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> Corresponding Author's Email Address: purwo-s-r@fk.unair.ac.id
> Author(s): Adi Pranoto, Zakaria Sendy Wardana, Misbakhul Munir, Hayuris Kinandita, Desiana Merawati, Sugiharto, Purwo Sri Rejeki
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Treadmill and Ergocycle Exercises Increase Insulin-Like Growth Factor-1 Levels in Obese Female

Adi Pranoto,[1] Zakaria Sendy Wardana,[2] Misbakhul Munir,[23] Hayuris Kinandita,[23] Desiana Merawati,[4] Sugiharto,[4] Purwo Sri Rejeki[23†]

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Abstract: Obesity increases the risk incidence of metabolic disorders, including insulin resistance, so that it causes an increase in blood glucose. Physical exercises, mediated by Insulin-Like Growth Factor-1 (IGF-1) have benefits in improving insulin sensitivity and lowering blood glucose. IGF-1 increases insulin sensitivity and maintain glucose homeostasis by activation of the Phosphoinositide 3-Kinase (PI3K) pathway and translocation of Glucose Transporter Protein-4 (GLUT-4). The purpose of the study was to analyze the comparison of a moderate-intensity treadmill and ergocycle exercise to the increasing of 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 18-22-year-old. Subjects were randomly divided into 3 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. Interventions were conducted 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 results were IGF-1 pre-exercise levels in CONT was (9.75±1.74) ng/mL, ERGO-Exercise was (9.79±3.00) ng/mL and TREAD-Exercise was (9.75±2.63) ng/mL (p=0.999). IGF-1 post-exercise levels in CONT was (9.45±2.44) ng/mL, ERGO-Exercise was (14.76±6.71) ng/mL and TREAD-Exercise was (14.98±2.84) ng/mL (p=0.022). IGF-1 delta (Δ) post – pre levels in CONT was (–0.29±2.33) ng/mL, ERGO-Exercise was (4.96±6.45) ng/mL and TREAD-Exercise was (5.22±2.31) ng/mL (p=0.015). These results showed that one session of a moderate-intensity treadmill and ergocycle exercise for 30 minutes increase IGF-1 levels compared to the control. It is necessary to conduct advanced research to analyzed chronic intervention (training) to the increasing of IGF-1 levels in obese females.

Keywords: IGF-1 levels, treadmill, ergocycle, obese female

跑步機和Ergocycle運動可增加肥胖女性的胰島素樣生長因子-1水平

摘要： 肥胖會增加包括胰島素抵抗在內的代謝異常的風險發生率，從而導致血糖升高. 由胰島素樣生長因子-1（IGF-1）介導的體育鍛煉可改善胰島素敏感性和降低血糖. IGF-1通過激活磷酸肌醇3-激酶（PI3K）途徑和轉運葡萄糖轉運蛋白4（GLUT-4）來提高胰島素敏感性並維持葡萄糖穩態。. 該研究的目的是分析中等強度的跑步機和健身操運動與肥胖女性中IGF-1水平增加的比較。. 這項研究是一項真正的實驗研究，採用了隨機的前測後測對照組設計。受試者為27名18-22歲的肥胖女性. 將受試者隨機分為3組，即CONT（n=9，無干預組），ERGO鍛煉（n=9，Ergocycle鍛煉）和TREAD-鍛煉（n=9，跑步機鍛煉）. 連續進行了30分鐘的TREAD運動和ERGO運動的干預. 運動前和運動後15分鐘採集血樣. 通過酶聯免疫吸附法（ELISA）檢測IGF-1水平. 使用ANOVA檢驗分析數據，並使用社會科學統計軟件包（SPSS）進行事後檢驗進行LSD事後檢驗. 結果是CONT中的IGF-1運動前水平為（9.75±1.74）ng/mL，ERGO運動為（9.79±3.00）ng/mL，TREAD運動為（9.75±2.63）ng/mL（p=0.999）. CONT中的IGF-1運動

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後水平為（9.45±2.44）ng/mL，ERGO運動為（14.76±6.71）ng/mL，TREAD運動為（14.98±2.84）ng/mL（p=0.022）. CONT前後的IGF-1增量（Δ）為（-0.29±2.33）ng/mL，ERGO鍛煉為（4.96±6.45）ng/mL，TREAD鍛煉為（5.22±2.31）ng/mL（p=0.015）. 這些結果表明，與對照組相比，一次中等強度的跑步機和ergocycle運動30分鐘可以增加IGF-1水平。. 有必要進行深入的研究以分析肥胖女性中IGF-1水平升高的慢性干預（培訓）.

关键词： IGF-1水平，跑步機，人體工程學，肥胖女性

Introductions

Obesity is a metabolic disease which has reached epidemic proportion [1]. Obesity is considered as an epidemic and recently, it has been a pandemic [2] and syndemic [3] . That is because obesity prevalence keep rising from year to year [4] . It is estimated that 1.9 billion people above 18 year old suffer from obesity, 650 million among them are obese, which consist of 11% male and 15% female [5]. Globally, more than a third of adult people suffer from obesity [6]. It is estimated that in year 2025, obesity prevalence will become 18% male and 21% female [7]. According to Riset Kesehatan Dasar (Riskesdas) 2018, obesity prevalence for people above 18 year old in Indonesia was 21.8%. This number was higher than obesity prevalence in 2013 (14.8%) and 2007 (10.5%) [8]. The high increase in obesity prevalence become serious problem which will threaten human resource quality [9] and health problem of countries in the world [10].

