# Patterns of pharmacologic and non-pharmacologic treatment, treatment satisfaction and perceived tolerability in patients with fibromyalgia: a patients' survey

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## ABSTRACT

**Objective.** *To evaluate the patterns of treatment among patients with fibromyalgia (FM) in Spain and to assess patient satisfaction and perceived tolerability of the treatment received.*

**Methods.** *An observational, cross-sectional study was conducted in Spain via internet from September 2015 to March 2017. We recorded sociodemographic and clinical information, including treatment satisfaction evaluated using a 10-point numerical rating scale (NRS) and adverse events.*

**Results.** *Evaluable subjects (n=915) were predominantly middle-aged, married women who presented with moderate to severe pain, sleep disturbance and affected quality-of-life. The most frequent non-pharmacologic treatments were physical exercise (85%), diet (47%), supplements such as magnesium and vitamins (47%), and psychotherapy (31%). The most frequently prescribed drugs were tramadol (40%), benzodiazepines (30%), duloxetine (22%), pregabalin (19%), amitriptyline (17%) and non-steroidal anti-inflammatory drugs (NSAIDs; 16%); 7.5% of patients received stronger opioids. After excluding benzodiazepines, NSAIDs, and paracetamol, 46% of patients received ≥2 drugs. Satisfaction with treatment (NRS mean score) was generally poor for pharmacologic treatment (4.1), exercise (4.7), psychotherapy (5.2), diet (5.0), physiotherapy (6.2) and acupuncture (6.3). The increase in the number of drugs prescribed was not associated with an increase in satisfaction, but rather with an increase in adverse events.*

**Conclusion.** *Patients with FM in Spain are overtreated with a combination of non-pharmacologic and pharmacologic therapies. Several of these therapies lack adequate support from randomised clinical trials and/or clinical practice guidelines. This overtreatment is not associated with relevant clinical benefits or patient satisfaction and, in the case of pharmacologic treatments, poses tolerability and safety issues.*

## Introduction

Fibromyalgia (FM) is a central sensitisation syndrome characterised by widespread pain that is frequently accompanied by symptoms such as anxiety, depression, sleep disturbance, fatigue and cognitive problems (1, 2). FM has a worldwide prevalence of 2.7% (3), predominantly affecting women with a female to male ratio of 3:1 (3) and, after osteoarthritis, is the most frequent disorder seen in rheumatology clinics (4). The presence of comorbid conditions, especially other central sensitisation syndromes (5, 6) and psychiatric disorders (7), is very frequent. FM is associated with a substantial burden for the individual and society (8-12).

It is generally agreed that the management of FM requires a multidisciplinary approach, combining non-pharmacologic treatments as the initial approach, mainly education, exercise and psychotherapy, and beginning pharmacologic treatments thereafter (13, 14). Among pharmacologic treatments, based on the results from clinical trials, the guidelines recommend pregabalin, duloxetine, milnacipran, amitriptyline, cyclobenzaprine and, in certain patients, tramadol as therapeutic options (13, 14). In addition to tolerability issues, none of these drugs improves all symptomatic domains of the disease, exhibits a large effect on the symptoms or has consistently demonstrated a greater overall efficacy compared with the others (15). Data from clinical practice also reflects this important limitation of the pharma-

cologic treatments for FM. According to a recent study undertaken in USA, after one year of initiating pharmacologic treatment, only 25% of the patients continue with the initial option, which requires switching the medication, a combination with another drug or simply a treatment discontinuation (16). Consistent with this finding, it has been reported that less than half of the patients with FM are satisfied with the medication they are receiving (17). In addition, it also appears that an important proportion of patients with FM do not receive appropriate treatment and that treatment adherence is poor (16). A wide variety of non-pharmacologic treatments are used in the clinical practice in patients with FM (9, 17-22), and although the information is very limited, perceived effectiveness and satisfaction with these therapies are also poor (9, 22).

