Treadmill and Ergo cycle Exercises Increase Insulin-Like Growth Factor-1 Levels in Obese Female

Adi Pranoto,[1] Zakaria Sendy Wardana,[2] Misbakhul Munir,[2,3] Hayuris Kinandita,[2,3] Desiana Merawati,[4] Sugiharto,[4] Purwo Sri Rejeki[2,3*]

[1]Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

[2]Sport Health Science, Faculty of Medicine Universitas Airlangga, Surabaya, Indonesia

[3]Department of Physiology, Faculty of Medicine Universitas Airlangga, Surabaya, Indonesia

[4]Sport Science Department, Faculty of Sport Science State University of Malang, Malang, Indonesia

Abstract: Obesity increases the risk incidence of metabolic disorders, including insulin resistance, causing an increase in blood glucose. Physical exercises, mediated by Insulin-Like Growth Factor-1 (IGF-1), contribute to improving insulin sensitivity and lowering blood glucose. IGF-1 increases insulin sensitivity and maintains glucose homeostasis by activating the Phosphoinositide 3-Kinase (PI3K) pathway and translocation of Glucose Transporter Protein-4 (GLUT-4). The purpose of the study was to analyze the effect of a moderate-intensity treadmill and ergo cycle exercises on the increasing IGF-1 levels in the obese female. This research was a true experimental study with the randomized pretest-posttest control group design. Subjects were 27 obese females aged 18-22. Subjects were randomly divided into three groups, that is CONT (n=9, group without intervention), ERGO-Exercise (n=9, Ergocycle Exercise), and TREAD-Exercise (n=9, Treadmill Exercise). Interventions for TREAD-Exercise and ERGO-Exercise were conducted continuously for 30 minutes, from 07.00-10.00 a.m. Blood samples were taken pre-exercise and 15 minutes post-exercise. IGF-1 levels were examined by the Enzyme-Linked Immunosorbent Assay (ELISA) method. Data were analyzed using ANOVA test and LSD post hoc test using Statistic Package for Social Science (SPSS). The research results showed that one session of a moderate-intensity treadmill and ergo cycle exercise for 30 minutes increases IGF-1 levels compared to the control. It is necessary to conduct advanced research to analyze chronic intervention (training) for increasing IGF-1 levels in obese females.

Keywords: IGF-1 levels, treadmill, ergo cycle, obese female

跑步机和人体工学循环运动可增加肥胖女性的胰岛素样生长因子-1 水平

摘要：肥胖会增加包括胰岛素抵抗在内的代谢异常的风险发生率，从而导致血糖升高。由胰岛素样生长因子-1（IGF-1）介导的体育锻炼有助于提高胰岛素敏感性和降低血糖。 IGF-1 通过激活磷酸肌醇 3-激酶（PI3K）途径和葡萄糖转运蛋白 4（GLUT-4）的易位来提高胰岛素敏感性并维持葡萄糖稳态。这项研究的目的是分析中等强度的跑步机和人体工学循环运动对肥胖女性中 IGF-1 水平升高的影响。这项研究是一项真正的实验研究，采用了随机的前测后测对照组设计。受试者是 27 名 18-22 岁的肥胖女性。将受试者随机分为三组，即 CONT（n = 9，无干预组），ERGO 锻炼（n = 9，Ergocycle 锻炼）和 TREAD-锻炼（n = 9，跑步机锻炼）。从上午 07.00-10.00 开始连续 30 分钟进行 TREAD 运动和 ERGO 运动的干预，在运动前和运动后 15 分钟采

集血样。通过酶联免疫吸附测定（ELISA）方法检查 IGF-1 水平。使用 ANOVA 检验对数据进行分析，并使用社会科学统计软件包（SPSS）对 LSD 事后检验进行分析。研究结果表明，与对照组相比，在中等强度的跑步机上进行一次持续 30 分钟的健身操，可以增加 IGF-1 的水平。有必要进行高级研究以分析肥胖女性中增加 IGF-1 水平的慢性干预（培训）。

