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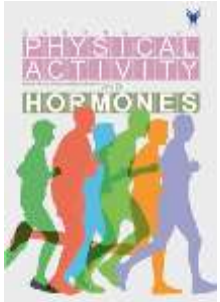

The effect of aerobic-resistance exercise on body composition, physical fitness, resting metabolism rate, serum cortisol, and leptin of children with hypothyroidism

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Abstract

Introduction: Hypothyroidism is a common condition and is caused by thyroid hormone deficiency. This makes your metabolism slow down. So, the purpose of this study was to compare the effect of aerobic-resistance training on body composition, physical fitness, resting metabolism rate (RMR), cortisol, and leptin of children with hypothyroidism.

Material & Methods: This research was a clinical trial with a statistical sample of 20 volunteers with hypothyroidism were randomly divided into two equal groups of exercise (EG) and control (CG). Before and after 8 weeks of resistance aerobic exercise (75 min, 3 session/week). Serum cortisol, leptin and body composition indices, and physical fitness components were measured. Data analysis was done through SPSS software version 26.

Results: The results of the present study showed that 8 weeks of aerobic-resistance training caused a significant decrease in waist-to-hip ratio (WHR), increased anaerobic power, agility, balance, and muscle endurance ($P<0.05$), but no significant were seen on resting metabolism rate (RMR), serum cortisol, TSH, T4 and leptin of female with hypothyroidism ($P<0.05$).

Conclusion: It seems that aerobic-resistance training may improve some of physical fitness and body composition of females with hypothyroidism, but it has no effect on RMR, serum cortisol, thyroid hormones, and leptin of patient.

1. Introduction

Primary hypothyroidism is the second most common endocrine disease worldwide after diabetes mellitus and is caused by thyroid hormone deficiency (1). Hypothyroidism is a pathological condition that is generally characterized by inadequate levels of serum TSH and normal levels of T3 and T4 hormones and in more severe conditions with deficiency of T3 and T4 hormones. The prevalence of this disease in children and adolescents has been less than 2%. Adequate concentration of thyroid hormones in childhood and adolescence is essential for normal growth and in the presence of thyroid disorders and untreated with drugs causes metabolic disorders and deterioration of growth in them (2-5).Some evidence suggests that moderate increases in TSH levels may be associated with mild metabolic disorders in childhood (6). On the other hand, hypothyroidism may lead to increased visceral fat in children (3). In this regard, the body composition of hypothyroid children showed that TSH levels improved following weight loss and lifestyle changes (7).Exercise is used as a treatment aid in many hormonal disorders today. Probably a short-term period of concurrent aerobic-resistance training may improve blood glucose hemostasis and body composition of adolescent girls with hypothyroidism (8). Some studies have suggested that exercise activities cause a decrease in some thyroid hormones (2). However, the effect of exercise on reducing thyroid gland hormones is unclear. In this regard, the contributing factor is the association between glucocorticoids' response to exercise activity and circulating thyroid hormones (9).

Cortisol is the most important glucocorticoid hormone that inhibits thyroid function in the hypothalamus-pituitary-thyroid axis (10). Many studies have pointed to the importance of cortisol as a marker of the stress hormone. On the other hand, changes in levels of this hormone are influenced by factors such as age, pubertal status, gender and type of exercise (11). So that one of the most important stimulants of this hormone secretion is strenuous physical activity. In this regard, Copeland et al. (2002) reported a decrease in cortisol following resistance and endurance training in a study of healthy individuals (12). In contrast, Alvarez et al. (2017) stated that performing resistance training with a 70% intensity of one repetition maximum, does not cause a significant change in cortisol (13).

The combination of endurance and resistance training in different forms as combined training has been considered by researchers as a training method. In this regard, researchers have investigated the effectiveness of simultaneous implementation of resistance and endurance training on basal metabolism, muscle fitness and endurance. In most of these researches, improvements in aerobic power due to combined training have been reported compared to endurance training and increased muscle strength in resistance training. Skeletal muscle as the target tissue of thyroid hormones can show a different function in hypothyroidism than exercise activity. Many studies show the effect of exercise in healthy children and adolescents and indicate that aerobic and resistance exercises can affect physical fitness in these individuals (7, 11-15).

