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The Effect of Eight Weeks of Endurance Training and Curcumin Supplementation on the Levels of Inflammatory Markers and Cardiopulmonary Function of Obese Girls with a History of Coronavirus Infection

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Abstract

Background: *This study aimed to investigate the discrete and combined effects of 8 weeks of endurance training and curcumin supplementation on the levels of inflammatory markers and pulmonary function in obese girls with a history of coronavirus infection.*
Methods: *This research was conducted by semi-experimental method and clinical trial in the form of pre-test and post-test. 40 obese women were selected randomly and allocated into 4 groups: exercise+curcumin supplement (Curcu+Exe), exercise+placebo (Exe), curcumin supplement (Curcu), and control (Control). The subjects in exercise groups participated in an eight-week aerobic exercise program. The subjects of the supplement groups took three to four capsules every day. The level of blood serum inflammatory indicators was measured using the ELISA kit. The pulmonary function indices were evaluated using a spirometer.*
Results: *The results of the present study showed that eight weeks of progressive endurance training along with curcumin supplementation in obese girls with a history of corona infection, led to a decrease in inflammatory indicators (IL-6 and TNF-a) and improved pulmonary function indicators in the experimental groups.*
Conclusions: *Curcumin supplementation along with progressive endurance exercises can lead to the improvement of inflammatory conditions and pulmonary function in obese girls with a history of corona disease. Therefore, these people can improve their body composition and general health through the combination of endurance activity and curcumin supplementation.*

Keywords: IL-6, TNF-a, Obesity, Physical activity, COVID-19.
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Introduction

Obesity is an underlying factor for the occurrence of many diseases, which is associated with an increased risk of type 2 diabetes, metabolic disorders, coronary artery disease, respiratory problems, and neurological diseases[1]. Overweight and obesity affect almost 60% of adults, and approximately one out of every three children live with overweight or obesity. The results of studies have shown that by 2030, about 51% of the world's people will be obese[2], which increases the risk of cardiovascular diseases and increases mortality from 20 to 80%[3]. There is a correlation between obesity, insulin resistance, and cytokines related to fat and carbohydrate metabolism[4]. Studies have shown that inflammatory cytokines such as Tumor necrosis factor alpha (TNF-α), and Interleukin-6 (IL-6) have higher levels in obese populations or related diseases than in people with normal weight[5]. The production of large amounts of inflammatory cytokines such as IL-6, IL-18, and TNF-α by adipose tissue plays a role in the development of insulin resistance, diabetes, and metabolic syndrome[6]. In addition, the coronavirus epidemic created a severe challenge for all societies, because it has caused a change in the social interactions of people and their lifestyles. The world is still facing this virus, which is still a serious threat to everyone. Excessive production of pro-inflammatory cytokines in hypermetabolic conditions is associated with oxidative stress caused by the virus, which causes severe damage to myocytes[7]. The development of the COVID-19 disease depends on the interaction between SARS-CoV-2, the host's immune system, and the individual's immune response[8].

Lifestyle changes, such as increasing the level of physical activity and using a low-calorie diet, are recommended as the first interventions to reduce body fat levels and prevent the development of metabolic diseases and complications[9]. There are continuous efforts to discover and evaluate natural compounds with minimal side effects for weight management[10]. One of these substances is curcumin. Curcumin is a polyphenolic compound that represents the most important curcuminoid isolated from the rhizome of plants[11]. Several studies have reported the broad-spectrum antimicrobial activity for curcumin including antibacterial, antiviral, antifungal, and antimalarial activities[12]. Curcumin is a potent medicinal agent that uses multiple molecular pathways to exert its effects on biological systems[13]. This suggests that this compound has the potential for the prevention (and future treatment) of obesity[14].

According to the mentioned materials, this research seeks to find an answer to this basic question: Does endurance training and curcumin supplementation have a significant effect on the levels of inflammatory markers and pulmonary function in obese girls with a history of corona? Evaluation of this issue may help professionals who work with this population (for example: physical therapists, exercise physiologists, etc.) to

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design better exercise programs for the rehabilitation of patients.

