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The Effect of Pregabalin on Weight Gain, Balance, Gait, Fatigue and Sleepiness in Patients with Fibromyalgia

Fibromiyalji Hastalarında Pregabalinin Kilo Alımı, Denge, Yürüme, Yorgunluk ve Uykululuk Üzerine Etkisi

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ABSTRACT Objective: Our aim was to evaluate the effect of low dose pregabalin on weight, balance, gait, fatigue, and sleepiness in fibromyalgia patients in a twelve-week follow-up period in this study. **Material and Methods**: Twenty-eight patients with fibromyalgia diagnosis were included in the study. All patients used 150 mg/day pregabalin during the study period and they were followed for twelve weeks. Weight, body mass index measurements, Tinetti Balance and Gait Test, Epworth Sleepiness Scale, and Fatigue Severity Scale were performed prior to the treatment, at the fourth week, and at the twelfth week of the study. The results at these time points were compared. **Results:** Among 28 patients who accepted to participate in the study, 11 patients dropped out of the study. Seven of these patients dropped out due to adverse effects. The weight significantly increased at the 4th (p=0.010) and 12th weeks of treatment (p=0.008) compared to the pretreatment measurements. The mean weight gain was 1.5±1.8 kg at the 4th week and 1.7±1.9 kg at the 12th week compared to the baseline. There were no statistically significant differences in the parameters of the Tinetti Balance Test, Tinetti Gait Test, Epworth Sleepiness Scale, and Fatigue Severity Scale scores before and after the treatment periods. **Conclusion:** Low dose pregabalin induces weight gain in patients with fibromyalgia. Pregabalin does not have a significant effect on gait, balance, sleepiness, and fatigue

Keywords: Fibromyalgia; pregabalin; weight gain; balance; fatigue

ÖZET Amaç: Bu çalışmada 12 haftalık bir takip döneminde düşük doz pregabalinin fibromiyalji hastalarında kilo, denge, yürüyüş, yorgunluk ve uyku hâli üzerine etkisini değerlendirmeyi amaçladık. **Gereç ve Yöntemler:** Fibromiyalji tanısı alan 28 hasta çalışmaya dâhil edildi. Çalışma süresince tüm hastalar 150 mg/gün pregabalin kullandı ve 12 hafta takip edildi. Tedaviye başlamadan önce, çalışmanın 4. haftasında ve 12. haftasında ağırlık, beden kitle indeksi ölçümleri, Tinetti Denge ve Yürüme Testi, Epworth Uykululuk Ölçeği ve Yorgunluk Şiddet Ölçeği uygulandı. Bu zaman noktalarında elde edilen sonuçlar birbirleriyle karşılaştırıldı. **Bulgular:** Çalışmaya katılmayı kabul eden 28 hastadan 11'i çalışmadan ayrıldı. Bu hastalardan 7'sinin, ayrılma sebebi yan etkilerdi. Tedavi öncesi ölçümlere göre vücut ağırlığında tedavinin 4. haftasında (p=0,010) ve 12. haftasında (p=0,008) anlamlı artış görüldü. Ortalama ağırlık artışı başlangıca göre 4. haftada 1,5±1,8 kg ve 12. haftada 1,7±1,9 kg idi. Tedavi öncesi ve sonrası değerler karşılaştırıldığında Tinetti Denge Testi, Tinetti Yürüme Testi, Epworth Uykululuk Ölçeği ve Yorgunluk Şiddet Ölçeği sonuçlarında istatistiksel olarak anlamlı bir fark saptanmadı. **Sonuç:** Düşük doz pregabalinin fibromiyalji hastalarında kilo alımını indüklediği, yürüyüş, denge, uykululuk ve yorgunluk üzerinde önemli bir etkisi olmadığı saptanmıştır.

Anahtar Kelimeler: Fibromiyalji; pregabalin; kilo alımı; denge; yorgunluk

Fibromyalgia (FM) is a syndrome involving chronic widespread pain, multiple muscular tender points, and associated symptoms like fatigue, sleep disturbances or cognitive problems.[1,2] Its prevalence varies according to geographic location and diagnostic criteria used ranging between 1% and 6%.[3,4] It is more prevalent in female gender. The exact pathogenesis of this disease is not completely understood. It is thought as a central sensitivity syndrome with altered pain processing in the central nervous system.[5,6] There has been no definitive treatment for FM yet and the current treatment options include pharmacological and non-pharmacological therapies or their combination.[7] Treatment is aimed at ameliorat-

