Research Paper

Effect of Home-based Resistance Training on the Serum Levels of Interleukin-6 and Cortisol in Recovered Women from COVID-19: A Pilot Study

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ABSTRACT

Background: COVID-19 is the most common cause of increased levels of cortisol and interleukin 6 (IL-6). The purpose of this pilot study was to examine the effect of home-based resistance training on the serum levels of IL-6 and cortisol in recovered women with COVID-19.

Materials and Methods: A pilot randomized controlled design was used. Twenty middle-aged women who recovered from COVID-19 were assigned randomly to the intervention and control groups. The height, weight, and body mass index (BMI) of all participants were measured both before and after the intervention period. Blood samples were taken in the morning to determine the serum levels of IL-6 and cortisol. Fitness (estimated VO_2 max) was assessed with a 1.6-km walking test. The intervention group followed eight weeks, three days per week, 1 hour per day of thera-band resistance training and body weight training at home. The control group did not participate in any sports program.

Results: At baseline, there were no significant differences between both groups in the mean IL-6, and cortisol levels (P>0.05). After the intervention, the mean IL-6 and cortisol levels significantly decreased in the intervention group (P<0.05).

Conclusion: Eight weeks of thera-band resistance band training program and bodyweight workout decreases the serum levels of cortisol and IL-6 and improves the immune system of recovered women with COVID-19. Additionally, there seem to be some indications that this training might have a positive influence on immune function. Further research in this area is highly recommended.

Keywords:
Immune system, Physical activity, Coronavirus disease 2019, COVID-19

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1. Introduction

In December 2019, the outbreak of a new type of acute viral respiratory disease (pneumonia) was reported in central China and the number of people infected with it increased rapidly. Specialists named the disease coronavirus disease 2019 (COVID-19) and identified its origin as a virus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 is a global health pandemic that has affected the physical and mental health of many people [1]. Coronavirus severely affects the immune system and many tissues, especially the lungs, by causing cytokine storms in the body [2]. Coronaviruses induce an increase in cytokines (interleukin 1 (IL-1) and IL-6), and inflammatory chemokines (chemokine (C-C motif) ligand 2 (CCL2) protein [3].

Four peptides called "cytokines" circulate in the blood and are usually associated with an immune response to infections, and two of them, IL-6 and tumor necrosis factor-α (TNF-α), can determine the severity of symptoms, complications, and risk of death in patients with COVID-19 [4]. The mechanisms of the immune system against this virus are not yet well understood. Inflammatory conditions that develop during this disease appear to increase apoptosis, fatigue, aging, and aging of immune system cells [5].

As a compensatory mechanism, the body increases serum levels of IL-6, TNF-α, and cortisol to counteract COVID-19. The results of the study by Lio et al on 69 patients showed that baseline serum levels of IL-6 were associated with the severity of COVID-19. A significant increase in basal IL-6 is positively correlated with maximal body temperature during hospitalization and basal increase in C-reactive protein (CRP), lactate dehydrogenase (LDH), ferritin, and D-dimer, and dynamic changes in IL-6 can serve as a marker for disease monitoring in patients [6].

On the other hand, the psychological pressure created in society and the fear and stress caused by COVID-19 through the production of cortisol in the body also cause a decrease in the function of the immune system [7]. Elevated cortisol is an important part of the body's stress response that causes adaptive changes in metabolism, cardiovascular function, and immune regulation [8]. Previous research has shown that there is a very close relationship between stress and immune system parameters. During stress, cortisol is constantly active, which can increase negative gastrointestinal symptoms and weaken the immune system. Cortisol levels are significantly higher in patients with COVID-19 than in those without the disease [8, 9].

According to the stages of COVID-19, after initial medical and supportive treatments, rehabilitation through exercise is suggested, which can play an important role in the recovery and health of patients after treatment [10]. Evidence suggests that moderate-intensity exercise, due to its anti-inflammatory effects as a drug, activates mechanisms that can be effective in curing many diseases [11-13].

The American College of Sports Medicine (ASCM) recommends strength training programs that do not require equipment, such as squats, sit-ups, stretches, lunges, and yoga exercises, which can be very helpful [14]. Thera-band resistance exercise as one type of resistance training is easy to do and safe. Elastic band training (EBT) serves as a safe and effective progressive overload method that does not require special infrastructure and can be used even at home to activate all muscle groups, as well as a time-saving method for Improving muscle strength and functional capacity throughout life [15].

