



ORIGINAL ARTICLE

The attitudes of Turkish physicians in the treatment of fibromyalgia; is “Pregabalinophobia” the new reality of pain medicine?

Türk hekimlerinin fibromiyalji tedavisindeki tutumları; pregabalinofobi ağrı tedavisinin yeni gerçeği mi?

📧 Sertaç KETENCI,¹ 📧 Birzat Emre GÖLBOYU,² 📧 Ender SALBAŞ,³ 📧 Bora UZUNER,⁴ 📧 Bahadır ÇİFTÇİ⁵

Summary

Objectives: This study aims to determine the treatment preferences of physicians interested in fibromyalgia treatment and to investigate their hesitations about prescribing pregabalin.

Methods: Our survey study was conducted between February 5 and 20, 2021. The survey forms were sent to the known email addresses and phone numbers of 1569 physical medicine and rehabilitation (PMR), algology, and rheumatology physicians. The replies to the surveys were checked for possible resubmissions. The pooled data were evaluated with the SPSS 22.0 statistical package program. Frequency distributions were calculated and presented as n, %.

Results: Four hundred and six PMR, rheumatology, and algology specialists fulfilled the study forms. About 59.0% of physicians stated that they prefer duloxetine as the first-line agent of fibromyalgia syndrome (FMS) treatment. Pregabalin was only 6.0% of the physicians' first choice for FMS. About 35.0% of the participating physicians stated that the PMR department should follow up FMS patients. About 44.3% of the participants noted that they refer FMS patients to other departments which interested in FMS treatment and do not want to follow-up FMS patients. About 81% agreed that pregabalin causes addiction. About 36.7% stated that at least 20% of the patients could abuse pregabalin and 97.8% of physicians stated that they were prejudiced about prescribing pregabalin to prisoners. Approximately two of the three physicians experienced an act of violence in their hospital regarding pregabalin prescribing.

Conclusion: These data showed that the “Pregabalinophobia” should be accepted. This condition is associated with life safety concerns of the physician not only from unreliability of the drug. It seems that the doctors have valid reasons to develop this prejudice.

Keywords: Drug abuse; fibromyalgia; pregabalin, pregabalinophobia.

Özet

Amaç: Bu çalışma, fibromiyalji tedavisi ile ilgilenen hekimlerin tedavi tercihlerini belirlemek ve pregabalin reçetelemek konusundaki tereddütlerini araştırmayı amaçlamaktadır.

Gereç ve Yöntem: Anket çalışmamız 5 Şubat 2021–20 Şubat 2021 tarihleri arasında gerçekleştirildi. Fiziksel tıp ve rehabilitasyon, algoloji ve romatoloji hekimlerinden oluşan 1569 kişinin bilinen e-posta adreslerine ve telefon numaralarına anket formları gönderildi. Anketlere verilen yanıtlar olası yeniden gönderimler açısından kontrol edildi. Veri havuzu SPSS 22.0 istatistik paket programı ile değerlendirildi. Frekans dağılımları hesaplandı ve n, % olarak sunuldu.

Bulgular: Dört yüz altı fiziksel tıp ve rehabilitasyon, romatoloji ve algoloji uzmanı çalışma formlarını tamamladı. Hekimlerin %59'u fibromiyalji tedavisinde birinci basamak ajan olarak duloksetin tercih ettiklerini belirtti. Pregabalin, hekimlerin fibromiyalji için ilk tercihinin sadece %6'sıydı. Çalışmaya katılan hekimlerin %35'i fibromiyalji hastalarının fiziksel tıp ve rehabilitasyon bölümlerinde takip edilmesi gerektiğini belirtti. Katılımcıların %44,3'ü fibromiyalji hastalarını, fibromiyalji tedavisi ile ilgilenen ve fibromiyalji hastalarını takip etmek isteyen diğer bölümlere sevk ettiklerini belirtti. Katılımcıların %81'i pregabalinin bağımlılığa neden olduğunu kabul etti. Katılımcıların %36,7'si fibromiyalji hastalarının en az %20'sinin pregabalinini kötüye kul-

¹Department of Rheumatology, Manisa City Hospital, Manisa, Türkiye

²Department of Pain, Manisa City Hospital, Manisa, Türkiye

³Department of Physical Medicine and Rehabilitation, Ömer Halisdemir University Faculty of Medicine, Niğde, Türkiye

⁴Department of Physical Medicine and Rehabilitation, Ondokuz Mayıs University Faculty of Medicine, Samsun, Türkiye

⁵Department of Anesthesiology and Reanimation, Medipol University, İstanbul, Türkiye

Submitted (Başvuru tarihi) 13.05.2021 Accepted after revision (Düzeltilme sonrası kabul tarihi) 01.09.2021 Available online date (Online yayımlanma tarihi) 06.07.2022

Correspondence: Dr. Bora Uzuner. Ondokuz Mayıs Üniversitesi Tıp Fakültesi, Fiziksel Tıp ve Rehabilitasyon Anabilim Dalı, Samsun, Türkiye.

Phone: +90 - 362 - 312 19 19 / 2338 **e-mail:** buzuner@hotmail.com

© 2022 Turkish Society of Algology

lanabileceğini belirtti. Hekimlerin %97,8'i mahkumlara pregabalin reçete edilmesi konusunda ön yargılı olduğunu belirtti. Üç hekimden yaklaşık ikisi hastanelerinde pregabalin reçete edilmesi ile ilgili bir şiddet olayına maruz kaldığını belirtti.

