

Iberian Journal of Applied Sciences and Innovations

2021 vol1, Issue 4

The Effect of Aerobic and Nonlinear Resistance Training on Inflammatory Factors and its Relationship with Pain and Function in Overweight Women with Osteoarthritis of the Knee

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Abstract— the aim of this study was to compare the effect of aerobic and nonlinear resistance training on inflammatory factors and its relationship with pain and function in overweight women with osteoarthritis of the knee. 21 women aged 50 to 60 years with knee osteoarthritis were randomly divided into three groups of aerobic exercise, nonlinear resistance training and control (7 people in each group). Exercises were performed for 12 weeks (3 sessions per week). Before and after the training period, the subjects were measured for pain and motor function and blood samples were taken from three groups after the 12-hour fasting period and levels of CRP and TNF-a were measured for each sample. Both types of exercises significantly reduced weight, BMI, pain and TNF-a and CRP levels and significantly improved motor function in women with osteoarthritis of the knee (P<0.05), but no significant difference was observed between the two types of exercise (P>0.05). Also, with decreasing inflammation, pain decreased and motor function increased (P<0.05). Training with weight loss and inflammatory factors in overweight women with osteoarthritis of the knee can reduce pain and improve motor function in these women. There is probably no Mohammad-Ali Kohanpour * Department of Physical Education, Lamerd Branch,

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significant difference between the effect of aerobic and nonlinear resistance training in this area.

Keywords— Knee osteoarthritis, Nonlinear resistance training, Inflammation, Overweight, Aerobic training

I. INTRODUCTION

Knee osteoarthritis is a disorder of the knee joint in the elderly that is caused by the effects of aging on the musculoskeletal system in the knee joint (1). The disease is multifactorial and involves a combination of factors such as muscle weakness and intra-articular changes such as inflammation, trabecular deformity, and cartilage erosion (1, 2). Among the weightbearing joints, the knee joint, whose function is essential in many daily activities such as going up and down stairs, getting up from a chair, and walking, is most affected (3, 4). Osteoarthritis involves the entire structure of the joint, cartilage, bone, ligament, and muscle, and causes changes such as reduced joint space, the formation of bone osteophytes, and sclerosis (4). Swelling of the joint, movement limitations in walking such as decreased speed and stride length, decreased range of motion and angular velocity of the joint, decreased muscle strength, impaired proprioception, and increased pain are some of the symptoms of this disease (5). Muscle weakness, especially quadriceps with pain is one of the first signs of knee osteoarthritis in patients (6, 7, 8, 9). In fact, muscle weakness before the onset of the disease may play a significant role in its onset (6). Because quadriceps and hamstrings act as stabilizers for the knee joint, major research has focused on focusing on quadriceps and hamstrings (10, 11).

In overweight people with osteoarthritis of the knee, exercise and diet can be effective and can lead to improved performance in these patients (12, 13). Exercise therapy is one of the ways to deal with knee osteoarthritis (14). In recent vears. the role of low-grade systemic inflammation in the pathogenesis of knee osteoarthritis has been established (15, 16, 17). In patients with osteoarthritis of the knee, high levels of proinflammatory cytokines have been reported with pain and worse function (18). It has been shown that there is a high correlation between levels of C-reactive protein (CRP) and osteoarthritis, so that in the samples of these patients, CRP levels were increased (19, 20). In addition, tumor necrosis factor-alpha (TNF- α), interleukin-6 (IL-6), and interleukin-1 (IL-1) are other inflammatory markers in knee osteoarthritis (21). Because the effects of exercise and weight loss interventions are known to reduce inflammation, the antiinflammatory effects of these interventions have been suggested as a potential therapeutic mechanism (22, 23). Unfortunately, most studies that have examined the effect of therapeutic interventions, including exercise, on the pathogenesis of osteoarthritis of the knee have not examined the levels of these proinflammatory cytokines.

Also, fewer studies have compared the effect of aerobic and resistance training in this regard. In this regard, non-linear resistance training is training that is similar to aerobic training in terms of training metabolism. The aim of this study was to compare the effect of aerobic exercise and nonlinear resistance training on inflammatory factors and its relationship with pain and function in overweight women with osteoarthritis of the knee.

