IMPACT OF AN INTENSIVE DYNAMIC EXERCISE PROGRAM ON OXIDATIVE STRESS AND ON THE OUTCOME IN PATIENTS WITH FIBROMYALGIA

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Abstract:

Objective: The aim is to investigate the effectiveness of intensive dynamic exercises on the oxidative status in patients with primary fibromyalgia (FM) and to explore the importance of these effects on the outcome of FM. Methods: We measured levels of stress oxidants (protein carbonyls, nitric oxide and thiobarbituric acid reactive substances) and antioxidant parameters (thiols and catalase) in blood samples from 40 FM patients and from healthy control (n=25) at presentation and after 12 weeks of intensive exercise program that is comprised of aerobic and strengthening exercises (lasting one hour three times per week). In the patients, pain was assessed using the visual analog scale (VAS), tender points count (TP), the fibromyalgia impact questionnaire (FIQ) and the Beck depression inventory (BDI) were undertaken at presentation and after 12 weeks of exercise therapy. Results: At presentation, the serum levels of the oxidative stress parameters were significantly higher (p<0.001), while the serum levels of antioxidant parameters were significantly lower (p<0.001) in patients with FM than in the controls. There was a higher significant decrease (p<0.001) in the oxidative stress parameters following the 12-week exercise regime, while the antioxidant parameters levels showed a higher significant increase (p<0.001) after the exercise treatment. TP, VAS, FIQ and BDI showed a higher
significant (p<0.001) improvement with exercise therapy. **Conclusion:** Twelve weeks of an intensive dynamic exercise program should be recommended to patients with FM as it was effective in decreasing the oxidative stress parameters, increasing the antioxidant parameters and improving the clinical outcome of this disease.

**Keywords:** Fibromyalgia; oxidative stress; fibromyalgia impact questionnaire (FIQ); exercise program.

1- **Introduction:**

Fibromyalgia syndrome (FMS) means a pain syndrome originating from the muscle and its connective tissues and it is characterized by widespread non-inflammatory pain, cognitive dysfunction, fatigue, sleep disturbance, and a heterogeneous complex of somatic symptoms [1]. It is more common in females with an estimated prevalence of 1–2% in the adult population [2]. FMS is still a disease of unknown etiology. There are many pathologic mechanisms, which are postulated as a possible etiology of FMS, one of them is local hypoxia which is suggested to play a potential role in the pathophysiology of disease manifestations [3].

Free radicals are synthesized as a product of redox reactions and normally antagonized by enzymatic (e.g., catalase, superoxide dismutase, glutathione peroxidase) and non-enzymatic (e.g., vitamin E, vitamin A, vitamin C, glutathione and uric acid) antioxidative mechanisms.[4]. In some pathological conditions, free radicals may be present in excess as a result of increased protein degradation and lipid peroxidation leading to tissue damage and altered membrane permeability. Oxidative stress refers to shift of the balance between free oxygen species and antioxidant levels in favor of oxidation and may contribute to the pathogenesis of many diseases including chronic fatigue syndrome and FMS [5,6].

Protein damage in response to the oxidative stress leads to the formation of protein carbonyl derivatives -through either alpha-amidation pathway or by oxidation of the
glutamyl residue—which are considered markers of protein oxidation [7]. Also, increased carbonyl stress is associated with decreased protein thiol (t-SH) groups levels which are considered a marker of antioxidant capacity [8].

Nitric oxide (NO) is an intracellular messenger molecule that is incorporated in many biological processes such as neurotransmission, vascular regulation and metabolic regulation of exercise [9]. NO is found to modulate free radicals levels in many cell verities [10]. NO is suggested to play an important role in pain pathway and is believed to have a potential role in the pathogenesis of chronic pain syndromes [11].

Treatment of FMS includes patient education, exercise, cognitive behavioral therapy, and medications [12]. No definite individual or combined therapy has been proven to cause definite resolution of disease symptoms. However, exercise may have beneficial role in the management of FMS [13] as many patients are found to have impaired aerobic fitness and poor muscle strength [14,15].

Exercise was defined in a Cochrane review of exercise for treatment of FMS to include aerobics, such as stepping and walking, and strengthening exercises such as resistance training and weight lifting and stretching for flexibility [13].

