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Original Article

Evaluation of the effects of neural therapy in patients diagnosed with fibromyalgia

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ABSTRACT

Objectives: This study aims to compare the effects of neural therapy and exercise on pain, quality of life, depression, anxiety, and functioning status in patients diagnosed with fibromyalgia syndrome (FMS).

Patients and methods: This multi-center study included a total of 72 patients (60 females, 12 males; mean age: 39.2±9.5 years; range, 22 to 53 years) who were diagnosed with FMS according to the 1990 American College of Rheumatology (ACR) criteria between January 2015 and June 2015. The patients were randomly divided into two groups: the first group (n=30) received an exercise program (strengthening, stretching, relaxation, and aerobic exercises, three days a week), and the second group (n=42) received a total of six sessions of neural therapy as one session a week in addition to the same exercise program. Pain severity was assessed with the Visual Analog Scale (VAS), emotional state with the Beck Depression Scale (BDS) and Beck Anxiety Inventory (BAI), quality of life with Short Form-36 (SF-36), and functioning status with the Fibromyalgia Impact Questionnaire (FIQ). The patients were evaluated at the end of treatment (week 6) and one month after the end of treatment.

Results: The mean disease duration was 34.3±9.3 months, the mean VAS score was 7.3±2.2, and the mean FIQ score was 58.4±13.2. There were significant improvements in the VAS, FIQ, SF-36, BDS, and BAI scores after the treatment in both groups ($p<0.05$). Post-treatment BDS and VAS scores were significantly lower in the neural therapy group ($p=0.038$; $p=0.049$; $p<0.05$). There was no significant difference in any parameter one month after the treatment between the groups ($p>0.05$).

Conclusion: When neural therapy is combined with exercise in FMS patients, it may be advantageous in terms of pain and depression, compared to exercise alone.

Keywords: Fibromyalgia, lidocaine, neural therapy.

Fibromyalgia syndrome (FMS) is a chronic disease with widespread musculoskeletal pain, fatigue, sleep disorders, and many central hypersensitivity syndromes are seen together.[1] It is observed by 2.9% and 3.8% in general population.[2] Numerous pharmacological and non-pharmacological methods are used for the treatment of FMS. Non-pharmacological methods are needed, particularly where pharmacological methods are insufficient. Several studies have found that every FMS patient uses complementary and alternative medicine at least once.[3] These approaches include exercise based therapies (Qigong, Tai Chi, Yoga), manipulative treatment methods (massage, chiropractic management), mind body interventions (i.e., mediation, hypnosis, biofeedback), acupuncture, hydrotherapy, balneotherapy, phytotherapy, homeopathy, and natural products.[4] Guidelines established by different countries seem to focus on non-pharmacological methods in recent years.[5]

Neural therapy is a form of treatment which can be applied in painful situations with local anesthetics administered in the tendon ligament scaring, ganglia, peripheral nerves, glands, trigger points, and other tissues.[6] Neural therapy treats the body not as a structure only, but as an electrical system. Each cell has a membrane potential. In conditions involving chronic pain, such as fibromyalgia, anomalies are present in the membrane potentials resulting in autonomic

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nervous system and hormonal system dysfunctions. Altered central nervous system is reflected on the peripheral system. The first step in neural therapy is to find the primary focus which sends this stimulus to the autonomic nervous system. Primary focus can sometimes be a tooth abscess, sinus pathology, or a scar tissue. Such structures may cause constant stimulation, disrupting the body's regulatory capacity.[6-8] The main goal of neural therapy is to correct the potential anomalies in nerve sheaths.[6-8] Local anesthetics used in neural therapy are known to have neuroprotective and anti-inflammatory effects on the nervous system.[9,10] Genetic factors, environmental factors, peripheral disorders, and central mechanisms are involved in the etiopathogenesis of fibromyalgia. In particular, past physical traumas, muscle-tissue dysfunctions, autonomic nervous system dysfunctions, hypothalamic-pituitary-adrenal, and neuroendocrinological anomalies, neuropeptide anomalies, central sensitization, and immune system dysfunctions are held responsible for the etiopathogenesis of the disease.[11-14]

Considering the mechanism of action of neural therapy, it is believed that it can be effective against many mechanisms which are held responsible for the etiopathogenesis of fibromyalgia.[3,4] Being one of the alternative and complementary treatments used by a great majority of patients, neural therapy has been in use for a long time in many European countries, mainly Germany.[6-8] In the literature, there is no study evaluating the efficacy of neural therapy in fibromyalgia patients. In the present study, therefore, we aimed to evaluate the effect of neural therapy on pain, quality of life (QoL), and emotional state in patients with fibromyalgia.