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ing symptoms and increasing the quality of life. Nonpharmacological therapies include exercise, massage, physical therapy, acupuncture and cognitive behavioral therapy.[7,8] Pharmacological therapies include tricyclic antidepressants, serotonin and norepinephrine reuptake inhibitors, selective serotonin reuptake inhibitors, cannabinoids and antiepileptics.[9] Pregabalin is an antiepileptic drug approved for the treatment of FM. It was reported to be effective in the treatment of pain and other symptoms of fibromyalgia.[10,11] Its use is currently increasing for the management of pain due to various causes.[12] The use of pregabalin is associated with several adverse effects. Dizziness, somnolence, peripheral edema, and weight gain were reported to be the most common side effects of pregabalin use due to various indications.[13] In this study, we wanted to evaluate the effects of low dose pregabalin on weight, balance, gait, fatigue, and sleepiness in FM patients in a twelve-week follow-up period.

MATERIAL AND METHODS

This prospective study was conducted in Niğde Ömer Halisdemir University, School of Medicine, Department of Physical Medicine and Rehabilitation. This study was carried out according to the Declaration of Helsinki 2008 and approved by the Niğde Ömer Halisdemir University Ethics Committee. Verbal and written informed consents were obtained from the participants. The participants were recruited among the patients admitted to the outpatient clinic in Physical Medicine and Rehabilitation Department of Niğde Ömer Halisdemir University. Twenty-eight patients with FM diagnosis who were found to be eligible for pregabalin use were included in the study. The diagnosis of FM was made using 2016 revised American College of Rheumatology (ACR) diagnostic criteria.[1] Patients who were pregnant or breast feeding, who had other comorbid medical conditions that could cause chronic pain like malignancies, multiple major surgeries, traumatic injuries, or rheumatologic diseases other than FM, patients with a history of surgery or medical condition (e.g., stroke or knee replacement or vestibular disorder) or the use of medications that may affect weight, fatigue, gait, balance were excluded. Those patients with neurologic or endocrine diseases that may affect sleep onset or maintenance were also excluded. All patients used 150 mg/day pregabalin during the study period. The participating patients were followed for twelve weeks. Weight, body mass index (BMI) measurements, Tinetti Balance and Gait Test, Epworth Sleepiness Scale (ESS) and Fatigue Severity Scale (FSS) were performed before the beginning of treatment, at fourth week, and at twelfth week of the study.

TINETTI BALANCE AND GAIT TEST

This test is also called performance-oriented mobility assessment scale.[14] It is developed to assess the functional mobility and stability in elderly patients.[15] It is relatively easy and simple to use in clinical setting. In the first part of the test, the balance of the patient and its maintenance are tested during nine maneuvers from daily life activities. The score from the first part indicates the balance core. In the second part, observation of the gait and mobility was performed and it is scored based on seven features of gait. The Turkish version of this test was found to be valid and reliable.[16]

EPWORTH SLEEPINESS SCALE

This questionnaire measuring day time sleepiness level was developed in 1991.[17] In this self-administered and simple questionnaire, the participants rate their chance of falling asleep during eight different situations of daily life in one of four scores from 0 to 3. The ESS score is obtained by adding the eight item scores. Higher scores demonstrate higher daytime sleepiness level. Its Turkish version was found to be reliable and valid for measuring of daytime sleepiness of Turkish patients.[18]

FATIGUE SEVERITY SCALE

This short, self-administered questionnaire was developed to measure the severity of fatigue and its effect on function.[19] It includes nine items related to the effects of fatigue on daily life and each item is rated from 1 to 7 by the participants. The arithmetic mean of the patients' scores for each item is calculated as the total score. The Turkish version of FSS was found to be valid and reliable for measuring the severity of fatigue in FM patients.[20]

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS version 20.0 (IBM Corporation, Armonk, NY). Quantitative data were expressed as the mean±standard deviations and qualitative data as proportions (%). Repeated measures ANOVA was used to compare the pretreatment, 4th and 12th post treatment week values of weight, BMI, Tinetti Balance, Tinetti Gait, ESS and FSS scores. Post hoc tests using the Bonferroni corrections were performed for the comparison of different time points. In all analyses, p values <0.05 were considered as statistically significant.

RESULTS

Among 28 patients who accepted to participate in the study, 11 patients dropped out of the study. Seven of these were due to adverse effects (5 patients due to somnolence and 2 patients due to dizziness) and 4 patients dropped out due to personal reasons. Seventeen patients completed the study. The mean age was 43.6±8.8 and all patients were female. The mean disease duration was 2.4±1.3 years.