Another factor regulating thyroid hormones is leptin. These hormones affect leptin-expressing genes to control its production or secretion (14). On the other hand, cortisol itself increases leptin (4). It has been reported that physical activity and exercise can affect leptin secretion by reducing fat stores and changing the activity of the hypothalamic-pituitary-adrenal axis. However, recent studies have shown that the behavior of leptin hormone and its secretion-regulating hormones may differ from intensity and intensity of exercise (5), body composition (12), and gender differences (3). In this regard, Rojo et al. (16) conducted a study on obese children aged 8-12 years and found that 12 weeks of aerobic exercise did not affect blood leptin levels. In addition, Palakis and colleagues (2010) also found that 8 months of moderate-intensity walking and running did not affect serum leptin in normal-weight and overweight children (17).

According to our knowledge, very little research has been done on the effects of exercise on patients with thyroid disorders, especially hypothyroidism (11, 18, 19). therefore, the present study was designed to investigate the effect of eight weeks of combined aerobic-resistance training on cortisol, leptin, and physical fitness indices in children with hypothyroidism.

2. Materials and methods

2.1. Sample

This clinical trial was registered in the Clinical Trial Registry Center with IRCT20150531022498N26 number. This study was conducted by the Ethics Committee, Rasht Branch, Islamic Azad University with IAU (RASHT. REC.1395.59). Among 104 children with hypothyroidism referred to 17 Shahrivar Hospital in Rasht, 20 patients (age 8-15 years) volunteered to participate in this research, and were randomly divided into two equal groups: exercise (EG) and control group (CG).

2.2. Aerobic-resistance exercise protocol

The duration of the exercises was 75 minutes. The exercise program started with 10 minutes of warm-up including slow running with 40-50% of the maximum heart rate, and active stretching exercises, then resistance exercises (25-30 min), aerobic exercises (30 Min), and Cool down (5 min) stretching exercises (Schroeder et al. (20), Table 1).

Table 1. *aerobic-resistance training program*

	Resistance exercises			aerobic exercises	
Week	**Number of sets**	**Number of repetitions**	**duration (minutes)**	**Intensity (% of maximum heart rate)**	**duration (minutes)**
1	3	13-15 rep	25-30	60-65	30
		to the point of exhaustion (40-50%1RM)			
2	3	8-10 rep	25-30	65-70	30
		to the point of exhaustion (40-50%1RM)			
3	3	8-10 rep	25-30	70-75	30
		to the point of exhaustion (50-60%1RM)			
4	3	8-10 rep	25-30	70-75	30
		to the point of exhaustion (60-65%1RM)			
5	3	10-12 rep	25-30	70-75	30
		to the point of exhaustion (50-60%1RM)			
6	3	10-12 rep	25-30	75-80	30
		to the point of exhaustion (50-60%1RM)			
7	3	10-12 rep	25-30	75-80	30
		to the point of exhaustion (60-65%1RM)			
8	3	10-12 rep	25-30	75-80	30
		to the point of exhaustion (60-65%1RM)			

2.3. Measuring Instruments

To measure participants' weight, the Beurer digital scale (Germany) was used with an accuracy of 0.1 g, and the height of the subjects was measured using the Sohnle Wall stadiometer (Germany). Body mass index (BMI) was calculated by dividing weight (kg) by square height (m2). Waist and hip circumferences were measured with a flexible, nonelastic band and were defined as the smallest abdominal girth between the lowest rib and the upper anterior iliac spine (waist) or the horizontal measurement at the maximal buttock circumference (hip), respectively. The researchers used the Standing Stork Test to describe the static balance ability. %BF is obtained as a %BF predicted by the Slaughter equation (21). For measuring agility, the 4×9 meters agility test was used to measure the ability to change the direction of movement of the body during running, and the sit-down test was used to measure muscle endurance.

Blood samples were taken before and after 8 weeks of intervention. The concentrations of Leptin (Zellbio, GmbH, Germany- Diaclone, GmbH, and French), and cortisol (Diametra Diagnostic, Italy/EU) hormones were determined by a colorimetric competitive enzyme-linked immunosorbent assay (ELISA) method. The intra-assay coefficient of variation and sensitivity were 6.3%, 0.2 ng/Ml for leptin, and cortisol was ⩽ 15%.

