p	n.s.	0.000001	0.000001	0.000001	

n.s.= not significant

during the three months of observation and the reduction was present since the first month for each index (Tables 1-4, Figures 2&3).

In group A, 18 patients (77.2%) reported a "perceived" improvement in pain symptoms and in general health conditions, along with a significant recovery of the motor function and the production capacity, while 4 patients (23,8%) did not report any symptoms improvement.

In Group B, 21 patients (87.5%) reported a "perceived" improvement in pain symptoms and in general health conditions, along with a significant recovery of the motor function and the production capacity, while 3 patients (12.5%) reported a so "mild" improvement in pain symptoms as not to affect the motor function and the production capacity at all. Statistical evaluation showed that these percentages were not statistically significant.

The improvement in FIQ and VAS score was more pronounced both in intensity and in tempestivity in the group B and this difference was particularly evident at the end of the period of observation (Tables 1-4).

The Tables 2 and 3 show respectively the values of the items Anxiety and Depression of the FIQ. Both items improve during treatment, but in the group B, the effect the therapy is stonger and earlier than in the group A.

The most frequently reported adverse effects were heartburn, nausea, asthenia, weakness, sweating, pseudo-dizziness, drowsiness, especially during the first 2-3 weeks of treatment. All symptoms were equally reported as episodic, thus not requiring suspending the treatment, by both groups of patients. In 5 cases, heartburn suggested a proton pump inhibitor (omeprazole, 20 mg tablets) to be added to

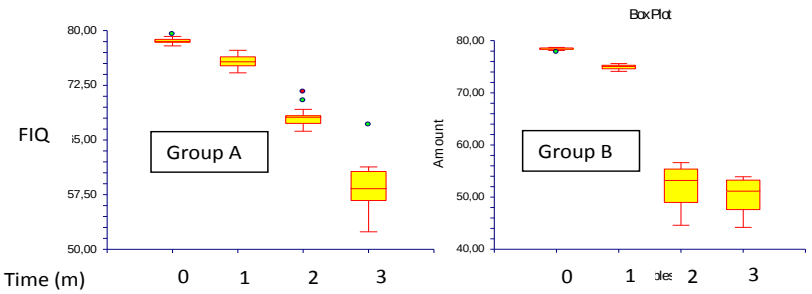

Figure 2: Fibromyalgia Impact Questionnaire: total score at time 0 and after 1, 2 and 3 months of therapy (M±SD) (A = patients of group A, n= 22; B= patients of group B, n= 24) (for statistical analysis, see Table 1).

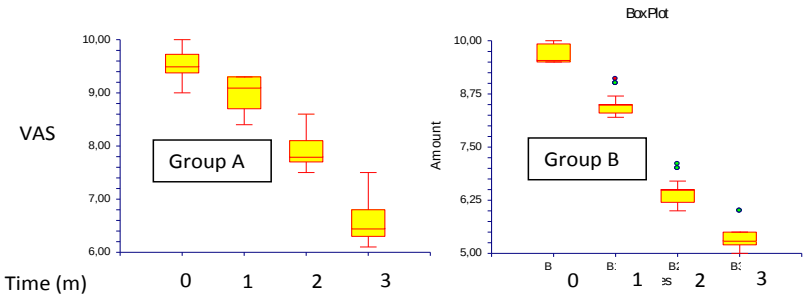

Figure 3: Visual Analogue Scale (VAS): total score at time 0 and after 1, 2 and 3 months of therapy (M±SD) (A = patients of group A, n= 22; B= patients of group B, n= 24) (for statistical analysis, see Table 2).

the treatment protocol for 2 weeks, which resulted in the disorder solution.

Only 29 patients (63.0%) completed the prescribed protocol of physical exercise: they defined the physical exercise as useful and 9 of them reported to have enjoyed it "*consistently*". On the other hand, 8 of these patients had to quit the exercise after a while (9-12 days, on average), mainly because of the difficulty in keeping up with the daily protocol. Finally, 12 patients reported a significant difficulty in practicing physical exercise for too long.