Obesity is a disease which has high risk in the incidence of 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, general factor which contribute to body weight increase is imbalance between energy intake and energy expenditure [20–22]. Life style modification is recommended for basic management in obesity treatment [12]. Life style modification with exercise-based non-pharmacological approach is the right strategy [23, 24]. Physical exercises is considered for very effective and efficient method in preventing the increase of obesity prevalence [25, 26]. It is because exercise increase energy expenditure and maintain glucose homeostasis which is mediated by Insulin-Like Growth Factor-1 (IGF-1) [10, 17].

IGF-1, also called as somatomedin C, is mostly synthesized by the liver and it is regulated by Growth Hormone (GH) which has main role in cell growth, cell development and energy homeostasis [17, 27]. Physical exercise was proved to increase IFG-1 levels in acute exercises and chronic exercises [28–30]. It is because physical exercises stimulate brain to activate the hypothalamus [31]. The hypothalamus secrete Growth Hormone Releasing Hormone (GhRH). This GHRH is transferred to 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 affect muscle strength and muscle mass [27]. Previous research showed various results. Research conducted by Tsai *et al.* [35] showed that acute response from moderate intensity exercise using ergocycle for 20

minutes increased IGF-1 serum levels significantly in 20-29 year old men. Nevertheless, exercise with intensity above 80% of VO_{2max} decreased IGF-1 levels significantly [18]. Mannerkorpi *et al.* [36] concluded that acute exercise using ergocycle with moderate and high intensity for 15 minutes increased IGF-1 serum levels significantly in healthy women. Research by Nishida *et al.* [37] showed that low-intensity aerobic training using ergocycle for 60 minutes decreased 9% of IGF-1 levels significantly. 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 ergocycle exercises to the increase of IGF-1 levels in obese female teenagers.

2. Material and Methods

2.1 Experimental Design

This research was true experimental study with the randomized pretest-posttest 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 3 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 procedure in this research was 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 ergocycle 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 exercise and ergocycle exercise were done with continuous method. Treadmill exercise and ergocycle exercises were conducted at 08.00 a.m. [40, 41]. Instruments used for this interventions were treadmill (Pulsar 4.0 HP Cosmos Sports & Medical, Nussdorf-Traunstein, Germany) and ergocycle (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 Physical Freshness Laboratory with a room temperature of 26±1 °C and humidity level in the room 50-70 %. Figure 1 shows treadmill and ergocycle exercise program in clearer detail.

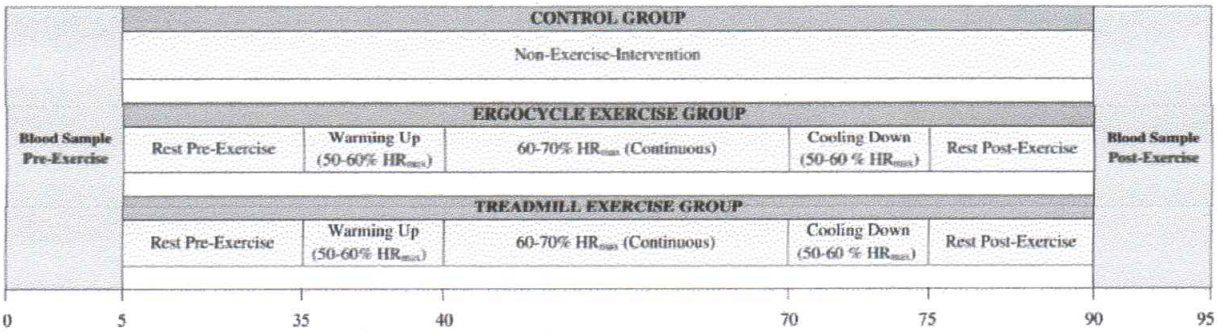

Fig. 1 Treadmill and ergocycle exercise program

2.3 Anthropometric Measurements

Body height of the subject was measured using a stadiometer (SECA, Chino, CA). Anthropometric measurements which are consist of body weight, BMI, PBF, fat mass (FM), free fat mass (FFM), muscle mass (MM), bone mass (BM) are 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 nondominant arm 3 times consecutively with a 1-2 minute interval between two measurements while 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 a 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 at 30 minutes after the intervention [42], whereas post-exercise blood samples were taken at 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 for analysis of IGF-1 levels on the next day [10].

2.6 IGF-1 Serum Levels Assessment

IGF-1 levels were examined by using 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). Test of Normality was conducted using Shapiro-Wilk test, whereas, test of Homogeneity was conducted test using Levene test. Statistical difference was tested by using 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 level of significance (P<0.05).

3. 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 subject

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
Percentage body fat (%)	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

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 means of subject's characteristics in each group. The results of ANOVA test showed that there was no difference in subject's characteristics on all variable of each group (P>0.05). Analytical results on pre-exercise and post-exercise IGF-1 levels are presented on Figure 1.

