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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-α were measured for each sample. Both types of exercises significantly reduced weight, BMI, pain and TNF-α 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 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 weight-bearing 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

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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 years, 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 anti-inflammatory 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 (non-steroidal 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 life-threatening 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

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none of the above was seen. Exclusion criteria also included non-regular visit of the patient in the training session, use of non-steroidal anti-inflammatory 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, 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 = 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.

Table1. Nonlinear resistance training program

Week	1	2	3	4	5	6	7	8	9	10	11	12
Session 1	L	L	M	VL	M	L	VL	H	L	M	L	VL
Session 2	M	VL	H	H	M	M	M	VL	L	M	M	H
Session 3	L	H	L	L	L	H	L	M	VH	VL	VL	L

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,

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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-α 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-α 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

Variable	group	Before training	After training	F	P	Effect size
Weight (Kg)	Aerobic Exercise	72 ± 3.46	68.14 ± 4.05	10.65	0.001 *	0.54
	Nonlinear resistance exercise	69.57 ± 3.95	67.28 ± 3.54			
	Control	70.85 ± 3.67	71.14 ± 3.67			
BMI (kg / m2)	Aerobic Exercise	26.11 ± 1.46	24.69 ± 1.92	12.90	0.001 *	0.58
	Nonlinear resistance exercise	25.35 ± 0.35	24.49 ± 0.38			
	Control	25.43 ± 0.81	25.61 ± 0.62			
the pain (VAS)	Aerobic Exercise	58.14 ± 7.03	65.42 ± 10.51	8.003	0.003 *	0.47
	Nonlinear resistance exercise	55.85 ± 7.26	65.71 ± 6.21			
	Control	61.28 ± 8.71	61 ± 9.14			
Function (KOOS)	Aerobic Exercise	61.71 ± 7.15	67.57 ± 6.05	8.91	0.002 *	0.49
	Nonlinear resistance exercise	56 ± 8.75	64 ± 8.48			
	Control	62 ± 9.69	60.42 ± 8.59			
CRP (ng/ml)	Aerobic Exercise	1939.28 ± 232.69	1386.14 ± 305.58	12.74	0.001 *	0.58
	Nonlinear resistance exercise	2140 ± 374.007	1503.57 ± 353.57			
	Control	1964.42 ± 318.17	1874.71 ± 408.19			
TNF-α (pg/ml)	Aerobic Exercise	11.56 ± 1.54	9.23 ± 1.35	9.18	0.001 *	0.50
	Nonlinear resistance exercise	10.60 ± 1.05	8.40 ± 1.06			
	Control	9.36 ± 1.30	9.52 ± 1.62			

* Significant at the level of P≤0.05

Table2. Results of Tukey post hoc test to compare pairs of groups

Variable	pair comparison	P
Weight	Aerobic training - nonlinear resistance training	0.22
	Aerobic training - control	0.001 *
	Nonlinear resistance training - control	0.028 *
BMI	Aerobic training - nonlinear resistance training	0.22
	Aerobic training - control	0.001 *

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	Nonlinear resistance training - control	0.011 *
the pain	Aerobic training - nonlinear resistance training	0.60
	Aerobic training - control	0.026 *
	Nonlinear resistance training - control	0.003 *
Function	Aerobic training - nonlinear resistance training	0.64
	Aerobic training - control	0.015 *
	Nonlinear resistance training - control	0.002 *
CRP	Aerobic training - nonlinear resistance training	0.75
	Aerobic training - control	0.002 *
	Nonlinear resistance training - control	0.001 *
TNF-α	Aerobic training - nonlinear resistance training	0.98
	Aerobic training - control	0.004 *
	Nonlinear resistance training - control	0.005 *

* Significant at the level of P≤0.05

Table3. Pearson correlation coefficient test results

Variables	Weight	BMI	the pain	Function	CRP	TNF-α
Weight	-	r= 0.99 p= 0.001 *	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= 0.002 *	r= -0.36 p= 0.10
Function	r= -0.65 p= 0.001	r= -0.66 p= 0.001	r= 0.62 p= 0.003 *	-	r= -0.41 p= 0.064	r= -0.44 p= 0.04 *
CRP	r= 0.26 p= 0.23	r= 0.32 p= 0.14	r= -0.63 p= 0.002 *	r= -0.41 p= 0.064	-	r= 0.68 p= 0.001 *
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= 0.001 *	-

* Significant at the level of P≤0.05

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-α 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-α, 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

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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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Relationship Between Anthropometric Characteristics and Player Experience with Speed, Agility and Scoring Statistics of Khorasan Razavi Women's Futsal Team Players in the Iranian Premier League

