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Comparison of the Effects of Ozone Therapy and Exercise with Algometer in Chronic Pain Fibromyalgia Patients Applying to Traditional Complementary and Medical Centers: Cross-sectional Study

Geleneksel ve Tamamlayıcı Tıp Merkezine Başvuran Kronik Ağrılı Fibromyalji Hastalarında Ozon Tedavisi ile Egzersizin Etkilerinin Algometre ile Karşılaştırılması: Kesitsel Çalışma

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ABSTRACT Objective: Ozone, which is applied in ozone therapy, is a chemical cousin of the oxygen molecule and can be added to the treatment of many diseases. In recent years, an increasing number of publications have reported that exercise therapy is safe and necessary for most patients. The aim of this study is to evaluate the effect of ozone and exercise on chronic pain threshold in fibromyalgia with an algometer. **Material and Methods:** Thirty-seven people with Fibromyalgia Syndrome (FMS) were included in the study. Patients using long-acting antiaggregant drugs and those using favism were excluded. They were randomly divided into 2 groups. The first group, the Ozone Group (n=19), received 1 session of major ozone therapy per week for 5 weeks. The 2nd group, the Ozone+Exercise Group (n=18), exercised 3 days per week in addition to major ozone therapy for 5 weeks and a home exercise program was used. At the beginning and end of the treatment, subjective pain levels were evaluated with visual analogue scale (VAS), quality of life with 36-Item Short Form Health Survey (SF-36), physical functions with Fibromyalgia Impact Questionnaire (FIQ), body flexibility with sit-lie flexibility table and pressure pain threshold of 6 anatomical points specific to FMS (total 12 points on the right and left) with algometer device. **Result:** No difference was found between the baseline VAS, SF-36, FIQ and flexibility values (p>0.05). In the pretreatment algometer values, the values of the 2nd point were significantly higher in the Ozone+Exercise group (p<0.05), and no difference was found between the groups in the remaining 5 evaluation points (p>0.05). Significant improvements were observed in VAS, SF-36, FIQ and flexibility values throughout the treatment in both groups (p<0.05).

Keywords: Exercise therapy; fibromyalgia; ozone therapy; pain

ÖZET Amaç: Ozon tedavisinde uygulanan ozon, oksijen molekülünün kimyasal kuzenidir ve birçok hastalığın tedavisine eklenebilir. Son yıllarda, egzersiz terapisinin çoğu hasta için güvenli ve gerekli olduğu giderek artan sayıda yayın tarafından bildirilmiştir. Bu çalışmada amaç fibromyaljide kronik ağrı eşiğine ozon ve egzersizin etkisini algometre ile değerlendirmektir. **Gereç ve Yöntemler:** Çalışmaya fibromiyalji sendromlu (FMS) 37 kişi dâhil edildi. Uzun etkili antiagregan ilaç kullanan ve favizm kullanan hastalar hariç tutuldu. Rastgele 2 gruba ayrıldılar. Birinci grup olan Ozon Grubu (n=19), 5 hafta boyunca haftada 1 seans majör ozon terapisi aldı. İkinci grup olan Ozon+Egzersiz Grubu (n=18), 5 hafta boyunca majör ozon terapisine ek olarak haftada 3 gün egzersiz yaptı ve ev egzersiz programı kullanıldı. Tedavi başlangıcında ve sonunda subjektif ağrı düzeyleri görsel analog skala [visual analogue scale (VAS)] ile, yaşam kalitesi 36 Maddelik Kısa Form Anketi [36-Item Short Form Health Survey (SF-36) ile, fiziksel fonksiyonlar Fibromiyalji Etki Anketi [Fibromyalgia Impact Questionnaire (FIQ)] ile, vücut esnekliği otur-yat esneklik masası ile ve FMS'ye özgü 6 anatomik noktanın (sağ ve sol toplam 12 nokta) basınç ağrı eşiği algometre cihazı ile değerlendirildi. **Sonuç:** Bazal VAS, SF-36, FIQ ve esneklik değerleri arasında fark saptanmadı (p>0,05). Tedavi öncesi algometre değerlerinde 2. noktanın değerleri Ozon+Egzersiz grubunda anlamlı olarak daha yüksekti (p<0,05), kalan 5 değerlendirme noktasında gruplar arasında fark saptanmadı (p>0,05). Her iki grupta da tedavi boyunca VAS, SF-36, FIQ ve esneklik değerlerinde anlamlı iyileşmeler gözlendi (p<0,05).