Patients that completed the prescribed program of physical exercise in the group B were 79,1% and in the group B were 45,0% of total subjects ($p < .05$).

Group B patients were administered a Satisfaction Index Test, which showed a positive assessment of the course planning (71.3%), of the methodology (74.6%), of the tutors competence and availability (83,5%) and of the benefits (77.4%) of a closer understanding of the disease.

Discussion

In this work, we show that a combined pharmacological and educational therapeutic approach might be a useful tool for the management of Primary Fibromyalgia Syndrome.

The association of a non-pharmacological approach (Cognitive Behavioral Model) to the pharmacological treatment has been chosen for several reasons: the poor proven efficacy of drug treatments so far used; our previous positive experience of migraine, pathology related to a neurotransmitter serotonin defect; and above all, the important role recognized to psycho-affective and psychosocial factors in the pathophysiology of the fibromyalgia syndrome.

Actually, one of the most recent and most accredited pathophysiologic assumptions is that PFS in classified within the group of "Central Sensitivity Syndrome", which includes, besides the Migraine, other pathologies commonly considered "functional" as Irritable Bowel Syndrome, Tensio-Type Headache, Temporomandibular Disorders, Myofascial Pain Syndrome, Post-traumatic Stress Syndrome, Premestrual Syndrome, Vulvodynia/ Vulvar Vestibulitis Syndrome, Female Urethral Syndrome, all of them expressions of the expansion of receptive field (pain beyond the area of peripheral nerve supply), prolonged electrophysiological dicharge and an after-stimulus unpleasant quality of the pain (burning, throbbing, tingling or numbness) [46].

Our data, even if limited by the relative small number of patients, might nevertheless highlight some few interesting aspects.

First, the considerable number of patients who - for several reasons - have abandoned our study (35.2%) clearly points, in our opinion, to a problem in patient management. A psychological prejudice resulting in distrust of the medical establishment might be likely to play a key role here, perhaps on account of several factors: the number of specialists involved, the discordant diagnoses, the considerable sums invested/disinvested in drugs too often overrated in effectiveness but not supported by any scientific evidence, the patient's apprehension about being affected by a "mysterious" or otherwise unidentifiable disease, the fear to be "blamed" and "misunderstood" either by the attending physician or by family members (both of whom might be "reassured" by tests proving negative or inconclusive, as with the so-called "functional" diseases). All these elements play up the patients' psychophysical vulnerability [47,48].

Evaluations by the two groups of patients during the first month of treatment - in case improvement in pain management (VAS) does not match an equal global improvement (FIQ) - might confirm a somewhat ingrained mistrust of the proposed treatment, however partially successful. Yet, the results showed by the two groups of patients, point to the possible effectiveness of a multi-drug treatment based on the minimum effective dose concept. Specifically, data reported by Group B patients (i.e. pharmacological approach combined with an MCE educational program), while emphasizing the importance of the relevant psycho-emotional component of the disease, might lead, in our opinion, to a deeper awareness during the monthly meetings not only of the known physio-pathological aspects, but also of our scarce acquaintance with this condition and, consequently, with the limits of current therapeutic approaches, to a discussion with medical professionals on various aspects of the disease (thus benefiting from a form of active listening) [49,50], and finally to the possibility of experience sharing, as evidenced by the positive opinion about the overall experience.

Conclusion

In conclusion, we think that a combined therapeutic, pharmacological and educational approach might be a useful tool for the management of a complex and heavily debilitating disease (especially on a personal, familiar, and social level) such as Primary Fibromyalgia Syndrome.