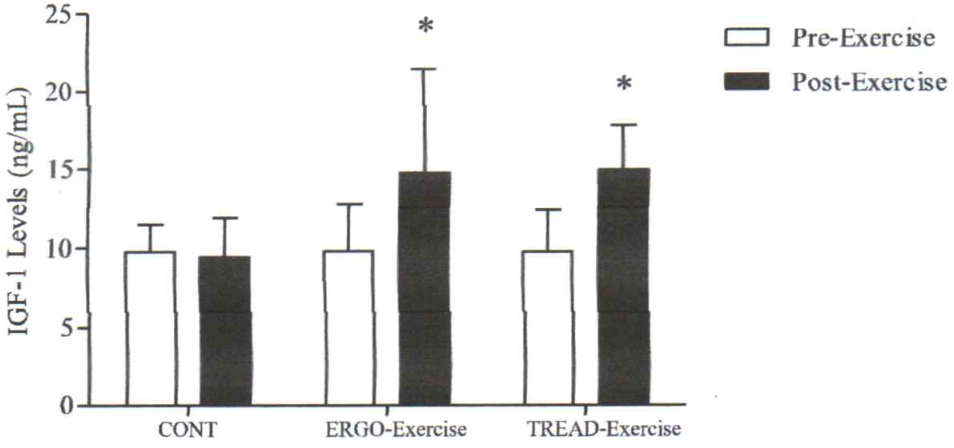

Fig. 1 IGF-1 levels pre-exercise vs. post-exercise. CONT: Control group; ERGO-Exercise: Ergocycle exercise group; TREAD-Exercise: Treadmill exercise group. Data are presented as mean±SD. p-Value were obtained using Paired Sample T-Test to compare post-exercise and pre-exercise IGF-1 level. *Significant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

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 1). 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 2.

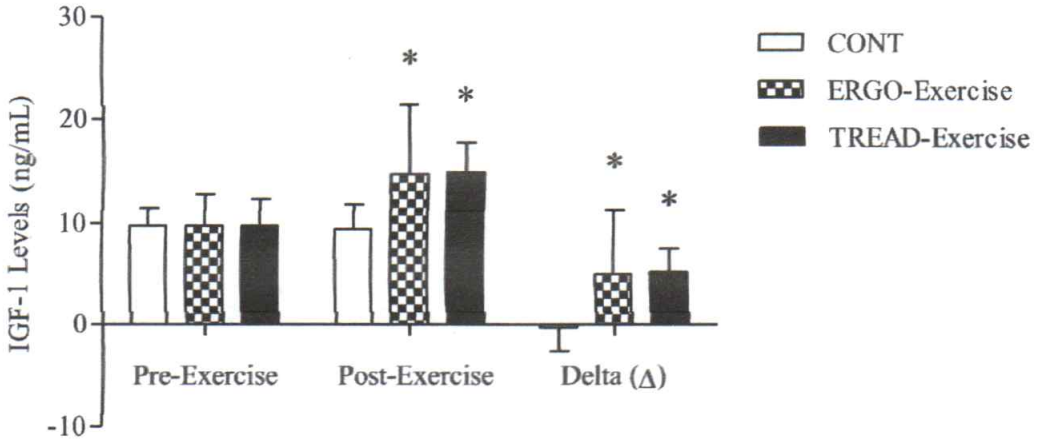

Fig. 2 IGF-1 levels pre-exercise, post-exercise and delta (Δ) post – pre. CONT: Control group; ERGO-Exercise: Ergocycle exercise group; TREAD-Exercise: Treadmill exercise group. Data are presented as mean±SD. p-Value were obtained using One way-ANOVA, followed by LSD post hoc test compare pre-exercise, post-exercise, delta (Δ) post – pre IGF-1 level in group. *Significant vs control group (CONT) (p<0.05).

Data in Figure 2 show that there is no singnificant 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 were 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), while ERGO-Exercise with TREAD-Exercise did not show a significant difference (P>0.05).

4. Discussion

This research was aimed to analyze the difference between tredmill and ergocycle exercise to the increase of IGF-1 levels in obese female. The results showed that there was no significant difference in pre-exercise IGF-1 levels among all groups (p=0.999). Therefore, three groups at this reseach had the same characteristics before treadmill and ergocycle 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 with the result from the research conducted by Berry *et al.* [28] concluded that treadmill exercise with intensity 60% of VO_{2max} increased IGF-1 mRNA levels significantly. Yoon *et al.* [43] in their research, conclude that moderate intensity exercise increased IGF-1 levels. The increase of IGF-1 levels in TREAD-Exercise was possibly because the effect of exercise. Physical exercises stimulate brain to activate the hypothalamus [31]. The hypothalamus secrete 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 between ERGO-Exercise and CONT (p=0.013). It was similar with the result from the research conducted by Mannerkorpi *et al.* [36] concluded that acute ergocycle exercise with moderate intensity increased IGF-1 serum levels significantly. Research conducted by Tsai *et al.* [35] concluded that acute response from moderate intensity

exercise increased IGF-1 serum levels significantly. The increase of IGF-1 in ERGO-Exercise was possibly because of the increase of 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 decrease. This, in turn, increase 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].