关键词：IGF-1 水平，跑步机，人为周期，肥胖女性

1. Introduction

Obesity is a metabolic disease that has reached epidemic proportions [1]. Obesity is considered an epidemic, and recently, it has been a pandemic [2] and syndemic [3]. That is because obesity prevalence keeps rising from year to year[4]. It is estimated that 1.9 billion people above 18 years old suffer from obesity, 650 million are obese, 11% male, and 15% female [5]. Globally, more than a third of adult people suffer from obesity [6]. It is estimated that in 2025, obesity prevalence will become 18% male and 21% female [7]. According to [8], obesity prevalence for people above 18 years old in Indonesia was 21.8%. This number was higher than the obesity prevalence in 2013 (14.8%) and 2007 (10.5%). The high increase in obesity prevalence becomes a serious problem that will threaten human resource quality [9] and the health problem of countries worldwide [10].

Obesity is a disease that has a high risk in the incidence of a very serious health problem that will threaten the world's public health [11, 12]. It is because obesity is one of many causes of disability and early death [6, 13], not only in adult people but also in children and teenagers around the world [1, 14]. Obesity triggers various health problems, such as increased incidence of cardiovascular diseases [15], type 2 diabetes mellitus, hypertension [12], stroke, some cancers, gallstone, osteoarthritis [16], respiratory disorders [1], muscle dysfunction [17], rheumatic diseases, metabolic syndrome [18]and metabolic disorders, including insulin resistance [19]. The cause of obesity is multifactorial. However, a general factor contributing to bodyweight increase is an imbalance between energy intake and energy expenditure [20–22]. Lifestyle modification is recommended for basic management in obesity treatment [12]. Lifestyle modification with an exercise-based non-pharmacological approach is the right strategy [23, 24]. Physical exercises are considered an effective and efficient method in preventing the increase in obesity prevalence [25, 26] because they increase energy expenditure and maintain glucose homeostasis mediated by Insulin-Like Growth Factor-1 (IGF-1) [10, 17].

IGF-1, also called somatomedin C, is mostly synthesized by the liver. It is regulated by Growth Hormone (GH), which plays the main role in cell growth, cell development, and energy homeostasis [17, 27]. Physical exercise was proven to increase IFG-1 levels in acute and chronic exercises [28–30]. It is because physical exercises stimulate the brain to activate the hypothalamus [31]. The hypothalamus secretes Growth Hormone Releasing Hormone (GhRH). This GHRH is transferred to the anterior pituitary [27, 32] and then stimulates GH secretion [29, 33]. GH modulates IGF-1 secretion from the liver to the blood circulation [17, 34]. IGF-1 in the circulation will bind to Insulin-Like Growth Factor Binding Protein 3 (IGFBP3) [17]. The binding of IGF-1 and IGFBP3 will affect energy balance, decrease body weight, and free fat mass [17]. It also affects muscle strength and muscle mass [27]. Previous research showed different results. As reported in [35], acute response from moderate-intensity exercise using ergo cycle for 20 minutes increased IGF-1 serum levels significantly in 20-29-year-old men. Nevertheless, exercise with an intensity above 80% of VO_{2max} decreased IGF-1 levels significantly [18]. It was concluded in [36] that acute exercise using an ergo cycle with moderate and high intensity for 15 minutes increased IGF-1 serum levels significantly in healthy women. Low-intensity aerobic training using an ergo cycle for 60 minutes decreased significantly by 9% of IGF-1 levels [37]. According to the previously mentioned research, it is still unclear whether exercise will decrease or increase IGF-1 levels. According to the background above, the objective of this research was to compare moderate-intensity treadmill and ergo cycle exercises to the increase of IGF-1 levels in obese female teenagers.

2. Materials and Methods

2.1. Experimental Design

This research was a true experimental study with the randomized pretest-post-test control group design. Subjects were 27 females, 18-22 year old, body mass index (BMI) 25.5-32.5 kg/m^2, percentage body fat (PBF) > 30%, fasting blood glucose (FBG) < 100 mg/dL,

normal hemoglobin (Hb), normal blood pressure, and normal resting heart rate. Subjects were randomly divided into three groups, that is CONT (n=9, group without intervention), ERGO-Exercise (n=9, Ergocycle Exercise), and TREAD-Exercise (n=9, Treadmill Exercise). All subjects received information verbally or in writing about the research. Subjects filled out and signed informed consent before participating in the study. All procedures in this research were approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia (309/EC/KEPK/FKUA/2019).