Anahtar Kelimeler: Egzersiz terapisi; fibromiyalji; ozon terapisi; ağrı

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Fibromyalgia Syndrome (FMS) is a chronic condition characterized by widespread chronic pain and certain tender points in the body, seen in the locomotor system.[1] FMS is a common chronic rheumatic disease, a syndrome that negatively affects individuals' physical, sensory functions and quality of life. Along with these negativities, pain, insomnia, fatigue, mental disorder and other physical findings can also be added.[2] In order for FMS patients to be diagnosed, there must be increased sensitivity with palpation in 11 of the 18 previously determined anatomical points in the body, in addition to the complaint of chronic pain.[1]

In a study conducted in our country, the prevalence of FMS in women is 6.8%. The disease is seen in all age groups, but it is more common in the middle age group. The ratio of women to men in individuals with FMS is 80-90% and it is more painful in women.[3,4]

Today, FMS treatment is divided into 3 as pharmacological, non-pharmacological and complementary treatments. Pharmacological treatments include antidepressants, antiepileptic drugs and other drugs, and also include different combinations of these drugs.[5] Non-pharmacological treatments include patient education, different types of exercises, physical therapy methods, breathing techniques, etc. Complementary treatments include major ozone therapy, acupuncture, homeopathy, phytotherapy and other complementary treatments.[6] The main purpose of FMS treatment is to achieve a higher quality of life by reducing patients' complaints and increasing their functional capacity. The most effective method in treatment is multidisciplinary treatment approaches where pharmacological, non-pharmacological and complementary treatment methods are applied together.[7] The scales used in this study include visual analogue scale (VAS), Fibromyalgia Impact Questionnaire (FIQ), and flexibility: vas is a subjective scale that shows the pain level of patients and expresses the pain level numerically between zero and 10. Zero means I have no pain, and 10 means I have unbearable pain. Questions about the patient's sleep quality are asked with the survey questions made with FIQ. With flexibility, the distance the patient can extend their hands is measured with a tape measure with the sit-and-reach test.

There are a limited number of studies in the literature investigating the effectiveness of ozone therapy in individuals with FMS. However, no study has been conducted in our country investigating the effectiveness of major ozone therapy and exercise therapy in patients diagnosed with FMS in terms of subjective pain, objective pain, the impact of the disease on daily life and quality of life values. Our aim with this study is to evaluate and weigh the effects of ozone and exercise on the pain thresholds of fibromyalgia patients with chronic pain using an algometer.

MATERIAL AND METHODS

INCLUSION CRITERIA

Diagnosed with fibromyalgia, aged between 18-65, not having glucose 6-phosphate enzyme deficiency, not having any allergies including ozone and citrus fruits, being literate in Turkish.

EXCLUSION CRITERIA

Not having fibromyalgia diagnosis, having ozone allergy, being under 18, being over 65, having any allergies, using long-acting antiplatelet drugs such as coumadin, transplant patients, pregnant women. The fibromyalgia patients who participated in the study were first asked to provide informed consent and the study was explained (Appendix 1). Then, they were asked to fill out the descriptive characteristics form, FIQ and 36-Item Short Form Health Survey (SF-36) questionnaires. Then, all participants were assessed for their pressure pain thresholds using the algometer device and their flexibility using the flexibility bench before the first session of ozone therapy. The patients were called back to the clinic within the following week after the 5-week treatment plan was implemented and the necessary data were obtained by collecting the same questionnaire and physical measurements.

In our study, the major ozone autohemotherapy (MAH) method will be applied. In the MAH application, the patient's own blood is taken with 200 cc ozone-resistant infusion sets with negative pressure, and after ozone gas insufflation from the generator, it is homogenized and reinfused to the patient in the same set (Figure 1, Figure 2, Figure 3).[8] The entire

FIGURE 1: Ozone generator and oxygen device

FIGURE 2: Ozone sensor device

process should be carried out under sterile conditions. New materials were used in each session. The materials must be resistant to ozone. Blood reinfusion should be slow. It is necessary to plan the session intervals for MAH by considering both the mechanisms of action of ozone and the citrate or heparin we use. A session lasts approximately 15-20 minutes. The application can be repeated in sessions at certain periods depending on the person, their condition, and the desired effect. Concentrations are determined with the standard unit of measurement of micrograms per milliliter.[9] In our study, in order to standardize the

FIGURE 3: Drop counter infusion system

number of ozone therapy sessions and amounts, 5 sessions of ozone therapy were applied to each patient at 10, 20, 30, 35, and 40 gamma, respectively.