Sonuç: Bu veriler “pregabalinofobi”nin kabul edilmesi gerektiğini göstermektedir. Bu durum, yalnızca ilacın güvenilmezliğinden değil, hekimin can güvenliği endişeleriyle de ilişkilidir. Görünüşe göre doktorlarda bu ön yargının oluşmasında geçerli nedenler vardır.

Anahtar sözcükler: Fibromiyalji; ilaç kötüye kullanımı; pregabalin; pregabalinofobi.

Introduction

Fibromyalgia syndrome (FMS) is a disorder with several symptoms, including chronic diffuse pain, fatigue, sleep disorders, cognitive dysfunction, and depressive episodes.^[1] FMS commonly affects women 30–50 years old, and studies indicate a prevalence of between 1.0% and 4.0% of the general population, ranging from 0.0 to 4.0% in men and 2.5 to 10.5% in women.^[2,3]

The primary concept of fibromyalgia was developed after researchers realized that its etiology was not the result of peripheral damage or inflammation but rather central neuronal mechanisms. Recent studies have shown that FMS is a multisymptomatic disorder characterized by dysfunction in the central pain mechanism, and today, the terms “central sensitivity” or “central pain syndrome,” “non-nociceptive pain,” and “chronic multisymptomatic diseases” are used.^[4] Due to the central mechanisms in FMS, pregabalin, a centrally acting analgesic with anxiolytic and anticonvulsant effects, is frequently used in the treatment of FMS.^[5]

Pregabalin is an $\alpha 2$ - δ calcium channel ligand and has been approved by the FDA as a first-line treatment for neuropathic pain. It has been reported that pregabalin showed improvements in pain, sleep disorders, and fatigue in FMS patients in randomized, double-blind, and placebo-controlled studies. Gabapentin has similar pharmacological effects as pregabalin and is also recommended for FMS treatment.^[6] These drugs provide effective pain control for FMS; however, they also have a significant side effect profile consisting of several symptoms in the neurological system, primarily somnolence, lethargy, and euphoria. Sometimes, these effects restrict the use of these drugs, and sometimes, people prefer off-label use of these drugs because of such effects.^[7]

Pregabalin abuse is increasing worldwide. People take higher-than-recommended doses of pregabalin due to its euphoric effects. There is a growing black

market for pregabalin in populations at high risk of abuse,^[8,9] such as prisons, where pregabalin is sometimes prescribed as a pain killer instead of opioids. Increased incidence of this kind of drug abuse makes physicians extremely reluctant to prescribe pregabalin for pain management. Given the fact that “opiophobia” is defined and accepted concerning opioid prescription, today, we suggest that the possible hesitation of physicians to prescribe pregabalin may be termed “Pregabalinophobia.”

Therefore, in this survey study, we have investigated the medical treatment preferences and possible concerns of algology, rheumatology, and physical medicine and rehabilitation (PMR) specialists who follow up with FMS patients in their clinics about pregabalin prescription to reveal the concept of “Pregabalinophobia.”

Material and Methods

Our study was undertaken between February 5 and 20, 2021, following the approval of the ethics committee. Before we commenced, 10 physicians who were not participating in the study were asked to read our survey for clarity, and a preliminary study was conducted.

Data collection

Survey data in the form of web data were obtained through an electronic data form. The survey forms were sent to the known email addresses and phone numbers of 1569 physicians. The replies to the surveys were checked for possible resubmissions.

There were a total of 30 questions in the survey form. The first part of the form consisted of seven questions collecting demographic data. The second part consisted of six questions for participants about their preferences concerning FMS management, maximum dose, and pregabalin side effects, their opinions about which department should follow up with FMS patients, and whether they refer patients.