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***Abstract*— the purpose of this study was to investigate the relationship between anthropometric characteristics and player experience with speed, agility and scoring statistics of Khorasan Razavi women's futsal team players. For this reason, 14 players of Khorasan Razavi women's futsal team were evaluated in the group stage of the Iranian Women's Futsal Premier League 1300-1499. Calendar age, physiological age, height, arm circumference, thigh circumference, leg circumference, chest circumference, shoulder width, waist circumference, hip circumference, waist-to-hip ratio, playing experience, experience playing in the Premier League, playing experience in the national team, scoring statistics, speed (15 m and 25 m) and agility (4.9 test) were measured. Pearson correlation coefficient test and SPSS software version 16 at the level of P≤0.05 were used for statistical analysis. Based on the results, experience is probably the most important factor for the success in scoring of women futsal players. As in the present study, as the age, years of playing, playing in the Premier League and playing in the national team increased, so did the scoring statistics. On the other hand, it seems that the smaller the circumference of the upper and lower limbs, the better the speed and agility performance, which is probably due to the smaller size of the muscle compared to fat and the reduction of fat in these limbs.**

Keywords*— *Futsal, Sports Performance, Anthropometric, Experience, Scoring Statistics

I. INTRODUCTION

Futsal is one of the most exciting and popular sports in the world and has a special place among the people in Iran. The Iranian men's national futsal team is the proudest futsal team in Asia and has won most of the Asian Cup. However, the Iranian women's national futsal

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team has also established itself as the top power in Asia in recent years and has won the Asian Cup in the last two seasons. Iranian women futsal players have shown that they have a very high potential, and if scientific work is done in this field and special attention is paid, they can take their honors higher than the Asian continent. Therefore, important factors for better athletic performance in futsal should be identified and their development should be planned in the short, medium and long term. Some factors should be considered in the field of sports talent and some in the field of training design.

Futsal is a sport that is played in 20 minutes of useful time, and due to the size of the playing field, a player constantly needs to use fast running in short and medium distances, change the direction and speed of running, shooting, etc. Therefore, speed and agility are two very important factors of physical fitness for a futsal player (1, 2). Alvarez et al. (2008) in a study of Spanish league players showed that the average distance traveled per game is 4313 meters and the average distance traveled per minute of the game is 117.3 meters. Among them, 397 meters of walking, 1762 meters of jogging, 1232 meters of moderate intensity running, 571 meters of high-intensity running and 349 meters of maximum speed running have been reported (3). It has been shown that athletes need to increase their speed and agility to reach the peak of their athletic performance (4). Also, although excellent performance requires improvement in physiological characteristics and fitness factors, it is also related to anthropometric characteristics (5). Identifying important anthropometric characteristics that are related to performance in futsal helps coaches make their plans to bring athletes to the highest level of athletic performance. Although many anthropometric features are used in sports talent identification and help coaches identify elite athletes, some anthropometric features, such as circumference of limbs, can be changed with practice. In fact, body size seems to be a good factor in predicting success in futsal (4).

The purpose of this study was to investigate the relationship between anthropometric characteristics and player experience with speed, agility and scoring statistics of Khorasan Razavi women's futsal team players.

I. METHODOLOGY

The method of this research is correlational. Due to the small statistical population, the total number sampling method was used and after the necessary coordination, 14 players of the Khorasan Razavi women's futsal team in the group stage of the Iranian Women's Futsal Premier League 1300-1400 were selected and evaluated as a statistical sample. Calendar age, physiological age (body composition test results), height (body composition test results), arm circumference, hip circumference, leg circumference, chest circumference, shoulder width, waist circumference, hip circumference, waist-to-hip ratio, gaming experience, Experience of playing in the Premier League, experience of playing in the national team, scoring statistics (group stage of the Premier League 1400-1399), speed (in two distances of 15 meters and 25 meters) and agility (4.9 test) were measured. Arm circumference, thigh circumference, leg circumference, chest circumference, shoulder width, waist circumference and hip circumference were also measured using a tape measure. The waist-to-hip ratio was also calculated by dividing the waist by the hip circumference. After collecting the data and for statistical analysis, the data were first described using the mean and standard deviation. Then the data distribution was examined by Kolmogorov-Smirnov test and it was found that the data have a normal distribution and permission to use the parametric correlation coefficient test was obtained. Thus, Pearson correlation coefficient test was used to determine the relationship between variables. SPSS statistical software version 16 was used for statistical analysis. A significance level of $P \leq 0.05$ was considered. In addition, due to the small sample size for correlational studies, the significance level of $P \leq 0.09$ was also considered as a near-significant level so that if the correlation was not significant at the level of $P \leq 0.05$ but at the level of $P \leq 0.09$ It was significant, it was likely to be significant in

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larger sample size and it was recommended to study in larger sample size.

II. Results

Results related to calendar age, physiological age, height, arm circumference, thigh circumference, leg circumference, chest circumference, shoulder width, waist circumference, hip circumference, waist-to-hip ratio, playing experience, Premier League playing experience, playing experience In the national team, the statistics of goals, speed (in two distances of 15 meters and 25 meters) and agility (4.9 test) are presented in Table 1. Also, the results of Pearson correlation coefficient test are reported in Table 2.