This research was approved by the Necmettin Erbakan University Health Sciences Scientific Research Ethics Committee with the decision numbered 2023/416 dated 05.04.2023 (ANNEX 6).

DATA ANALYSIS

Data analysis was performed with the R 4.4.2 (R Core Team, 2024) program. Mean and standard deviation for numerical variables; frequency and percentage statistics for categorical variables were given.

T-test and mixed effects models were used in the analysis of numerical variables. chi square or Fisher exact test was used in the analysis of categorical variables. Least square mean was used in "post hoc" pairwise comparisons. $p<0.05$ was considered statistically significant.

RESULTS

Demographic and descriptive characteristics of all individuals participating in the study (age, height, weight, time of diagnosis, gender, education status, exercise habits) are given in Table 1.

The individuals participating in the study were compared in terms of age, height, weight and diagnosis Time (Table 1). Since (p>0.05) was found for these 4 values, there is no significant difference. In terms of age, height, weight and diagnosis time, ozone and Ozone+Exercise groups are identical groups. The values of gender, education status and exercise habit of both groups were compared with Fisher's exact test. Since (p>0.05) was found for all the features, there is no statistical significance. It can be stated that both groups are identical in terms of these features.

When the pre-treatment VAS, FIQ and flexibility values of the individuals participating in the study were compared, no statistical significance was found between the groups (p>0.05) (Table 2). It can be stated that these 2 groups were identical in terms of subjective pain, physical impact and body flexibility.

When the sub-parameter values of the SF-36 questionnaire belonging to the groups were compared, all scale values were found to be statistically similar (p>0.05). It can be stated that both groups are identical in terms of quality of life.

TABLE 1: Comparison of demographic information of participants

	Ozone (n=19) $\bar{X}$±SD	Ozone+Exercise (n=18) $\bar{X}$±SD	p value[1]
Age (years)	48.89±6.94	47.44±7.45	0.54
Long (cm)	165.05±7.95	165.44±9.91	0.90
Weight (kg)	75.05±14.36	76.44±12.67	0.76
Diagnosis time (years)	7.37±6.38	8.67±5.79	0.52
	n (%)	n (%)	p value[2]
Gender			
Woman	15 (79%)	15 (83%)	>0.99
Man	4 (21%)	3 (17%)	
Educational status			0.42
Primary	4 (21%)	2 (11%)	
High school	2 (11%)	3 (17%)	
Associate degree	0 (0%)	0 (0%)	
Licence	11 (58%)	7 (39%)	
Master's degree	2 (11%)	4 (22%)	
Doctorate	0 (0%)	2 (11%)	
Exercise habit			
No there's not	9 (47%)	12 (67%)	
1 in mounth	1 (5.3%)	0 (0%)	0.46
1-2 in week	5 (26%)	5 (28%)	
3-4 in week	4 (21%)	1 (5.6%)	

SD: Standard deviation

TABLE 2: Comparison of pre-treatment VAS, FIQ and flexibility values of the groups

	Ozone (n=19) $\bar{X}$±SD	Ozone+Exercise (n=18) $\bar{X}$±SD	p value
VAS	7.00±1.49	6.61±1.50	0.461
FIX	61.04±12.24	64.46±12.77	0.483
Flexibility	21.49±9.63	22.17±8.27	0.808

SD: Standard deviation; VAS: Visual analogue scale;
FIQ: Fibromyalgia Impact Questionnaire; FIX

TABLE 3: Comparison of pre-treatment SF-36 subparameter values of the groups

SF-36	Ozone (n=19) $\bar{X}$±SD/Med (Q1-Q3)	Ozone+Exercise (n=18) $\bar{X}$±SD/Med (Q1-Q3)	p value
Physical function	58.42±26.20	56.22±21.12	0.760
Physical role difficulty	0.00(0.00-25.00)	20.00(5.00-60.00)	0.286
Emotional role difficulty	0.00(0.00-33.33)	0.00(0.00-66.67)	0.396
Energy/vitality	31.05±17.84	34.17±15.27	0.589
Mental health	50.32±12.95	52.89±10.85	0.536
Social functioning	47.37±18.90	53.47±15.93	0.315
Pain	28.95±18.49	33.33±18.31	0.465
General health perception	33.95±19.05	39.72±15.29	0.316

SD: Standard deviation; SF-36: 36-Item Short Form Health Survey

When the pressure pain threshold values measured on the right and left from 6 regions of the body before treatment were compared, no statistical significance was observed when the pressure pain thresholds of the 1st, 3rd, 4th, 5th and 6th points were compared between the groups (p>0.05) (Table 4). It can be assumed that the 2 groups are identical in terms of pain thresholds at these points. A statistically significant difference was observed in the comparison of the pressure pain threshold of the 2nd point (p<0.05). It can be said that these 2 groups are not identical for the region represented by the 2nd point (Femoral medial condyle).