2.2. Exercise Protocol

The exercise program was applied and supervised by professionals at the Fitness Center of the Malang City Health Department, East Java, Indonesia. Treadmill exercise and ergo cycle exercise were conducted with moderate-intensity 60-70% of HR_{max} for 40 minutes. It was consist of 5 minutes warming up (50-60% HR_{max}), 30 minutes core exercise (60-70% HR_{max}), and 5 minutes cooling down (50-60 HR_{max}) [38, 39]. Treadmill exercises and ergo cycle exercises were done with the continuous method at 08.00 a.m. [40, 41]. Instruments used for this intervention were treadmill (Pulsar 4.0 HP Cosmos Sports & Medical, Nussdorf-Traunstein, Germany) and ergo cycle (Monark 828 E, Version 1010 Art. No: 7950-296, Vansbro, Sweden). Monitoring heart rate during exercise using a polar heart rate monitor (Polar H10 Heart Rate Sensor, Inc., USA). This study was carried at the Physical Freshness Laboratory with a room temperature of $26 \pm 1°C$ and humidity level in the room 50-70 %. Figure 1 shows the treadmill and ergo cycle exercise program in clearer detail.
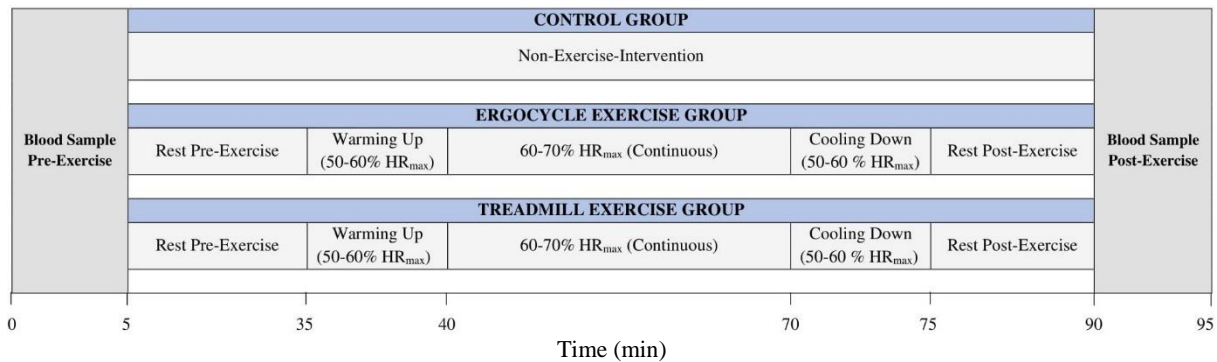

Fig. 1 Treadmill and ergo cycle exercise program

2.3. Anthropometric Measurements

The body height of the subject was measured using a stadiometer (SECA, Chino, CA). Anthropometric measurements included body weight, BMI, PBF, fat mass (FM), free fat mass (FFM), muscle mass (MM), bone mass (BM). These measurements were conducted using TANITA (Body Composition Analyzer DC3607601(2)-1604 FA, TANITA Corporation of America, Inc).

2.4. Physiological Condition

Blood pressure was measured using an automated device (OMRON Model HEM-7130 L, Omron Co., JAPAN) at the non-dominant arm three times consecutively with a 1-2 minute interval between two measurements while the participants were in a seated position. Measurement of resting heart rate (RHR) using a Pulse Oximeter (PO 30 Pulse Oximeter, Beurer North America LP, 900 N Federal Highway, Suite 300, Hallandale Beach, FL 33009).

2.5. Blood Samples

Four milliliters of blood samples were taken from the cubital vein after 12-hour overnight fasting (pre-exercise) [36, 42]. At the time of drawing blood, the subject was in a sleeping position. Pre-exercise blood samples were taken 30 minutes after the intervention [42], whereas post-exercise blood samples were taken 15 minutes after the intervention [36]. Blood samples were centrifuged for 10 minutes at 3000 rpm [17]. Serum was collected and saved at $-80°C$ to analyze IGF-1 levels on the next day [10].