IGF-1 is also called as somatomedin C. It is mostly synthesized by the liver and regulated by GH which has main role in cell growth, cell development, and energy metabolism [17, 27]. IGF-1 play a role in body composition and it is related to the alteration of lean body mass and fat mass [28]. IGF-1 also have a role in increasing insulin sensitivity and maintaining glucose homeostasis [44]. Besides that, IGF-1 play a role in tissue homeostasis, anti-apoptotic, mitogenic, anti-inflammation, antioxidant, metabolism, skeletal muscle plasticity, maintenance of muscle strength and mass, as well as neural and cardiovascular protection [27, 45, 46]. IGF-1can 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]. Exercise induce IGF-1secretion through activation of the hypothalamus [31]. The hypothalamus secrete GhRH which then be transferred to the anterior pituitary through hypothalamic-hypohyseal 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 and free fat mass [17], as well as 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 the application of the results of this research are can not 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 in 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 researches will have the benefit of perfecting optimal exercise programs for obesity treatment in the future.

5. Conclusion

Results from this research showed that one session of moderate-intensity treadmill and ergocycle exercise for 30 minutes increase 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.

Conflict of interest

The authors declare that they have no competing interests.

Acknowledgment

No financial support was provided for this project. We would like to express our gratitude to Faculty of Sport Science State University of Malang that has provided facilities in the screening process of a prospective research subject and Fitness Center of the Malang City Health Department that has provided facilities well. Also, we greatly appreciate and wish to thank Palang Merah Indonesia (PMI) Blood Transfusion Unit (UTD) Malang that has assisted the blood sampling and blood centrifuge processes. This includes but is not limited to all the parties of to Physiology Laboratory Faculty of Medicine Universitas Brawijaya Malang who has helped the analysis process of IGF-1 level and all volunteer who have participated in this study.

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Dear Editor-in-Chief
Prof. Yi Weijian
Journal of Hunan University Natural Sciences

December, 26th 2020

Thank you very much for your helpful review. We have carefully studied the comments and suggestions and revised our paper accordingly. The following are our point-by-point responses to the comments. We hope that the revisions are acceptable and that our responses adequately address the comments. Thank you for your consideration.

Sincerely,

Purwo Sri Rejeki and coauthors

Responses to comments from Reviewers #1

1. Please add the purpose of the study to the abstract.

   Response:
   - The purpose of the study was to analyze the comparison of a moderate-intensity treadmill and ergocycle exercise to the increasing of IGF-1 levels in the obese female.

2. Please describe the scientific novelty of your research compared to the current regulations in science.

   Response:
   - The novelty of this study is a comparison of a moderate-intensity treadmill and ergocycle exercise to the increasing of IGF-1 levels in the obese female. Treadmill and ergocycle 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}). Whereas, previous studies only used ergocycle exercises, an example of research conducted by Tsai et al. (2014) by providing ergocycle exercise interventions for 20 men aged 20-29 years. Likewise, research conducted by Mannerkorpi et al. (2017) by providing acute exercise with moderate and high intensity carried out for 15 minutes using an ergocycle to healthy female. In addition, our study also focuses on obesity, especially in female.

3. Please describe the research methods in more detail (to the maximum of your ability).

Response:

- **Experimental Design**

This research was true experimental study with the randomized pretest-posttest 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 3 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 procedure in this research was approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia (309/EC/KEPK/FKUA/2019).

- **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 ergocycle 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 exercise (60-70% HR_{max}), and 5 minutes cooling down (50-60 HR_{max}). Treadmill exercise and ergocycle exercise were done with continuous method. Treadmill exercise and ergocycle exercises were conducted at 08.00 a.m. Instruments used for this interventions were treadmill (Pulsar 4.0 HP Cosmos Sports & Medical, Nussdorf-Traunstein, Germany) and ergocycle (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 Physical Freshness Laboratory with a room temperature of 26±1 °C and humidity level in the room 50-70 %. Figure 1 shows treadmill and ergocycle exercise program in clearer detail.