INTRAGROUP COMPARISON OF VALUES BEFORE AND AFTER TREATMENT OF GROUPS

When the post-treatment values of the Ozone group are examined in terms of VAS, FIQ scale values and flexibility, a significant improvement is observed for all 3 parameters compared to the pre-treatment values (p<0.05) (Table 5).

TABLE 4: Comparison of pre-treatment pressure pain threshold values of groups

		Ozone (n=19) X̄±SD	Ozone+Exercise (n=18) X̄±SD	p value
Point 1	Right	26.58±9.32	31.93±9.21	0.068
	Left	27.53±9.88	30.49±6.65	0.309
Point 2	Right	45.16±15.45	60.43±10.53	**0.007**
	Left	43.06±14.65	56.14±15.60	**0.021**
Point 3	Right	31.89±10.88	36.20±14.74	0.313
	Left	33.02±14.33	34.36±8.34	0.753
Point 4	Right	45.31±17.59	48.02±12.40	0.583
	Left	45.37±17.53	47.75±11.97	0.630
Point 5	Right	54.57±22.83	53.84±15.87	0.899
	Left	52.85±16.70	56.00±18.12	0.586
Point 6	Right	67.69±24.10	78.13±17.46	0.101
	Left	70.12±25.70	74.26±14.42	0.512

SD: Standard deviation

TABLE 5: Comparison of VAS, FIQ and flexibility values of the Ozone group before and after treatment

	Treatment pre- X̄±SD	Treatment post- X̄±SD	p value
VAS	7.00±1.49	3.67±1.85	**0.000**
FIX	61.04±12.24	35.34±19.83	**0.000**
Flexibility	21.49±9.63	23.92±8.06	**0.011**

SD: Standard deviation; VAS: Visual analogue scale;
FIQ: Fibromyalgia Impact Questionnaire; FIX:

INTRAGROUP COMPARISON OF VALUES BEFORE AND AFTER TREATMENT OF GROUPS

When the post-treatment values of the Ozone group are examined in terms of VAS, FIQ scale values and flexibility compared to the pre-treatment values, a significant improvement is observed for all 3 parameters ($p<0.05$) (Table 5).

When the post-treatment SF-36 scale values of the Ozone group are examined, a significant improvement is observed in all scale sub-parameters compared to the pre-treatment values ($p<0.05$).

COMPARISON OF PRESSURE PAIN THRESHOLD VALUES OF THE OZONE GROUP BEFORE AND AFTER TREATMENT

When the post-treatment pressure pain threshold values of the Ozone group are examined, it is seen that the improvement in all measured points compared to the pre-treatment values is not statistically significant ($p>0.05$). Among the obtained results, the right side p values of the 3rd and 4th points are close to 0.05.

COMPARISON OF VAS, FIQ AND FLEXIBILITY VALUES OF OZONE+EXERCISE GROUP BEFORE AND AFTER TREATMENT

When the post-treatment values of Ozone+Exercise group are examined in terms of VAS, FIQ scale values and flexibility compared to pre-treatment values, a significant improvement is observed for all three parameters ($p<0.005$) .

When the post-treatment SF-36 scale values of Ozone+Exercise group are examined, a significant improvement is observed in Physical Function, Physical Role Difficulty, Emotional Role Difficulty, Energy, Pain and General Health Perception subparameters compared to pre-treatment ($p<0.05$). The improvement in the Mental Health and Social Functioning subparameters of the group is not significant ($p>0.05$).

COMPARISON OF PRESSURE PAIN THRESHOLD VALUES OF OZONE+EXERCISE GROUP BEFORE AND AFTER TREATMENT

When the pressure pain threshold values of Ozone+Exercise group were examined after treatment, it was seen that the pain threshold on the right side of Point 2, Point 3 and Point 5 improved significantly compared to before treatment ($p<0.05$). It is

seen that the improvement in the other measured points is not statistically significant ($p>0.05$). Among the obtained results, the p values of point 4 on the left side and point 6 on both sides approached 0.05.