PATIENTS AND METHODS

This multi-center study included a total of 72 patients (60 females, 12 males; mean age: 39.2±9.5 years; range, 22 to 53 years) who were diagnosed with FMS according to the 1990 American College of Rheumatology (ACR)[15] criteria between January 2015 and June 2015. The ethics approval (No. 2015/31) of the study was received from Medicine Faculty of Kocaeli University. A written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki. All patients were questioned in detail and physical examination was performed. Patients with diseases that could cause secondary FMS (systemic lupus erythematosus, scleroderma, Sjögren's syndrome); those with rheumatic diseases such as polymyalgia rheumatica; patients with neurological diseases as infectious pathologies, thyroid gland disorders, neuropathies, myopathies, myositis and multiple sclerosis; patients reporting any allergy to lidocaine and its components; those with infections, open wounds or vascular pathologies in the application site, patients with severe systemic diseases, severe mental disorders or known severe psychiatric diseases; patients with a history of malignancy or the use of anticoagulants and patients who received physiotherapy and rehabilitation and injection applications were excluded from the study.

Sociodemographics of all patients were recorded. Patients' disease duration, morning stiffness duration, pain levels and the number of painful points among 18 precision points based on the 1990 ACR FMS diagnostic criteria[16] were also recorded. The pain level was assessed with the Visual Analog Scale (VAS) using a 10-cm ruler. All patients were told that no pain corresponded to 0, the most severe pain to 10, and moderate pain to five points and asked to describe their pain accordingly. Determination of the tender points was carried out by applying a force of 4 kg on the 18 tender points specified in the FMS diagnostic criteria[16] with the thumb, until the nail bed blanches. The painful points were recorded.

The emotional state of the patients was assessed with the Beck Depression Scale (BDS) and the Beck Anxiety Inventory (BAI). The BDS consists of a total of 21 items. The total score is between 0 and 63 points. The patients were asked to mark the most appropriate option for each item considering their situation in the last week. According to this scale, 14-18 points indicates mild, 19-28 points moderate, and 29-63 points severe depression in the Turkish society. The Turkish validity and reliability of the scale were performed by Hisli et al. The BAI is a 21-question scale with the total score assessed in the range of 0-63 points.[17,18] The Turkish validity and reliability study were conducted by Ulusoy et al.[19,20]

The QoL was assessed using the Short-Form 36 questionnaire (SF-36). The SF-36 evaluates QoL in eight subtitles including physical functioning, social role functioning, physical role functioning, emotional role functioning, mental health, energy/vitality, bodily pain, and general health perceptions.[21] The Turkish validity and reliability study were conducted by Kocyigit et al.[22] The functional status was assessed with the Fibromyalgia Impact Questionnaire (FIQ). The FIQ was developed by Burckhardt et al.[23] to measure the functional status and, reliability and

validity of the scale specific to Turkey was performed by Sarmer et al.[24]

The patients were randomized according to the order of inclusion into the study and divided into two treatment groups. The patients were randomized using a closed envelope method. The patients in both groups were informed about their disease. Drugs taken for FMS were allowed, providing the dose not to be changed. All patients were informed about their disease and the exercises that were asked to be done. The first treatment group received an exercise program consisting of strengthening, stretching, and relaxation exercises, while the second group received neural therapy applications in addition to the same exercise program. Neural therapy was scheduled as once a week for six weeks. A total of six sessions were performed. All patients were assessed before the treatment, at the end of treatment, and one month after the end of treatment.