Table1. Mean and standard deviation of the studied variables

Variables	mean ± Standard deviation
Calendar age (years)	23.14 ± 5.68
Physiological age (years)	23.31 ± 5.95
Height (cm)	163.28 ± 5.96
Arm circumference (cm)	26.17 ± 2.62
Hip circumference (cm)	51.78 ± 5.12
Leg circumference (cm)	34.39 ± 2.82
Chest circumference (cm)	82.25 ± 5.58
Shoulder width (cm)	42.28 ± 2.52
Waist circumference (cm)	68.92 ± 5.38
Hip circumference (cm)	94.96 ± 7.02
Waist to hip ratio	0.72 ± 0.02
Game history (years)	10.85 ± 4.09
Premier League history (year)	5 ± 4.5
National team history (year)	4.42 ± 4.01
Scoring statistics (number of goals)	4.64 ± 6.45
The first record for sprinting 15 meters (seconds)	2.97 ± 0.12
The second record for sprinting 15 meters (seconds)	2.93 ± 0.18
The record for sprinting 25 meters (seconds)	4.42 ± 0.17
9.4 agility running record (seconds)	10.76 ± 0.58

The results showed that the players of the Khorasan Razavi women's futsal team have an average of more than 10 years of playing experience, about 5 years of playing in the Premier League and more than 4 years of playing in the national team, which according to the average age is 23.14 years. Due to its good age, this team has a high level of game experience. Calendar age was closely and positively correlated with scoring statistics (P = 0.09 and r = 0.46). Physiological age was significantly and positively associated with the 25-meter sprint record (P = 0.02 and r = 0.60). Height was significantly and negatively with the first record of 15 meters (P = 0.031 and r = -0.57) and the record of 25 meters (P = 0.047 and r = -0.53) and almost significantly and negatively with the second record of 15 meters. M (P = 0.07 and r = -0.49) were related. Arm circumference was significant and positive with a running record of 25 meters (P = 0.001 and r = 0.76) and close to significant and positive with a second running record of 15 meters (P = 0.51 and r = 0.059) and a running record of agility (P = 0.53 and r = 0.058). Thigh circumference was significantly and positively associated with the 25-meter running record (P = 0.002 and r = 0.76) and the agility running record (P = 0.029 and r = 0.60). Leg circumference was significantly and positively related to the 25-meter sprint record (P = 0.08 and r = 0.47). Chest circumference was significantly and positively associated with the 25-meter sprint record (P = 0.002 and r = 0.74). Shoulder width was closely and positively correlated with agility running record (P = 0.061 and r = 0.53). Waist circumference was significantly and positively related to the 25-meter sprint record (P = 0.002 and r = 0.78) and the agility running record (P = 0.047 and r = 0.58) and was also significantly and positively related to the second 15-meter sprint record (P = 0.09 and r = 0.48). Hip circumference was significantly and positively related to the 25-meter running record (P = 0.01 and r = 0.65) and the agility running record (P = 0.004 and P = 0.74) and it was also closely and positively related to the 15-meter sprint records in the first test (P = 0.07 and r = 0.48) and in the second test (P = 0.09 and r = 0.45). Goal statistics positively and significantly was related with playing history (P = 0.02 and r = 0.60), playing history in the Premier League (P = 0.63 and r = 0.01) and playing history in the national team (P = 0.64 and r = 0.01).

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Table2. Pearson correlation coefficient test results

Variables	The first record of 15 meters sprint	The second record of 15 meters sprint	25-meter sprint record	4.9 agility running record	Scoring statistics
Chronological age	r= 0.20 p= 0.47	r= 0.03 p= 0.91	r= 0.42 p= 0.12	r= 0.07 p= 0.81	r= 0.46 p= 0.09 *
Physiological age	r= 0.26 p= 0.35	r= 0.11 p= 0.68	r= 0.60 p= 0.02 **	r= 0.22 p= 0.46	r= 0.41 p= 0.14
Height	r= -0.49 p= 0.07 *	r= -0.57 p= 0.031 **	r= -0.53 p= 0.047 **	r= -0.025 p= 0.93	r= 0.18 p= 0.52
Arm circumference	r= 0.31 p= 0.26	r= 0.51 p= 0.059 *	r= 0.76 p= 0.001 **	r= 0.53 p= 0.058 *	r= -0.23 p= 0.41
Round thigh	r= 0.27 p= 0.33	r= 0.37 p= 0.18	r= 0.76 p= 0.002 **	r= 0.60 p= 0.029 **	r= -0.035 p= 0.90
Round leg	r= -0.025 p= 0.93	r= 0.16 p= 0.56	r= 0.47 p= 0.08 *	r= 0.27 p= 0.36	r= 0.05 p= 0.84
Around the chest	r= 0.17 p= 0.54	r= 0.43 p= 0.11	r= 0.74 p= 0.002 **	r= 0.40 p= 0.17	r= -0.09 p= 0.75
Shoulder width	r= -0.11 p= 0.70	r= 0.12 p= 0.67	r= 0.31 p= 0.27	r= 0.53 p= 0.061 *	r= 0.13 p= 0.64
Waist	r= 0.39 p= 0.18	r= 0.48 p= 0.09 *	r= 0.78 p= 0.002 **	r= 0.58 p= 0.047 **	r= 0.16 p= 0.59
Hip circumference	r= 0.48 p= 0.07 *	r= 0.45 p= 0.09 *	r= 0.65 p= 0.01 **	r= 0.74 p= 0.004 **	r= -0.17 p= 0.55
Waist to hip ratio	r= -0.30 p= 0.31	r= 0.03 p= 0.91	r= 0.15 p= 0.62	r= -0.31 p= 0.31	r= -0.15 p= 0.62
Game history	r= 0.086 p= 0.77	r= -0.13 p= 0.65	r= 0.15 p= 0.60	r= -0.06 p= 0.82	r= 0.60 p= 0.02 **
Premier League history	r= 0.068 p= 0.81	r= -0.04 p= 0.89	r= 0.08 p= 0.76	r= -0.20 p= 0.49	r= 0.63 p= 0.01 **
National team history	r= 0.031 p= 0.91	r= 0.021 p= 0.94	r= 0.037 p= 0.89	r= -0.14 p= 0.64	r= 0.64 p= 0.01 **
Scoring statistics	r= -0.28 p= 0.31	r= -0.47 p= 0.08 *	r= -0.13 p= 0.64	r= 0.07 p= 0.80	-