The values and comparison of study parameters were given in Table 1. The weight of patients significantly increased after the treatment at the 4th week (p=0.010) and at the 12th week (p=0.008) compared to pretreatment measurements. The mean weight gain was 1.5±1.8 kg at the 4th week and 1.7±1.9 kg at the 12th week compared to the baseline. There was no significant difference between weight measurements after the treatment at the 4th and 12th weeks. Fifteen (88%) out of 17 patients had weight gain after the treatment at the 4th week and 12th weeks. There were no statistically significant differences in the parameters of the Tinetti Balance, Tinetti Gait, ESS and FSS scores before and after the treatment periods (Table 1).

DISCUSSION

In this study, a significant increase in the body weight and BMI was recorded in the fourth and twelfth weeks of the treatment compared to the baseline in patients with FM. But other parameters like Tinetti Balance and Gait scores, ESS and FSS scores did not change significantly compared to the baseline. Weight gain is an adverse event frequently reported in the studies evaluating pregabalin for the treatment of fibromyalgia.[10] Cabrera et al. reported that nearly 17% of the patients on pregabalin treatment for various indications had 7% weight gain from baseline in a meta-analysis.[21] They also reported that FM patients had a mean weight gain of 2.0 kg and a 2.74% mean weight gain compared to the baseline. Our patient group also had 1.5±1.8 kg mean weight gain at the 4th week and 1.7±1.9 kg mean weight gain at the 12th week compared to the baseline. None of our patients dropped out of study due to weight gain. The results of this study are compatible with those of the previous studies and indicate that pregabalin treatment is associated with weight gain in FM patients.

Somnolence, dizziness, fatigue, and daytime sleepiness were other frequently reported side effects of pregabalin use.[22] Especially somnolence and dizziness were reported as the most common side effects leading to drug discontinuation.[10] Due to these common side effects, we investigated the effect of prega-

TABLE 1: Change in BMI, weight, Tinetti Balance and Gait, ESS and FSS.

	Baseline (n=17)	4th week (n=17)	12th week (n=17)	
	Mean±SD	Mean±SD	Mean±SD	p
BMI	29.3±4.1[a]	29.9±4.2[b]	30.±4.2[b]	<0.001
Weight	73.1±7.4[a]	74.5±7.7[b]	74.7±7.8[b]	<0.001
Tinetti balance	25.2±1.2[a]	25.08±1.4[a]	25.2±1.2[a]	0.379
Tinetti gait	8.6±0.6[a]	8.7±0.6[a]	8.7±0.6[a]	0.332
ESS	6.7±5.1[a]	7.2±4.3[a]	6.8±4.3[a]	0.518
FSS	4.7±1.4[a]	4.2±1.4[a]	3.9±1.3[a]	0.226

Means that have no superscript in common are significantly different from each other. p values in the table demonstrate the significance of difference among groups .
BMI: Body mass index; ESS: Epworth Sleepiness Scale; FSS: Fatigue Severity Scale; SD: Standard deviation.

balin on gait and balance using Tinetti Balance and Gait test. Caglar Okur et al. also investigated the effect of pregabalin used for low back pain on gait and balance.[23] They found a decrease in the balance and gait scores at the first week but the scores at the 4th and 12th week were not different from baseline. Similar to their study, the scores at the 4th and 12th were not different from the scores at the baseline in our study. These results suggest that pregabalin did not have unfavorable effects on balance and gait in patients with FM in the short period.

In a study evaluating the effect of pregabalin in patients with restless leg syndrome, it was reported that day-time sleepiness was more prevalent in patients on pregabalin treatment compared to the placebo group especially in higher doses.[24] We did not find a difference in the ESS scores of patient compared to the baseline in our study. This may be due to low (150 mg/day) dose of pregabalin used in our study. These results suggest that pregabalin did not increase sleepiness in patients with FM in 150 mg dose.

Pregabalin was also found to be associated with fatigue in several studies in indications other than FM.[25] Other studies reported that pregabalin was not effective in reducing fatigue in FM patients.[26] We evaluated fatigue using FSS in FM patients and did not find significant difference in FSS scores during the twelve-week treatment period. Our results also suggest that pregabalin has no positive or negative effect on fatigue symptoms in FM patients.

There are several limitations of this study. Firstly, the number of participants were low due to high dropout rate. Seven out of 28 (25%) patients dropped out due to adverse events. Similar to our study, the dropout rate due to adverse events is high in patients using pregabalin and it was reported to be nearly 20% in patients with FM.[25,26] Secondly, only a single test was used to evaluate the change in each of the symptoms. We tried to choose the most practical tests and tests which were found to be reliable and valid for Turkish patients. Thirdly, pregabalin was used as a low fixed dose (150 mg/day) during the study period in this study.

In conclusion, the results of this prospective cohort study suggest that low dose pregabalin induces weight gain in patients with FM. It does not have a significant effect on gait, balance, sleepiness, and fatigue.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

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