This study was designed to investigate the role of modalities that improve and positively influence immune system function to counter the viral load of COVID-19. To the best of our knowledge, no study has investigated the effect of home-based resistance training exercises on women who recovered from COVID-19. Therefore, this study aimed to investigate the effect of eight weeks of thera-band resistance exercise and body weight on the serum levels of cortisol and IL-6 in recovered women with COVID-19.

2. Materials and Methods

Study design and participants

A pilot randomized controlled design was used. Twenty female volunteers who had recovered from COVID-19 two months before their enrollment in the study were included. All subjects received an explanation of the purpose, methods, potential risks, and benefits of the study, and written informed consent was obtained from all participants. Participants' ages ranged from 35 to 50 years old. They were divided randomly into two control (n=10) and intervention (n=10) groups.

We compared changes at baseline and improvements between the intervention and control groups on serum levels of cortisol and IL-6 levels after eight weeks of a home-based resistance training program. Subjects were recruited from Isfahan City, Iran, upon invitation through online advertisements via social media channels (Telegram, WhatsApp, and Instagram).

They received phone calls or face-to-face interviews once a week to make sure the study did not alter their physical activity. In these weekly visits, health problems, functional problems, as well as drug use were recorded by a trained researcher. Exclusion criteria were active smoking, history of heart disease, recent fracture or orthopedic surgery within the past six months, neurological or orthopedic pathological conditions potentially affecting movement, and kidney or liver failure. The intervention group performed an exercise intervention, and the control group was instructed not to perform any kind of physical activity and to follow habitual daily routines.

Blood sample collection

Blood samples were taken in the morning (8:30-9:30) by collecting 10 mL of venous blood. Participants were asked to stop any exercise for at least 24 hours before blood sampling. The blood was centrifuged at 3000 rpm for 15 min at 4°C. We measured serum levels of IL-6 and cortisol and analyzed their levels with ELISA Pars kits made in Iran.

Intervention

The subjects of the intervention group were instructed and familiarized with the execution of the resistance training protocol by experts in exercise prescription, before the beginning of the experimental procedures. The first session of the resistance-training program was performed at home with the presence and supervision of the investigators to verify the subjects' independence to exercise execution. Therefore, the intervention group performed home-based resistance thera-band training with an elastic band and body weight exercise at home in three sessions a week and 1h a day for eight weeks.

The exercises were performed according to the guidelines of the ACSM recommended for patient resistance training. In addition, the subjects were trained to control exercise intensity using the targeted number of repetitions (TNRs) and the OMNI-resistance exercise scale (OMNIRES) in the first two sessions [16, 17]. The thera-band resistance bands were used for each movement determining maximal strength with one repetition maximum method in three colors (yellow, red, and blue) as three sets and 15 repeats. The elastic bands were used as yellow for one and two weeks, red for three and five weeks, and blue for 6six and eight weeks. Each resistance training with an elastic band (35-40 minutes) was performed in a controlled and slow manner for each of the six muscle groups (legs, back, abdomen, chest, shoulder, and arm). The training session ended with a 5-minute cooldown.

In order to adhere to the principle of overload after every two weeks of training, the intensity of exercise was increased by using elastic band discoloration. Accordingly, they were changed from yellow to red and blue. In addition, training volume increased with increasing the number of sets from one to two sets and progression-based [5, 13]. The body weight training program consisted of squats, lunges, sit-ups, seated cable rows, push-ups, pull-ups, planks, and step-ups, one set of 12 to 15 repetitions, 20 bodyweight squats, ten push-ups, ten walking lunges (each leg), ten Dumbbell rows (using a milk jug or other weights), and 15 seconds of plank. It should be noted that all training programs were performed daily between 8:00 and 12:00 AM.

Statistical analysis

All values are expressed as Mean±SE. The measurement values were normality distributed in both groups evidenced by the Shapiro-Wilk test. The Levene's test was used to determine the homogeneity of variance. Analysis of covariance (ANCOVA) was used to evaluate the effect of resistance training on serum IL6 and cortisol levels. The significance level was set at $P<0.05$. SPSS software, version 21 was used for statistical analysis.