II. METHODOLOGY

This quasi-experimental study was conducted with a pretest and posttest design with a control group. 21 women aged 50 to 60 years with osteoarthritis of the knee were purposefully selected and participated in this study voluntarily. After selecting the subjects, they were randomly divided into three groups of aerobic training, nonlinear resistance training and control (7 people in each group). Before starting the research, the nature, goals and risks of this study were explained to the subjects in a face-to-face meeting and written consent was obtained from them to participate in this study. Inclusion criteria included: women with knee pain for 6 months or more (having chronic pain and acute pain exacerbation) being in functional level II and III (based on clinical and radiological symptoms), not in the acute stage of the disease, Willingness to participate in the study, age 50-60 years, no intra-articular injection from 3 months ago, no oral (nonsteroidal anti-inflammatory drug) from one week before enrollment, no history of trauma, injury or surgery And lower limb fractures, BMI 25 and above but less than 30, no history of lifethreatening joint diseases (osteonecrosis, diabetes, osteoporosis, rheumatoid arthritis, neuromuscular disease, history of any symptoms of collagen vascular disease, psoriatic arthritis) Gout and gout-like arthritis (lack of a long history of drug use affecting the musculoskeletal system and lack of addiction). All these cases were studied by a specialist in the subjects. In addition, all subjects were examined for factors affecting lower limb misalignment, which is one of the causes of early osteoarthritis, in which none of the above was seen. Exclusion criteria also included non-regular visit of the patient in the training session, use of non-steroidal antiinflammatory drugs during the study, exacerbation of symptoms and pain, and unwillingness of the patient to continue treatment.

Initially, the form of data collection, through which age, weight, height, amount of physical activity, history of disease or medications used, the presence of injury, trauma or surgery in the knee joint of individuals, was determined by sports and orthopedic specialists It was confirmed and completed by the examiner in the form of face-to-face interview and the health or illness and injury conditions of these individuals were monitored. The specimens were then examined by an orthopedic physician and radiographs were taken from each knee in two views (anterior-posterior view, lateral view). All radiographs were observed by a radiologist and evaluated according to Kellgren-Lawrence criteria (reduction of joint space, osteophyte formation, sclerosis of subcutaneous bone) and the status of each view was reported. Then, the clinical and radiological symptoms were divided into the following degrees by a specialist examining the knee and osteoarthritis of the knee: 1- No symptoms or pathological findings are evident. Findings indicate mild degenerative changes (osteoarthritis) in the knee. The findings indicate moderate degenerative changes (osteoarthritis) in the knee. Findings indicate advanced or severe degenerative changes (osteoarthritis) in the knee. After explaining to the subjects about the purpose of the study, the global and localized questionnaire KOOS (Knee injury and osteoarthritis outcome score) which was used to measure the rate of osteoarthritis and severity of knee pain, symptoms, motor function in daily activities, Sports-recreation and quality of life in the knee joint are designed (29), completed by the examiner in person. The KOOS questionnaire has 42 patient-centered questions that include 5 patient-related concepts including pain (9 questions), other symptoms (swelling, dryness, stiffness, etc.) related to the disease (7 questions), and activities of daily living (up and down). Examining stairs, standing, bathing, etc. (17 questions), sports-

recreational activities (jumping, running, spinning) (5 questions) and quality of life in relation to knee problems (4 questions) are examined (24). Subjects answered the questions based on a 5-point Likert scale (no = 0, little = 1, $\frac{1}{2}$ moderate = 2, severe = 3, infinitely severe = 4). Each subscale is defined individually and qualitatively based on the Visual Analogue Scale (VAS). An eye analog scale is a line segment with one end zero and the other end 100. The number 100 indicates no problem and zero is considered the worst case (24). Subjects answered the questions based on a 5-point Likert scale (no = 0, little = 1, moderate = 2, severe = $\frac{1}{2}$ 3. infinitely severe = 4). Each subscale is defined individually and qualitatively based on the Visual Analogue Scale (VAS). An eye analog scale is a line segment with one end zero and the other end 100. The number 100 indicates no problem and zero considered the worst case (24).

Exercises were performed for 8 weeks (3 sessions per week). During this period, the two training groups performed their own exercises and the control group did not receive any intervention and only engaged in their normal daily activities. The nonlinear resistance training program includes weight training in different intensities with emphasis on muscle endurance and a flexible timing pattern.

-	rubien robiniteur resistance training program											
Week	1	2	3	4	5	6	7	8	9	10	11	12
Sessi on 1	L	L	М	V L	М	L	V L	Н	L	М	L	V L
Sessi on 2	М	V L	Н	Н	М	М	М	V L	L	М	М	Н
Sessi on 3	L	Н	L	L	L	Н	L	М	V H	V L	V L	L
T									(TT)			

Table1. Nonlinear resistance training program

Intensity very light (VL), light (L), medium (M), heavy (H) and very heavy (VH)

Aerobic exercise three sessions per week, each session consisting of eight minutes of warm-up and eight minutes of running with an intensity of 75 to 85% of the maximum reserve heart rate in the first session, both sessions increased the subjects' running time by one minute until later. From 12 weeks, the running time was 26 minutes and the last 5 minutes of each session were cooling.