Many studies showed a relief of pain and fatigue and improvements in fatigue, mood and sleep quality in patients with FMS treated with regular physical exercise [13, 15 -16]. Possible mechanisms of improved disease manifestation were attributed to improved tissue oxygenation, increased energy phosphate level [17, 18].

The aim is to investigate the effectiveness of intensive dynamic exercises on the oxidative status in patients with primary fibromyalgia (FM) and to explore the importance of these effects on the outcome of FM.

2- Patients and methods:

Type of study: it is a case control study followed by an interventional prospective study

2.1. Participants:

Forty three female patients, fulfilling the revised American College of Rheumatology (ACR) criteria for FMS [19] were included as the study group from the in-
patients and out–patients’ clinic of the Rheumatology, Rehabilitation and Physical Medicine department of Benha university hospitals between December 2014 and June 2015. Twenty five age matched apparently healthy non-smoker females from the hospital personnel, medical and nursing staffs were also included as a control group. Certain inclusion criteria should be presented in all participants, such as ability to cycle, willing to exercise three times weekly on a fixed schedule, having no serious psychiatric disease and acceptance to complete a questionnaire.

We excluded patients with secondary FMS, smokers, patients with any condition that can interfere with exercising such as severe chest, cardiac, neurological or musculoskeletal diseases, those who have participated in regular exercise programs within 6 months prior to the study, those who take antioxidants or antidepressant medications.

Patients’ evaluation included full history taking with the recording of the disease duration, thorough clinical, physical and functional evaluation at presentation and after 12 weeks of the designated exercise program, with particular focus on body mass index (BMI), visual analog scales (VAS) to evaluate the pain intensity, the tenderness points (TP) were evaluated and recorded over 18 specific body points by applying pressure (4 kg/cm²). Four-item Jenkins’ Sleep Questionnaire to assess the sleep disturbance [20], Beck Depression Inventory (BDI) [21] and the modified health assessment questionnaire (MHAQ)[22] were assessed in all the patients.

The FM Impact Questionnaire (FIQ) to assess the severity of FMS symptoms and the functional status was also used. It is a multidimensional instrument composed of 10 items (physical impairment, feel good, work missed, interference in job, pain, fatigue, morning tiredness, stiffness, anxiety and depression) with a maximal total score of 100. Higher value indicates more impairment [23].

The local ethical committee of our institution (at Faculty of Medicine, Benha University, e) approved the study and all the participants gave a written informed consent before being enrolled into the study.

2.2. The exercise program:

The exercises program was explained to patients to get their cooperation and consent. The patients were guided and carefully observed during sessions for any complaint. In
cases of extra pain lasting for more than 2 hours and occurring within 24 hours after training, the exercise load was temporarily decreased. The exercise program consisted of warming up for 10 minutes of peripheral and spinal range of motion exercises associated with walking, followed by cycling using a stationary bicycle for 15-20 minutes, the target heart rate was initially adjusted to 60–70% of the age adjusted maximal heart rate (220-age in years), then strengthening exercises to the upper limb, lower limb and trunk muscles were performed using dumbbells, shoulder press, elevation of the shoulder against resistance, hip flexion and extension and standing hip exercises using weights of 1 to 2 kg and two sets of 8–10 repetitions. The exercise session was concluded by a cooling down period of -10-15 minutes of stretches followed by relaxing exercises. The program took up 45-60 minutes per session, three times per week for 12 week.

Three patients refused to complete exercise program so excluded from the study. Only 40 patients completed the exercise therapy and assessments at the allocated time.

2.3. Laboratory Investigation

Blood samples were collected after an overnight fasting from patients and control group in heparinized and non heparinized tubes. Then, serum and plasma specimens were stored at -80°C until analysis. Serum and plasma specimens are collected at baseline and at the end of the exercise program and analyzed for:

**Measurement of Protein Carbonyl (PC) Levels**

Protein Carbonyl levels in plasma were measured using Cayman’s Protein Carbonyl Colorimetric Assay Kit. The kit utilized the DNPH reaction as described by Levine et al. [24].

**Measurement of thiobarbituric acid reactive substances (TBARS)**

TBARS were measured in plasma by colorimetric determination of malondialdehyde (MDA) the product of lipid peroxidation using Cayman’s TBARS Assay Kit according to manufacture instructions (Armstrong and Browne)[25].