Materials and Methods

This research was carried out using a semi-experimental method and a clinical trial in the form of pre-test and post-test. The statistical population included inactive obese girls with an age range of 25-35 years with a body mass index of 35±5 and a history of corona disease, referring to sports clubs in Kermanshah city in 2023. None of the subjects had a history of chronic diseases such as cardiovascular diseases, diabetes, various cancers, kidney and digestive disorders, or any type of injury or problem that prevents them from participating in physical activities. To select the sample, first, a notice was distributed among all the sports clubs in Kermanshah city, and people with the age range and BMI required for this research were asked to cooperate, and they were asked to volunteer in this research if they wished. Based on this, among the people who volunteered to participate in the research, 40 qualified people were randomly invited to participate in the briefing session and were randomly divided into four experimental groups: experimental group of progressive aerobic exercise+curcumin supplement 10 people (Curcu+Exe), experimental group of progressive aerobic exercise+placebo 10 people (Exe), curcumin supplement experimental group 10 people (Curcu) and control/no intervention experimental group 10 people (Control). All participants gave informed consent before participating in the study. After grouping the subjects, two days before the start of the intervention period, initial evaluations including anthropometric indicators (height, weight, body mass index, and waist to hip circumference) of each subject were measured in the laboratory. The height of the subjects was measured with a Seka measuring tape (made in Germany) with an accuracy of 0.5, and the weight of the subjects was measured with a Seka scale with an accuracy of 0.1 kg with minimal clothing. Then, the body composition of the people was calculated using the Jawon model body analysis machine made in South Korea. To measure the waist circumference, the circumference of the abdomen in the area of the navel, and to measure the circumference of the hips, the widest part of the hips was measured with a tape measure. Then, the WHR (Waist–hip ratio) size was obtained by dividing the waist circumference by the hip circumference. After measuring the physical and physiological indicators according to the experimental groups, the subjects participated in the training protocol for eight weeks (three days a week).

To implement the progressive aerobic exercise program, the subjects of the experimental and control groups participated in an eight-week aerobic exercise program, three sessions a week, each session lasting 60 minutes with an intensity of 65 to 85% of the maximum heart rate according to Table 1. The program training session included 10 minutes of warm-up, 40 minutes of aerobic exercises (aerobics), running and local movements (belly crunches, butterfly, circle in the air, climbing stomach, and other similar things), and 5 minutes of cooling down with an intensity of 65%. The maximum heart rate at the beginning and every two weeks was increased by 5% until they reached 85% of the maximum heart rate in the last week.

Table 1. Protocol of progressive endurance exercises

Week	Time (min)	Intensity (%HRmax)
1-2	40	65
3-4	45	70
5-6	50	75
7-8	55	80

Regarding the way of supplementing curcumin, the subjects of the supplement groups took three to four capsules every day for eight weeks according to the method of taking curcumin supplement made by Karen company, made in Iran with the license of Food and Drug Organization and registration number 4106933222644050 consumed. For the blinding of the intervention, the placebo group also received three to four capsules containing prepared starch; as the capsules received in both placebo and supplement groups were the same in size. The distribution and consumption of capsules were randomly distributed by the laboratory supervisor between the intervention group and the placebo group by the laboratory officials without the knowledge of the subjects from other groups, and the researchers were not aware of the results of the randomization and the type of packaging that they delivered. Before the initial evaluations of the pre-test stage, the participants were asked to observe some points, 48 hours before the evaluation, avoid doing any physical activity beyond daily life, and 24 hours before the evaluation of the consumption of everything they eat in Report the nutrition record sheet. After 12 hours of fasting, at 8-10 am and with the presence of a nursing expert from the Kermanshah health center, the subjects were present at the Parsian laboratory in Kermanshah city, and five milliliters of blood was taken from them to measure the serum levels of the index profile. Inflammatory tests were taken. The first blood sample was taken 48 hours before the beginning and the second sample was taken 48 hours after the end of the eight-week supplementation period. The blood samples were centrifuged at a speed of three thousand revolutions per minute and after separating the serum, they were kept at minus 70 degrees Celsius. In the present study, inflammatory indices (IL-6: Interleukin 6; TNF-a: Tumor necrosis factor alpha) were measured using the ELISA kit of Carmania Parsgene Company, made in Iran, with the kit series HIL6230615 and HTNF230519. A spirometer test was used for lung function evaluation using a spirometer (Spirolab New) brand (MIR) made in Italy to record the pulmonary function index (VC: Vital capacity; FVC: Forced vital capacity; FEV1: Forced expiratory Volume in 1 second).