Overall, with the exception of a survey conducted in Latin America and Europe (20) and a recent study conducted in the United Kingdom (22), most of the information we have on the patterns of treatment and patient perceptions of those treatments comes from studies conducted in USA, and data on treatment satisfaction as well as patient perception of tolerability are limited. This study aimed to evaluate the patterns of treatment among patients with FM in Spain and to assess patient satisfaction and perceived tolerability with the treatment received.

## Materials and methods

### *Study design*

This was an observational, cross-sectional study conducted in Spain between September 2015 to March 2017. Participation in the survey was solicited through several patient associations in every region of Spain and diffusion through social networks. Participants were briefly informed at the beginning of the survey of its objectives and that they should be aged 18 or older and have been diagnosed with FM; due to the nature of the survey, diagnosis relied on patients' report and could not be confirmed by the study investigators. Participants were also informed that answering the survey was equivalent to consent to participate in the study and that their data would be used for investigational purposes. Since the questionnaire was anonymous, no written informed consent was required. The study was approved by the Human Research Ethics Committee of the University of Granada.

The survey consisted of five blocks of questions (it is available at http://goo.gl/forms/UAO7RKC6ks. See Annex 1 for an English translation of the survey): sociodemographic information, clinical data, data on pharmacologic treatments, data on non-pharmacologic treatments, and an assessment of patient satisfaction with treatment. Sociodemographic data included age, sex, marital status, educational level, and employment status. Clinical data comprised information on duration of diagnosis, comorbidities, and five questions that used a 10-point numerical rating score (NRS) to evaluate the impact of the disease on daily life, pain intensity, sleep quality, level of depression and level of anxiety. Except for the sleep scale, the greater the score, the greater the impact or symptom; the reverse was applicable for the sleep rating scale. Data on pharmacologic treatment included who prescribed the treatment; medications and dosage that the patient was currently receiving; whether the patient was taking any vitamin, supplement, probiotic/prebiotic or any alternative natural/herbal medicines; and whether the patients experienced any disturbances associated with the current treatment. Data on non-pharmacologic treatment included information on physical exercise (type and frequency), psychotherapy (type and frequency), diet, and an open question on other treatments. Finally, patient satisfaction with treatment was evaluated with a 10-point NRS where 1 indicated a lack of satisfaction and 10 that the patient was completely satisfied; there were 5 NRS, one for each type of treatment.

### *Data analysis*

The statistical analyses were mostly descriptive, using means and standard deviation for quantitative variables and absolute and relative frequencies for qualitative variables. Difference in the mean satisfaction according to the number of drugs received was analysed using one-way analysis of variance (ANOVA). Mean satisfaction of each non-pharmacologic treatment was compared with the mean satisfaction of pharmacologic treatment using an unpaired t test. We performed two exploratory multiple linear regression analyses. In the first model, treatment satisfaction as evaluated with the NRS was the dependent variable and the independent variables were age (years), sex, time from diagnosis (categorised as <1 year, 1-5 years and >1year), number of diseases associated with FM, performing physical exercise, receiving psychological treatment, receiving dietetic treatment, number of drugs received, presence of side-effects, and the scores in the NRS for pain intensity, sleep quality, depressive symptomatology and anxious symptomatology. In the second model, performed only in patients who were receiving pharmacologic treatment, the dependent variable was the score in the NRS of impact on daily-life and the independent variables were the same as in the first model. All comparisons were two-tailed and considered significant if $p<0.05$. All analyses were performed using IBM SPSS Statistics for Windows, v. 25.0. (Armonk, NY: IBM Corp).