**Measurement of Nitric Oxide (NO) LEVELS**
NO production was determined by measuring total nitrate/nitrite—the stable end product of NO metabolism, in serum in a two step process using BioVision's Nitric Oxide Colorimetric Assay Kit (#K262-200, BioVision Research Product, USA) according to manufacture instructions.

**Measurement of Catalase Activity**

Catalase activity was measured in plasma by colorimetric method using catalase assay kit purchased from Biodiagnostic Co., Cairo, Egypt according to the method of Aebi [26].

**Measurement of Thiol (T-SH) Levels**

T-SH levels were measured in plasma using The SensoLyte® Thiol Quantitation Assay kit (Ana Spc, Inc.) utilizing the widely used Ellman’s reagent for colorimetric measurement of thiol concentrations according to manufacturer’s instructions of the kit (Dickinson et al)[27].

**Statistical analysis:** The collected data were analyzed using SPSS version 16 (Chicago, SPSS Inc. U.S.) Categorical data were presented as number and percentages while continuous variables were presented as mean and SD. Paired t-test, unpaired t-test and pearson’s correlation coefficients were used as tests of significance. The results is considered significant at p value <0.05.

**3- Results:**

Forty female patients with FMS (ages ranged from 23 to 55 years) with a mean of 39.3±9.1 years, and twenty five age matched apparently healthy females (ages ranged from 22 to 53 years) with a mean of 38.7±9.3 years were included in the study. Patients’ clinical and laboratory features are shown in (Table 1). The mean plasma and serum levels of oxidative stress parameters were significantly higher at baseline in the FM patients compared to their mean plasma levels in the control. The mean plasma and serum levels of NO, protein carbonyl and TBARS were found to be significantly higher in FMS group than the control group (p<0.001 and p< 0.001, respectively). The mean plasma levels of antioxidant capacity parameters were significantly lower in the FMS compared to their
mean plasma levels in the controls. The mean catalase, and T-SH plasma levels were found to be significantly lower in FMS group compared to the control group (p<0.001 and p<0.001, respectively); (Table 1).

Regarding the effect of the exercise program, all the clinical parameters significantly improved with exercise. There was a statistically significant decrease in the mean VAS (p<0.001), number of tender points (p<0.001), FIQ (p<0.001), BDI (p<0.001) , Jenkins’ Sleep Questionnaire(p <0.001) and MHAQ (p <0.001) after the exercise program compared to their mean before the exercise program; (Table 2).

Regarding the effect of the exercise program on the oxidative stress parameters, there were statistically significant decrease in the mean serum and plasma levels of NO, protein carbonyl and TBARS (p<0.001) after the exercise program compared to their mean before after the exercise program, while there were statistically significant increase in the mean plasma levels of catalase (p<0.001) and T-SH (p<0.001) after the exercise program compared to their mean before the exercise program; (Table 2).

The plasma protein carbonyl levels at baseline showed a statistically significant positive correlation with TP (r=0.47, p<0.05), and Plasma TBARS levels at baseline showed a statistically significant positive correlation with BMI (r=0.46, p <0.05), FIQ (r=0.48, p <0.05) , MHAQ (r= 0.52, p<0.05) ;(Table 3).

Serum NO levels at baseline showed a statistically significant positive correlation with VAS (r=0.51, p <0.05), -TP (r=0.54, p <0.05), FIQ (r= 0.52, p<0.05), MHAQ (r= 0.53, p<0.05). There was a statistically significant negative correlation between catalase level at baseline and TP (r= -0.45, p <0.05), MHAQ (r= -0.46, p<0.05); (Table 3).