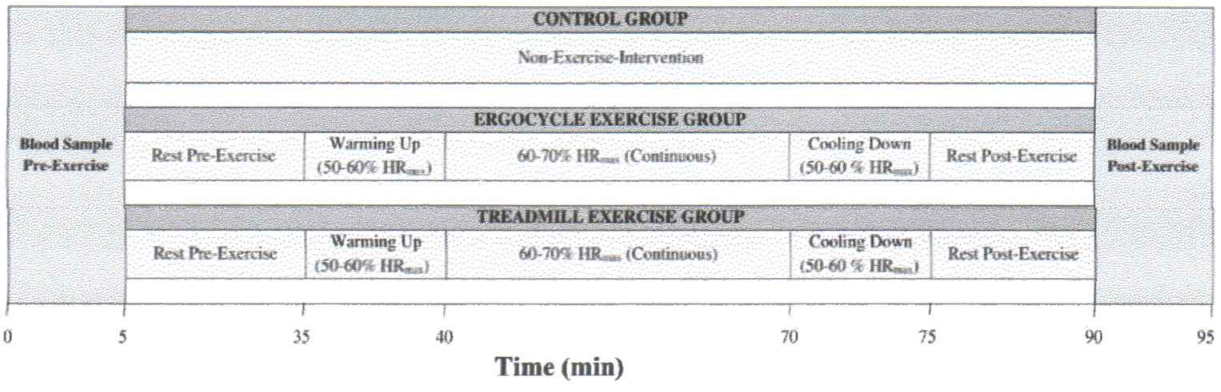

Figure 1. Treadmill and Ergocycle Exercise Program

- **Anthropometric Measurements**

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

- **Physiological Condition**

Blood pressure was measured using an automated device (OMRON Model HEM-7130 L, Omron Co., JAPAN) at the nondominant arm 3 times consecutively with a 1-2 minute interval between two measurements while 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).

- **Blood Samples**

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

- **IGF-1 Serum Levels Assessment**

IGF-1 levels were examined by using 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).

- **Statistical Analysis**

Data were analyzed by Statistic Package for Social Science (SPSS) Statistics for Windows, version 16 (SPSS Inc., Chicago, IL, USA). Test of Normality was conducted using Shapiro-Wilk test, whereas, test of Homogeneity was conducted test using Levene test. Statistical difference was tested by using 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 level of significance ($P<0.05$).

4. Please describe you Results: Now that you have explained how you gathered your research, you are to report what you actually found. In this section, taking no more than 4 pages, outline the main findings of your research. You need not include too many details, particularly if you are using tables and figures. While writing this section use the smallest number of words necessary to convey your statistics. Use appendices or supplementary materials if you have too much data.

Response:

- The main findings of this study are one session of moderate-intensity treadmill exercise and moderate-intensity ergocycle exercise for 30 minutes increase IGF-1 levels compared to the control group. However, moderate-intensity treadmill exercise was more effective in increasing IGF-1 levels than moderate-intensity ergocycle exercise. For more details, the research data are presented in tables 1-3.

The basic profiles of the subject's, 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 subject's

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
Percentage body fat (%)	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

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 means of subject's characteristics in each group. The results of ANOVA test showed that there was no difference in subject's characteristics on all variable of each group (P>0.05). Analytical results on pre-exercise and post-exercise IGF-1 levels are presented on Table 2.

Table 2 Statistical analysis on pre-exercise and post-exercise IGF-1 levels

Group	Time		Paired Sample T-Test
	Pre-exercise	Post-exercise	*P*-value
CONT	9.75±1.74	9.45±2.44	0.710
ERGO-Exercise	9.79±3.00	14.76±6.71*	0.045
TREAD-Exercise	9.75±2.63	14.98±2.84*	0.000

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

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 (P>0.05). However, the ERGO-Exercise and TREAD-Exercise group showed a significant difference in mean IGF-1 levels between pre-exercise and post-exercise (P<0.05). 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 Table 3.

Table 3 IGF-1 levels pre-exercise, post-exercise and delta (Δ) post – pre in all groups.

Time	Group			ANOVA *P*-value
	CONT	ERGO-Exercise	TREAD-Exercise	
	mean±SD (ng/mL)	mean±SD (ng/mL)	mean±SD (ng/mL)	
Pre-exercise	9.75±1.74	9.79±3.00	9.75±2.63	0.999
Post-exercise	9.45±2.44	14.76±6.71*	14.98±2.84*	0.022
(Δ) post – pre	–0.29±2.33	4.96±6.45*	5.22±2.31*	0.015

CONT: Control group; ERGO-Exercise: Ergocycle exercise group; TREAD-Exercise: Treadmill exercise group. One way-ANOVA, followed by LSD post hoc test, was used to compare the differences among groups. Data are presented as mean±SD. *Significant vs control group (CONT) ($p<0.05$).

Data in Table 3 show that there is no singnificant 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 were significant difference between ERGO-Exercise and CONT IGF levels (sig. 0.018 and $P<0.05$), as well as TREAD-Exercise and CONT (Sig. 0.014 and $P<0.05$); whereas, ERGO-Exercise and TREAD-Exercise IGF-1 levels showed no significant difference (Sig. 0.919 and $P>0.05$). Likewise, delta (Δ) (post – pre) showed a significant difference in mean IGF-1 levels between ERGO-Exercise and CONT (Sig. 0.013 and and $P<0.05$), TREAD-Exercise with CONT (Sig. 0.010 and $P<0.05$), while ERGO-Exercise with TREAD-Exercise did not show a significant difference (Sig. 0.897 and $P>0.05$).

5. Clarify the scope of the article results.

Response:

- The scope of this study is physiology.

6. Please specify the applied value of your results.

Response:

- All statistical analysis was conducted using level of significance ($P<0.05$).

7. Clarify the practical limitations of the application of the results.

Response:

- We have added a research limitation to the last paragraph of the discussion section. The limitations of the application of the results of this research are can not 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 in 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 researches will have the benefit of perfecting optimal exercise programs for obesity treatment in the future.

