Journal of Exercise and Health Science, Vol. 02, No. 03, Summer 2022, Page 67-80

Research Paper

The Effect of Two Weeks of Interval Training with and without Blood Flow Restriction on Growth Indices (GH, IGF-1, LA) in Active Adolescent

Mohammad Tanhaie[1], Javad Vakili[2], Saeed Nikokheslat[3]

1. MSc in Exercise Physiology, Faculty of Physical Education and Sports Sciences, Tabriz University, Tabriz, Iran (Corresponding Author)
2. Associate Professor, Faculty of Physical Education and Sports Sciences, Tabriz University, Tabriz, Iran
3. Associate Professor, Faculty of Physical Education and Sports Sciences, Tabriz University, Tabriz, Iran

Received: 2022/08/09 **Accepted: 2022/12/14**

Abstract

Exercise with blood flow restriction (BFR)is likely to have a profound effect on the levels of growth hormone markers. The purpose of this study was to determine the effect of two weeks of interval training with and without BFR on the serum levels of growth hormone, IGF-1 and lactate in active adolescent boys. Twenty-four active male adolescents (mean age of 17.56±5.69 years, height of 171±47 cm, body mass index 22.06±2.9kg/m^2) were selected as the Subjects and randomly divided into two groups of training with BFR and without BFR The training protocol was performed Up to 60-75% of Maximum heart rate, two sessions a week, three repetitions in the first week and four repetitions of 400 meters in the second week. The rest between repetitions was 60-80 seconds. The cuff pressure for thighs during exercise was between 140 and 180 mmHg. Blood samples were taken to measure IGF-1 and GH indices before exercise and 48 hours after the last exercise session and lactate immediately after. To analyze the data, 2x2 ANOVA statistical test and independent t test were used at a significance level of P<0.05. The findings showed a significant increase in the levels of blood lactate and GH in the BFR group (p = 0.001). However, there was no significant change in the IGF-1 levels for BFR or BFR groups (p = 0.099). Accordingly, it can be said that performing interval exercises with BFR is likely more effective in increasing growth and performance indices in adolescents compared to exercises without BFR.

Keywords: Interval training, Blood flow restriction, Growth hormone, IGF1, Lactate.

1. Email: m.super_star@yahoo.com
2. Email: vakili@tabrizu.ac.ir
3. Email: sa_nikoo@yahoo.com

Introduction

Regular physical activity is important throughout life, especially during childhood and adolescence, and its beneficial effects on the physical, intellectual and psychological development of children and adolescents should not be ignored. Adolescence have the greatest impact on physical health and other indicators related to health and increasing performance in adulthood. Growth indicators such as growth hormone (GH) during childhood and adolescence are the factors that stimulate the growth of long bones (in arms and legs) and are the main and final regulators of height. This hormone also controls the growth of soft tissues such as muscles and tendons [1]. During sport activities, the hormonal system, similar to the nervous system, has a strong effect on the body's response to any specific activity and the coordination of different mechanisms of the body, including the energy production mechanism to help to perform the activity. The reactions of the hormonal system change according to the variables of each specific sport and different physiological and psychological states [2].The secretion of GH slowly decreases with increasing age after adolescence and finally at very old ages it reaches about 25% of youth. Many physiological states such as sleep, hunger, stress, reduced glucose concentration, obesity, hormones, amino acids (arginine), age and sex, and physical activity, stimulate the secretion of GH by reducing the amount of somatostatin secretion or increases secretion Growth-hormone-releasing hormone (GHRH)[3].

GH is one of the most important hormones in the body, which, along with a group of other hormones, is necessary for the normal growth of the body. This hormone is necessary to continue growth in children and teenagers and maintain weight and protein in adults. Since growth can be considered as an increase in the living body mass, or an increase in the amount of proteins, the main target of this hormone is to stimulate the process of protein synthesis and provide the necessary energy for the protein biostructure. However, GH has a less direct effect on the growth process and many aspects of growth in the body are influenced by a substance called somatomedin, which is mainly produced in the liver as it is known. Normal growth has a direct relationship with the plasma concentration of somatomedin or insulin-like growth factor (IGF-1)[3].