References

1. Light KC, White AT, Tadler S, Iacob E, Light AR. Genetics and gene expression involving stress and distress pathways fibromyalgia with and without comorbid chronic fatigue syndrome. Pain Res Treat. 2012; 1-13.
2. Okifuji A, Turk DC. Stress and psycho physiological dysregulation in patients with fibromyalgia syndrome. Appl Psychophysiol Biofeedback. 2002; 27: 129-141.
3. Centonze V, Bassi A, Cassiano MA, Munno I, Dalfino L, Causarano V. Migraine, daily chronic headache and fibromyalgia in the same patient: an evaluative "continuum" of non organic chronic pain? About 100 clinical cases. Neurol Sci. 2004; 25: S292.
4. Palmieri VO, Centonze V, Pappagallo F, Mascolo A, Mele A, Santovito D, et al. Psychiatric Disorders, Stress Reaction and Fibromyalgia Syndrome [FMS]: report of an Experience on 48 Patients. Ann Depress Anxiety. 2014; 1: 1-4.
5. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al. The American College of Rheumatology 1990: criteria for the classification of fibromyalgia. Report of the Multicenter Criteria Committee. Arthr Rheum. 1990; 33: 160-172.
6. Wolfe F, Clauw DJ, Fitzcharles MA, Goldenberg DL, Katz RS, Mease P, et al. The American College of Rheumatology: preliminary diagnostic criteria for Fibromyalgia and measurement of symptoms severity. Arthr Care Res. 2010; 62: 600-610.
7. Wolfe F, Claw DJ, Fitzcharles MA, Goldenberg DL, Hauser W, Katz RS, et al. Fibromyalgia criteria and severity scales for clinical and epidemiological studies: a modification of the ACR Preliminary Diagnostic criteria for Fibromyalgia. J Rheumatol. 2011; 16: 1113-1122.
8. Schweinhardt P, Sauro KM, Bushnell MC. Fibromyalgia: a disorder of the brain? Neuroscientist. 2008; 14: 415-421.
9. Toussaint L, Vincent Ann, McAllister SJ, Wipple M. Intra-and Inter-Patient Symptom Variability in Fibromyalgia: Results of a 90-day Assessment. Musculoskeletal Care. 2015; 13: 93-100.
10. Lipkovich IA, Choy EH, Van Wambeke P, Deberdt W, Sagman D. Typology of patients with fibromyalgia: cluster analysis of duloxetine study patients. BMC Musculoskeletal Disorders. 2014; 15: 450-461.
11. Crofford LJ, Young EA, Engleberg NC, Korszun A, Brucksch CB, McClure LA, et al. Basal circadian and pulsatile ACTH and cortisol secretion in patients with fibromyalgia and/or chronic fatigue syndrome. Brain Behav Imm. 2004; 18: 314-325.
12. McCrae CS, O'Shea AM, Boissoneault J, Vatthauer KE, Robinson ME, Staud R, et al. Fibromyalgia patients have reduced hippocampal volume compared with healthy controls. Journal of Pain Research. 2015; 8: 47-52.
13. Van Houdenhove B, Egle UT. Fibromyalgia: a stress disorder? Piecing the biopsychosocial puzzle together. Psychoter Psychosom. 2004; 7: 267-275.
14. Mease PJ, Dundon K, Sarzi-Puttini P. Pharmacotherapy of fibromyalgia. Best Pract Res Clin Rheumatol. 2011; 25: 285-297.
15. Clark S, Tindall E, Bennett RM. A double blind crossover trial of prednisone versus placebo in the treatment of fibrositis. J Rheumatol. 1985; 12: 980-983.
16. Ngian GS, Guymer EK, Littlejohn GO. The use of opioids in fibromyalgia. Int J Rheum Dis. 2011; 14: 6-11
17. Bennett RM, Kamin M, Karim R, Rosenthal N. Tramadol and acetaminophen combination tablets in the treatment of fibromyalgia pain: a double-blind, randomized, placebo-controlled study. Am J Med. 2003; 114: 537-545.
18. Hauser W, Wolfe F, Tolle T, Uceyler N, Sommer C. The role of antidepressants in the management of fibromyalgia syndrome: a systematic review and meta-analysis. CNS Drugs. 2012; 16: 297-307.
19. Painter JT, Crofford LJ. Chronic opioid use in fibromyalgia syndrome: a clinical review. J Clin Rheumatol. 2013; 16: 72-77.
20. Calandre EP, Rico-Villademoros F. The role of antipsychotics in the management of fibromyalgia. CNS Drugs. 2012; 16: 135-153.