Treadmill and Ergocycle Excercises Increase Insulin-Like Growth Factor-1 Levels in Obese Female

by Adi Pranoto

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

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Abstract: Obesity increases the risk incidence of metabolic disorders, including insulin resistance, so that it causes an increase in blood glucose. Physical exercises, mediated by Insulin-Like Growth Factor-1 (IGF-1) have benefits in improving insulin sensitivity and lowering blood glucose. IGF-1 increases insulin sensitivity and maintain glucose homeostasis by activation of the Phosphoinositide 3-Kinase (PI3K) pathway and translocation of Glucose Transporter Protein-4 (GLUT-4). The objective of this research was to analyze the comparison of moderate-intensity treadmill and ergocycle exercise to the increasing of IGF-1 levels in obese female. This research was a true *experimental study with the randomized pretest-posttest control group design*. Subjects were 27 obese females 18-22-year-old. Subjects were randomly divided into 3 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. Interventions were conducted 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 results were IGF-1 pre-exercise levels in CONT was (9.75±1.74) ng/mL, ERGO-Exercise was (9.79±3.00) ng/mL and TREAD-Exercise was (9.75±2.63) ng/mL (p=0.999). IGF-1 post-exercise levels in CONT was (9.45±2.44) ng/mL, ERGO-Exercise was (14.76±6.71) ng/mL and TREAD-Exercise was (14.98±2.84) ng/mL (p=0.022). IGF-1 delta (Δ) post – pre levels in CONT was (-0.29±2.33) ng/mL, ERGO-Exercise was (4.96±6.45) ng/mL and TREAD-Exercise was (5.22±2.31) ng/mL (p=0.015). These results showed that one session of a moderate-intensity treadmill and ergocycle exercise for 30 minutes increase IGF-1 levels compared to the control. It is necessary to conduct advanced research to analyzed chronic intervention (training) to the increasing of IGF-1 levels in obese females.

Keywords: IGF-1 levels, treadmill, ergocycle, obese female

Introductions

Obesity is a metabolic disease which has reached epidemic proportion [1]. Obesity is considered as an epidemic and recently, it has been a pandemic [2] and syndemic [3] . That is because obesity prevalence keep rising from year to year [4] . It is estimated that 1.9 billion people above 18 year old suffer from obesity, 650 million among them are obese, which consist of 11% male and 15% female [5]. Globally, more than a third of adult people suffer from obesity [6]. It is estimated that in year 2025, obesity prevalence will become 18% male and 21% female [7]. According to Riset Kesehatan Dasar (Riskesdas) 2018, obesity prevalence for people above 18 year old in Indonesia was 21.8%. This number was higher than obesity prevalence in 2013 (14.8%) and 2007 (10.5%) [8]. The high increase in obesity prevalence become serious problem which will threaten human resource quality [9] and health problem of countries in the world [10].

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Obesity is a disease which has high risk in the incidence of 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, general factor which contribute to body weight increase is imbalance between energy intake and energy expenditure [20–22]. Life style modification is recommended for basic management in obesity treatment [12]. Life style modification with exercise-based non-pharmacological approach is the right strategy [23, 24]. Physical exercises is considered for very effective and efficient method in preventing the increase of obesity prevalence [25, 26]. It is because exercise increase energy expenditure and maintain glucose homeostasis which is mediated by Insulin-Like Growth Factor-1 (IGF-1) [10, 17].

IGF-1, also called as somatomedin C, is mostly synthesized by the liver and it is regulated by Growth Hormone (GH) which has main role in cell growth, cell development and energy homeostasis [17, 27]. Physical exercise was proved to increase IFG-1 levels in acute exercises and chronic exercises [28–30]. It is because physical exercises stimulate brain to activate the hypothalamus [31]. The hypothalamus secrete Growth Hormone Releasing Hormone (GhRH). This GHRH is transferred to 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 affect muscle strength and muscle mass [27]. Previous research showed various results. Research conducted by Tsai *et al.* [35] showed that acute response from moderate intensity exercise using ergocycle for 20 minutes increased IGF-1 serum levels significantly in 20-29 year old men. Nevertheless, exercise with intensity above 80% of VO_{2max} decreased IGF-1 levels significantly [18]. Mannerkorpi *et al.* [36] concluded that acute exercise using ergocycle with moderate and high intensity for 15 minutes increased IGF-1 serum levels significantly in healthy women. Research by Nishida *et al.* [37] showed that low-intensity aerobic training using ergocycle for 60 minutes decreased 9% of IGF-1 levels significantly. 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 ergocycle exercises to the increase of IGF-1 levels in obese female teenagers.

Material and Methods

Experimental Design

This research was true experimental study with the randomized pretest-posttest 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 3 groups, that is CONT (n=9, group without intervention), ERGO-Exercise (n=9, Ergocycle Exercise), and TREAD-Exercise (n=9, Treadmill Exercise). All procedure in this research was approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia (309/EC/KEPK/FKUA/2019).