2.6. IGF-1 Serum Levels Assessment

IGF-1 levels were examined using an Enzyme-Linked Immunosorbent Assay (ELISA) kit (Catalog No. E-EL-H0086; Elabscience, Inc., China, 2019) with a standard curve range 1.56–100 ng/mL and sensitivity up to 0.94 ng/mL. FBG was measured in mg/dL using ACCU-

CHEK (ACCU-CHEK® Performa, Mannheim, Germany). Hb was measured in g/dL using Easy Touch (Easy Touch GCHb, Taiwan).

2.7. Statistical Analysis

Data were analyzed by Statistic Package for Social Science (SPSS) Statistics for Windows, version 16(SPSS Inc., Chicago, IL, USA). Normality was tested using the Shapiro-Wilk test, whereas Homogeneity was measured using the Levene test. Statistical difference was tested using the Paired Sample T-Test, ANOVA, and Least Significant Difference (LSD) post hoc test. All data were presented in mean±SD. All statistical analysis was conducted using the level of significance ($P<0.05$).

3. Research Results

The basic profiles of the subjects, including age, body weight, body height, body mass index, percentage body fat, fat mass, free fat mass, muscle mass, bone mass, resting heart rate, systolic blood pressure, diastolic blood pressure, fasting blood glucose, and hemoglobin are displayed in Table 1.

Table 1 Characteristics of the subjects

Variable	CONT (n = 9)	ERGO-Exercise (n = 9)	TREAD-Exercise (n = 9)	ANOVA P-Value
Age (years)	20.78±0.97	20.33±1.00	20.89±0.78	0.415
Body Weight (kg)	73.49±7.96	68.21±7.88	71.15±7.43	0.367
Body Height (m)	1.60±0.05	1.55±0.05	1.57±0.04	0.173
Body mass index (kg/m^2)	28.49±1.57	28.244±2.39	28.61±1.67	0.918
Body fat percentage (%)	42.92±2.43	43.48±4.01	43.72±2.67	0.857
Fat mass (kg)	34.19±6.44	30.69±5.25	33.31±4.50	0.381
Free fat mass (kg)	40.67±3.78	41.08±4.40	40.99±3.20	0.972
Muscle mass (kg)	38.28±3.47	38.64±4.02	38.57±2.93	0.973
Bone mass (kg)	2.39±0.314	2.43±0.38	2.42±0.27	0.956
Resting heart rate (bpm)	75.33±7.81	74.67±6.93	78.78±7.99	0.479
Systolic blood pressure (mmHg)	114.44±5.27	115.55±5.27	112.22±4.41	0.370
Diastolic blood pressure (mmHg)	74.44±5.27	76.67±5.00	75.55±5.27	0.666
Fasting blood glucose (mg/dL)	90.22±7.90	90.67±4.21	88.22±8.23	0.737
Hemoglobin (g/dL)	15.03±0.93	14.42±1.32	14.89±1.46	0.567

Note: One way-ANOVA. Data are presented as mean±SD. CONT: Control group; ERGO-Exercise: Ergocycle exercise group; TREAD-Exercise: Treadmill exercise group.

Data in Table 1 show the means of the subjects' characteristics in each group. The ANOVA test results showed no difference in the subjects' characteristics on all variables of each group ($P>0.05$). Analytical results on pre-exercise and post-exercise IGF-1 levels are presented in Figure 2.