21. Hauser W, Wlitt B, Fitzcharles MA, Sommer C. Review of pharmacological therapies in fibromyalgia syndrome. Arthritis Res Ther. 2014; 16: 201-212.
22. Younger J, Parkitny L, McLain D. The use of low-dose naltrexone [LDN] as a novel anti-inflammatory treatment for chronic pain. Clin Rheumatol. 2014; 33: 451-459.
23. Patkar AA, Mesand PS, Krulewicz S, Mannelli P, Peindl K, Beebe KL. A randomized, controlled trial of controlled release paroxetine in fibromyalgia. Am J Med. 2007; 120: 448-454.
24. Straube S, Derry S, Moore RA, McQuay HJ. Pregabalin in fibromyalgia: mea-analysis of efficacy and safety from company clinical trial reports. Rheumatology. 2010; 49: 706-715.
25. Arnold LM, Rosen A, Pritchett YL, D'Souza DN, Goldstein DJ, Iyengar S, et al. A randomized, double-blind, placebo-controlled trial of duloxetine in the treatment of women with fibromyalgia with or without major depressive disorder. Pain. 2005; 119: 5-15.
26. Clauw DJ, Mease P, Palmer RH, Gendreau RM, Wang Y. Milnacipran for the treatment of fibromyalgia in adults: a 15-week, multicenter, randomized, double-blind, placebo-controlled, multiple dose clinical trial. Clin Ther. 2008; 30: 1988-2004.
27. Mease PJ, Clauw DJ, Gendreau RM, Rao SG, Kranzler J, Chen W, et al. The efficacy and safety of Milnacipran for treatment of fibromyalgia. A randomized, double-blind, placebo-controlled trial. J Rheumatol. 2009; 36: 398-409.
28. HauserW, Petzke F, Sommer C. Comparative efficacy and harms of duloxetine, Milnacipran and pregabalin in fibromyalgia syndrome. J Pain. 2010; 11: 505-521.
29. Grossman P, Tiefenthaler-Gilmer U, Raysz A, Kesper U. Mindfulness training as an intervention for fibromyalgia: evidence of postintervention and 3-year follow-up benefits in well-being. Psychother Psychosom. 2007; 76: 226-233.
30. Bernardy K, Fuber N, Kollner V, Hauser W. Efficacy of cognitive-behavioral therapies in fibromyalgia syndrome-a systematic review and meta analysis of randomized controlled trials. J Rheumatol. 2010; 37: 1991-2005.
31. Ang DC, Jensen MP, Steiner JL, Hilligoss J, Graacely RH, Saha C. Combining Cognitive-Behavioral Therapy and Milnacipran for Fibromyalgia: a Feasibility Randomized-controlled Trial. Clin J Pain. 2013; 29: 747-754.
32. Gonzales-Viejo MA, Avellanet M, Hernandez-Morcuende MI. A comparative study of fibromyalgia treatment: ultrasonography and physiotherapy versus sertraline treatment. Ann Readapt Med Phys. 2005; 48: 610-615.
33. Sim J, Adam N. Systematic review of randomized controlled trials of non pharmacological interventions for fibromyalgia. Clin J Pain. 2002; 18: 324-336.
34. Mannerkorpi K, Ahlmen M, Ekdahl C. Six-and 24- month follow-up of pool exercise therapy and education for patients with fibromyalgia. Scand J Rheumatol. 2002; 31: 306-310.
35. Cedraschi C, Desmeules J, Rapiti E, Baumgartner E, Cohen P, Finckh A, et al. Fibromyalgia: A randomized, controlled trial of a treatment programme based on self management. Ann Rheum Dis. 2004; 63: 290-296.
36. Williams DA, Cary MA, Groner KH, Chaplin W, Glaer LJ, Rodriguez AM, et al. Improving physical functional status in patients with fibromyalgia: A brief cognitive behavioral intervention. J Rheumatol. 2002; 35: 1280-1286.
37. Thieme K, Gracely RH. Are psychological treatments effective for fibromyalgia pain? Curr Rheumatol Rep. 2009; 11: 443-450.
38. Price DD, McGrath A, Rafii A, Buckingham B. The Validation of Visual Analogue Scales as Ratio Scale Measures for Chronic and Experimental Pain. Pain. 1983; 17: 45-56.
39. Burckhardt CS, Clark SR, Bennet RM. The Fibromyalgia Impact Questionnaire: Development and validation. Journal of Rheumatology. 1991; 18: 728-733.
40. Centonze V, Polito MB, Cassiano MA, Albano MG, Ricchetti G, Bassi A, et al. Patient Education and Migraine: a pilot study. Funct Neurol. 1998; 13: 117-123.
41. Ukai K, Kimura H, Arao M, Aleksic B, Yamamuchi A, Ishihara R, et al.