Exercise Protocol

Treadmill and ergocycle 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 and ergocycle exercise were done with continuous method. Intervention using treadmill and ergocycle exercises were conducted at 08.00 a.m. [40, 41]. Instruments used for this interventions were treadmill (Pulsar 4.0 HP Cosmos Sports & Medical, Nussdorf-Traunstein, Germany) and ergocycle (Monark 828 E, Version 1010 Art. No: 7950-296, Vansbro, Sweden). Pre-exercise blood samples was taken at 30 minutes before intervention [42], whereas post-exercise blood samples were taken at 15 minutes after intervention [36]. Monitoring heart rate during exercise using a polar heart rate monitor (Polar H10 Heart Rate Sensor, Inc., USA). Figure 1 shows treadmill and ergocycle training program in clearer detail.

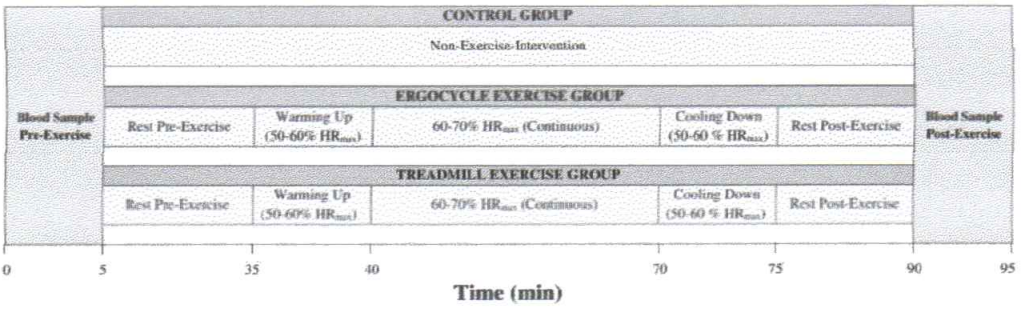

Figure 1. Treadmill and Ergocycle Exercise Program

Anthropometric Measurements

Body height of the subject was measured using a stadiometer (SECA, Chino, CA). Anthropometric measurements which are consist of body weight, BMI, PBF, fat mass (FM), free fat mass (FFM), muscle mass (MM), bone mass (BM) are conducted using TANITA (Body Composition Analyzer DC3607601(2)-1604 FA, TANITA Corporation of America, Inc). Blood pressure was measured using an automated device (OMRON Model HEM-7130 L, Omron Co., JAPAN) at the nondominant arm 3 times consecutively with a 1-2 minute interval between two measurements while participants were in a seated position.

Blood Samples

Four milliliters of blood samples were taken from cubital vein [36, 42]. Blood samples were centrifuged for 10 minutes at 3000 rpm [17]. Serum was collected and saved at -80°C for analysis of IGF-1 levels on the next day [10].

IGF-1 Serum Levels Assessment

IGF-1 levels were examined by using 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).

Statistical Analysis

Data were analyzed by Statistic Package for Social Science (SPSS) Statistics for Windows, version 16 (SPSS Inc., Chicago, IL, USA). Test of Normality was conducted using Shapiro-Wilk test, whereas, test of Homogeneity was conducted test using Levene test. Statistical

difference was tested by using 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 level of significance ($P<0.05$).

Results

Descriptical analysis of subject's characteristic and analytical results of IGF-1 levels are presented on Table 1 and Figure 1.

TABLE 1. Characteristics of the subject

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
Weight (kg)	73.49±7.96	68.21±7.88	71.15±7.43	0.367
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
Percentage body fat (%)	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

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 means of subject's characteristics in each group. The results of ANOVA test showed that there was no difference in subject's characteristics on all variable of each group ($P>0.05$). Analytical results on pre-exercise and post-exercise IGF-1 levels are presented on Figure 1.

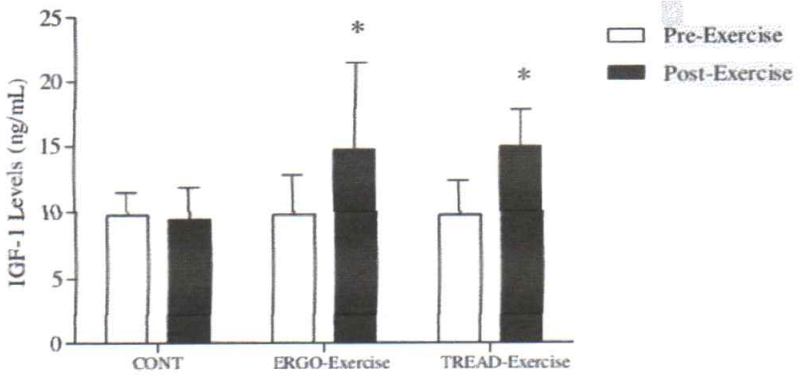

FIGURE 1. IGF-1 levels pre-exercise vs. post-exercise. CONT: Control group; ERGO-Exercise: Ergocycle exercise group; TREAD-Exercise: Treadmill exercise group. Data are presented as mean±SD. p-Value were obtained using Paired Sample T-Test to compare post-exercise and pre-exercise IGF-1 level. *Significant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

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 1). 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 2.