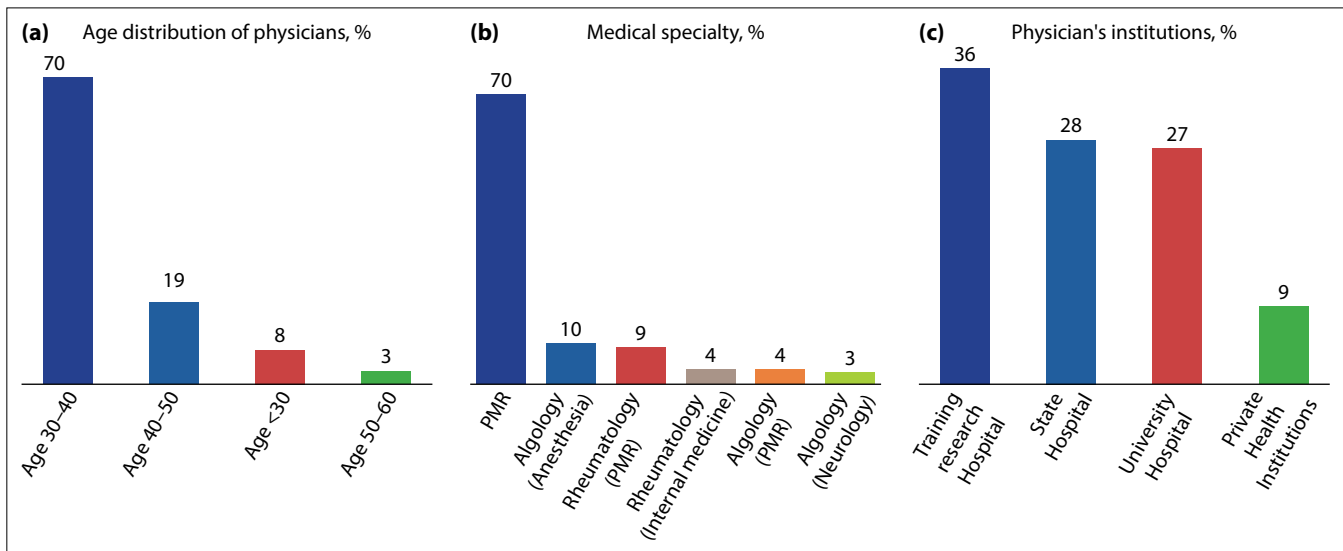


Figure 1. (a) Age distribution of physicians, (b) medical specialty, and (c) physician's institutions. PMR: Physical medicine and rehabilitation.

The third part consisted of five questions designed to reveal participants' views on the current "health practice statement" notification about prescribing pregabalin, and the last part consisted of questions about participants' concerns with regard to pregabalin prescription.

Statistical analysis

The pooled data were evaluated on a computer using the SPSS 22.0 statistical package program. Frequency distributions were calculated and presented as n, %. Pearson's Chi-squared test and Kruskal-Wallis H-test were used to compare the categorical data between the groups.

Results

Our survey was sent to 1569 physicians through telephone and e-mail. Only physicians who returned their responses within a certain period (14 days) were included in the study. This resulted in 406 PMR, rheumatology, and algology specialists being included in the study. Of these participants, 36.0% worked in training and research hospitals and 27.0% worked in university hospitals. Approximately half of the participants have been working as specialists for 5 years or fewer, 78.0% of them have been working as specialists for 10 years or fewer. In addition, 70.0% of the participating physicians were below 40 years old, and the female-to-male ratio was 56:44 (Fig. 1).

In response to the question about the first preferred agent of FMS treatment, most of the physicians

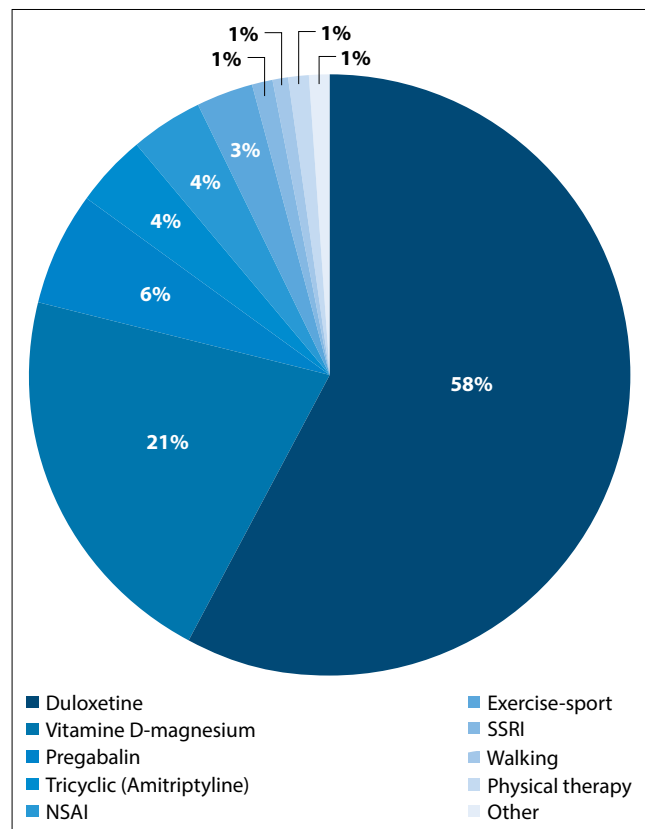


Figure 2. First-choice treatment method in FMS.

(59.0%) stated that they prefer duloxetine. Only 6.0% of participating physicians indicated pregabalin as their first choice; however, the preference for nonsteroidal anti-inflammatory drug (NSAID) was 4.0%, similar to the preference for tricyclic antidepressants (TSA). No significant difference was found between the first-choice agents preferred by the physicians in the study according to the physicians' department (Fig. 2).

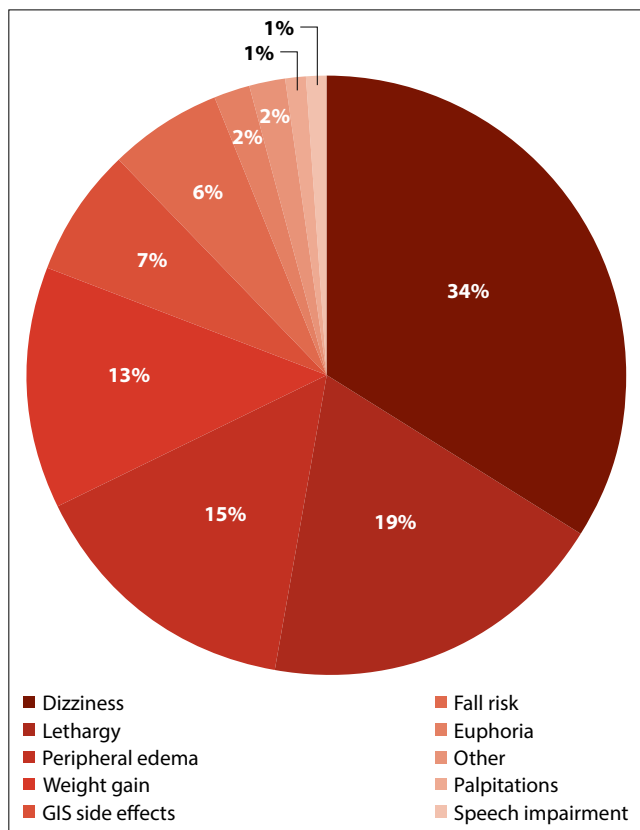


Figure 3. The most common side effects of pregabalin according to physician.