The level of both forms of IGF-1 was assessed pre-exercise and post-exercise. The results of the Paired Sample T-Test in the CONT group showed that there was no significant difference in the mean IGF-1 levels between pre-exercise and post-exercise (9.75±1.74 vs. 9.45±2.44 ng/mL, (p-value=0.710)) (Figure 1). However, the ERGO-Exercise group showed a significant difference in mean IGF-1 levels between pre-exercise and post-exercise (9.79±3.00 vs. 14.76±6.71 ng/mL, (p-value=0.045)) (Figure 2). Likewise, the TREAD-Exercise group showed a significant difference in mean IGF-1 levels between pre-exercise and post-exercise (9.75±2.63 vs. 14.98±2.84 ng/mL, (p-value=0.000))

(Figure 1). The results of the analysis of IGF-1 levels pre-exercise, post-exercise, and delta (Δ) post – pre in all groups can be seen in Figure 3.
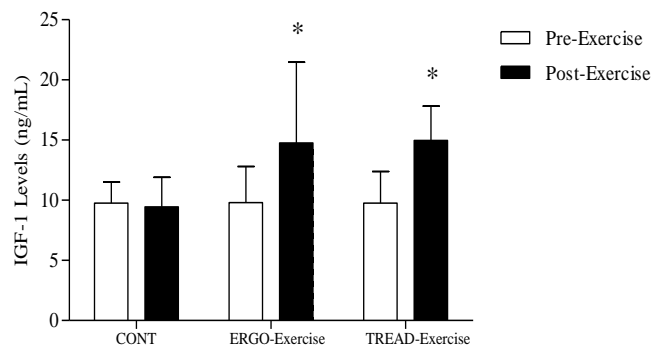

Fig. 2 IGF-1 levels pre-exercise vs. post-exercise. CONT: Control group; ERGO-Exercise: Ergocycle exercise group; TREAD-Exercise: Treadmill exercise group. Data are presented as mean±SD. p-Value was obtained using Paired Sample T-Test to compare post-exercise and pre-exercise IGF-1 levels
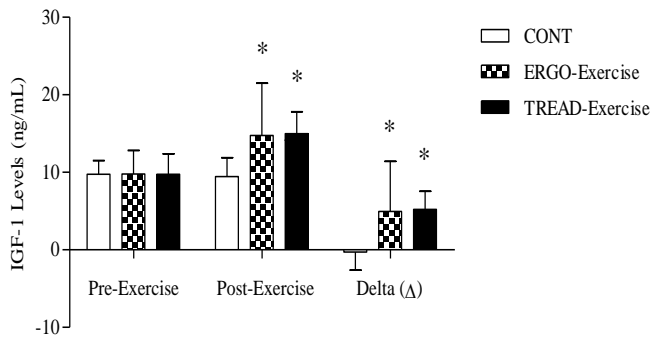*Significant vs pre-exercise ($p<0.05$)

Fig. 3 IGF-1 levels pre-exercise, post-exercise, and delta (Δ) post – pre. CONT: Control group; ERGO-Exercise: Ergocycle exercise group; TREAD-Exercise: Treadmill exercise group. Data are presented as mean±SD. p-Values were obtained using one way-ANOVA, followed by an LSD post hoc test compare pre-exercise, post-exercise, delta (Δ) post – preIGF-1 level in the group *Significant vs control group (CONT) (*p*<0.05).

Data in Figure 3 show no significant difference in pre-exercise IGF-1 levels in all groups (*P*>0.05). However, post-exercise and delta (Δ) (post – pre) IGF-1 levels differ significantly in all groups(*P*<0.05). LSD post hoc test showed that there was a significant difference between ERGO-Exercise and CONT IGF levels (p=0.018), as well as TREAD-Exercise and CONT (p=0.014); whereas, ERGO-Exercise and TREAD-Exercise IGF-1 levels showed no significant difference (p=0.919). Likewise, delta (Δ) (post – pre) showed a significant difference in mean IGF-1 levels between ERGO-Exercise and CONT (p=0.013), TREAD-Exercise with CONT (p=0.010). In contrast, ERGO-Exercise with TREAD-Exercise did not show a significant difference (*P*>0.05).

4.   Discussion

This research aimed to analyze the difference between treadmill and ergo cycle exercise to increase IGF-1 levels in obese females. The results showed no significant difference in pre-exercise IGF-1 levels among all groups (p=0.999). Therefore, the three groups in this research had the same characteristics before the treadmill and ergo cycle intervention.