**Table I.** Demographic characteristics.

| Characteristic | n=915 |
|---|---|
| Age (years), mean (SD) | 47.0 (9.3) |
| Sex (female), n (%) | 866 (94.6) |
| Marital status, n (%) | |
| Married/living with a partner | 625 (68.3) |
| Divorced | 141 (15.4) |
| Single | 127 (13.9) |
| Widowed | 22 (2.4) |
| Employment status, n (%) | |
| Employed | 338 (36.9) |
| Housework | 154 (16.8) |
| Disabled | 88 (9.6) |
| Unemployed | 195 (21.3) |
| Student | 9 (1.0) |
| Retired (age) | 17 (1.9) |
| Retired (disease) | 114 (12.5) |

n: number of patients; SD: standard deviation.

## Results

Overall, 1,166 subjects responded to the questionnaire. After removing duplicates (n=103) and questionnaires from countries other than Spain (n=148), we

**Table II.** Characteristics of the disease.

| Characteristic | n=915 |
|---|---|
| Time since diagnosis, n (%) | |
| <1 year | 111 (12.1) |
| 1-5 years | 267 (29.2) |
| >5 years | 537 (58.7) |
| Associated symptoms[a], mean (SD) | |
| Pain intensity | 7.2 (2.0) |
| Sleep quality | 3.4 (2.3) |
| Depression | 5.8 (2.7) |
| Anxiety | 6.3 (2.6) |
| Impact on daily life, mean (SD) | 7.7 (2.1) |
| Frequent (≥5%) comorbid diseases, n (%) | |
| Anxiety disorder | 555 (60.7) |
| Chronic fatigue syndrome | 539 (58.9) |
| Depressive disorder | 496 (54.2) |
| Irritable bowel syndrome | 448 (49.0) |
| Arthrosis | 400 (43.7) |
| Tension-type headache | 374 (40.9) |
| Migraine | 383 (41.9) |
| Temporomandibular dysfunction | 346 (37.8) |
| Interstitial cystitis | 144 (15.7) |
| Rheumatoid arthritis | 143 (15.6) |
| Multiple chemical sensitivity syndrome | 120 (13.1) |
| Disc herniation | 65 (7.1) |

[a]All symptoms were evaluated in a NRS (1-10); the greater the score, the poorer the clinical status, except for sleep quality, for which the reverse was applicable.
n: number of patients; SD: standard deviation.

**Table III.** Most frequent (≥5%) types of non-pharmacologic treatment.

| Type of treatment[a] | n (%) |
|---|---|
| Physical exercise | 777 (84.9) |
| Walking | 604 (66.0) |
| Swimming | 119 (13.0) |
| Pilates | 83 (9.1) |
| Cycling | 68 (7.4) |
| Supervised Gym | 50 (5.5) |
| Diet | 432 (47.2) |
| Hypocaloric | 155 (16.9) |
| Gluten-free | 121 (13.2) |
| Supplements | 427 (46.7) |
| Magnesium | 177 (19.3) |
| Vitamin D | 76 (8.3) |
| Complex B Vitamins | 68 (7.4) |
| Multivitamin complex | 62 (6.8) |
| Vitamin B12 | 52 (5.7) |
| Psychotherapy | 287 (31.4) |
| Cognitive behavioural therapy | 140 (15.3) |
| Relaxation techniques | 112 (12.2) |
| Mind-body therapy | 52 (5.7) |

[a]Patients could be receiving several treatments.

had 915 evaluable questionnaires. Subjects were predominantly middle-aged, married women (Table I). Patients had an established diagnosis of FM for more than 5 years and exhibited moderate to severe pain, sleep disturbance and an impact on daily life (Table II); they also presented with a high number of comorbidities, mainly with other central sensitisation entities, psychiatric disorders and musculoskeletal disorders.