24 hours before the first intervention session and 48 hours after the last intervention session,

measurements of pain and motor function were taken from the subjects and blood samples were taken from three groups at 8 o'clock in the morning and in a fasting position for 12 hours Samples of CRP and TNF- α levels were measured. TNF- α levels were measured using a kit from the French company Diaclone with a sensitivity of 8 pg / ml. Levels of C-reactive protein (CRP) were obtained by ELISA method and using ELISA commercial kit, Ontario Canada with a sensitivity of 10 ng / ml. In order to compare and evaluate the changes of variables in the three research groups and in two measurement times (pre-test and post-test), the statistical test of mixed-variance between-intra subjects was used. A significance level of P≤0.05 was considered and all statistical calculations were performed using SPSS software version 16.

III. RESULTS

The results of mixed analysis of variance, Tukey post hoc test and Pearson correlation coefficient are reported in Tables 1, 2 and 3, respectively. Weight, BMI, pain and levels of TNF-a and CRP were significantly decreased in both exercise groups compared to the control group (P<0.05) and motor function was significantly increased in both exercise groups compared to the control group (P<0.05). However, no significant difference was observed between the effects of the two types of exercise on any of the variables (P>0.05). There was also a significant relationship between TNF-a and CRP levels with pain and motor function. With decreasing CRP levels, pain was reduced (P<0.05). Also, with decreasing TNF- α levels, an increase in performance was observed (P<0.05).

Table1. Results of mixed analysis of variance to compare the changes of the three groups

Variabl e	group	Before trainin g	After trainin g	F	Р	Effec t size
Weight (Kg)	Aerobic Exercise Nonline ar resistanc	$72 \pm$ 3.46 69.57 \pm 3.95	$68.14 \pm 4.05 $ 67.28 ± 3.54	10.6 5	0.00 1 *	0.54

	e					
	exercise					
	Control	70.85 ± 3.67	71.14 ± 3.67			
	Aerobic	26.11	24.69			
	Exercise	± 1.46	± 1.92			
D) (I	Nonline					
BMI	ar	25.35	24.49	12.9	0.00	0.58
(kg / m2)	resistanc e	± 0.35	± 0.38	0	1 *	0.38
1112)	exercise					
		25.43	25.61			
	Control	± 0.81	± 0.62			
	Aanahia	58.14	65.42			
	Aerobic Exercise	± 7.03	±			
		± 7.05	10.51			
	Nonline			0.00	0.00	
the pain	ar	55.85	65.71	8.00	0.00	0.47
(VAS)	resistanc	± 7.26	± 6.21	3	3 *	
	e exercise					
		61.28	61 ±			
	Control	± 8.71	9.14			
	Aerobic	61.71	67.57			
	Exercise	± 7.15	± 6.05			
Functio	Nonline					
n	ar	$56 \pm$	64 ±		0.00	
(KOOS	resistanc	8.75	8.48	8.91	2 *	0.49
)	e exercise					
	exercise	$62 \pm$	60.42			
	Control	9.69	± 8.59			
	4 1 1	1939.2	1386.1			
	Aerobic Exercise	$8 \pm$	$4 \pm$			
	Exercise	232.69	305.58			
	Nonline					
CRP	ar	2140 ±	1503.5	12.7	0.00	0.50
(ng/ml)	resistanc	374.00	7 ± 353.57	4	1 *	0.58
	e exercise	7	555.57			
	CACICISE	1964.4	1874.7			
	Control	2 ±	10/4./ 1 ±			
		318.17	408.19			
	Aerobic	11.56	9.23 ±			
	Exercise	± 1.54	1.35			
	Nonline					
TNF-α	ar	10.60	$8.40 \pm$		0.00	0.50
(pg/ml)	resistanc	± 1.05	1.06	9.18	1 *	0.50
10 /	e exercise					
		$9.36 \pm$	$9.52 \pm$			
	Control	1.30	1.62			
* Significant at the level of P<0.05						

* Significant at the level of $P \le 0.05$

Table2. Results of Tukey post hoc test to compare

	pairs of groups	
Variable	pair comparison	Р
	Aerobic training - nonlinear resistance training	0.22
Weight	Aerobic training - control	0.001 *
	Nonlinear resistance training - control	0.028 *
BMI	Aerobic training - nonlinear resistance training	0.22
	Aerobic training - control	0.001 *