COMPARISON OF VAS, FIQ AND FLEXIBILITY VALUES OF THE GROUPS AFTER TREATMENT

When the VAS, FIQ and flexibility values of the individuals participating in the study were compared after treatment, no statistical significance was observed between the groups ($p>0.05$). It can be stated that the exercise applied in addition to ozone treatment did not cause a significant change in terms of subjective pain, physical effect and body flexibility.

When the subparameter values of the SF-36 questionnaire belonging to the groups were compared at the end of the treatment, the value of the subparameter titled Mental Health was found to be statistically higher in the Ozone group ($p<0.05$). There was no statistically significant difference in terms of physical function, physical role difficulty, energy, social functionality, pain and general health perception ($p>0.05$).

COMPARISON OF PRESSURE PAIN THRESHOLD VALUES OF THE GROUPS AFTER TREATMENT

When the pressure pain threshold values after treatment were compared between the groups, a significant difference was observed on both the right and left sides of the 2nd and 6th points ($p<0.05$). When we examined the values, the right side value of the 1st point approached the statistical significance rate. The difference between the values of the left side of the 1st point, the right and left side localizations of the 3rd, 4th and 5th points was found to be statistically insignificant ($p>0.05$).

DISCUSSION

The aim of our study was to evaluate the effects of major ozone therapy applied to individuals with FMS who applied to the Getat center in terms of pain, quality of life, physical function effects and pressure pain threshold by comparing it with exercise. In the literature review, we did not find any study comparing major ozone therapy with any exercise treatment.

37 individuals who met the inclusion criteria were included in the study. The Ozone group consisted of 19 participants and the Ozone+Exercise group consisted of 18 participants. We have listed the important results we obtained as a result of our study below.

In the study conducted by Moreno-Fernández et al. investigating the effects of ozone autohemotherapy on 20 fibromyalgia patients, a total of 10 sessions were performed by applying 30 gamma in the 1st 3 sessions, 40 gamma in the 4th session, 50 gamma in the 5th session, and 60 gamma in the last 5 sessions.[10] Serotonin and oxidative stress parameters (reactive oxygen species (ROS), lipid oxidation products, PC) values were examined in the study: a significant decrease was detected in LP and PC, where serotonin levels statistically increased, a significant decrease in the number of tender points, and a significant decrease in the FIQ score was also detected.[10] In our study, the decrease in FIQ scores was similar, but while the total number of tender points was evaluated in this study, in our study, in addition to the material method, the pressure pain threshold of the tender points was also evaluated with an algometer.

In a randomized placebo-controlled double-blind study conducted by Sucuoğlu et al. (n=54, treatment group=26, control=28), fibromyalgia patients were given both major and minor ozone twice a week.[11] Before and after the treatment, they applied the FIQ, Pittsburgh Sleep Quality Index (PSQI) and Short Form-12 (SF-12) questionnaire. As a result, a significant improvement was found in the subjective FIQ and PSQI scales in the treatment group ($p<0.05$).[11] In our study, we obtained similar findings in terms of the total score decrease in the FIQ scale.

In a prospective cross-sectional study conducted by Gazioğlu Türkyılmaz et al, 13 sessions of major ozone therapy were applied to fibromyalgia patients (n=40, treatment group=13).[12] The applied ozone therapy was arranged as 2 sessions per week for the first 5 weeks and 1 session per month for the last 3 months. Patients completed the FIQ and the SF-36 at the beginning (PRE), in the 5th week after 10 MAH sessions [Prothrombin-time test (PT)], in the ninth week after 11 sessions (PT1) and in the 17th week after 13 sessions (PT3). Significant improvements were found in the FIQ and SF-36 assessment scales used before and after the treatment in all periods.

Significant improvements were observed in FIQ and SF-36 scores in all periods compared to the previous period ($p<0.05$). The most significant improvements in both FIQ scores ($p<0.01$) and SF-36 scores between 2 consecutive measurements were observed between the baseline and PT period ($p<0.01$). In addition, significant improvements occurred in all SF-36 subscale scores between PT and PT3 ($p<0.02$).[12] In our study, we found similar improvement rates in SF-36 and FIQ scores.