** Significant at the level of P≤0.05
* Significant at the level of P≤0.09 (close to significant at the level of P≤0.05)

III. Discussion

Based on the present findings, calendar age was closely significant and positively related to scoring statistics. So that in larger specimens, the results may be significant and with age, the scoring rate may increase. These results, of course, are obtained in a team with favorable age conditions, and such results may not be observed with excessive age. Therefore, experience may be an important factor in scoring statistics when the age is not too high. In this regard, the present results showed that the experience of the game has a significant relationship with the scoring statistics, if the playing history, playing history

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in the Premier League and playing history in the national team (all three) had a significant positive relationship with scoring statistics of players. They were all desirable. So that with increasing playing experience, playing experience in the Premier League and playing experience in the national team, the number of goals scored by players increases significantly. Therefore, experience may be an important factor in scoring statistics when the age is not too high. In this regard, the present results showed that the experience of the game has a significant relationship with the scoring statistics. The playing history, playing history in the Premier League and playing history in the national team (all three) had a significant positive relationship with the scoring statistics of the players, the intensity of these relationships were all favorable. So that with increasing playing experience, playing experience in the Premier League and playing experience in the national team, the number of goals scored by players increases significantly.

Physiological age was significantly and positively related to the 25-meter sprint record, which was also favorable. As the physiological age increases, the speed record of 25 meters increases or in fact the speed decreases in this distance. Physiological age is probably an important factor in speed performance at higher distances, and if this age is lower, the athlete can perform better at speeds over distances above 20 meters. But this variable (physiological age) does not seem to be an important factor for speed performance over short distances (such as 15 meters). However, more studies are needed in this area, but it should be noted that such an interpretation is relevant to puberty. Height was significantly and negatively related to the first record of 15 meters and the record of 25 meters and was significantly and negatively related to the second record of 15 meters, the intensity of these relationships was moderate. It seems that with increasing height, the sprint record decreases or, in fact, the speed performance in both distances improves. This correlation is probably due to the effect of longer stride length on better speed performance.

Arm circumference was significantly and positively related to the 25-meter sprint record, and it was also significantly and positively correlated with the second 15-meter sprint record and agility running record, so that with increasing arm circumference, the sprint record also increases. (Speed performance decreases). Also, hip circumference was significantly and positively related to the 25-meter running record and agility running record, so that with increasing hip circumference, speed performance (at a distance of 25 meters) and agility decrease. Chest circumference was significantly and positively related to the 25-meter running record and leg circumference was significantly and positively related to the 25-meter running record. As the chest and leg circumference increase, the speed performance at a distance of 25 meters may decrease. Shoulder width was also closely related to the agility running record. Also, waist circumference was significantly and positively related to the 25-meter sprint record and agility running record, and was closely and positively related to the second 15-meter sprint record. Hip circumference also showed a relationship similar to waist circumference, and in addition, it was closely related to the first record of 15 meters. These findings suggest that performance and agility are likely to decline as these body sizes increase. However, attention should be paid to the body composition of these limbs. Although we measured body composition in another study from the same research project, it is better to study the body composition of different limbs separately in future studies. For example, as increasing arm and hip circumference causes a decrease in speed and agility, it should be noted that increasing the circumference of these limbs with fat can lead to such an effect. But because a kilogram of muscle is less than a kilogram of fat, it is possible that reducing the size of these limbs, if lost or gained by muscle, can lead to improved speed and agility. The results also showed that the scoring statistics were closely and negatively related to the second record of 15 meters running, so that with decreasing the record of 15 meters (increasing speed), the scoring statistics increase. Of course, since this relationship has been close to significant, it is better to examine in the future in a larger sample

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size, for example, all the players of the Women's Futsal Premier League.