3. Results

At baseline, there were no significant differences between the groups in age, height, and body mass index (BMI) ($P>0.05$). The demographic and physical characteristics of participants at baseline are shown in Table 1.

Within-group comparisons showed that IL-6 levels significantly decreased in the intervention group after eight weeks of treatment ($P<0.05$), while it showed no significant differences in the control group ($P>0.05$). Within-group comparison results are shown in Table 2.

Between-group comparisons showed that at baseline, there were no significant differences between groups in IL-6 and cortisol levels ($P>0.05$). IL-6 and cortisol serum levels significantly decreased in the intervention group compared to the control group after eight weeks of intervention ($P<0.05$). The between-group comparisons are shown in Table 3 ($F=11.26$ and $P=0.004$).

4. Discussion

Our study showed that eight weeks of home-based resistance training (thera-band resistance and body weight exercise) significantly decreased serum levels of IL-6 and cortisol in the intervention group compared to the control group.

Table 1. Physical characteristics of the study samples (n=20)

Variables	Groups	Mean±SE	P
Age (y)	Intervention	35.20±2.53	0.058
	Control	34.20±2.55	0.057
Height (cm)	Intervention	165.80±1.65	0.055
	Control	163.90±1.84	0.056
Weight (kg)	Intervention	66.50±2.07	0.057
	Control	68.60±2.52	0.056
BMI (kg/m^2)	Intervention	23.46±0.35	0.054
	Control	23.54±0.33	0.055

ImmunoRegulation

Table 2. Independent repeated measures ANCOVA on IL-6 and cortisol levels at baseline and eight weeks after the intervention in the groups

Variables	Groups	Baseline	Mean±SE	P*
Cortisol (mcg/dL)	Intervention	Baseline	24.54±0.15	0.015
		After intervention	23.95±0.13	0.016
	Control	Baseline	22.39±0.12	0.013
		After intervention	22.45±0.14	0.014
Interleukin-6 (pg/mL)	Intervention	Baseline	28.26±0.25	0.011
		After intervention	27.06±0.18	0.012
	Control	Baseline	8.01±0.23	0.014
		After intervention	8.14±0.24	0.017

*Statistically significant.

ImmunoRegulation

Table 3. ANCOVA results for post-test corrected from pre-test for the intervention and control groups, respectively

Variables	Source of Variance	Sum of Squares	Mean Square	F	P	η^2	Test Power
Interleukin-6 (pg/mL)	Covariate	7.29	7.29	0.001	0.99	0.001	0.05
	Effect of experiment	5.71	5.71	11.26	0.004	0.398	0.88
	Error	8.62	0.50				
Cortisol (mcg/dL)	Covariate	0.005	0.005	0.02	0.876	0.001	0.05
	Effect of experiment	10.91	10.91	50.51	0.0001	0.748	0.99
	Error	3.67	0.21				

ImmunoRegulation

This study is unique as it is the first clinical trial that demonstrated that home-based resistance training could be an adjunct intervention for women covered with COVID-19 to enhance their immunity. This observation is in agreement with the findings of previous studies [18-20] on adolescent male runners who had completed a 21-km run and also adult athletes after endurance exercise [21]. A recovery has also been reported by some studies [22, 23]. The decrease of serum cardiac troponin I (cTnI) levels supports the previous notion that exercise-induced release of serum cardiac troponins in athletes with less clinical suspicion of a cardiac problem might simply indicate transient cytosolic leakage propagated by membrane damage, rather than cardiomyocyte necrosis [21]. Thus, it might be argued that after a youth soccer game, a small but statistically significant increase in cTnI may occur, which may not necessarily be of clinical significance or indicate risk, at least since prolonged values are within the normal range. However, the results of some previous studies have shown that exercise decreases the risk of duration and severity of various viral infections, including COVID-19, and directly strengthens the immune system [22, 24]. The results of some other studies that compared serum levels of IL-6 between athletes with high and moderate-intensity exercise programs during the COVID-19 epidemic showed a significant decrease in the moderate-intensity exercise group.