GIS: Gastrointestinal system.

The study also showed that most of the physicians prefer 300 mg/day as the maximum dose for pregabalin (56.7%). The second most common preferred maximum dose was 150 mg/day; however, 14.0% of physicians preferred an increased dose of 450 mg/day as the maximum dose in FMS indication.

When the side effects of pregabalin use were asked, 35.0% of the participating physicians indicated dizziness, 19.0% indicated lethargy, and 15.0% indicated peripheral edema as the most common side effect (Fig. 3).

When participants were asked which department should follow-up with FMS patients, 35.0% of the participating physicians stated that the PMR department should follow up, and when participants were asked to choose just one department, most of them (74.6%) preferred PMR. All physicians in the study (algology, PMR, and rheumatology) possessed a license to treat FMS; however, about half of them (44.3%) stated that they refer FMS patients to other departments. The opposite statement was also valid; 91.9% of the participants reported that FMS patients are

referred to them by other physicians with licenses to treat FMS (Table 1). When subgroups are examined; it is seen that internal medicine rheumatologists referred FMS patients to other departments significantly more than other branches. In terms of referral rates there was no statistically significant difference according to institutions and code white event exposure (Table 2).

When the primary hesitation was asked about pregabalin, 81% of the physicians stated that pregabalin causes addiction; 32.5% stated that they investigate the history of addiction before the prescription. About 36.7% of the participants stated that at least 20% of the patients could abuse pregabalin, 70% stated that they have prescribed pregabalin even though they felt threatened. Approximately one out of three physicians experienced a white code event; two of the three physicians experienced an act of violence in their hospital (Table 3). About 97.8% of physicians stated that they were prejudiced about prescribing pregabalin to prisoners; the prejudice rate was 87.2% for young male patients even if they are not prisoner (Table 4).

Discussion

Our study showed that pregabalin, the gold standard treatment for FMS, is chosen slightly as the first-choice treatment; most physicians believe that the drug is being abused by the patients, are threatened to prescribe this drug, therefore, they have serious prejudices about prescribing pregabalin, especially in special groups such as prisoners and young male patients, indicating a real "Pregabalinophobia" in current practice.

Today, there is no definitive therapy for fibromyalgia; treatment aims to reduce symptoms, preserve, and improve quality of life.^[10] In clinical practice, drug therapy is combined with non-pharmacologic treatment approaches such as physical therapy, exercise, and cognitive-behavioral therapy, and the treatment protocols treating fibromyalgia as a systemic disease rather than a muscle disorder are preferred.^[11] Methods using a single treatment modality cannot achieve full efficacy in fibromyalgia patients, and multidisciplinary therapy is considered the most effective method.^[12]

The choice of drug therapy should be based on the patient's clinical characteristics, side effect profile, and treatment response.^[13] Drugs with proven effi-

Table 1. Behaviors of the physicians about the follow-up and referral of FMS patients

	n	%
What do you think would be if FMS patients were followed by only one department?		
Algology	41	10.1
PMR	303	74.6
Psychiatry	44	10.8
Orthopedics	–	
Neurology	1	0.2
Rheumatology	17	4.2
Have you ever referred FMS patients to another clinician?		
Yes	180	44.3
No	226	55.7
What is the frequency of referral patients for pregabalin to another specialist although FMS patients can follow?		
Several times a day	75	18.5
A few times a week	115	28.3
Several times a month	129	31.8
Several times a year	54	13.3
Never	33	8.1

FMS: Fibromyalgia syndrome.

cacy in fibromyalgia are TSA, cyclobenzaprine, tramadol, serotonin-noradrenaline reuptake inhibitors, and several antiepileptics.^[14] Most of the drugs used for treatment such as paracetamol and NSAIDs are without proven efficacy and not recommended in guidelines.^[15,16] However, also in our study, physicians equally preferred a classical treatment agent TSA in FMS treatment as the first choice and NSAID drugs without a role in the treatment. Even more interestingly, pregabalin, one of the gold standard agents of FMS treatment, was the first choice with 6%, almost the same as NSAID with 4%.

The results of two pregabalin reviews showed that pregabalin reduces pain in fibromyalgia patients and improves sleep disorder and functions.^[17,18] Analysis of a randomized, prospective study on 209 patients conducted in 2016 showed that pregabalin has a favorable effect on sleep disorder.^[19] Despite all these favorable effects, supplemental treatments are not included in the guidelines, such as Vitamin D and magnesium which were almost 4 times more likely to be the first-choice treatment than pregabalin in our survey.