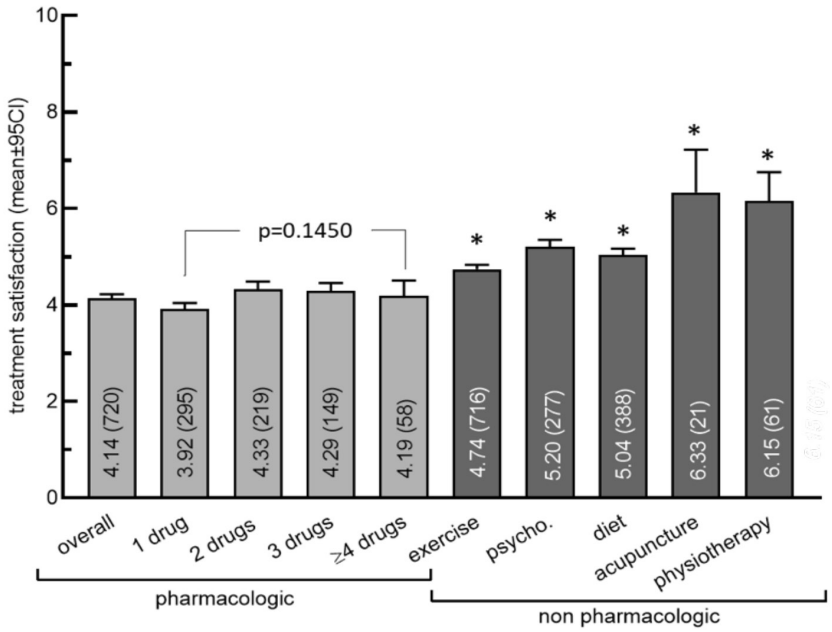


**Fig. 1.** Treatment satisfaction with pharmacologic and non-pharmacologic treatments for fibromyalgia. *$p<0.0001$ *vs*. overall pharmacologic treatment.

*Non-pharmacologic treatment*

The most frequent non-pharmacologic treatment was physical exercise (85%), most commonly walking (66%) (Table III); 33% of the participants performed physical exercise more than 3 days in a week and 44% of patients 2–3 days per week. A specific diet was followed by almost half of the participants, with hypocaloric and gluten-free diets used most frequently. Almost half of the participants were taking supplements, mainly magnesium and several kinds of vitamins. Finally, only one-third of patients were receiving psychotherapy; however, the majority of such participants (73%) received it less than 1 day a week.

*Pharmacologic treatment*

Pharmacologic treatment was received by 87% of participants and was prescribed in almost half of the participants by a family physician alone (18.3%), a rheumatologist alone (15.1%) or both specialists (14.7%) (Supplementary Fig. 1). Overall and regardless other coprescribers, the most frequent prescribers were a family physician (58.8%), a rheumatologist (56.3%), a psychiatrist (33.3%) and a pain physician (20.0%). The most frequently prescribed drugs were tramadol (40%) and benzodiazepines (30%) and to a lesser extent duloxetine (22%), pregabalin (19%), amitriptyline (17%) and NSAIDs (16%); 7.5% of participants received other opioids different from tramadol (Table IV). When only considering drugs for the treatment of FM supported by at least one randomised clinical trial (*i.e*. excluding benzodiazepines, NSAIDs, and paracetamol), 46% of participants were receiving two or more drugs and the most frequently used drug was tramadol, either used as monotherapy or in combination (Table IV). Mean drug dosages are also presented in Table IV. There were some differences when the single prescriber was a rheumatologist (n=135) or a family physician (n=188). Among participants whose pharmacologic treatment was prescribed by a rheumatologist, there was a higher frequency of prescription of tramadol (40% *vs*. 32%), duloxetine (22% *vs*. 15%), amitriptyline (22% *vs*. 14%), pregabalin (17% *vs*. 13%), NSAIDs (16% *vs*. 13%), other opioids (11% *vs*. 5%), and fluoxetine (10% *vs*. 6%); in contrast, they showed a lower prescription frequency of paracetamol (4% *vs*. 7%) and paroxetine (4% *vs*. 7%), (data

on differences of less than 3% are not reported herein).