Neural therapy application

For neural therapy injections, 10% or 2% lidocaine was used. Lidocaine was diluted with normal saline and used as 0.5% lidocaine. The Quaddel injection was made with 0.1 to 0.2 mL lidocaine as intracutaneous injection. In the local application, the Quaddel injection was made to the painful points found by palpation in the shoulders, back, waist, or any part of the body. In the segmental application, bilateral Quaddel injection was performed into the interspinous spaces between cervical 1 (C1) and sacral 1 (S1) vertebrae and 2 cm lateral to the midline at the level of the spinous process level. In the sternum injection, a quaddel injection was made in the middle of two breast lines. In the abdominal Hopfer's application, the Quaddel injection was performed as two-row circles around the umbilicus with 2 cm intervals. The Quaddel injection was also made in the trigeminus outlets (supraorbital, infraorbital, mentalis). In addition, jugular veno-lymphatic drainage and belt injection were performed. For the thyroid application, two Quaddel injections were made in each one inch (finger) lateral to left and right of the midpoint between the thyroid cartilage located in the neck and incisura of the sternum. A 5-M application was performed as two Quaddel injections in each 3-inch lateral to left and right of the symphysis pubis, two Quaddel injections in 2-inch cranial to these points, and one injection to one inch cranial to the symphysis pubis. For the scar applications, subcutaneous injections were performed as 2 mL lidocaine per 10 cm^2 area depending on the scar size.

Applications carried out during the treatment are shown in the Figure 1. Neural therapy group received a total of six sessions of therapy once a week.[25]

1. Session
   a) Local application: quaddel injection to the painful points found with palpation in the shoulders, waist, lower back and anywhere in the body
   b) C1-S1 segmental application
   c) Sternum injection
   d) Abdominal Hopfer crown
   e) 5 M application
   f) Thyroid application
   g) Mastoid, Vaccine and umblicalus scar injection
   h) Jugular veno-lymphatic drainage and belt injection
2. Session
   a) Local application: quaddel injection to the painful points found with palpation in the shoulders, waist, lower back and anywhere in the body
   b) C1-S1 segmental application
   c) Sternum injection
   d) Abdominal Hopfer crown
   e) Quaddel injection to the outlets of trigeminus
   f) Jugular veno-lymphatic drainage and belt injection
3. Session
   a) Local application: quaddel injection to the painful points found with palpation in the shoulders, waist, lower back and anywhere in the body
   b) C1-S1 segmental application
   c) Sternum injection
   d) Abdominal Hopfer crown
   e) 5 M application
   f) Thyroid application
   g) Other scars
4. Session
   a) Local application: quaddel injection to the painful points found with palpation in the shoulders, waist, lower back and anywhere in the body
   b) C1-S1 segmental application
   c) Sternum injection
   d) Abdominal Hopfer crown
   e) Quaddel injection to the outlets of trigeminus
   f) Jugular veno-lymphatic drainage and belt injection
5. Session
   a) Local application: quaddel injection to the painful points found with palpation in the shoulders, waist, lower back and anywhere in the body
   b) C1-S1 segmental application
   c) Sternum injection
   d) Abdominal Hopfer crown
   e) 5 M application
   f) Thyroid application
   g) Mastoid, Vaccine and umblicalus scar injection
   h) Jugular veno-lymphatic drainage and belt injection
6. Session
   a) Local application: quaddel injection to the painful points found with palpation in the shoulders, waist, lower back and anywhere in the body
   b) C1-S1 segmental application
   c) Sternum injection
   d) Abdominal Hopfer crown
   e) Quaddel injection to the outlets of trigeminus
   f) Jugular veno-lymphatic drainage and belt injection

Figure 1. Neural therapy program.

Table 1. Demographic data of patients

	Exercise group (n=30)			Neural therapy group (n=42)			
	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (year)			39.7±1.4			38.9±1.5	0.472†
Body Mass Index (kg/m^2)			28.3±0.2			29.1±0.9	0.564†
Sex							
Female	25			35			
Male	5			7			0.547†
Current smoker	14	46.6		20	47.6		0.112‡
Education (University)	5	16.6		8	19.0		0.098‡
Housewife/employed	20/10			30/12			0.147‡
Duration of illness			32±7.2			31±7.8	0.485†
Number of tender points			13±2.4			13±2.7	0.241†

SD: Standard deviation; † Student t-test; ‡ Yates Continuity Correction.