Shuttle Run test was used to measure maximum oxygen consumption (VO2 max). The test consists of 21 stages and is run as round-trip shuttles on a 20-meter track. The validity of this formula for children and adolescents is reported to be 0.71. The VO2max level of the subjects was evaluated using the following formula:

$VO_{2max} = 31.025 + 3.238\ X - 3.248A + 0.1536\ A.$

X: Shuttle speed traveled, A: age in years.

Anaerobic power was measured using the RAST test. This test consists of 6 stages of 15-meter running with 10-second resting intervals. The validity of this test was shown for children (37). The formula then calculated the anaerobic power in each sprint:

Anaerobic Power = (Body Mass 3 ×Distance2)/Time3.

The RMR was then estimated using standard equations of Mifflin-St Jeor (Mifflin et al., 1990) equations:

Men: (10 × weight in kg) + (6.25 × height in cm) - (5 × age in years) + 5.

Women: (10 × weight in kg) + (6.25 × height in cm) - (5 × age in years) - 161.

2.4. Statistical Methods

Statistical analyses of data obtained before and after the exercise training were performed with "SPSS for Windows Version 26.0" software. the normality of data distribution was determined by the Shapiro-Wilk test. A paired t-test was used to compare the pre and post-exercise training data of the study groups and an independent t-test to compare the groups. Statistical significance level was chosen as p values less than 0.05.

3. Results

The descriptive characteristics of the two groups are presented in Table (2).

Table 2. *Describe the characteristics of the subjects with compare pre and post test*

	EG			CG		
Age (years)	12.40±1.71			11.80±2.20		
Height(cm)	154±0.03			153±0.04		
	Pre-test M±SD	**Post-test M±SD**	**Paired t-test sig**	**Pre-test M±SD**	**Post-test M±SD**	**Paired t-test sig**
Weight (kg)	61.80±3.64	60.25±3.79	.03*	62.80 ±4.46	63.70±4.46	.04*
BMI (kg/m2)	26.84±2.34	25.28±0.89	.049*	26.02 ±4.00	26.92±2.03	.45
WHR (ratio)	0.76±0.10	0.76±0.10	.01*	0.76±0.04	0.76±0.04	.08
Subcutaneous fat (mm)	38.03±4.08	32.53±5.80	.01*	34.96 ±7.36	34.10±5.91	.69
aerobic power (ml/kg/min)	38/47±3/72	38/71±2/80	.06	±3/74 39/23	/24±3/75 39	.90
anaerobic power (watt)	34/20±29/903	3/00±30/88 64	.01*	19/98 3/30± 50	1±23/29 349/0	.37
Agility (Second)	21/10±1/43	23/02±1/74	.01*	±2/97 21/06	/42±3/12 21	.38
Balance (Second)	14/40±3/62	17/40±3/27	.01*	±3/33 15/60	/30±4/08 15	.43
Muscular endurance numbers/) (min	15/90±9/46	17/80±8/28	.01*	±4/90 16/50	/30±5/01 16	.34
RMR Kcal/ day	11/57±67/25 38	1/97±21/34 174	.04*	93/33 1/20± 154	1±67/50 1160/8	.68
Cortisol (micrograms /dl)	14/65±5/56	15/02±8/64	.85	±2/06 17/68	/08±4/38 18	.77
leptin (ng/ml)	44/20±10/22	4/57±20/39 0	.46	18/13 3/31± 1	9±14/09 28/6	.59
TSH, μu/mL	4.17 ± 1.8	6.31 ± 5.2	0.29	4.99 ± 2.54	5.27 ± 2.36	0.55
T4, μg/mL	6.89 ± 1.07	7.58 ± 0.9	0.18	6.37 ± 1.29	7.31 ± 2.3	0.14

EG: Experimental group, CG: Control group, RMR: Resting Metabolism Rate, WHR: Waist to Hip Ratio, mm: millimeter, ml: milliliter, min: minute, dl: deciliter

The results of the paired t-test in experimental group showed decrease in weight, BMI, WHR, and increase in anaerobic power, agility, balance, muscular endurance, and RMR. However, no significant changes were observed in leptin, cortisol, TSH, and T4 and aerobic power of the samples. During this period, no significant changes were observed in the control group.