*Treatment satisfaction and adverse events*

Regardless of the treatment modality, satisfaction was low (Fig. 1) but was significantly higher for any non-pharmacologic approach than for pharmacologic treatments. With a score over 6.0 in the 10-point NRS, acupuncture and physiotherapy were the interventions associated with the highest satisfaction. The increase in the number of drugs prescribed for the treatment of FM was not associated with statistically significant increase in satisfaction (Fig. 1). Satisfaction did not greatly differ between drugs used as monotherapy with a mean (SD) score in the 10-point NRS of 4.1 (2.2) for tramadol, 3.9 (2.2) for amitriptyline, 3.6 (1.7) for duloxetine, and 3.5 (2.1) for pregabalin. The use of tramadol in participants receiving combination therapy was associated with a slight increase of satisfaction when combined with another drug (with tramadol 4.6 [2.3] *vs*. without tramadol 4.1 [2.3]) but remained the same when used in polytherapy (with tramadol 4.3 [2.2] *vs*. without tramadol 4.2 [2.0]).

Adverse events were common and increased as the number of coprescribed drugs increased (Table V). In general, the type of side effect was concordant with the adverse reaction profile of the most frequently prescribed drugs.

**Table IV.** Most frequent (≥5%) pharmacological treatment.

| Drug | n (%) | Daily dose (mg/day), mean (SD) |
|---|---|---|
| Overall (n=915) | | |
| Tramadol | 368 (40.2) | 190.90 (127.1) |
| Benzodiazepine[a] | 276 (30.2) | NA |
| Duloxetine | 204 (22.3) | 69.72 (51.2) |
| Pregabalin | 176 19.2) | 161.41 (109.4) |
| Amitriptyline | 157 (17.2) | 32.88 (24.7 |
| NSAIDs[a] | 143 (15.6) | NA |
| Paracetamol[a] | 93 (10.2) | NA |
| Fluoxetine | 84 (9.2) | 32.00 (25.6) |
| Trazodone | 77 (8.4) | 95.48 (42.8) |
| Other opioids[a] | 69 (7.5) | NA |
| Gabapentin | 58 (6.3) | 902.55 (589.4) |
| Paroxetine | 54 (5.90) | 26.33 (10.7) |
| Cyclobenzaprine | 51 (5.6) | 28.33 (40.0) |
| Venlafaxine | 50 (5.5) | 182.75 (104.0) |
| Escitalopram | 47 (5.1) | 18.38 (10.1) |
| **By number of drugs (n=915)[b]** | | |
| One drug | 295 (32.2) | |
| Tramadol | 92 (10.1) | |
| Duloxetine | 52 (5.7) | |
| Amitriptyline | 41 (4.5) | |
| Pregabalin | 31 (3.4) | |
| Fluoxetine | 18 (2.0) | |
| Two drugs | 219 (23.9) | |
| Duloxetine+tramadol | 28 (3.1) | |
| Amitriptyline+tramadol | 18 (2.0) | |
| Fluoxetine+tramadol | 14 (1.5) | |
| Pregabalin+tramadol | 12 (1.3) | |
| Duloxetine+pregabalin | 12 (1.3) | |
| Three drugs | 149 (16.3) | |
| Duloxetine+pregabalin+tramadol | 12 (1.3) | |
| Duloxetine+trazodone+tramadol | 8 (0.9) | |
| Four drugs | 42 (4.6) | |
| ≥Five drugs | 15 (1,6) | |

n: number of patients; NA: not applicable; SD: standard deviation.
[a]Each category comprises several drugs or combinations of drugs and therefore, no mean dose can be calculated.
[b]For these analyses we only considered drugs for the treatment of fibromyalgia supported by at least one randomised clinical trial (*i.e*. benzodiazepines, non-steroidal anti-inflammatories, and paracetamol were excluded).

*Exploratory multivariate analysis*

The only factor negatively associated with treatment satisfaction was the presence of side-effects (β=-0.138, $p<0.001$). The factors positively associated with treatment satisfaction were the score in the sleep quality (β=0.236, $p<0.001$) and the score in pain intensity (β=0.087, $p=0.049$). The number of prescribed drugs was not associated with treatment satisfaction (β=0.031, $p=0.414$).