All patients in both groups were instructed how to perform home-based exercises and asked to regularly take these exercises two days a week for six weeks. The patients were invited to the clinic for control and regulation of the exercises by the physiotherapist once in every two weeks. When necessary, some small adjustments were made according to the medical conditions of the patients and a rehabilitation program consisting of exercises and patient education was applied.[26]

Statistical analysis

Statistical analysis was performed using the Number Cruncher Statistical System (NCSS) 2007 (Kaysville, Utah, USA) software. Descriptive data were expressed in mean ± standard deviation (SD), median (min-max), number, and frequency. The Student's t-test was used for two group comparison of parameters showing normal distribution. The chi-square test was used and Yates' correction was applied to compare the association between two categorical variables. Intragroup comparison of the normally distributed parameters was carried out using the repeated measures test (variance analysis in repeated measures) and paired comparisons were made using the corrected Bonferroni test. *P* values of <0.01 and <0.05 were considered statistically significant.

RESULTS

The mean disease duration was 34.3±9.3 months, the mean VAS score was 7.3±2.2, and the mean FIQ score was 58.4±13.2. No statistically significant difference was found between the groups in terms of age, sex, disease duration, smoking, marital status, and educational status (Table 1).

Pre-treatment VAS scores did not show any statistically significant difference between the treatment groups (p>0.05). Post-treatment VAS scores were significantly lower in both exercise and neural therapy groups (p=0.038; p<0.05). No significant difference was observed between both groups in terms of the post-treatment first-month VAS scores (p=0.001; p<0.01). According to the paired comparisons, changes in the VAS scores were found to be statistically significant in both exercise and neural therapy groups (p=0.001; p<0.01), (p=0.001; p<0.01) (Table 2).

Pre-treatment BDS scores were not statistically significant between the groups (p>0.05). However, post-treatment changes in the BDS scores were found to be statistically significant in both exercise and neural therapy groups (p=0.049; p<0.05). There were no statistically significant differences between the groups in terms of pre-, post-treatment, and post-treatment first month BAI scores (p>0.05). According to the paired comparisons, changes in the BAI scores

Table 2. Visual Analog Scale between groups

	Exercise group (n=30)	Neural therapy group (n=42)	
	Mean±SD	Mean±SD	*p*†
Visual Analog Scale			
Pre-treatment	7.7±1.2	7.2±1.3	0.824
Post-treatment	5.3±1.0	4.3±0.9	0.038*
Post-treatment first month	4.1±0.7	3.1±1.0	0.069
P value	0.001**‡	0.001**‡	

SD: Standard deviation; † Student t-test; ‡ Repeated measures ANOVA test; * p<0.05, ** p<0.01 statistically significant.

Table 3. Beck Depression and Anxiety Scores between groups

	Exercise group (n=30)	Neural therapy group (n=42)	
	Mean±SD	Mean±SD	*p*†
Beck Depression Score			
Pre-treatment	15.1±3.2	15.7±3.2	0.824
Post-treatment	12.0±2.4	10.1±2.6	0.049*
Post-treatment first month	10.2±1.8	9.3±2.2	0.839
	0.001**‡	0.001**‡	
Beck Anxiety Score			
Pre-treatment	19.5±3.5	19.8±3.8	0.736
Post-treatment	16.6±3.7	15.6±3.9	0.314
Post-treatment first month	15.0±3.1	14.0±3.6	0.221
	0.001**‡	0.001**‡	

SD: Standard deviation; † Student t-test; ‡ Repeated measures ANOVA test; * p<0.05; ** p<0.01.

between pre- and post-treatment values were found to be statistically significant in both exercise and neural therapy groups (p=0.001; p<0.01) (Table 3).