**Table (1):** Comparison between patients and control groups as regards clinical parameter and serum levels of Protein carbonyl, NO, Catalase and T-SH before 12 week exercise therapy.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patient group</th>
<th>Control group</th>
<th>P-value</th>
</tr>
</thead>
</table>


<table>
<thead>
<tr>
<th></th>
<th>n=40</th>
<th>n=25</th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>Mean±SD</td>
<td>Mean±SD</td>
<td>P</td>
</tr>
<tr>
<td>Age( year)</td>
<td>39.3±9.1</td>
<td>38.7±9.3</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Disease duration(Year)</td>
<td>3.96±7.3</td>
<td>--------</td>
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</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.2±4.1</td>
<td>27.1±1.8</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>TP</td>
<td>16.5±1.36</td>
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<tr>
<td>VAS</td>
<td>6.11±1.44</td>
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<tr>
<td>FIQ</td>
<td>57.44±16.2</td>
<td>--------</td>
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<tr>
<td>BDI</td>
<td>23.65±12.50</td>
<td>--------</td>
<td></td>
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<tr>
<td>Jenkins’ Sleep Questionnaire</td>
<td>9.14± 4.11</td>
<td>--------</td>
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<tr>
<td>MHAQ</td>
<td>2.1±0.89</td>
<td>--------</td>
<td></td>
</tr>
<tr>
<td>TBARS (µM)</td>
<td>3.92 ± 0.27</td>
<td>3.4 ± 0.24</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Protein carbonyl (mmol/ mg)</td>
<td>1.5 ±0.62</td>
<td>0.72 ±0.32</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>NO</td>
<td>42.27 ± 6.32</td>
<td>28.53 ± 8.1</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Catalase (kU/l)</td>
<td>39.03 ± 8.03</td>
<td>50.65 ±9.84</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>T-SH(µM)</td>
<td>259.28 ± 46.12</td>
<td>391.70 ± 75.96</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

BMI= Body mass index ,TP= tender points. VAS= Visual analog Scale, FIQ= Fibromyalgia Impact Questionnaire, BDI =beck depression inventory, MHAQ =modified health assessment questionnaire , TBARS= thiobarbituric acid reactive
substance, T-SH= thiol, NO= nitric oxide,* Highly significant (p<0.001). unpaired t-test is the statistical test used

Table (2): Comparison between FM patients as regards clinical parameter and serum levels of oxidative stress and anti-oxidant both groups before and after 12 week of exercise therapy.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patients group before exercise therapy</th>
<th>Patients group after exercise therapy</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=40</td>
<td>n=40</td>
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<tr>
<td>Mean±SD</td>
<td>Mean±SD</td>
<td></td>
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</tr>
<tr>
<td>TP</td>
<td>16.5±1.36</td>
<td>6.5±1.21</td>
<td>P&lt;0.001*</td>
</tr>
<tr>
<td>VAS</td>
<td>6.11±1.44</td>
<td>4.53 ± 1.33</td>
<td>P&lt;0.001*</td>
</tr>
<tr>
<td>FIQ</td>
<td>57.44±16.2</td>
<td>48.13 ± 7.61</td>
<td>P&lt;0.001*</td>
</tr>
<tr>
<td>BDI</td>
<td>23.65±12.50</td>
<td>19.50 ± 11.24</td>
<td>P&lt;0.001*</td>
</tr>
<tr>
<td>Jenkins’ Sleep Questionnaire</td>
<td>9.14± 4.11</td>
<td>5.4 ± 3.28</td>
<td>P&lt;0.001*</td>
</tr>
<tr>
<td>MHAQ</td>
<td>2.1±0.89</td>
<td>0.31±0.80</td>
<td>P&lt;0.001*</td>
</tr>
<tr>
<td>TBARS (μM)</td>
<td>3.92 ± 0.27</td>
<td>3.14 ± 0.52</td>
<td>P&lt;0.001*</td>
</tr>
<tr>
<td>Protein carbonyl (mmol/ mg)</td>
<td>1.5 ± 0.62</td>
<td>1.04 ±0.23</td>
<td>P&lt;0.001*</td>
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<tr>
<td>---------------------------</td>
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<tr>
<td>NO</td>
<td>42.27 ± 6.32</td>
<td>31.53 ± 5.1</td>
<td>P&lt;0.001*</td>
</tr>
<tr>
<td>Catalase (kU/l)</td>
<td>39.03 ± 8.03</td>
<td>53.05 ± 13.89</td>
<td>P&lt;0.001*</td>
</tr>
<tr>
<td>T-SH(μM)</td>
<td>259.28 ± 46.12</td>
<td>342.40± 55.96</td>
<td>P&lt;0.001*</td>
</tr>
</tbody>
</table>

TP= tender points, BMI= Body mass index ,VAS= Visual analog Scale, FIQ= Fibromyalgia Impact Questionnaire, BDI =beck depression inventory, TBARS= thiobarbituric acid reactive substance, T-SH= thiol, NO= nitric oxide MHAQ =modified health assessment questionnaire ; * Highly significant (p<0.001). paired t-test is the used statistical test

Table (3): Correlation between oxidative stress parameters at baseline and different variables in FMS patients.