Results from this research showed that there was a significant difference in post-exercise IGF-1 levels between TREAD-Exercise and CONT (p=0.014). Likewise, delta (Δ) (post – pre) showed a significant difference in mean IGF-1 levels between TREAD-Exercise with CONT (p=0.010). It was similar to the result from the research conducted in [28] concluded that

treadmill exercise with intensity 60% of VO_{2max} increased IGF-1 mRNA levels significantly. As reported in [43], moderate-intensity exercise increased IGF-1 levels. The IGF-1 levels possibly increased in TREAD-Exercise because of the effect of exercise. Physical exercises stimulate the brain to activate the hypothalamus [31]. The hypothalamus secretes GhRH and, then, GhRH stimulates GH secretion[32, 33]. GH modulates IGF-1 secretion from the liver to the blood circulation [34].

There was a significant difference in post-exercise IGF-1 levels between ERGO-Exercise with CONT (p=0.018). Likewise, delta (Δ) (post – pre) showed a significant difference in mean IGF-1 levels betweenERGO-Exercise and CONT (p=0.013). It was similar to the research results reported in [36], revealing that acute ergo cycle exercise with moderate intensity increased IGF-1 serum levels significantly. As concluded in [35], the acute response from moderate-intensity exercise increased IGF-1 serum levels significantly. The increase of IGF-1 in ERGO-Exercise was possible because of increased energy needs for muscle contraction for exercise. When exercising, there is an increase in energy needs and glucose uptake for muscle contraction, so that energy stored in muscle decreases. This decrease, in turn, increases IGF-1 release to the blood circulation. The increase of IGF-1 secretion to the circulation activates Phosphoinositide 3-Kinase (PI3K) pathway and Glucose Transporter Protein-4 (GLUT-4) translocation for maintaining glucose homeostasis and energy balance during exercise [44].

GF-1, or somatomedin C, is mostly synthesized by the liver and regulated by GH, which plays the main role in cell growth, cell development, and energy metabolism [17, 27]. IGF-1 plays a role in body composition related to the alteration of lean body mass and fat mass [28]. IGF-1 also plays a role in increasing insulin sensitivity and maintaining glucose homeostasis[44]. Besides that, IGF-1 is significant for tissue homeostasis, anti-apoptotic, mitogenic, anti-inflammation, antioxidant, metabolism, skeletal muscle plasticity, muscle strength and mass maintenance, and neural and cardiovascular protection [27, 45, 46]. IGF-1 can be synthesized through endocrine, paracrine, and autocrine mechanism [29]. Acute and chronic exercise both can increase IGF-1 levels in plasma and serum [28, 29]. Exercises induce IGF-1 secretion through activation of the hypothalamus [31]. The hypothalamus secretes GhRH, which then should be transferred to the anterior pituitary through hypothalamic-hypophyseal portal vessels [32]. GhRG stimulates GH secretion [33]. GH modulates IGF-1

secretion from the liver to the blood circulation[34]. IGF-1 in the circulation will bind to IGFBP3[17]. The binding of IGF-1 and IGFBP3 will affect energy balance, decrease body weight, free fat mass [17], and the maintenance of muscle strength and mass [27].

There was no significant difference in post-exercise IGF-1 levels between TREAD-Exercise with ERGO-Exercise (p=0.999). Likewise, delta (Δ) (post – pre) there was no significant difference in IGF-1 levels between TREAD-Exercise with ERGO-Exercise (p=0.897). The limitations of applying this research results cannot be applied to the elderly and people who have a high risk, such as hypertension, coronary heart disease (CHD), stroke, respiratory disorders, etc. Other than that, the limitation of this study is that we only analyzed one dependent variable, namely the IGF-1 level. The intervention given in this study was only acute exercise. It is necessary to conduct advanced research to analyzed chronic intervention (training) in obese female teenagers with the addition of several dependent variables, such as growth hormone (GH), Growth Hormone Releasing Hormone (GhRH), Insulin-Like Growth Factor Binding Protein 3 (IGFBP3), blood glucose, insulin, and homeostasis model assessment of insulin resistance (HOMA-IR). Hopefully, the results of these future research will benefit from perfecting optimal exercise programs for obesity treatment in the future.

6. Conclusion

This research showed that one session of the moderate-intensity treadmill and ergo cycle exercises for 30 minutes increases IGF-1 levels compared to the control.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Acknowledgment

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