The nature of the futsal game is such that sprints and short starts are often used. Having the ability to run at high speeds and start allows players to accelerate the game, reach the stray balls earlier than the opponent, or hit the ball earlier than the opponent (2). Research shows that elite futsal players run 5 to 12 percent of their playing time fast during the game and do high-intensity running (speeds above 15 km / h) (3). Therefore, running fast can greatly contribute to the high performance of individual and team futsal. Also, due to the size of the futsal court and the number of players on the court, rarely does a player use fast runs of 20 meters or more. In fact, short-distance sprints, especially in futsal, lead to the physical superiority of the players and the better performance of tactical tasks in group games, as well as the release from the pressure of the opponent. Speed players in futsal in less than a second must decide and perform the desired skill. Because short speed is not only due to the shortening of muscle fibers and the composition of muscle fibers, but also the rapid use of the nervous system and faster reaction can play an important role in this regard. Therefore, the simultaneous use of the nervous-muscular system can improve the ability to perform short runs such as 5 meters and 10 meters and lead to superiority over the opponent. Therefore, in future studies, this issue should also be considered and it is better to measure the neuromuscular characteristics and speeds of decision and reaction of players to achieve better results. Also, futsal, due to its nature, requires a lot of sudden changes of direction and physical deceptions, which require high agility. However, James et al. (2008) showed that there is no significant difference between the agility of selected and unselected players for the Australian national youth soccer team (6), which is probably due to the nature of the game of football; Because football requires less agility than futsal, Dogramaci and Watsford (2011) showed a higher ability to change direction in elite players than in lower level players (7).

IV. CONCLUSION

Probably the most important factor for the success of women futsal players is experience. As in the present study, as the age, years of playing, playing in the Premier League and playing in the national team increased, so did the scoring statistics. Also, speed over short distances may play a role in scoring statistics, and the better the speed of the athlete over short distances, the better the performance in this regard, which should be examined in the future in a larger sample size. Be placed so that conclusions can be concluded with more confidence. On the other hand, it seems that the smaller the circumference of the upper and lower limbs, the better the speed and agility performance, which is probably due to the smaller size of the fat than the muscle and the reduction of fat in these limbs. . It is better in future studies to measure the body composition (subcutaneous fat) of these organs to lead to a more accurate interpretation in this regard. Finally, it seems that lower physiological age is an important factor for better speed performance over long distances, but no conclusions can be drawn before conducting additional studies in larger samples. It is suggested that next season, such a study be conducted on all players in the Women's Futsal Premier League.

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The Effect of Saffron Supplementation with Aerobic Training on Inflammatory Factors and Cognitive Status in Elderly Men

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***Abstract*— the aim of this study was to evaluate the effect of 12 weeks of aerobic training and saffron supplementation on cognitive status and serum levels of IL-1β and TNF-α in elderly men. Forty men aged 60 to 70 years were purposefully selected and randomly divided into 4 groups: aerobic training, saffron, aerobic training + saffron and placebo (10 people in each group). Interventions were performed for 12 weeks. Aerobic training consisted of 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 running time by one minute until after 12 weeks, the running time reached 26 minutes. Saffron extract was taken as a capsule with a dose of 500 mg in two meals in the morning and after exercise. IL-1β and TNF-α levels were significantly reduced in both training and saffron groups, but in the training + saffron group, their decrease was greater (P<0.05). Cognitive status in the three intervention groups increased significantly compared to the placebo group, which was higher in the exercise + saffron group (P<0.05). It is possible that taking saffron supplement along with aerobic training for 12 weeks, by improving the cognitive status in older men by reducing inflammatory factors, can prevent cognitive disorders and eventually Alzheimer's.**

Keywords*— *Aerobic training, Saffron, Cognitive status, Inflammation, Elderly

I. INTRODUCTION

The population aged over 60 years in Iran reaches around 10 million in 2020 and over 26 million up to 2050 that will be 23% of the total population (1). Cognitive impairment represents one of the common disorders in the elderly such that around 35% of them present with it at different severities and Alzheimer's disease is the progressive stage of this disorder (2). In cognitive impairment, attention, memory, language, orientation, actions, executive performance, judgement, and problem-solving are impaired mostly due to brain memory loss (3). The normal functioning of the various brain systems is responsible for cognitive function, and cognitive impairments arise as the age increases and the elements involved in these systems develop. Also, various inflammatory processes and cytokines play a key role in the pathogenesis of Alzheimer's disease (4). The expression of most cytokines in normal tissues is normal, but in neurodegenerative diseases, their

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expression is increased. For example, proinflammatory cytokine expression of tumor necrosis factor alpha (TNF-α) is increased in neurodegenerative diseases (5, 6). In this regard, it has been shown that the safety profile of patients with mild cognitive impairment changes (7).