Table 3. *Independent t-test results to compare the post-test of the control group and the training group*

Indicator	Difference of means	F	t	Sig
BMI ($kg/hight^2$)	0.81	2.35	0.55	0.58
WHR ratio	0.004	5.68	2.19	0.04*
Subcutaneous fat (mm)	0.74	3.57	1.87	0.07
aerobic power (ml/kg/min)	0.24	3.73	1.88	0.07
anaerobic power (watt)	-22.00	0.001	-9.98	0.01*
Agility (Second)	1.44	0.38	2.56	0.01*
Balance (Second)	-3.30	0.01	-5.70	0.01*
Muscular endurance (numbers/ min)	-2.10	5.44	-4.20	0.01*
RMR Kcal/ day	30.41	1.65	1.42	0.17
Cortisol (micrograms /dl)	0.03	0.24	0.01	0.99
leptin (ng/ml)	3.25	6.95	0.44	0.44

***Significant difference between groups**

EG: Experimental group, CG: Control group, RMR: Resting Metabolism Rate, WHR: Waist to Hip Ratio, mm: millimeter, ml: milliliter, min: minute, dl: deciliter

According to the results, compared to the control group, a significant decrease in WHR, and improve in anaerobic power, Agility, Balance, and Muscular endurance was observed in the experimental group ($p<.05$).

4. Discussion

The results of the present study showed that despite no change in thyroid hormones, leptin, cortisol, RMR, and aerobic power (VO2 max), eight weeks combined exercises had a positive effect on some indicators of physical fitness, including anaerobic power, agility, balance, muscular endurance WHR, and muscular endurance of children with hypothyroidism. In line with the present results, Lee and his colleagues showed that simultaneous (aerobic-resistance) circular exercises (70-80% of 1RM) and aerobic exercises (60-80% of HR max) can improve the anaerobic capacity of obese children (12-14 years). However, contrary to the results of the present study, they showed that these exercises were also effective in improving the aerobic capacity of children (22). In addition, Cao et al. (23) compared football training and HIT for 12 weeks in obese boys aged 11 to 13 years, which showed that despite similar changes in body mass and composition in both groups, upper body anaerobic power in The soccer group was more of a HIT workout. They attributed the possible increase to reduced body mass and more jumping and explosive arm movements compared to HIIT exercises, which can improve upper body performance. Regarding the improvement of anaerobic power, it can be said that sports exercises increase power by using more movement units and by increasing the explosive abilities of muscles. In the review of previous studies, it has been shown that neuromuscular adaptations with better activation and co-contraction of cooperating muscles, as well as increasing the inhibition of opposing muscle activity, are likely to contribute to increasing anaerobic power (24). Therefore, in our study, the improvement of anaerobic power through combine resistance-endurance exercises may be due to increased motor unit and neuromuscular adaptations. Regarding the improvement of muscular endurance, it can be mentioned that muscular endurance depends a lot on the ability of the heart and blood circulation and the ability of the lungs, and with more blood circulation in the active muscle, the muscles of that area will have more endurance. Because as a result of exercise, the required energy is provided faster and waste materials from metabolism are also transported out faster (25). As a result, there is a possibility that with the improvement of physical fitness indicators such as anaerobic capacity following aerobic and resistance sports, muscular endurance will also increase (26). Regarding agility, Soares et al. (27) compared football training and HIT for 12 weeks in obese boys (age 11 to 13 years), which showed a greater increase in agility in the soccer group compared to HIT in these people. They considered the reason for the superiority of soccer training to be the nature of this training in agility performance. On the other hand, as a result of aerobic and resistance exercises, the neuromuscular system increases, which causes the sympathetic nervous system to function better (28).