The results of a database published in 2009 showed that 150 mg/day dose is not different from a pla-

cebo, the best treatment response is obtained by a dose of 450 mg/day, and 600 mg/day does not provide additional benefit.^[18]

Resistance to prescribe pregabalin in our survey suggests whether the prescribed average dose is lower than the optimal dose. In studies on pregabalin dose in FMS treatment, significant improvements have been obtained in the fibromyalgia efficacy survey at both 450 mg/day and 600 mg/day doses.^[6] A study performed in Japanese showed that pregabalin treatment provided significant improvement in the fibromyalgia effect survey, especially in resting sleep, pain, and fatigue scores.^[20] In a comparative meta-analysis published in 2016 about FMS treatment, it was reported that no superiority was found in terms of efficacy and safety between duloxetine 60 mg, pregabalin 300 mg, and milnacipran 100 mg and 200 mg treatments.^[21] Seventeen studies and 7739 patients were included in a review to compare pregabalin, duloxetine, and milnacipran. It was concluded that the incidence of discontinuation for these three drugs was similar in terms of 30% pain relief and adverse effects. Duloxetine and pregabalin had higher efficacy on pain and sleep disorder as compared to milnacipran; while the effect of duloxetine on depressive mood was higher

Table 2. Referring ratios of fibromyalgia patients to other departments

	Refers to another department n=180 (44%)		Not refers to another department n=206 (56%)		p
	n	%	n	%	
Specialty					
Algology (anesthesia)	19	46	22	54	0.001*
Rheumatology (internal medicine)	16	94	1	6	
PMR	105	37.5	175	62.5	
Algology (PMR)	7	46	8	54	
Rheumatology (PMR)	24	61	15	39	
Algology (Neurology)	9	64	5	36	
Institution					
State hospital	55	48	59	52	0.084*
Training and research hospital	68	46	77	54	
University hospital	47	43	61	57	
Private Health Institution	16	41	23	59	
White code individual					
Yes	47	37	80	63	0.052
No	133	47	146	53	
White code institutional					
Yes	119	45	142	55	0.493
No	61	42	84	58	

n, % Chi-square test. *Kruskal-Wallis H-test; p<0.05. PMR: Physical medicine and rehabilitation.

as compared to the other two drugs, milnacipran and pregabalin reduced fatigue more than duloxetine.^[22] Although most pregabalin studies reported that up to 600 mg/day drug could be prescribed with a safe side effect profile, only 12% of the physicians in our survey reported that they prescribed 600 mg/dose as the maximum dose. This is acceptable considering that the repayment institution in Turkey pays pregabalin 450 mg/day as the maximum dose for FMS diagnosis, however, 73% of physicians in our survey stated that they do not use a maximum dose of 450 mg/day. Furthermore, it has a similar side effect and safety profile with duloxetine, however, duloxetine is the first choice in 56.8%, while pregabalin is preferred only 6%, so it is evident that the physicians do not prefer pregabalin due to reasons other than side effects.

Supporting this assumption, the physicians in our survey did not report any life threatening or serious side effects during pregabalin use; the most commonly reported side effects were drowsiness, lethargy, and pe-

ripheral edema. Literature studies are also in line with similar observations. A review of eight studies showed that adverse effects such as somnolence, drowsiness, weight gain, and peripheral edema are common with pregabalin, however, they are mild to moderate and the drug is well tolerated.^[23] The most common side effects of pregabalin treatment are dizziness and drowsiness with an incidence of 40–50% and 30–45%, respectively.^[6,24,25] Central side effects include blurred vision, attention deficit, balance problems, vertigo, and euphoria. These side effects are mild to moderate and rarely lead to discontinuation of the drug.^[26] Apart from these, side effects such as mild dry mouth, increased appetite, and constipation may occur.

Despite its acceptable side -effect profile, there should be another reason to not prefer this effective drug. Pregabalin is a safe drug to be used in several conditions. In Turkey, the Ministry of Health has approved its indication in peripheral neuropathic pain, fibromyalgia, and partial epilepsy in 150–600 mg/

Table 3. Physicians' approach to patients while pre-
scribing pregabalin in FMS

	n	%
Are you getting consent?		
Yes	41	10.1
No	365	89.3
Are you taking a history of addiction?		
Yes	274	67.5
No	132	32.5
Do you think pregabalin is addictive?		
Yes	329	81
No	77	19
Do you think what is the pregabalin misuse rate?		
1-5	48	11.8
5-10	115	28.3
10-20	94	23.2
>20	149	36.7
Have you been prescribed pregabalin even though you feel threatened?		
Yes	284	70
No	122	30%
Have you experienced the "white code" incident?		
Yes	127	31.3
No	279	68.7
Has there been a "white code" incident in the institution that you work for?		
Yes	261	64.3
No	145	35.7

FMS: Fibromyalgia syndrome.

day. Despite this broad indication area, recent case reports showing that pregabalin has the abuse potential and addiction which are increasing.^[27-29]

These types of reports are primarily indicated in anxiety disorder, then other studies on its use for other psychiatric diseases have been raised. Especially in addiction studies, case reports are showing that pregabalin relieves the symptoms of withdrawal syndrome.^[30,31] However, these promising results about addiction are overshadowed by the Swedish National Register of adverse drug reactions/SWEDIS data showing that 16 of 198 reported adverse events of abuse and addiction were associated with pregabalin. Thirteen cases had a previous history of different psychotropic substance abuse. One of the cases empties the pregabalin capsule and sniffs it, while one dissolves it in water and injects himself, and others use it orally.^[32] Again, in the database review of the German Federal Institute for Drugs and Medical Devices (BfArM), 55 pregabalin cases were reported as of September 6, 2012, 44 of them were addictive and 11 were abuse cases. The doses were between 400 mg/g and 6000 mg/g. Of the 35 patients with patient files, 22 of them have a history of present and 27 of them have a previous history of different psychotropic substance abuse/addiction.^[27]