The normal distribution of the research variables was investigated using the Kolmogorov-Smirnov normality test in the research groups. Levene's test was also used to check the homogeneity of variances. After determining the normal distribution of the data, one-way analysis of variance and Tukey's post hoc test were used to compare the physiological and biochemical variables between groups, and the correlated t-test was used to compare the differences within groups. All calculations were done using SPSS version 29 software. Finally, the significance level of the tests was considered P-value≥0.05.

Results

The results using the Shapiro-Wilk test revealed that the distribution of the co-variables in the research is normal, so parametric tests were used to perform statistical calculations. Using the one-way analysis of variance test on the pre-test values of the indicators in Tables 2 and 3 showed that there is no significant difference between the groups.

Performing statistical operations on the difference in the scores of the indices obtained in tables 2, 3 and P-value showed that there is significant difference in the IL-6 (P-value=0.001 and F=8.04), TNF-a (P-value=0.001 and F=19.58), VC (P-value=0.004 and F=5.29), FVC (P-value=0.001 and (F=8.07) and FEV1 (P-value=0.001 and F=8.86) differences between the four groups were significant. Using Tukey's follow-up test, it was found that this difference in regarding TNF-a index, between Exe group and Control group (P-value=0.002), Exe group with Curcu+Exe group (P-value=0.012), Curcu group with Control group (P-value=0.042), Curcu group with Curcu+Exe group (P-value=0.001) and Curcu+Exe group with the Control group (P-value=0.001), regarding the VC index, between the Exe group with the Control group (P-value=0.048), the Curcu group with the Curcu+Exe group (P-value=0.05), and the Curcu+Exe group with the Control group (P-value=0.006), regarding the FVC index, between the Exe group and the Control group (P-value=0.038), the Curcu group and the Curcu+Exe group (P-value=0.005), and the Curcu+Exe group and the Control group (P-value=0.001 and 0) and also about the FEV1 index, it is between the Curcu+Exe group and the Control group (P-value=0.001). On the other hand, the analysis of the correlation t-test on the values of the indicators in Tables 2 and 3 showed that there is a significant difference between the average of the research variables in the Exe, Curcu, and Curcu+Exe groups after the test compared to the pre-test. The difference according to the results of the percentage of changes and also the data related to the effect size of the variables shows that it is effective not only from a statistical point of view but also from a practical point of view.

Table 2. Inflammatory indices in the experimental groups

Variable	Groups	Measurement time		Percentage change	Paired-Sample-t-test	P-value within a group	Cohen's d	F	Intergroup P-value
		Pre-Test	Post-Test						
IL-6 (pg/mL)	Exe	9.41±1.42	7.14±1.52*	↓ 24.12	19.16	0.001	0.375	8.04	0.001
	Curcu	9.38±1.88	8.29±1.88*	↓ 11.62	30.60	0.001	0.113		
	Curcu+Exe	9.50±1.47	6.01±1.16*	↓ 36.74	22.26	0.001	0.726		
	Control	9.44±1.98	9.63±2.18	↑ 2.01	0.82	0.434	0.758		
	Pre-P-value	0.99	-	-	-	-	-		
TNF-a (pg/mL)	Exe	14.41±1.49	12.03±1.61*	↓ 16.52	34.49	0.001	0.218	19.58	0.001
	Curcu	15.38±1.88	13.12±1.84*	↓ 14.69	65.40	0.001	0.109		
	Curcu+Exe	14.90±1.36	9.60±1.52*	↓ 35.57	18.91	0.001	0.886		
	Control	14.94±1.71	15.17±1.65	↑ 1.54	-0.98	0.353	0.747		
	Pre-P-value	0.62	-	-	-	-	-		

IL-6: Interleukin 6; TNF-a: Tumor necrosis factor alpha. *Significant difference with the control group at the level of P-value≥0.05.