Based on studies, physical activities and proper Exercise training can affect the height growth, increasing muscle mass and improving the metabolism of three substances (carbohydrates, fat and protein) by stimulating the secretion of GH and subsequently IGF1. However, blood lactate elevation is one of the main causes of GH secretion, especially in intense sports activities. Therefore, high-intensity exercises that produce more lactate can lead to an increase in GH hormone, so that it is known that the increase in acidity and decrease in blood and muscle pH in intense exercise stimulates metabolic receptors. These

receptors send nerve messages from the active muscles to the adrenocortical peptide system and in this way, increase the secretion of GH and IGF-1[4].
Coaches and athletes are always looking to obtain and use the most efficient training methods in order to achieve the best results and adapt training at the most appropriate time. Interval training is one of these training methods that includes repetition of activities that are alternately used with periods of rest or lighter activity, so the individual can perform very intense activities for a long time. In interval training, the least fatigue and the fastest recovery period occur. These trainings have many advantages such as the precise control of training intensity, improvement of energy devices involved in the desired sports field, activity with intensities close to competition intensity [6]. Due to the fact that in these exercises, the Intensity of exercise is high and lactate production is high in the Training stages, it can be a very good stimulus for GH and IGF-1. But teenagers and children have a low capacity of the anaerobic system and the tolerance of this activity in this system is low for them, so researchers are looking for a method that can apply such methods on the physiological structures of the body [5].
Therefore, researchers have always wanted to develop safe and effective methods to maintain and develop muscle strength for a wide range of people who cannot tolerate high training intensities [7, 8]. So, researchers have proposed a type of exercise as exercise with blood flow restriction (BFR) [9]. In this training method, the blood flow to the active muscle during training is limited or stopped by tying a flexible rubber tourniquet around the proximal part of the arm or thigh [10]. The intensity of these exercises is usually between 20 to 30% of a maximum repetition (it is considered almost equivalent to the intensity of daily activity of people, so it is tolerable for people with different physical characteristics) [11, 13, 12]. This action causes the creation of a temporary blood pool in the organ, and after that, the accumulation of metabolic substances, especially lactic acid, increases locally in the organ, which increases the concentration of metabolites, acidifies the muscle environment, increases H+ ions, and decreases tissue availability the internal oxygen from the hypothalamus-pituitary axis of the blood and finally causes the release of anabolic hormones such as GH [15,14], so it seems that using this training method is effective to stimulate the secretion of LA, GH and IGF-1 in adolescents and youths.
Attarzadeh Hosseini et al. (2013) investigated the acute response of lactate, GH and IGF-1 to two exercise protocols with blood flow restriction in 20 adolescent and found that the level of GH, IGF-1 and lactate increased immediately after walking in the BFR group compared to the group without blood flow restriction [16]. Homaei et al. (2012) studied the effect of eight weeks of intermittent and

continuous training on the resting serum levels of GH and IGF-1 after single-session exercise and they observed significant increase in GH and IGF-1 levels of active adolescent males. In addition, compared to the continuous training, the interval protocol led to more increase in the level of serum GH and IGF-1 [17]. In contrast, Taylor et al. (2016) and Basereh et al. (2016) reported that katsu exercise had no significant effect on serum GH levels [18, 19]. Therefore, investigation the changes in hormones that are effective in the strength and growth of young people, which undergoes changes in response to new exercises, can be considered as an interesting topic among the studies related to the science of exercise and improving muscle strength. Due to some different results in these issue, the researcher aimed at investigating the effect of two weeks of interval exercise with and without blood flow restriction on serum levels of GH, IGF-1 and lactate in active male adolescents.

Materials and Methods

Subjects

The present research was conducted in the form of a semi-experimental design with two group including an exercise group with blood flow restriction (BFR) and an exercise group without blood flow restriction (WFR). In this study, 24 men were selected among football players aged 17.75 ± 0.75 years old with at least one year of football experience, no injuries (especially in the lower limbs) and no use of drugs or supplements in the last six months. The percentage of body fat of subjects were measured using a skin thickness gauge and the seven-point formula of the American College of Sports Medicine, and then they performed the $VO2_{max}$ test with the shuttle run test and were randomly assigned to one of the two groups of performing interval exercise with and without BFR. All subjects were selected by attending the coordination meeting and after fully explaining the goals and practice protocol of the measurement methods, by completing the consent form and the health questionnaire. All procedures of the present study were approved by the Ethical board of the Tabriz University in accordance with internationally standard principles.

Table 2 shows the bassline Demographic characteristics of the study groups. Demographic data were compared between groups using ANOVA test. The results of one-way ANOVA showed that there is no significant difference between the groups in the demographic characteristics of the participants

Table 2- Descriptive characteristics of study groups at baseline.