<table>
<thead>
<tr>
<th></th>
<th>Protein carbonyl</th>
<th>TBARS</th>
<th>NO</th>
<th>T-SH</th>
<th>Catalase</th>
</tr>
</thead>
<tbody>
<tr>
<td>I)Demographic variables:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.23</td>
<td>0.21</td>
<td>0.21</td>
<td>-0.12</td>
<td>-0.17</td>
</tr>
<tr>
<td>Disease duration</td>
<td>0.26</td>
<td>0.18</td>
<td>0.24</td>
<td>-0.23</td>
<td>0.12</td>
</tr>
<tr>
<td>BMI</td>
<td>0.09</td>
<td>0.46*</td>
<td>0.05</td>
<td>0.12</td>
<td>0.14</td>
</tr>
<tr>
<td>II)Disease related variables at baseline:</td>
<td></td>
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<tr>
<td>VAS</td>
<td>0.22</td>
<td>-0.35</td>
<td>0.51</td>
<td>-0.12</td>
<td>-0.28</td>
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</tr>
<tr>
<td>TP</td>
<td>0.47 *</td>
<td>0.42</td>
<td>0.54 *</td>
<td>-0.25</td>
<td></td>
</tr>
<tr>
<td>FIQ</td>
<td>0.26</td>
<td>0.48 *</td>
<td>0.52 *</td>
<td>-0.34</td>
<td></td>
</tr>
<tr>
<td>BDI</td>
<td>0.32</td>
<td>0.38</td>
<td>0.28</td>
<td>-0.096</td>
<td></td>
</tr>
<tr>
<td>MHAQ</td>
<td>0.34</td>
<td>0.52 *</td>
<td>0.53 *</td>
<td>-0.34</td>
<td></td>
</tr>
</tbody>
</table>

TP= tender points, BMI= Body mass index, VAS= Visual analog Scale, FIQ= Fibromyalgia Impact Questionnaire, BDI =beck depression inventory, TBARS= thiobarbituric acid reactive substance, T-SH= thiol, NO= nitric oxide MHAQ =modified health assessment questionnaire, * Spearman’s correlation coefficient (r) denote significant correlation.

4. Discussion:

Fibromyalgia syndrome (FMS) is a chronic condition characterized by evident pain and somatic symptoms that may be associated with possible disability in spite of normal physical examination, laboratory and radiological investigations.[28]. The underlying pathophysiology is multifactorial, potential etiologies may include central sensitization, alteration in the autonomic nervous system, genetic predisposition, neurotransmitters imbalance, dysfunction of the hypothalamic-pituitary-adrenal axis, pain modulation and oxidative stress[9].

Oxygen radicals, such as, superoxide anion and hydrogen peroxide, are produced mainly in the mitochondria[29]. About 1–4% of oxygen that react with the respiratory chain is involved in the production of superoxide radicals (O$_2^-$)[30]. Free radicals can play both beneficial as well as deleterious roles. At low physiological levels, it plays a potential role as a messenger in some of the intracellular signal transduction pathways [31]. However, when produced in excess, it can cause oxidative damage to many cellular
components through macromolecules modification as lipids peroxidation and proteins oxidation. There is a dynamic relationship between production of Free radicals and antioxidant capacity. Oxidative stress occurs when the antioxidant capacity fail to neutralize the deleterious effect of Free radicals [32].

In our study, serum levels of the oxidative stress parameters were statistically significantly elevated in the FMS patients compared to their levels in the serum of healthy controls. Also, FMS patients had a significantly lower antioxidant capacity as compared to healthy controls. We also found these levels to be significantly correlated with the clinical and functional parameters of the disease especially pain, tender points and FIQ. Our results confirmed the results reported by other studies [4, 33 -34].