In the present study, the amount of VO2max did not change. In line with the present study, Swamy (2013) found in a 6-month study in women aged 45-65 with hypothyroidism that aerobic exercise with an intensity of 60-75% of the HR max improves the VO2max (29). On the other hand, in another study in 43 adolescent boys aged 12-16 years old, it was shown that both aerobic exercises for 40-60 minutes and resistance exercises until exhaustion, for 12 weeks, both improve the VO2max (30). It has also been shown that 12 weeks of aerobic exercise in healthy obese children aged 8-12 years with an intensity of 80% of the HR max for 30-60 minutes has improved the VO2max (31). It seems that the reason for the difference in the obtained results can be attributed to the difference in age, the length of the training period, the physical condition of the subjects, adverse effects of hypothyroidism on organs, and the duration of the training. In justifying the lack of improvement in VO2max, it seems that a program that includes both types of aerobic and resistance exercises causes a challenge in the muscle fibers. Those muscle fibers that are called in one of the types of activities, face a dilemma and must try to find a compromise with oxidative stimuli to increase their aerobic performance or at the same time with stimuli from strength training. Find adaptation to increase their contraction force by increasing contractile protein. Therefore, this process may cause disturbances in simultaneous exercises. Other reasons for not improving the VO2max can be attributed to their lower growth level and the body composition of these patients (9, 10, 31). Since children with hypothyroidism have a lower level of physical fitness, their physical performance is low due to their inactive lifestyle. As a result, the possible reasons for the lack of effect of these exercises on aerobic power can be weak physical fitness, the type of training protocol, adverse effects of hypothyroidism on organs and the lack of nutritional control.

The results of our research showed that resting metabolism was not affected by exercise training. Consistent with our study, Church et al. (32) showed that 40 minutes of high-intensity resistance training (10 repetitions in 2 sets of 8 movements with 80% of 1RM) 19 hours after exercise did not have a significant difference in energy consumption, in this study, which was conducted on healthy women, RMR measurements were evaluated 25 weeks after resistance training. In contrast to the present study, Yu et al. (33) showed that the amount resting metabolism even 21 hours after resistance exercise has increased by about 10% compared to the previous day. In the Yu et al. (2021) study, the intensity of the exercises was 50-60% of 1RM.

Our results indicated no significance change in the amount of cortisol. The results of the present study are in line with the research of Rios et al., Goto et al., and West et al. It seems that the insufficient volume and intensity of the exercises and the different subjects are the reasons for the lack of change in cortisol. However, Copeland et al. (2002) in a study on 30 healthy trained women aged 16 to 69 years, after both endurance and resistance training, reported a decrease in cortisol following resistance and endurance training. The decrease in cortisol levels in Copeland's research can be seen as a reflection of the hormone's circadian change and its increase before the start of exercise in response to a specific blood sampling method. In addition, the decrease in cortisol after exercises is probably due to the increase in the removal of cortisol from the bloodstream or the decrease in the activity of adrenocorticotropic hormone. The changes of serum cortisol depend on the type, intensity and duration of activity, so that one of the most important stimuli for the release of this hormone is intense physical activity. Also, increasing the central body temperature increases the secretion of cortisol. Therefore, it is possible that the increase in cortisol following endurance training is due to hypoxia or an increase in core body temperature that is not caused by resistance training (14-16, 34).

In our research, it was found that eight weeks of training has no effect on serum leptin level. In line with the results of the present research, in a research of 12 weeks of aerobic training and interval training, none of them had an effect on blood leptin levels. The most important function of leptin is to regulate energy consumption. leptin hormone changes are not only dependent on body fat mass and other factors such as hormonal changes, diet, intensity and type of exercises are involved, and the complexity of leptin hormone behavior is related to the type of exercise, its intensity and how Applying these exercises will be effective. One of the most important limitations of this study was puberty, since puberty can be a factor affecting the secretion of hormones, a similar study should be conducted comparing children before and after puberty. The length of the study is another limitation, many changes in hormones usually occur over a long period of time, and in our study, the 8-week intervention determined based on previous studies may not be enough to improve the factors. In addition, due to the difference in the response of the body in healthy people and those with thyroid disorders and the interaction of hypothyroidism with leptin, cortisol and other factors, therefore, it is suggested that future research compares the effects of exercise training on thyroid hormones and hormones affecting metabolism among patients with hypothyroidism and healthy people.

5. Conclusion

Our results showed that concurrent aerobic-resistance training increased some indicators of physical fitness in females with hypothyroidism. However, this was not significant in cortisol, thyroid, and leptin hormones. Based on our knowledge, the current study probably the first research to determine the effects of cortisol, leptin, and changes in physical fitness in hypothyroidism children. In general, it can be concluded from this study that the short period of combined aerobic-resistance training provides beneficial adaptations such as BMI reduction and improvement of some physical fitness indices including anaerobic power, agility, balance and muscular endurance in children with hypothyroidism.

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