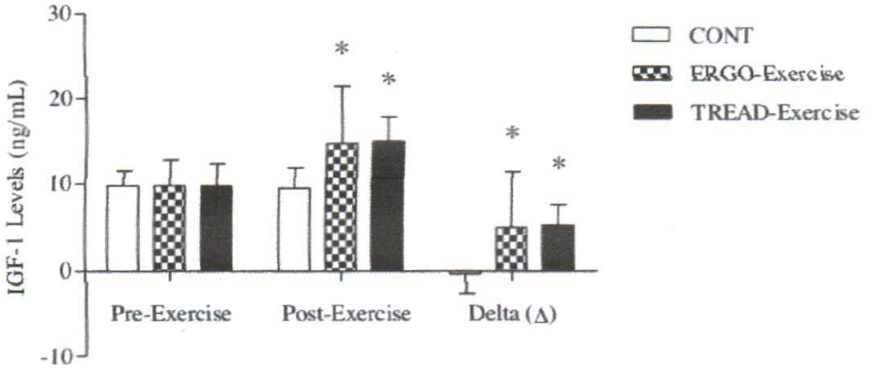

FIGURE 2. IGF-1 levels pre-exercise, post-exercise and delta (Δ) post – pre. CONT: Control group; ERGO-Exercise: Ergocycle exercise group; TREAD-Exercise: Treadmill exercise group. Data are presented as mean±SD. p-Value were obtained using One way-ANOVA, followed by LSD post hoc test compare pre-exercise, post-exercise, delta (Δ) post – pre IGF-1 level in group. *Significant vs control group (CONT) (p<0.05).

Data in Table 2 and Figure 2 show that there is no singnificant difference in pre-exercise IGF-1 levels (P>0.05), however, post-exercise and delta (Δ) (post – pre) IGF-1 levels differ significantly (P<0.05). LSD post hoc test showed that there were 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), while ERGO-Exercise with TREAD-Exercise did not show a significant difference (P>0.05).

Discussion

This research was aimed to analyze the difference between tredmill and ergocycle exercise to the increase of IGF-1 levels in obese female. The results showed that there was no significant difference in pre-exercise IGF-1 levels among all groups (p=0.999). Therefore, three groups at this reseach had the same characteristics before treadmill and ergocycle 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 with the result from the research conducted by Berry *et al.* [28] concluded that treadmill exercise with intensity 60% of VO_{2max} increased IGF-1 mRNA levels significantly. Yoon *et al.* [43] in their research, conclude that moderate intensity exercise

increased IGF-1 levels. The increase of IGF-1 levels in TREAD-Exercise was possibly because the effect of exercise. Physical exercises stimulate brain to activate the hypothalamus [31]. The hypothalamus secrete 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 between ERGO-Exercise and CONT (p=0.013). It was similar with the result from the research conducted by Mannerkorpi *et al.* [36] concluded that acute ergocycle exercise with moderate intensity increased IGF-1 serum levels significantly. Research conducted by Tsai *et al.* [35] concluded that acute response from moderate intensity exercise increased IGF-1 serum levels significantly. The increase of IGF-1 in ERGO-Exercise was possibly because of the increase of 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 decrease. This, in turn, increase 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].

IGF-1 is also called as somatomedin C. It is mostly synthesized by the liver and regulated by GH which has main role in cell growth, cell development, and energy metabolism [17, 27]. IGF-1 play a role in body composition and it is related to the alteration of lean body mass and fat mass [28]. IGF-1 also have a role in increasing insulin sensitivity and maintaining glucose homeostasis [44]. Besides that, IGF-1 play a role in tissue homeostasis, anti-apoptotic, mitogenic, anti-inflammation, antioxidant, metabolism, skeletal muscle plasticity, maintenance of muscle strength and mass, as well as neural and cardiovascular protection [27, 45, 46]. IGF-1can 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]. Exercise induce IGF-1secretion through activation of the hypothalamus [31]. The hypothalamus secrete GhRH which then be transferred to the anterior pituitary through hypothalamic-hypohyseal 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 and free fat mass [17], as well as 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). 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 researches will have the benefit of perfecting optimal exercise programs for obesity treatment in the future.

Conclusion

Results from this research showed that one session of moderate-intensity treadmill and ergocycle exercise for 30 minutes increase 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.

Conflict of interest

The authors declare that they have no competing interests.

Acknowledgment

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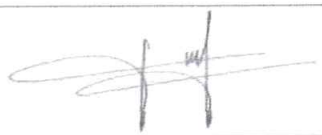
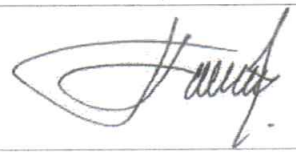
1	Adi Pranoto		December, 25th 2020
2	Zakaria Sendy Wardana		December, 25th 2020
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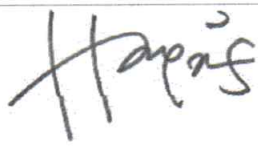
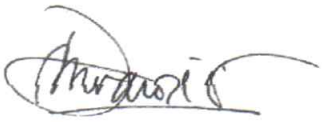
4	Hayuris Kinandita		December, 27th 2020

5	Desiana Merawati		December, 26th 2020
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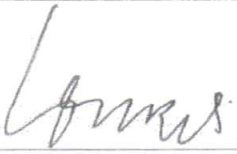
7	Purwo Sri Rejeki		December, 25th 2020