Effectiviness of low-dose Milnacipran for a patient suffering from pain disorder with delusional disorder [somatic type] in the orofacial region. Psychogeriatrics. 2013; 13: 99-102.

42. van Koulil S, van Lnkveld W, Kraaimaat FW, van Helmond T, Vedder A, van Hoom H, et al. Tailored cognitive- behavioral therapy and exercise training improves the physical fitness of patients with fibromyalgia. Ann Rheum Dis. 2011; 70: 2131-2133.

43. Valim V, Natour J, Xiao Y, Pereira AF, Lopes BB, Pollak DF, et al. Effects of physical exercise on serum levels of serotonin and its metabolite in fibromyalgia: a randomized pilot study. Rev Bras Reumatol. 2013; 53: 538-541.

44. Daenen L, Varkey E, Kellmann M, Nijs J. Exercise, not to exercise, or how to exercise in patients with chronic pain? Applying science to practice. Clin J Pain. 2015; 31: 108-114.

45. Vural M, Berkol TD, Erdogdu Z, Pekedis K, Kucukserat B, Aksoy C. Evaluation of the Effectiveness of an Aerobic Exercise Program and the Personality Characteristics of Patients with Fibromyalgia Syndrome: A Pilot Study. J Phys Ther Sci. 2014; 26: 1561-1565.

46. Yunus MB. Editorial review: an update on central sensitivity syndromes and the issues of nosology and psychobiology. Curr Rheumatol Rev. 2015; 11: 70-85.

47. Jimenez-Rodroguez I, Garcia-Leiva JM, Jimenez-Rodriguez BM, Condes-Moreno E, Rico-Villaermosa F, Calandre EP. Suicidal ideation and the risk of suicide in patients with fibromyalgia: a comparison with non-pain controls and patients suffering from low-back pain. Neuropsychiatr Dis Treat. 2014; 10: 625-630.

48. Calandre EP, Navajas-Rojas MA, Ballesteros J, Garcia- Carrillo J, Garcia-Leiva JM, Rico- Villademoros F. Suicidal ideation in patients with fibromyalgia: a cross-sectional study. Pain Pract. 2014; 17: 168-174.

49. Luciano JV, D'Amico F, Cerda-Lafont M, Pennarubia-Maria MT, Knapp M, Cuestas-Vargas A, et al. 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 Res Ther. 2014; 16: 451-459.

50. Kohl A, Rief W, Glomblewski JA. Do fibromyalgia patients benefit from cognitive restructuring and acceptance? An experimental study. J Behav Ther Exp Psychiatry. 2014; 45: 467-474.

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