	Nonlinear resistance training - control	0.011 *
	Aerobic training - nonlinear resistance training	0.60
the pain	Aerobic training - control	0.026 *
	Nonlinear resistance training - control	0.003 *
	Aerobic training - nonlinear resistance training	0.64
Function	Aerobic training - control	0.015 *
	Nonlinear resistance training - control	0.002 *
	Aerobic training - nonlinear resistance training	0.75
CRP	Aerobic training - control	0.002 *
	Nonlinear resistance training - control	0.001 *
	Aerobic training - nonlinear resistance training IF-α Aerobic training - control	
TNF-α		
	Nonlinear resistance training - control	0.005 *
* Sig	$r_{\rm prificant}$ at the level of P \leq	0.05

Table3. Pearson correlation coefficient test results

Variabl es	Weig ht	BMI	the pain	Functio	CRP	TNF -α
Weight	-	r= 0.99 p= 0.00 1 *	r= - 0.31 p= 0.16	r= - 0.65 p= 0.001 *	r= 0.26 p= 0.23	r= 0.28 p= 0.21
BMI	r= 0.99 p= 0.001 *	-	r= - 0.37 p= 0.09	r= - 0.66 p= 0.001 *	r= 0.32 p= 0.14	r= 0.29 p= 0.19
the pain	r= - 0.31 p= 0.16	r= - 0.37 p= 0.09	-	r= 0.62 p= 0.003 *	r= - 0.63 p= 0.00 2 *	r= - 0.36 p= 0.10
Functio n	r= - 0.65 p= 0.001	r= - 0.66 p= 0.00 1	r= 0.62 p= 0.00 3 *	-	r= - 0.41 p= 0.06 4	r= - 0.44 p= 0.04 *
CRP	r= 0.26 p= 0.23	r= 0.32 p= 0.14	r= - 0.63 p= 0.00 2 *	r= - 0.41 p= 0.064	-	r= 0.68 p= 0.00 1 *
TNF-α	r= 0.28 p= 0.21	r= 0.29 p= 0.19	r= - 0.36 p= 0.10	r= - 0.44 p= 0.044 *	r= 0.68 p= 0.00 1 *	-

* S	igni	ficant	at	the	level	of P≤0.05
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IV. DISCUSSION

Based on the findings of the present study, 12 weeks of exercise (both aerobic and nonlinear resistance) significantly reduced weight, BMI, pain and TNF-a and CRP levels and significantly improved motor function in women with osteoarthritis of the knee, but no significant difference was observed between the effects of the two types of exercise. Also, there was a significant relationship between changes in inflammatory factors with pain and function of these women, so that with decreasing inflammation, pain decreased and motor function increased. Consistent with the present findings, Runhaar et al. (2019) showed that as a result of exercise therapy, by reducing the levels of inflammatory agents IL-6, TNF-a, IL-1sR and CRP, pain and motor function in overweight patients Heals osteoarthritis of the knee (14). These findings suggest that weight loss and BMI, which are associated with a reduction in inflammatory factors, may be associated with improved pain and motor function in patients with osteoarthritis of the knee (14). Of course, in addition to inflammatory factors, other factors such as improving joint condition, increasing muscle strength and psychological factors may also play a role in this field, which should be considered in future studies (14). Regarding the reduction of inflammatory factors with exercise, Lee et al. (2015) also showed that IL-6, TNF- α and CRP levels are significantly reduced due to 8 weeks of combined aerobic and strength training. (25). However, not all studies are consistent and in one study, no significant changes in IL-6 and TNF-α levels were observed after 6 weeks of isokinetic and aerobic training (26). Regarding the positive effect of exercise in patients with osteoarthritis, our findings are consistent with the findings of Taglietti et al. (2018) (27). They reported that exercise in water could reduce pain and improve function in patients with osteoarthritis of the knee (27). However, some findings, in contrast to the present findings, indicate that there is no significant effect of exercise on the performance of these patients (29, 28), which may be due to insufficient short-term variables of exercise (intensity, volume and Exercise intensity). These differences are probably due to differences in training protocol or sample size that should be considered in future research. Also, one of the

reasons for the difference between the different findings could be the exact control or lack of control of the subjects' diet, which was one of the limitations of the present study. Finally, we suggest that concurrent training (both aerobic and nonlinear resistance) be considered in the future.

V. CONCLUSION

It seems that 8 weeks of exercise (both aerobic and nonlinear resistance) with weight loss and inflammatory factors in overweight women with osteoarthritis of the knee can reduce pain and improve motor function in these women. Given that nonlinear resistance training is metabolically similar to aerobic training, similar effects are likely to have occurred. However, we need more research in the future to reach a definitive conclusion.

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