Variable	BFR	WFR	P-value

Age (Yr)	17.28±5.82	17.85±5.52	0.724
Height (cm)	175.00±5.68	174.14±4.25	0.365
Weight (kg)	71.71±7.13	73.71±11.38	0.671
BMI (kg/m^2)	21.85±2.26	22.28±3.54	0.426

Interval Training Program

The training program of the current study was two weeks of intermittent training (two sessions per week) on the treadmill with an intensity of 60-75% Maximum heart rate, three repetitions of 400 meters in the first week and four repetitions in the second week, which was done at Fajr Miandoab Club. Each training session included 10 minutes of general warm-up and 10 minutes of specific warm-up on the treadmill and the main training program with the desired intensity. The rest interval between exercise repetitions was 60-80 seconds (See table 1).

Table 1. Characteristics of theinterval training program (with & without BFR)

The training intensity of the first week	60 – 65% of MHR
The training intensity of the second week	65 – 75% of MHR
The number of sets in the first week	3 Sets of 400 meters running on treadmill
The number of sets in the second week	4 Sets of 400 meters running on treadmill
The rest interval between sets	60 – 80 seconds

Blood Flow Restriction

In order to limit the blood flow and increase the pressure on the muscle in the training group with BFR, a canvas cuff with the dimensions of 85 cm length and 6 cm wide was used, inside which was a rubber tube with a diameter of 3 cm and a length of 15 cm. There was a meter that had two ducts, one for air entry and the other for installing a barometer, the pressure inside of which could be increased up to 300 mm of mercury. The pressure of the cuff for the thighs was between 180 and 140 mm Hg during the execution stages of the exercise [20]. For the training group with BFR, cuffs were used close the proximal part of the legs and were removed during rest. While the WBR group did their training program without using cuffs. In order to determine the validity of the cuff, Pakzad et al have used researcher-made cuffs in their study and the reliability of the cuff was checked using a pressure gauge before and after the exercise, and no change was observed in the cuff pressure.

IGF-1, GH and Lactate Assay

Blood samples were taken in two phases at baseline (before) and 48 hours after the completion of the training protocol to measure the serum levels of IGF-1 and

GH. The blood sample taken from the subject's brachial vein was placed in tubes containing the anticoagulant ethylenediaminetetraacetic acid (EDTA) and kept at -80°C until the time of index measurement. TOSOH device and immunoenzymometric method were used to determine the amount of GH hormone in each blood sample. And to determine the amount of IGF-1, a diameter brand ELISA kit was used with a sensitivity of 0.025 microliter units per milliliter. One of the reasons for using these methods is that there is no need to use radioactive materials. On the other hand, unlike other methods, a large amount of antibody is used in such methods, so that the hormone is trapped in the antibody-hormone complex, so the amount of hormone in the test sample is suitable for the amount of the product.

Blood samples for measuring lactate were also taken immediately after the anaerobic test. All measurements of GH, IGF-1 and lactate were performed in the pathology and medical diagnosis laboratory.

Data Analyzes

Kolmogorov Smirnov test was used to determine the normal distribution of data, two-way ANOVA and independent t-test were used to check the difference between stages and between groups. The obtained data were analyzed using SPSS version 21 software with a significance level of P<0/05

Results

The average of the measured indices of the two groups in the pre-test and post-test stages are shown in the table 3.

Tabl 3-The Mean±SD for studied variables of two groups in pre and post-test phases.

Variable	Group	Pre-test	Post-test
GH (ng/ml)	BFR	0.80±0.13	1.04±0.18
	WFR	0.82±0.14	0.92±0.21
IGF-1 (ng/ml)	BFR	330±25.16	398±15.55
	WFR	333±32.42	380±13.15
Lactate (mmol/L)	BFR	13.59±0.67	15.69±1.10
	WFR	13.78±0.61	14.19±0.66

Table. 4 shows the results of two-way analysis of variance for the variables According to Table. 4 The results show a significant main effect of Time (p = 0.0077), indicating that GH levels changed significantly from Pre-test to Post-test, regardless of the Group. However, there was no significant main effect of Group (p = 0.3224), nor a significant interaction between Group and Time (p = 0.1962).

The results show a significant main effect of Time (p < 0.0001), indicating that IGF-1 levels changed significantly from Pre-test to Post-test, regardless of the

Group. However, there was no significant main effect of Group (p = 0.0712), nor a significant interaction between Group and Time (p = 0.2274).

The results show significant main effects of Group (p < 0.0001) and Time (p < 0.0001), as well as a significant interaction between Group and Time (p = 0.0021). This indicates that Lactate levels were significantly different between the BFR and WFR groups, and they also changed significantly from Pre-test to Post-test, with the change being different between the two groups.