No statistically significant differences were found between the groups in terms of pre-, post-treatment, and post-treatment first month measurements of

Table 4. Short-Form 36 Quality of Life scores between groups

	Exercise group (n=30)	Neural therapy group (n=42)	
Short-Form 36	Mean±SD	Mean±SD	*p*†
Physical Functioning Scores (pre-treatment)	54.4±4.7	53.1±5.0	0.736
Physical Functioning Scores (post-treatment)	57.9±4.4	58.5±5.3	0.314
Physical Functioning Scores (post-treatment first month)	62.8±4.3	62.1±5.0	0.221
Intragroup comparisons (p value)	0.001‡	0.001‡	
Physical Role Function Scores (pre-treatment)	55.3±3.6	54.9±5.2	0.666
Physical Role Function Scores (post-treatment)	59.7±3.7	57.8±5.2	0.086
Physical Role Function Scores (post-treatment first month)	61.3±4.0	60.3±4.1	0.120
Intragroup comparisons (p value)	0.001‡	0.001‡	
Bodily Pain Score (pre-treatment)	56.2±4.3	55.1±5.3	0.372
Bodily Pain Score (post-treatment)	61.8±5.3	59.7±4.6	0.090
Bodily Pain Score (post-treatment first month)	63.3±5.2	61.3±3.6	0.106
Intragroup comparisons (p value)	0.001‡	0.001‡	
General Health Perception Scores (pre-treatment)	54.7±3.8	54.7±5.6	0.955
General Health Perception Scores (post-treatment)	58.9±4.8	57.9±5.1	0.578
General Health Perception Scores (post-treatment first month)	60.5±5.2	60.5±4.7	0.571
Intragroup comparisons (p value)	0.001‡	0.001‡	
Vitality Scores (pre-treatment)	56.8±5.2	55.0±5.4	0.167
Vitality Scores (post-treatment)	61.7±5.1	61.4±5.3	0.784
Vitality Scores (post-treatment first month)	66.0±3.7	63.9±5.1	0.056
Intragroup comparisons (p value)	0.001‡	0.001‡	
Social Functioning Scores (pre-treatment)	57.5±4.5	56.6±4.9	0.438
Social Functioning Scores (post-treatment)	64.1±4.5	63.0±5.3	0.107
Social Functioning Scores (post-treatment first month)	65.9±4.2	64.5±5.3	0.291
Intragroup comparisons (p value)	0.001‡	0.001‡	
Emotional Role Functioning Scores (pre-treatment)	56.9±5.1	55.5±5.3	0.268
Emotional Role Functioning Scores (post-treatment)	63.5±5.2	62.5±5.4	0.146
Emotional Role Functioning Scores (post-treatment first month)	66.0±5.7	65.5±5.0	0.294
Intragroup comparisons (p value)	0.001‡	0.001‡	
Mental Healthy Scores (pre-treatment)	57.5±4.7	55.0±5.5	0.056
Mental Healthy Scores (post-treatment)	60.4±4.9	57.9±9.9	0.068
Mental Healthy Scores (post-treatment first month)	63.9±4.7	62.3±5.0	0.104
Intragroup comparisons (p value)	0.001‡	0.001‡	

SD: Standard deviation; † Student t-test; ‡ Repeated measures ANOVA test.

Table 5. Fibromyalgia Impact Questionnaire measurements of groups

	Neural						
	Exercise group (n=30)			Neural therapy group (n=42)			
FIQ measurements	Mean±SD	Mean	Min-Max	Mean±SD	Mean	Min-Max	*p*†
Pre-treatment	56.4±3.0	57	49-61	56.2±2.9	56.5	49-61	0.766
Post-treatment	55.2±4.6	55	48-64	54.3±3.3	53	49-62	0.136
Post-treatment first month	42.4±2.7	42	38-49	41.2±3.1	49	41-55	0.711
p value		0.001**‡			0.001**‡		

FIQ: Fibromyalgia Impact Questionnaire; SD: Standard deviation; Min: Minimum; Max: Maximum; † Student t-test; ‡ Repeated measures ANOVA test; ** p<0.01 statistically significant.

SF-36 physical functioning, physical role functioning, bodily pain, general health perceptions, vitality, social functioning, emotional role functioning, and mental health subscales (p>0.05). According to the paired comparisons, changes in the SF-36 physical functioning measurements were found to be statistically significant in both exercise and neural therapy groups (p=0.001; p<0.01) (Table 4).