Apart from these medical reports, in a publication compiling web reports based on personal narrations in eight European countries on 203 websites; pregabalin has been reported by users as an ideal psychotropic that may be used for recreational purposes

Table 4. Prejudices about the use of pregabalin in special patient groups

	Absolutely I agree		I agree		I'm fickle		I do not agree		I strongly disagree	
	n	%	n	%	n	%	n	%	n	%
I have prejudices about imprisoned patients	339	83.5	58	14.3	6	1.5	3	0.7	-	-
I have prejudices about the young men	244	60.1	110	27.1	30	7.4	20	4.9	2	0.5
I will have bias after if I face with a white code event	242	59.6	118	29.1	26	6.4	14	3.4	6	1.5
I have prejudices when a patient who has prescribed pregabalin by a different physician	189	46.6	160	39.4	35	8.6	18	4.4	4	1

similar to alcohol/GHB/benzodiazepine for its euphoric and dissociative effects. In this review, it was stated that the oral use of pregabalin is common, however, it may also be used by intravenous, rectal, and nasal by emptying the contents of the capsule.^[33] The euphoric effect of pregabalin (1–10%) was reported by more patients than placebo (0.5%). This euphoric effect is suggested to increase the risk of pregabalin abuse.^[34]

Our study showed 89% of the physicians defined pregabalin as an addictive drug, however, only 33% of the physicians enquire the addiction history in daily practice. About 59% of physicians stated that they expected abuse at least 10% or more in patients on pregabalin; 36.7% of the participants think that the abuse rate is 20% or more. These rates show that the physicians expect serious pregabalin abuse in patients on pregabalin, and it was one of the reasons for the low rates of pregabalin prescription in FMS treatment.

Identified risk factors for pregabalin abuse have been showed in the literature as male sex, young age, previous substance abuse history, and use of large amounts of other drugs with potential abuse.^[35] In Turkey, İlhanlı et al.^[36] found that the use of pregabalin with antipsychotic/antidepressants was high in prisons. In our survey, 97.8% of the physicians stated that they were prejudiced in prescribing pregabalin to the prisoners. The prejudice rate for abuse is also very high for young male patients: 87.2%. From the point of view of participants who think pregabalin may be seriously addictive, these results are not surprising. Fibromyalgia is commonly observed in women and 90% of the patients are women.^[37] Therefore, the physician may prejudice when a young male requests a pregabalin prescription despite the low probability of fibromyalgia. Moreover, in Turkey, "code white" alarm condition during an act of violence is observed mostly for young men and prisoners. A study showed that 81.6% of violence cases are associated with males.^[38]

About 31.3% of the physicians who participated in our survey stated that they had violent crimes requiring a white code with the patients who were prescribed pregabalin, and approximately 2/3 of them had witnessed an act of violence in the institution because of pregabalin. Another truth revealed

by our survey is that 70% of physicians stated that they prescribed pregabalin feeling threatened at least once. It is a shocking data that most of the participating physicians undergo the act of violence and threats, even though they were at the beginning of their professional lives according to demographic data. Our data showed that almost all physicians who prescribe pregabalin for FMS treatment may undergo an act of violence at least once during their professional life. This may be the reason for the serious prejudice for the males and prisoners with a high risk of a criminal event.

It has been observed that the abovementioned conditions such as addiction, abuse, violence, threats, and forensic events negatively affect the Turkish physicians' approach to pregabalin, a very effective agent in FMS treatment. There were additional results in our survey showing that the participants do not prefer to prescribe pregabalin as much as possible. These include: 95% of physicians have hesitations about continuing pregabalin treatment initiated by another physician; approximately half of them refer their patient to another department for pregabalin prescription; and 91.9% stated that FMS patients were referred to them from another specialist who has authorization and to follow up FMS patients. This serious prejudice against pregabalin resembles the "Opiophobia" condition observed for opiates.

"Opiophobia" means to avoid prescribing opioid drugs due to side effects and abuse potential, was first used in the medical literature in 1985 by American pharmacologist John Morgan.^[39] Reluctance to prescribe opioids in physicians is associated with addiction concerns, possible side effects, and opiophobia of health-care personnel. Besides, literature studies showed that physicians consider that it's illegal to prescribe opioids in patients with non-cancerous chronic pain and patients with a history of substance abuse, and optimal pain treatment with opioids cannot be performed in patients with a history of substance abuse and severe chronic pain.^[40,41] In this study, we showed that just like "opiophobia;" physicians have a severe prejudice and hesitations about prescribing pregabalin, especially in terms of the abuse potential, and we termed this as "Pregabalinophobia" since not previously named in literature.

The limitations of our study are as follows: A face-to-face survey was not possible due to the pandemic, relatively limited number of participants, the participants could not reach the investigator when they did not understand the question, a small number of participants, especially from the rheumatology and algology departments, so they could not be adequately represented. Significant aspects of our study are as follows: We have reached almost 10% of PMR physicians in the country, so PMR physicians, the main department in FMS treatment, were well represented, exclusion of non-physician participation by accessing verified physician e-mails and phones, it includes a sufficient number of doctors who have graduated from every region in Turkey and several different institutes, it represents not only the stereotypical behavior of the limited clinics but also the physicians homogeneously all over the country.