It is important to consider interventions to prevent cognitive impairment and therefore Alzheimer's and measuring the inflammatory factors following these interventions can lead to a better understanding of the observed effects. Consumption of medicinal plants is one of such interventions that have attracted attention (8, 9). Meanwhile, saffron (Crocus sativus L.) is a perennial plant of the iris genus (Iridaceae) with a height of 10 to 30 cm and has a hard, round, fleshy onion covered with thin, brown membranes. The four major bioactive compounds in saffron are crocin, crocetin, picrocrocin and safranal, which are involved not only in the sensory characteristics of saffron (color, taste and aroma, respectively) but also in its health-improving properties (11). Numerous studies have shown that crocin and crocetin (which are the active compounds of saffron) are able to exert various protective medicinal effects that are attributed to the antioxidant capacity of these compounds (12). Several studies have reported that saffron extract and its two main components, crocin and crocetin improve memory and learning skills in mice whose learning behavior is impaired by ethanol induction. These results suggest that oral administration of saffron can be useful in the treatment of neurodegenerative diseases and related memory disorders (10). According to the results of Pitsikas et al. in 2006 and 2007, saffron-derived crocins fight diagnostic memory-related disorders in healthy rats, indicating the role of these carotenoids in memory (13). Saffron also has an anti-inflammatory effect (14) and as mentioned, the levels of inflammatory factors in cognitive disorders increase (4-7). In general, the effects reported for saffron include antioxidant, anti inflammatory, memory and learning improvements, anti tumor, anti depressant, reduces fat and lowers insulin resistance (15, 16).

However, so far no research has investigated the effect of consumption of this plant on cognitive status and related factors in the elderly. On the other hand, exercise as a low-cost treatment method can have a positive effect on cognitive function, which may be achieved by reducing inflammatory factors; Because cross-sectional studies have shown that active individuals have better cognitive function than inactive counterparts (17), the anti-inflammatory effect of training has also been reported (18). Considering that cognitive disorders are one of the most common problems in old age and these disorders are the beginning of a path that will eventually lead to Alzheimer's and of course death and considering that no definitive treatment for Alzheimer's has been introduced yet, the use of preventive interventions is very important. Also in this field, the use of medicinal plants is of special importance due to its naturalness and no side effects (9). Since exercise and physical activity have a proven role in improving cognitive function (17) and inflammatory factors (18) has it, it is important to study the effect of combining training and plant in this field. However, so far no research has investigated the simultaneous effect of aerobic training and saffron supplementation on inflammatory factors and its relationship with the cognitive status in the elderly.

The aim of this study was to evaluate the effect of 12 weeks of aerobic training and saffron supplementation on cognitive status and serum levels of IL-1β and TNF-α in elderly men.

II. METHODOLOGY

This research was conducted by quasi-experimental method with pre-test and post-test design with control group. Eighty seven people aged 60-70 years volunteered to participate in the study after advertising our study among different elderly populations living in Shiraz County. Then, the Mini–Mental State Examination (MMSE) was administered to volunteers. The MMSE, developed by Folstein et al. in 1975, consists of 11 subscales: Orientation to time and place, registration, attention and calculation, memory, language, executive skills, reading, writing, and doing fine

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works (19). The subjects that do not have any problems in these subscales are given the score 30; the scores < 20 represent in-depth cognitive disabilities and the scores 20-25 represent partial cognitive damage. The reliability (Cronbach's alpha) of the MMSE has been reported 0.87 with sensitivity and specificity of 90% and 84%, respectively (20). Forty volunteers who attained the MMSE scores 21-25 randomly divided into 4 groups: aerobic training, saffron, aerobic training + saffron, and placebo (10 people in each group). Inclusion criteria included being a man, being 60 to 70 years old, being able to attend intervention sessions, being evaluated by a physician to determine general health and participating in aerobic exercise, and not being on medication to treat cognitive disorders. Exclusion criteria also included absenteeism in interventions, lack of independence in daily activities, having various physical or mental illnesses, medication use, unwillingness to continue research and treatment for various cognitive disorders. Interventions were performed for 12 weeks. Saffron supplement in the amount of 500 mg in two stages, after breakfast one capsule (250 mg) and immediately after the exercise session (250 mg) or at the same time in the afternoon for the saffron group without exercise to consumed with 100 ml of water. The placebo group also used empty but completely similar capsules with the same instructions. Preparation of saffron supplement was such that saffron flower heads and bottoms were collected from saffron orchards in Bidokht city located in Khorasan Razavi province in Iran in November. It was then dried in the shade for 10 days. Saffron was divided into flower and flower parts. Different parts of saffron were powdered with Chinese mortar. 250 mg of each part of saffron was encapsulated and prepared for consumption. Aerobic training was 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 that 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 (21). 24 hours before and 48 hours after the interventions, 5 ml of blood was taken from the brachial vein of the subjects in a 12-hour fasting state. In order to isolate the serum, blood samples were centrifuged at 2000 rpm for 10 minutes after clotting. Samples were stored in the freezer at -20 ° C until the variables were measured. IL-1β and TNF-α levels were measured with the sensitivity of 8 and 2 pg/ml, respectively, using a kit (Diaclone, France). Cognitive states were measured using the MMSE. Data were described by average and standard deviation. Inter- and intra-subject mixed ANOVA was used to investigate inter- and intra-group changes and tukey's test were used to compare the changes in the variables among the groups. To investigate the association between the changes in the variables, Pearson correlation coefficient was used to investigate the association between the changes in the variables. The level of significance (p) was considered ≤ 0.05. Data analysis was conducted in SPSS 16.