The factors associated with a greater impact on daily life were pain intensity (β=0.736, $p<0.001$), severity of anxious symptomatology (β=0.084, $p=0.017$), time from diagnosis (β=0.046, $p=0.049$), and being male (β=0.048, $p=0.028$). The only factor associated with lesser impact on daily life was performing physical exercise (β=-0.044, $p=0.049$).

## Discussion

These results indicate that patients with FM in Spain are usually treated with a combination of drugs and non-pharmacologic strategies. Satisfaction with most treatment approaches is poor, and the treatment that patients are receiving appears inadequate in a substantial proportion of patients due to the following reasons: overuse of tramadol and stronger opioids, use of low doses for some drugs such as pregabalin, use of polypharmacy without increasing treatment satisfaction but increasing adverse events, inconsistent use of effective non-pharmacologic approaches such psychotherapy, and use of therapies that lack proven effectiveness such as diets, magnesium or vitamins. In contrast, exercise was a generalised practice among these patients.

Our study has several limitations that should be considered when interpreting the results. First, we used a cross-sectional design which, although adequate for evaluating prescription patterns, is subjected to survival bias. That is, only patients who continue with the prescribed treatment (*i.e*. those with better efficacy and/or tolerability results) were captured by our study. In other words, we had an optimistic snapshot of treat-

**Table V.** Adverse events overall and by number of drugs.

| System organ/side-effects, n (%) | Overall n=720 | 1 Drug n=295 | 2 Drugs n=219 | 3 Drugs n=149 | ≥4 Drugs n=57 |
|---|---|---|---|---|---|
| Gastrointestinal side-effect | 358 (49.7) | 124 (41.9) | 116 (53.0) | 76 (51.0) | 42 (73.7) |
| Nausea/vomiting | 167 (23.2) | 66 (22.3) | 54 (24.7) | 29 (19.5) | 18 (31.6) |
| Abdominal pain/heartburn | 142 (19.7) | 45 (15.3) | 43 (19.6) | 35 (23.5) | 19 (33.3) |
| Constipation/diarrhoea | 49 (6.8) | 13 (4.4) | 19 (8.7) | 12 (8.1) | 5 (8.8) |
| Central nervous system side-effect | 404 (56.1) | 145 (49.0) | 119 (54.3) | 91 (61.1) | 49 (86.0) |
| Somnolence/sedation/fatigue | 166 (23.1) | 56 (19.0) | 54 (24.7) | 37 (24.8) | 19 (33.3) |
| Dizziness/vertigo | 118 (16.4) | 43 (14.6) | 36 (16.4) | 26 (17.4) | 13 (22.8) |
| Anxiety/nervousness/irritability | 31 (4.3) | 13 (4.4) | 8 (3.6) | 3 (2,0) | 7 (12.3) |
| Cognitive impairment | 45 (6.3) | 15 (5.1) | 9 (4.1) | 14 (9.4) | 7 (12.3) |
| Other organs/systems side-effects | 93 (12.9) | 33 (11.2) | 15 (6.9) | 29 (26.2) | 16 (28.1) |