Conclusion

This study revealed that the Pregabalinophobia condition should be accepted. This condition is associated with life safety concerns of the physician not only from unreliability to the drug. The doctors have valid reasons to develop this prejudice, however, a group of physicians who approach almost all prisoners with prejudice will inadequately treat patients when the patients need treatment. It is essential that the necessary environment is provided quickly because of inadequate treatment and preventing the right to access treatment, and more importantly, clinicians should not work under any pressure, they should work without concern for life safety and violence.

Ethical Approval: The study was approved by The Istanbul Medipol University Non-interventional Clinical Research Ethics Committee (Date: 04/02/2021, No: 128).

Conflict-of-interest issues regarding the authorship or article: None declared.

Financial Disclosure: This study has no funding or sponsor.

Peer-review: Externally peer-reviewed.

References

- Bennett RM, Jones J, Turk DC, Russell IJ, Matallana L. An internet survey of 2,596 people with fibromyalgia. *BMC Musculoskelet Disord* 2007;8:27. [CrossRef]
- Forseth KO, Gran JT, Husby G. A population study of the incidence of fibromyalgia among women aged 26-55 yr. *Br J Rheumatol* 1997;36:1318-23. [CrossRef]
- Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L. The prevalence and characteristics of fibromyalgia in the general population. *Arthritis Rheum* 1995;38:19-28. [CrossRef]
- Yunus MB. Central sensitivity syndromes: A new paradigm and group nosology for fibromyalgia and overlapping conditions, and the related issue of disease versus illness. *Semin Arthritis Rheum* 2008;37:339-52. [CrossRef]
- Güler N, Kaptanoğlu E, Şahin Ö, Hizmetli S, Elden H. The effectiveness of gabapentine in female patients with fibromyalgia. *Cumhuriyet Med J* 2010;32:40-7.
- Arnold LM, Russell IJ, Diri EW, Duan WR, Young JP Jr, Sharma U, et al. A 14-week, randomized, double-blinded, placebo-controlled monotherapy trial of pregabalin in patients with fibromyalgia. *J Pain* 2008;9:792-805. [CrossRef]
- Zaccara G, Gangemi P, Perucca P, Specchio L. The adverse event profile of pregabalin: A systematic review and meta-analysis of randomized controlled trials. *Epilepsia* 2011;52:826-36. [CrossRef]
- Cairns R, Schaffer AL, Ryan N, Pearson SA, Buckley NA. Rising pregabalin use and misuse in Australia: Trends in utilization and intentional poisonings. *Addiction* 2019;114:1026-34. [CrossRef]
- Schifano F. Misuse and abuse of pregabalin and gabapentin: Cause for concern? *CNS Drugs* 2014;28:491-6. [CrossRef]
- Fitzcharles MA, Ste-Marie PA, Goldenberg DL, Pereira JX, Abbey S, Choinière M, et al. 2012 Canadian Guidelines for the diagnosis and management of fibromyalgia syndrome: Executive summary. *Pain Res Manag* 2013;18:119-26.
- Sindel D, Saral I, Esmailzadeh S. Management approaches in fibromyalgia syndrome. *Turk J Phys Med Rehab* 2012;58:136-43.
- Sarzi-Puttini P, Atzeni F, Salaffi F, Cazzola M, Benucci M, Mease PJ. Multidisciplinary approach to fibromyalgia: What is the teaching? *Best Pract Res Clin Rheumatol* 2011;25:311-9. [CrossRef]
- Kia S, Choy E. Update on treatment guideline in fibromyalgia syndrome with focus on pharmacology. *Biomedicines* 2017;5:20. [CrossRef]
- Macfarlane GJ, Kronisch C, Dean LE, Atzeni F, Häuser W, Fluß E, et al. EULAR revised recommendations for the management of fibromyalgia. *Ann Rheum Dis* 2017;76:318-28.
- Halpern R, Shah SN, Cappelleri JC, Masters ET, Clair A. Evaluating guideline-recommended pain medication use among patients with newly diagnosed fibromyalgia. *Pain Pract* 2016;16:1027-39. [CrossRef]
- Margolis JM, Prinic N, Smith DM, Abraham L, Cappelleri JC, Shah SN, et al. Development of a novel algorithm to determine adherence to chronic pain treatment guidelines using administrative claims. *J Pain Res* 2017;10:327-39.
- Clair A, Emir B. The safety and efficacy of pregabalin for treating subjects with fibromyalgia and moderate or severe baseline widespread pain. *Curr Med Res Opin* 2016;32:601-9. [CrossRef]
- Moore RA, Straube S, Wiffen PJ, Derry S, McQuay HJ. Pregabalin for acute and chronic pain in adults. *Cochrane Database Syst Rev* 2009;CD007076. [CrossRef]
- Roth T, Bhadra-Brown P, Pitman VW, Resnick EM. Pregaba-