III. RESULTS

Descriptive data, the results of inter- and intra-subject mixed ANOVA and Tukey's test, and Pearson correlation coefficients are shown in Tables 1-3, respectively.

There was a significant difference between changes in weight, body mass index, cognitive status, TNF-α and IL-1β in the four groups over time (P=0.001). Weight and BMI in the two groups of training + saffron and training were significantly reduced compared to the two groups of saffron and control (P<0.05). There was no significant difference between weight and BMI changes between the two groups of training and training + saffron (P>0.05) and the two groups of saffron and placebo (P>0.05). Cognitive status was significantly increased in the three intervention groups compared with the placebo group (P<0.05). The increase in cognitive status in the training + saffron group was significantly more than the two groups of training and saffron alone (P<0.05), but the changes in cognitive status in the two groups of training and saffron alone were not significantly different (P=0.99). TNF-α and IL-1β were significantly reduced in the three intervention groups compared with the placebo group

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(P<0.05). The decrease in TNF-α and IL-1β in the training + saffron group was significantly greater than the two training and saffron groups alone (P<0.05), but changes in TNF-α and IL-1β in the two groups of training and saffron alone were not significantly different (P>0.05).

The results showed that there was a significant negative relationship between weight and BMI changes with cognitive status changes (P<0.05) and a significant positive relationship between weight and BMI changes with TNF-α and IL-1β changes (P<0.05). Regarding the relationship between cognitive status changes and changes in inflammatory factors, the results showed that with decreasing serum TNF-α levels in the elderly, their cognitive status increased significantly (r=-0.70 and p=0.001); And with decreasing serum IL-1β levels in the elderly, their cognitive status increased significantly (r=-0.65 and p=0.001).

Table1. Comparison of variables between four groups (ANOVA)

variables	groups	Before	After	F value	P value	Effect Size
Weight (kg)	training + saffron	78±3.80	75.10±6.04	13.36	0.001*	0.52
	training	76.90±5.50	74.50±2.75			
	saffron	79.40±6.48	79±5.56			
	placebo	78±5.79	78.50±5.81			
BMI (kg/m^2)	training + saffron	26.48±2.69	25.48±0.54	14.50	0.001*	0.54
	training	25.74±2.86	25.95±0.82			
	saffron	25.35±2.33	25.22±0.61			
	placebo	25.32±2.86	25.48±0.93			
Cognitive State (MMSE)	training + saffron	23.20±1.68	27±1.76	13.38	0.001*	0.52
	training	24.50±1.58	26.10±1.19			
	saffron	24.70±1.05	26.20±0.91			
	placebo	26.30±1.63	25.80±0.63			
TNF-α (pg/ml)	training + saffron	8.85±1.05	5.26±0.85	18.16	0.001*	0.60
	training	8.91±1.10	7.13±1.44			
	saffron	8.84±1.54	7.26±1.21			
	placebo	7.06±1.42	7.30±1.53			
IL-1β (pg/ml)	training + saffron	3.81±0.41	2.31±0.37	26.80	0.001*	0.69
	training	3.56±0.56	2.89±0.66			
	saffron	3.46±0.70	3.09±0.67			
	placebo	3.001±0.72	3.23±0.67			

*Significant at 0.05.

Table2. The results of Tukey's test regarding the points of significant difference

Pair wise Comparison	Weight	BMI	Cognitive State	TNF-α	IL-1β
training + saffron / training	0.85	0.75	0.013 *	0.007 *	0.001 *
training + saffron / saffron	0.002 *	0.001 *	0.009 *	0.002 *	0.001 *
training + saffron / placebo	0.001 *	0.001 *	0.001 *	0.001 *	0.001 *
training / saffron	0.014 *	0.012 *	0.99	0.98	0.46
training / placebo	0.001 *	0.001 *	0.019	0.002 *	0.001 *
saffron / placebo	0.48	0.48	0.028	0.006 *	0.021 *

*Significant at 0.05.