In the study conducted by Kuculmez, 10 major ozone sessions were applied to fibromyalgia patients 2-3 times a week.[13] VAS and FIQ were applied before and after the treatment, and as a result, significant improvement was detected in both VAS and FIQ scores from the 1st month. In our study, we reached similar results after 5 sessions. We think that this result was achieved in a longer period of time because the group conducting the study always used the same dose of 25 mcg/ml, and in our study, we achieved positive effects in a total of 5 sessions by gradually increasing the dose (10, 20, 30, 35, 40 gamma).[13]

In a review discussing the use of therapeutic medical ozone in musculoskeletal pain control, 27 studies from 9 different countries on this subject using different ozone application methods (intradiscal, intracarpal, MH, intraforaminal, subcutaneous, subacromial bursa, endoscopically administered to the epidural space) were examined; device safety was emphasized in the studies, and each application method of ozone was recommended as a safe treatment method, highly effective (77.8% without any side effects) in musculoskeletal pain. As a side effect (local ecchymosis, local pain at the injection site, hypotension-hypoglycemia was observed in only 1 person systemically.[14] Tirelli et al. applied ozone therapy to fibromyalgia patients for more than 2 years.[15] As a result of this study, Tirelli et al. suggested that ozone therapy could be recommended to fibromyalgia patients who could not get sufficient results from existing treatments because it does not have any side effects.[15] We also did not encounter any side effects during our study. In this respect, we support the reliability of ozone therapy.

In a randomized controlled study conducted in 2017 comparing stretching and strengthening exercises with placebo and each other, stretching exercises were found to be superior to strengthening exercises and placebo in improving physical function, pain and quality of life, and strengthening exercises were found to be more effective than stretching exercises and placebo in reducing depression.[16] In our study, the improvements in physical function and pain observed in our Ozone+Exercise group including exercise therapy are consistent with the contributions of this study to the literature.

In a randomized controlled study conducted in 2019, only aerobic exercise and aerobic exercise+ stretching exercises were compared. The aerobic exercise+stretching group was found to be significantly more effective in pain, quality of life and sleep compared to only aerobic exercise.[17] The benefits of the additional stretching exercises are consistent with the results in our study in the Ozone+Exercise group.

RECOMMENDATIONS

We recommend that exercise be added to ozone therapy in individuals with FMS who feel more back pain. Major ozone therapy provides short-term free radicals to the organism and exercises the immune system, thus improving chronic pain. We believe that it may be a suitable option for those looking for a safe, effective and natural painkiller. We believe that the positive effects of ozone therapy obtained in the short term will spread to the long term with the exercises performed and we state that long-term studies are needed in this area.

Objective data analyses including digital algometers and multi-center studies with high participant numbers and longer-term treatments and therefore longer patient follow-ups are needed in the literature. We believe that our study provides valuable information about the potential of ozone therapy, however, we emphasize that the need for longer-term studies using different exercise programs to fully demonstrate the comparative effectiveness of exercise in pain management continues and the importance of continuing studies in this direction.

LIMITATIONS

There were some limitations in our study.

These are: Since the materials of major ozone therapy were purchased in euros, it increased the cost of treatment and therefore, it was studied with a low sample size. In the plan of our study, there was no control group that did not receive treatment. Therefore, a comparison could not be made with the group that did not receive any treatment. Again, since it was not a group that only followed exercise, it was not possible to evaluate the effects of isolated exercise. Since the participants who were evaluated before and after the treatment were not re-evaluated after a long period, the long-term effectiveness of the treatments was not evaluated.

CONCLUSSION

This study was conducted to evaluate the effects of major ozone therapy applied in the treatment of individuals with FMS and to compare it with exercise. According to this study, both ozone therapy and exercise treatments are treatment methods that can be used to increase the quality of life of individuals with FMS and to eliminate chronic fatigue. Our study shows that major ozone therapy has a healing effect on subjective pain level, body flexibility, quality of life and the level of physical function. Exercises combined with ozone therapy increased the pressure pain threshold especially in the lumbar region. When we look at the point by point, we found that the combined application of ozone therapy with exercise significantly increased the pressure pain threshold of the tender points in the medial knee, suboccipital and medial upper corner of the scapula.

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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.

Authorship Contributions

Idea/Concept: *Hayriye Alp;* ***Design:*** *Hayriye Alp;* ***Control/Supervision:*** *Hayriye Alp;* ***Data Collection and/or Processing:*** *Şerife Aydın;* ***Analysis and/or Interpretation:*** *Şerife Aydın;* ***Literature Review:*** *Hayriye Alp, Şerife Aydın;* ***Writing the Article:*** *Hayriye Alp, Şerife Aydın;* ***Critical Review:*** *Hayriye Alp;* ***References and Fundings:*** *Hayriye Alp;* ***Materials:*** *Hayriye Alp, Şerife Aydın.*

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