- lin improves fibromyalgia-related sleep disturbance. *Clin J Pain* 2016;32:308–12. [\[CrossRef\]](#)
20. Ohta H, Oka H, Usui C, Ohkura M, Suzuki M, Nishioka K. A randomized, double-blind, multicenter, placebo-controlled phase III trial to evaluate the efficacy and safety of pregabalin in Japanese patients with fibromyalgia. *Arthritis Res Ther* 2012;14:R217. [\[CrossRef\]](#)
21. Lee YH, Song GG. Comparative efficacy and tolerability of duloxetine, pregabalin, and milnacipran for the treatment of fibromyalgia: A Bayesian network meta-analysis of randomized controlled trials. *Rheumatol Int* 2016;36:663–72.
22. Häuser W, Petzke F, Sommer C. Comparative efficacy and harms of duloxetine, milnacipran, and pregabalin in fibromyalgia syndrome. *J Pain* 2010;11:505–21. [\[CrossRef\]](#)
23. Gerardi MC, Atzeni F, Batticciotto A, Di Franco M, Rizzi M, Sarzi-Puttini P. The safety of pregabalin in the treatment of fibromyalgia. *Expert Opin Drug Saf* 2016;15:1541–8.
24. Pauer L, Atkinson G, Murphy TK, Petersel D, Zeiher B. Long-term maintenance of response across multiple fibromyalgia symptom domains in a randomized withdrawal study of pregabalin. *Clin J Pain* 2012;28:609–14. [\[CrossRef\]](#)
25. Straube S, Derry S, Moore RA, McQuay HJ. Pregabalin in fibromyalgia: Meta-analysis of efficacy and safety from company clinical trial reports. *Rheumatology (Oxford)* 2010;49:706–15. [\[CrossRef\]](#)
26. Pauer L, Winkelmann A, Arsenault P, Jespersen A, Whelan L, Atkinson G, et al. An international, randomized, double-blind, placebo-controlled, phase III trial of pregabalin monotherapy in treatment of patients with fibromyalgia. *J Rheumatol* 2011;38:2643–52. [\[CrossRef\]](#)
27. Gahr M, Franke B, Freudenmann RW, Kölle MA, Schönfeldt-Lecuona C. Concerns about pregabalin: Further experience with its potential of causing addictive behaviors. *J Addict Med* 2013;7:147–9. [\[CrossRef\]](#)
28. Filippetto FA, Zipp CP, Coren JS. Potential for pregabalin abuse or diversion after past drug-seeking behavior. *J Am Osteopath Assoc* 2010;110:605–7.
29. Grosshans M, Mutschler J, Hermann D, Klein O, Dressing H, Kiefer F, et al. Pregabalin abuse, dependence, and withdrawal: A case report. *Am J Psychiatry* 2010;167:869.
30. Bobes J, Rubio G, Terán A, Cervera G, López-Gómez V, Vilardaga I, et al. Pregabalin for the discontinuation of long-term benzodiazepines use: An assessment of its effectiveness in daily clinical practice. *Eur Psychiatry* 2012;27:301–7.
31. Oulis P, Masdrakis VG, Karakatsanis NA, Karapoulios E, Kouzoupis AV, Konstantakopoulos G, et al. Pregabalin in the discontinuation of long-term benzodiazepine use: A case-series. *Int Clin Psychopharmacol* 2008;23:110–2. [\[CrossRef\]](#)
32. Schwan S, Sundström A, Stjernberg E, Hallberg E, Hallberg P. A signal for an abuse liability for pregabalin--results from the Swedish spontaneous adverse drug reaction reporting system. *Eur J Clin Pharmacol* 2010;66:947–53. [\[CrossRef\]](#)
33. Schifano F, D'Offizi S, Piccione M, Corazza O, Deluca P, Davey Z, et al. Is there a recreational misuse potential for pregabalin? Analysis of anecdotal online reports in comparison with related gabapentin and clonazepam data. *Psychother Psychosom* 2011;80:118–22. [\[CrossRef\]](#)
34. Baldwin DS, Ajel K, Masdrakis VG, Nowak M, Rafiq R. Pregabalin for the treatment of generalized anxiety disorder: An update. *Neuropsychiatr Dis Treat* 2013;9:883–92. [\[CrossRef\]](#)
35. Bodén R, Wettermark B, Brandt L, Kieler H. Factors associated with pregabalin dispensing at higher than the approved maximum dose. *Eur J Clin Pharmacol* 2014;70:197–204. [\[CrossRef\]](#)
36. İlhanlı İ, Güder N, Gül M. Gabapentinoids in penitentiaries: An abuse and addiction research. *Turk J Phys Med Rehabil* 2017;63:318–28. [\[CrossRef\]](#)
37. Arout CA, Sofuoglu M, Bastian LA, Rosenheck RA. Gender differences in the prevalence of fibromyalgia and in concomitant medical and psychiatric disorders: A national veterans health administration study. *J Womens Health (Larchmt)* 2018;27:1035–44. [\[CrossRef\]](#)
38. Aktaş E, Aydemir İ. The determination of views of health professionals who exposed to violence about the "White Code" implementation. *Turk Klin J Med Sci* 2018;3:32–47.
39. Sykes NP. Morphine kills the pain, not the patient. *Lancet* 2007;369:1325–6. [\[CrossRef\]](#)
40. Furlan AD, Sandoval JA, Mailis-Gagnon A, Tunks E. Opioids for chronic noncancer pain: A meta-analysis of effectiveness and side effects. *CMAJ* 2006;174:1589–94. [\[CrossRef\]](#)
41. Kalkman GA, Kramers C, van Dongen RT, van den Brink W, Schellekens A. Tackling rising numbers of opioid prescriptions users. *Lancet Public Health* 2020;5:e139. [\[CrossRef\]](#)