ment. The cross-sectional design and the lack of information on other important variables (*e.g.* fatigue or cognition) make that our multivariate analyses of factors associated with treatment satisfaction and with the impact on daily life can only be considered exploratory. The source of data were people aware of the survey through patient associations and social networks; this is likely to affect the representativeness of our sample, which probably includes patients with greater awareness of the disease. We believe that to a certain extent, this could have also contributed to capture an optimistic snapshot. It is important to perform further studies with a more representative sample of patients with FM recruited from the general population. The diagnosis of FM was self-reported and due to the anonymous nature of the study could not be confirmed by a member of the research team. Finally, our survey was conducted in a single European country, thus contributing to the limitations of its representativeness. Pharmacologic treatments are dominated by tramadol, either as a monotherapy or combination therapy. This probably reflects the severity of pain and associated disability in these patients, as well as the general limitation of all available pharmacologic treatments for ameliorating pain. It should be bear in mind that, although only performed as an exploratory analysis, the strongest factor associated with a greater impact on daily life was pain intensity; thus, for each point increase in the score of pain intensity, the score in the impact on daily life increased over 0.7 points. In addition, not only was tramadol the predominant pharmacologic approach, but the use of stronger opioids was also relatively frequent (7.5%), and in approximately 20% of the participants, pain units were involved in pharmacologic management. This frequent use of tramadol has been consistently reported in studies conducted in the US across the last 10 years (9, 16, 17, 23). In Europe, a recent survey conducted in the UK showed that codeine and tramadol were among the 5 more commonly tried drugs in patients with FM (22). In our view, this use of tramadol is not justified by the evidence, which is limited to two randomised controlled trials evaluating its effect on pain when administered orally as monotherapy (24) or in combination with paracetamol (25). However, our results also indicate that, although treatment satisfaction was generally poor, tramadol was associated with a slightly higher satisfaction than other drugs. We believe that this result is likely to reflect the better results obtained on pain with tramadol than with other drugs. The effect of tramadol is limited to pain and therefore its use as a monotherapy is difficult to justify. The use of other stronger opioids was lower than that reported in the US (9, 17) but was nevertheless high (7.5%) indicating that the abuse of opioids for treating chronic pain is a problem not limited to the US but also appears to affect European countries such as Spain or, as shown in a recent survey, the UK (22). According to the Center for Disease and Prevention guidelines for the use of opioids in chronic pain, they only should be used when benefits for pain and function are expected to outweigh the risks at the lowest effective dose and their continuation should be reevaluated every three months, among other recommendations (26). Under these conditions, it is unlikely that opioids could play a significant role in patients with FM. In our view, if the initial treatment for the amelioration of pain failed, the combination of pregabalin with either duloxetine or, where available, milnacipran as well as the combination of low doses of amitriptyline with an antidepressant or with melatonin are better alternatives than opioids with some support from clinical trials (27-31). The addition of NSAIDs to the standard treatment is not associated with an additional clinical benefit on pain (32, 33) and should not be recommended.

As mentioned in the introduction, the effects of available evidence-based drugs for the treatment of FM (namely, duloxetine, milnacipran, amitriptyline, cyclobenzaprine, pregabalin, and tramadol) are limited to a few symptoms and are usually small or doubtful in their clinical relevance (15, 34). Therefore, although the evidence on combinations of drugs for the treatment of FM is far from being robust (35), it is not surprising that patients required more than one pharmacologic treatment. Further on the usefulness of combination therapy for pain, which has been recently analysed in a systematic review (35), the use of some combinations, such as melatonin and amitriptyline, fluoxetine and amitriptyline, and pregabalin and duloxetine, has also been associated with greater overall improvement compared to monotherapy (27, 28, 30, 31) and in some reports, to a greater benefit on the quality of life (28, 31). In our study, the combination of amitriptyline with melatonin was used in 1 participant and with fluoxetine in 4 participants, and the combination of duloxetine and pregabalin was used in 12 participants. Bearing in mind that 24% of patients were receiving two drugs, our results indicate that most patients receive combinations that lack the support of any randomised clinical trial. Nearly 22% of participants were receiving three or more drugs without exhibiting higher satisfaction (neither in the bivariate analysis, nor in the multivariate analysis) and presented with more adverse events than those who were receiving

two drugs. Thus, this polypharmacy, in addition to not being supported by research evidence, does not appear to be clinically justified and should be avoided. In addition to worsening tolerability, polypharmacy in these patients increases the risk of drug-drug interactions, especially if we take into consideration that many of the prescribed drugs are inhibitors and/or substrates of CYP2D6 of the cytochrome P450 (36).