Wang et al. [35] suggested that peripheral and central sensitization can be mediated by the oxidative stress that can cause hyperalgesia at both local and spinal levels. Also, isoprostanes, a product of lipid peroxidation, can cause increased excitability of type C nociceptors [36].

Cells of the central nervous system may be more sensitive to the deleterious effect of free radicals than other body organs due to their high rate of metabolic activity and a low level of antioxidant capacity, and the high concentrations of oxidizable unsaturated fatty acids in their cell membranes [37]. Also, free radicals and NO disturb the permeability of blood brain barrier and increase excitability of dorsal root ganglion [9].

Not all studies reported increases in the oxidative stress parameters in FMS patients. Chung et al. [38], measured F2-isoprostane in the urine of 48 FMS patients for evaluation of the oxidative stress and found no significant difference as compared to the control group. They attributed this discrepancy to the difference in the molecule (F2-isoprostanes) measured to assess the oxidative stress.

In our study all the clinical parameters, such as pain, tender points , FIQ, sleep disturbance and depression showed a significant decrease (p<0.001) following the 12-week exercise regime as compared to their levels at baseline. Many studies have shown the
benefit of different types of exercises in the management of FMS with improvement of the quality of life and reduction of pain in patients with FMS [34, 39 - 40].

McLoughlin et al. [41] confirmed the association of reduction of pain perception and the increase in the accelerometer-monitored physical activity. The pain reduction related to aerobic exercises is usually termed (exercised-induced analgesia), which can be explained by activation of the sympathetic nervous system, which may be linked to supraspinal pain modulatory mechanism[42] as endogenous opioids may be released along adrenaline leading to temporary analgesic effect[43].

Dinler et al. [44], found aerobic exercises to reduce pain and fatigue due to increased peak oxygen uptake and Busch et al. [45] reported that strength and mixed exercises to be associated with marked improvements in the global well-being and physical function while they reported that the adverse events related to exercise such as pain and fatigue to be not uncommon.

On the other hand, Redondo et al. [46] applied an 8-week program consisting of aerobic, strength, and stretching exercises to FMS patients and they found improvement only in the FIQ and fatigue, while no improvement was found regarding pain and depression. Also, Alentorn-Geli et al.[47] did not found any significant improvement regarding FIQ, pain, fatigue and depression following a 6-week program of aerobic and stretching exercises plus patient education. This discrepancy can be related to the shorter duration of their exercise program.

In our study there was a significant decrease in the oxidative stress parameters TBARS, Protein carbonyl, and NO following the 12-week exercise regime as compared to their levels at baseline. T-SH and catalase levels also showed a significant increase (p<0.001) following the 12-week exercise regime as compared to their levels at baseline. The same results were found by Sarıfakıoğlu et al. [34], who found a decrease in the oxidative stress parameters following an exercise program applied to 30 patients with FMS.

Although free radicals production can be stimulated by acute exercises with a subsequent oxidative stress, many studies documented the up regulation of the antioxidant capacity as
a result of repeated exercise training in an attempt to avoid future free radical increase [34, 48-49].

Peake et al. [50] found skeletal muscles to be capable to adapt in response to repeated exercise by a process termed ‘repeated bout effect’ through modification of their cellular structure to become less susceptible to injury after repetition of the same exercise as noticed by decreased leukocyte cell surface receptors expression. Also, Ji et al. [51] found trained individuals to have lower oxidative stress parameters at rest and post exercise as compared to untrained individuals.

Previous studies investigated the effect of exercise on FMS and other studies evaluated stress oxidant levels in FMS patients. Only a previous study have assessed the relationship between exercise treatment and oxidative stress parameters in FMS patients [34].

In the current study we found that a 12-week intensive exercise therapy is effective in improving the severity of the FMS symptoms and the functional status as well as reduction of the oxidative load in FMS patients, so exercise regimen should be recommended and encouraged in these patients and we should focus on reducing oxidative stress in the treatment of FMS. Further studies are recommended with different exercise programs to obtain more results and select the best exercise regime that can reduce the oxidative stress.

In conclusion, 12 weeks of an intensive dynamic exercise program should be recommended to patients with FM as it was effective in decreasing the oxidative stress parameters, increasing the antioxidant parameters and improving the clinical outcome of this disease.

Conflict of interest: None

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