In addition, there was no statistically significant difference in the pre-, post-treatment, and post-treatment first month FIQ scores between the groups (p>0.05). According to the paired comparisons, changes in the FIQ scores were found to be statistically significant both in exercise and neural therapy groups (p=0.001; p<0.01) (Table 5).

DISCUSSION

The search for complementary and alternative medicine (CAM) methods is extremely common among patients with FMS. The rate of consultation for CAM methods is 42% in the general population, while the rate of consultation for any CAM method reaches almost 100% in FMS cases.[27,28] The main reason for seeking alternative treatment modalities is the lack of a treatment method which provides full recovery, as FMS is a chronic disease and adversely affects QoL.[3] Abnormality in membrane potentials of nerve fibrils and ganglia occurs in many chronic diseases, resulting in autonomic nervous system dysfunction.[6] Neural therapy is a regulative treatment to normalize the dysfunctional autonomic nervous system.[29] This form of treatment uses regulatory mechanisms and plastic features of the nervous system. Generation of targeted stimuli and destruction of other stimuli provide positive feedback in the cycle of pain, affecting both the organization of the nervous system and tissue perfusion.[6,8,29]

In our study, neural therapy and exercise therapy was found to be more advantageous in the early period, compared to the exercise therapy in FMS patients. However, no significant difference was observed between the groups in terms of pain one month following the treatment. Six-session neural therapy might be a short-term treatment for our study population which included the patients with long disease of duration and high pain scores. Nevertheless, positive effects of neural therapy on pain were observed in the early period. Similarly, Atalay et al.[30] reported the positive effects of five sessions of neural therapy on pain in their studies evaluating the efficacy of neural therapy and physiotherapy in chronic low back pain. In a study evaluating the long-term efficacy of neural therapy in patients with chronic pain, patients were followed for one year, and medical treatment for pain was reduced.[31] However, further studies are needed to evaluate the long-term efficacy of neural therapy.

Local anesthetics are known to cause vasodilatation by increasing capillary permeability with anti-inflammatory, antimicrobial, and sympatholytic effects.[32] Certain percentages of lidocaine or procaine are used in neural therapy applications. To the best of our knowledge, there is no study in the literature evaluating effectiveness of neural therapy in FMS patients. However, there are several studies about various forms of lidocaine applications in FMS.[33-35] Staud[33] proposed that somatic hyperalgesia in FMS can be normalized with local anesthetic application into the painful muscle. Lidocaine is thought to inhibit ectopic neuronal discharges[36] by blocking peripheral and central sodium channels.[37] Decreased central sensitization and reduced neuropathic pain are reported after intravenous lidocain application.[33] Schafranski et al.[38] applied intravenous 2% lidocaine with increasing doses for five days in 23 patients diagnosed with FMS and found improvements in the FIQ and VAS pain scores after infusions and 30 days after infusions. In another study, various doses of lidocaine and saline injections were applied into the trapezius and gluteal muscles in patients with FMS and significant reductions were observed in mechanical and thermal hyperalgesia in the group

receiving lidocaine.[39] The authors reported that lidocaine might show its anti-hyperalgesic effects by reducing the tonic peripheral impulse and central sensitization.[39] In our study, positive effects of neural therapy on pain in FMS might result from the aforementioned effects of lidocaine and particularly decreased central sensitization might show positive effects on pain in these patients.

Limitations of this study include small sample size, lack of intravenous administration and ganglionic administrations in the administration protocol, the number of sessions being limited to six, and the use of lidocaine solution instead of procaine, which is known to be more potent, since lidocaine is more easily accessible. Another limitation is the lack of standardization in CAM therapies. Such treatments have a holistic effect, and treatment affects the whole body. In our study, the ACR 1990 fibromyalgia diagnostic criteria were used. Therefore, the effects on somatic symptoms in the new diagnostic criteria have not been evaluated. Therefore, the effect of neural therapy on somatic symptoms of fibromyalgia may be the subject of further studies.

In conclusion, neural therapy can provide additional benefits in terms of pain and depression at an early stage, besides exercise therapy, in patients with fibromyalgia. However, further, more comprehensive studies are warranted in which a higher number of patients are included, and different doses and protocols are used with a higher number of sessions.

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