Table 3. Pulmonary function in the experimental groups

Variable	Groups	Measurement time		Percentage change	Paired-Sample-t-test	P-value within a group	Cohen's d	F	Intergroup P-value
		Pre-Test	Post-Test						
VC	Exe	4.30±1.11	5.73±0.85*	↑ 32.25	-14.59	0.001	0.313	5.29	0.001
	Curcu	4.42±1.04	4.71±0.99*	↑ 3.56	-13.48	0.001	0.067		
	Curcu+Exe	4.40±1.07	4.83±0.90*	↑ 36.90	-24.23	0.001	0.184		
	Control	4.36±1.07	4.35±1.06	0.23	0.33	0.748	0.086		
	Pre-P-value	0.99	-	-	-	-	-		
FVC	Exe	3.95±0.65	4.99±0.83*	↑ 26.32	-11.84	0.001	0.227	8.07	0.004
	Curcu	4.09±0.71	4.32±0.70*	↑ 5.62	-10.78	0.001	0.067		
	Curcu+Exe	4.03±0.72	5.57±0.84*	↑ 32.21	-26.91	0.001	0.181		
	Control	4.02±0.70	4.01±0.72	↓ 0.25	0.04	0.966	0.072		
	Pre-P	0.97	-	-	-	-	-		
FEV1	Exe	3.86±0.77	4.44±0.99*	↑ 15.03	-4.86	0.001	0.376	8.86	0.001
	Curcu	4.07±0.73	4.31±0.86*	↑ 5.89	-11.70	0.001	0.066		
	Curcu+Exe	4.22±0.94	5.63±0.87*	↑ 33.41	-31.60	0.001	0.140		
	Control	3.97±0.72	3.94±0.73	↓ 0.76	0.89	0.397	0.099		
	Pre-P-value	0.77	-	-	-	-	-		

VC: Vital capacity; FVC: Forced vital capacity; FEV1: Forced expiratory Volume in 1 second. *Significant difference with the control group at the level of P-value≥0.05.