Table3. Pearson correlation coefficients to examine

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the association between the changes in variables

variables	Weight	BMI	Cognitive State	TNF-α	IL-1β
Weight	-	r= 0.99 p= 0.001 *	r= - 0.45 p= 0.003 *	r= 0.64 p= 0.001 *	r= 0.53 p= 0.001
BMI	r= 0.99 p= 0.001 *	-	r= - 0.46 p= 0.003 *	r= 0.66 p= 0.001 *	r= 0.56 p= 0.001
Cognitive State	r= - 0.45 p= 0.003 *	r= - 0.46 p= 0.003 *	-	r= - 0.70 p= 0.001 *	r= - 0.65 p= 0.001 *
TNF-α	r= 0.64 p= 0.001 *	r= 0.66 p= 0.001 *	r= - 0.70 p= 0.001 *	-	r= 0.68 p= 0.001 *
IL-1β	r= 0.53 p= 0.001 *	r= 0.56 p= 0.001 *	r= - 0.65 p= 0.001 *	r= 0.68 p= 0.001 *	-

*Significant at 0.05.

IV. DISCUSSION

After 12 weeks, both training and saffron groups showed a significant increase in cognitive status and a significant decrease in inflammatory factors (IL-1β and TNF-α). However, in the group that both exercised and took saffron supplements (training + saffron), a greater increase in cognitive status and a greater decrease in IL-1β and TNF-α were observed. Also, according to the findings of the present study, with weight loss and body mass index of the elderly, their cognitive status increases and their TNF-α and IL-1β levels decrease. In addition, the present results showed that with decreasing TNF-α and IL-1β, the cognitive status in the elderly increases. Therefore, although these relationships do not constitute the effect of cause and effect; however, a significant relationship between changes in cognitive status and inflammatory factors indicates that the reduction of inflammatory factors may play a role in increasing the cognitive status of the elderly following aerobic exercise and saffron consumption.

Studies have been done on the effect of saffron on cognitive status and memory. For example, in a study by Ghadami et al. (2009), intraperitoneal injection of crocin for six consecutive days improved the destructive effects of scopolamine on the learning and memory in rats in a dose-dependent manner (22). Also in the study of Khalili et al. (2012) the use of crocin as a treatment for three weeks in rats in which Alzheimer's disease was induced by intraventricular injection of streptozotocin, significantly improved spatial learning, memory and cognitive skills (23). In addition, in a study by Hosseinzadeh et al. (2012) in which saffron extract and its active ingredient crocin were selected as the treatment, it improved cognitive deficits induced by cerebral hypoperfusion in rats (24). Khalili et al. (2009) also observed similar results to Hosseinzadeh et al. (2012) in experimental Alzheimer's mice (25). In general, the beneficial effects of saffron extract on the brain have been reported (26, 27, 28). It has been suggested that the positive effect of saffron on learning and memory processes is due to the antioxidant activity of its active compounds (29). Crocin seems to be the main compound and antioxidant in saffron, the effect of improving the effects of saffron extract on cognitive status (24). Due to the reduction of inflammatory factors due to the consumption of saffron extract in the present study, it may be possible to attribute the improvement in the cognitive status of the elderly due to saffron extract to the reduction of inflammatory factors due to this extract. It has been observed that saffron has an anti-inflammatory effect (14). In any case, we need more detailed and controlled studies in this regard in the future.

Regarding exercise and consistent with the present findings, Farinha et al. (2015) evaluated TNF-α and IL-1β in 23 untrained women before and after 12 weeks of treadmill training without changing diet. Their results showed that a period of aerobic training significantly reduced serum levels of TNF-α and IL-1β (30). But Isanejad et al. (2015) reported that 8 weeks of endurance training resulted in a significant increase in IL-1β and a significant decrease in TNF-α (31).

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Knudsen and Pedersen (2015) investigated the effect of training on inflammatory factors in patients with type 2 diabetes, reported that training leads to an increase in interleukin 6 by inhibiting TNF-α and by stimulating IL-1 receptor antagonist and thus limited IL-1β signaling leads to anti-inflammatory effects (18). In the present study, both a decrease in inflammatory factors and an increase in cognitive status were observed with aerobic training. In this regard, Miller et al. (2012) reported that there is a significant and positive relationship between cognitive status and physical activity (32) which it can be attributed to the reduction of oxidative stress and inflammation, increased angiogenesis, secretion of neurotrophins and catecholamines, and neurogenesis, especially in the hippocampal structure (33).

Regarding the effect of saffron consumption along with training on inflammatory factors and cognitive status, so far no research has been done, especially in the elderly. Therefore, the interpretation of the findings becomes difficult due to the impossibility of comparison with other findings. In any case, based on the present findings, it seems that two simultaneous interventions of saffron extract consumption and aerobic training can have a double effect on reducing inflammatory factors and increasing the cognitive status in the elderly; But as mentioned, this is the first time this research has been done and we need more research in this regard.

It is possible that both aerobic training and saffron supplementation, by improving the cognitive status of the elderly by reducing their inflammatory factors, can prevent or delay cognitive disorders and Alzheimer's disease in old age. It seems that the combination of two intervention methods (aerobic training + saffron supplement) leads to better prevention in this regard. Reducing inflammation may play an important role in this preventative measure, but other mediators should be considered in future research.

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