Satisfaction with pharmacologic treatment was very poor regardless of the drugs or whether they were used as monotherapy or in combination and was poorer than non-pharmacologic approaches. This is somewhat consistent with the results of the survey conducted in UK where, although effectiveness of both types of intervention were similar, acceptability, measured as the ratio between effectiveness and tolerability, was higher with non-pharmacologic approaches (22). Our results regarding satisfaction are especially remarkable since, due to our design, we captured information on patients who are tolerating the drug and probably exhibiting the greatest long-term efficacy; that is, as mentioned above, we are looking at the best possible scenario. The fact that satisfaction with pharmacologic treatments was consistently lower than with any other type of non-pharmacologic treatment reinforces the importance of enhancing the prescription of those non-pharmacologic approaches which are supported by enough evidence such as some forms of exercise (*i.e.* aerobic or strengthening exercise) (37, 38) and psychotherapies (*i.e.* cognitive-behavioural and, possibly, mindfulness-based interventions) (39, 40). Psychotherapy appears underused, bearing in mind the need to incorporate coping strategies by these patients and the high proportion of patients who exhibited anxiety or depressive symptoms; unfortunately, this type of therapy is not fully incorporated into the Spanish national health system. Conversely, supplements appear to be overused since there is no evidence that supports such frequent use of magnesium, vitamins or other complementary remedies (41, 42). This overuse of supplements could be related to self-prescription practices; however, it is likely that nurses and physicians could also contribute to this practice (43). Diets were frequently used in our study. Diets could have a non-specific beneficial impact on some symptoms (*e.g.* gastrointestinal) (39), and could possibly be recommended for some selected patients but not to the extent as was seen in our study. However, in some patients, diet and exercise could be part of a personal strategy for having a healthy lifestyle, and as such, is welcomed. Overall, the frequent use of complementary treatments in our sample is consistent with the results of other studies (9, 19) and could be related with the high levels of pain and disability (18).

Interestingly, although the sample size was small, the interventions associated with the highest satisfaction were acupuncture and physiotherapy. Acupuncture added to the standard treatment has been shown to be effective in reducing pain in patients with FM and is well-tolerated, and thus is included among the recommended treatment options in the EULAR guidelines (14). The results regarding physiotherapy are difficult to interpret since it was assessed by an answer to an open-ended question ("other treatments") and therefore, it is likely to include a variety of physical interventions. A recent overview of systematic reviews considered that only low to moderate intensity endurance and strength training are recommended (44); in fact, EULAR guidelines recommend against the use of some types of physical therapies, such as chiropractic care and massage, while strongly recommending aerobic and strengthening exercises (14). We believe that the greater satisfaction with acupuncture, physiotherapy and other non-pharmacologic approaches is likely to be related to their improved tolerability over pharmacologic treatments and thus, their better benefit-risk ratios.

In conclusion, patients with FM in Spain are overtreated with a combination of non-pharmacologic and pharmacologic therapies, and several of these therapies lack adequate support from randomised clinical trials and/or clinical practice guidelines. This overtreatment is not associated with any relevant clinical benefit or patient satisfaction and, in the case of pharmacologic treatments, poses tolerability and safety issues. Overall, there is a wide room for improvement in the management of these patients by all the stakeholders involved: physicians improving the rational use of drugs and other interventions, and providing a better patient education on their disease and its therapeutic alternatives; patients avoiding the use of supplements and other complementary therapies that lack of sufficient evidence and initiating or enhancing healthy habits (*e.g.* aerobic exercise); healthcare managers improving access to the few evidence-based effective therapeutic alternatives (*e.g.* psychotherapy); and national health authorities and organisations providing funding for research favouring the inclusion of the search for and evaluation of new therapeutic, possibly multimodal, alternatives for these patients in the research agenda.

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