Discussion

Obesity is associated with various diseases such as cardiovascular diseases, diabetes, high blood pressure, metabolic syndrome, and chronic inflammation. Most of the studies conducted about the causes and risks of obesity have shown that doing regular sports activities is a suitable way to deal with obesity. According to the findings of the present study, after eight weeks of progressive aerobic exercises with curcumin supplementation in obese girls with a history of coronavirus, the values of IL-6 and TNF-a in the experimental group showed a significant decrease. It is consistent with Osali et al.[15], Goldhammer et al.[16], and McFarlin et al.[17]. Mechanisms have been proposed to explain how exercise training may reduce chronic inflammation. It is known that in addition to adipose tissue, active skeletal muscle is a potential source of cytokines. IL-6 produced by myocytes through the activation of AMP-activated protein kinase (AMPK) with sufficient physical activity has anti-inflammatory effects, in contrast to IL-6 secreted by adipose tissue, which causes the release of IL- 10 and interleukin-1 receptor antagonist (IL-1RA), along with the inhibition of TNF-α production during activity and a few hours after training sessions. Another possible mechanism is the decreased expression of nuclear transcription factor κB (NFκB) receptors on monocytes and macrophages, possibly related to heat shock protein levels and hormones, increased lipolysis, and decreased monocyte counts reported in some studies. In addition, recent evidence suggests that exercise training may increase angiogenesis and blood supply, thereby reducing hypoxia and associated inflammation in adipose tissue. Today, various mechanisms have been proposed for curcumin's anti-inflammatory properties, including the NF-κB transcription factor, which is bound to the IKβ inhibitor and exists in an inactive form in the cell cytoplasm[18]. Cytokine stimulation activates IKβ kinase (IKK). IKK, by phosphorylating IKβ, causes the separation of this inhibitor from NF-κB. Phosphorylated IKβ binds to ubiquinone and degrades. While NF-κB is transferred into the nucleus and transcribes various genes, the most important of which are genes related to inflammatory cytokines and enzymes involved in inflammation. By binding to IKK, curcumin deactivates it and prevents it from being phosphorylated, and thus IKβ is separated. In this way, the mRNA production of all cytokines and molecules caused by the binding of NF-κB to DNA is stopped[19]. Another mechanism of curcumin in inhibiting NF-κB is increasing the expression of histone deacetylases. Histone deacetylase causes deacetylation of histones and binding of histone to DNA, which leads to inhibition of NF-κB binding to DNA. Curcumin prevents inflammation by inhibiting NF-κB[20]. In a normal state, the inflammatory stimulation of the immune system causes the activation of extracellular signal-regulated kinases (ERK1 and ERK2), which causes the phosphorylation of phospholipase A2 (PLA2) and its activation. Phospholipase A2 reaches the endoplasmic reticulum membrane with the help of Ca^{2+} and breaks the membrane phospholipid and produces arachidonic acid. This acid is converted into prostaglandin or leukotriene by being placed in one of the two pathways of cyclooxygenase or lipoxygenase, which results in inflammation and pain. Curcumin stops this process at different points, for example by binding to ERK it prevents the phosphorylation of PLA2, by inhibiting NF-κB it stops the production of cyclooxygenase 2 (COX2)[21] and by binding to the active site It deactivates cyclooxygenase and lipoxygenase enzymes, and in addition to reducing inflammation, it also reduces pain[22]. It inhibits the production of cytokine TNF.α, IL8, IL6, IL1 and various chemokines[23]. In addition, curcumin also affects the expression of binding molecules on the cell surface[24]. Previous studies on serum or plasma cytokine levels and their concentration have evaluated the acute effects of exercise[25]. Based on the findings reported in the previous study as well as the present one, it can be hypothesized that major weight loss associated with exercise training is necessary to adjust the levels of inflammatory indicators[26]. In this regard, some previous studies have shown a significant decrease in the concentration of C-reactive protein, which is another important indicator of systemic inflammation following the consumption and supplementation of curcumin[27]. Another result of the present study showed that eight weeks of endurance training with curcumin supplementation causes an increase in VC, FVC, and FEV1 variables, as well as a decrease in systolic blood pressure, diastolic blood pressure, and heart rate variables. It was also found that there is a significant difference between the average of the studied variables in the Curcu exercises group, the Exe group, and the Curcu+Exe group in the post-test compared to the pre-test, which is more in the Curcu+Exe group than in the Curcu group and the Exe group. In this regard, it should be acknowledged that the results of the present study are consistent with the findings of Ravashdeh et al.[28], Awto et al.[29], Irandoost et al.[30], and Gracebrook et al.[31] are not aligned. In previous research, various possible mechanisms have been pointed out, in this regard, we should mention the study of Ravashdeh et al, who admitted that the improvement of pulmonary function occurs more as a result of the expansion of the lungs during the period of high-intensity sports activity, which leads to the entry of a larger volume of air into the airways and the expansion of the respiratory tract. In another study, Park and Han[32] stated that high-intensity aerobic exercise increases oxygen consumption and activates inactive air sacs, and frequent inhalation and exhalation stimulation increases air sac capacity and The FVC result increases. At the same time that more passive airbags are activated, more air enters into the airbags, and increasing the capacity of the airbags can be used to increase the elasticity of the lung and exhale more air. They attributed more.

Now, in the present study, it was found that sports activity along with curcumin supplementation has a beneficial effect on IL-6, TNF-a, VC, FVC, and FEV1. It was also found that this is more in the Curcu+Exe group compared to Curcu and Exe alone. Therefore, according to the results of the present study, it can be concluded that curcumin supplementation and progressive endurance exercises can improve inflammatory conditions and cardiopulmonary function in obese girls with a history of corona disease. Therefore, these people can improve their body composition and general health by combining endurance activity and curcumin supplement consumption.

Ethical Considerations

This research was conducted after ethical approval with the ethics ID IR.ILAM.REC.1402.003 from the secretariat of the

National Ethics Committee based at Ilam University and with the clinical trial ID IRCT20221213056809N2.

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Conflict of Interest

None to declare.

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