Our results align with previous research in this area [25, 26]. Soori et al. [27] reported that combined exercise decreases IL-6 levels [27]. According to Nieman and Sakaguchi [28], adequate participation in moderate to vigorous physical activity (MVPA) is linked to a lower likelihood of experiencing acute respiratory infections (ARIs) [28]. Filgueira et al. [29] showed that a supervised exercise protocol for 12 weeks could alleviate inflammation in adults after COVID-19 compared to an unsupervised home exercise protocol [29]. However, Libardi et al. (2012) and the study of Khajeh Landi et al. (2020), which did not report a significant decrease in serum levels of IL-6 [30, 21].

It has been shown that the anti-inflammatory response induced by regular exercise activity is mediated by skeletal muscle contraction through the release of muscle-derived cytokines [31]. Myokine IL-6 suppresses the secretion of pro-inflammatory cytokines in several tissues and helps to create an anti-inflammatory environment for several hours after exercise [18]. Another finding of this study showed that eight weeks of resistance training with Thera band and body weight at home had a significant effect on cortisol levels in women recovering from COVID-19 and decreased cortisol levels. The findings of Yar Ahmadi et al. [32], Taha et al. [33], Gavan et al. [16], and Tan et al. [17] are in line with the results of this part of the present study. Yarahmadi et al. [32] showed that six weeks of badminton practice had a significant effect on reducing basal cortisol levels and subsequently reduced stress in non-athlete female students [32]. Ramezani et al. [9], in their research on the role of anxiety and cortisol in patients with coronary artery disease, showed higher levels of cortisol and anxiety and depression in patients who died of coronary artery disease compared to survived patients [9]. They found that anxiety and depression were correlated with patients' outcomes and psychological interventions could improve the mental health of vulnerable groups during coronary heart disease [9].

Taha and Mounir [33] assessed the acute response to cortisol at different intensities of resistance training in the elderly and showed that cortisol levels in the low- and moderate-intensity training groups had a significant decrease. They concluded that an acute period of low-to-moderate-intensity exercise is more effective in reducing cortisol and stress in the elderly than an acute period of high-intensity resistance exercise [33].

Güven et al. (2021) showed a significant positive relationship between total serum cortisol levels and mortality in patients with coronary heart disease and high levels of cortisol are associated with disease severity and mortality of coronary heart disease [16].

Tan et al. (2020) reported that cortisol levels were higher in patients with coronary artery disease than in healthy individuals. Also, high levels of CRP in these patients indicate the severity of the disease [17].

In general, in people without stress, cortisol is released on a daily basis, and its levels peak in the early morning and late evening. Any acute illness or trauma leads to a change in the daily secretion of cortisol. Increased cortisol secretion due to acute stress in COVID-19 is an adaptive mechanism in the body that regulates cardiovascular, immune, and metabolic functions [34]. The results of some studies suggest that resting levels of cortisol in the exercise program can occur without significant changes in adrenocorticotropic hormone (ACTH) levels. This suggests that ACTH receptors in the adrenal gland may be down-regulated. The decrease in exercise-induced cortisol response is also enhanced by a decrease in ACTH responses [35].

The findings of the present study showed that in people recovering from COVID-19 following resistance training, the level of catabolic hormones decreases, which can lead to increased protein synthesis and the creation of a favorable anabolic environment. Since the level of cortisol in the blood is related to muscle mass and in this study, strength resistance exercises with stretching have been used, it can be expected that the subjects' cortisol levels will decrease after the intervention.

5. Conclusion

We provide evidence that eight-week home-based thera-band resistance training with stretching and body weight can reduce serum levels of IL-6 and cortisol in recovered women from COVID-19. People who recover from COVID-19 can improve their immune system. Therefore, we recommend this kind of activity to COVID-19-covered women. Other factors of the immune system and systemic inflammation in adaptation to exercise activities in COVID-19 patients should also be examined.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of Shahed University (Code: IR.SHAHED. REC1400.142).

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Authors' contributions

Conceptualization, methodology, investigation: All authors; Methodology, writing Nahid Talebi, Zohreh Shah Mansori, Fatemeh Hassani; Funding acquisition and resources: Nahid Talebi; Supervision: Nahid Talebi and Fatemeh Hassani.

Conflicts of interest

The authors declared no conflict of interest.

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