Table No. 4- The result of two-way variance analysis

Variable	Source	Sum of Squares	df	Mean Squares	F	p-value
Growth Hormone (GH)	Group	0.0372	1	0.0372	1.01	0.32
	Time	0.030	1	0.304	8.34	0.007
	Group*Time	0.064	1	0.064	1.76	0.196
	Error	0.802	22	0.365		
Insulin-like Growth Factor 1 (IGF-1)	Group	2352.00	1	2352.00	3.5953	0.071
	Time	25600.00	1	25600.00	39.1408	0.000
	Group*Time	1008.00	1	1008.00	1.5408	0.2274
	Error	14392.00	22	654.18		
Lactate	Group	11.0408	1	11.0408	26.3438	0.000
	Time	19.6875	1	19.6875	47.0052	0.000
	Group*Time	5.0408	1	5.0408	12.0275	0.0021
	Error	9.2208	22	0.4192		

Discussion

Based on the results of the present research, the blood lactate concentration in the BFR group increased significantly compared to the WFR training group. In line with the results of the present results, Takano et al (2005) reported that, in a blocked blood flow, lactate concentrations increased significantly after low-intensity training in the blocking group at three times (immediately, 10 and 30 minutes after training), but in training group without blocking blood flow, lactate level was increased immediately after training [37]. Shimizu et al. (2016) studied 40 healthy elderly in two groups of resistance training with and without blood flow restriction. They reported that four weeks of training with 20% 1RM caused a further increase in vascular endothelial growth factor, GH and lactate ratio of the group without blood flow restriction in healthy elderly subjects [25].

In a research, Attarzadeh Hosseini et al (2013) investigated the acute response of lactate, GH and IGF-1 to two exercise protocols with blood flow restriction in male adolescents and concluded that the lactate level in both exercise groups increased significantly [126].

Reeves and colleagues (2006) compared the hormonal responses of male subjects in two types of training, light resistance training with limitation and hard resistance training without limitation. The training intensity for the limited training group was 30% of 1RM and for the unrestricted training group was 70% of 1RM. The results showed that the level of lactate increased significantly in both training groups [23]. Fujita et al (2007) reported that following two weeks of resistance training with blood flow restriction with a pressure of about 200 mm Hg, plasma lactate concentration in the experimental group with blood flow restriction elevated significantly immediately after exercise and up to 40 minutes. In addition, after training, the lactate level was high in the control group (same training intensity and conditions but without blood flow restriction). The lactate concentration was significantly higher in the experimental group compared to the control group [26].

In the study of Takarada and colleagues (2000), it has been shown that a session of resistant training with BFR in men significantly increases the concentration of norepinephrine and lactate in comparison with the traditional resistance training group [30].

Because lactate is one of the important metabolites and the final product of anaerobic glycolysis [27]. While resting, the muscles slowly release lactate into the blood. During exercise, especially short-term exercises with high intensity, muscles rapidly produce lactate, while lactate clearance slows down, this leads to an increase in the intracellular lactate concentration, which ultimately results in an increase in net lactate excretion. It is associated with blood from muscles [28]. Lactate is a very important metabolic mediator that acts as a precursor of the gluconeogenesis process in the liver. It is also an oxidative substrate for muscles, the increase in its level indicates an increase in dependence on glycolytic metabolism during activity, and it is considered one of the main causes of fatigue [29]. Most of the lactate produced during exercise is excreted from the body in the form of glycogen and amino acids after the end of exercise, and after a short period of time, the level of lactic acid returns to baseline values [29].

In BFR exercises, the purpose of added pressure is to limit the blood flow to the working muscles, which causes blood to accumulate in the capillaries of the body. With the accumulation of blood in the veins, the amount of blood that goes to the heart and as a result the arterial blood flow also decreases[1]. When the blood flow to the muscles decreases, the amount of oxygen and nutrients, especially glucose, decreases to a great extent, which is the adaptation factor of the muscles to low oxygen. Hypoxic conditions created by blood flow restriction increase the release of growth hormone, norepinephrine, IFG-1 [2] and other hormones related to hypertrophy adaptation and strength increase [3].

In BFR training or Katsu training, after performing a set of movements, the concentration of lactic acid in the body increases and stimulates receptors in the brain. By increasing the concentration of lactic acid in the blood, the growth hormone-secreting areas in the brain are stimulated, which increases the secretion of growth hormone, adrenaline, and anabolic hormones. Increasing lactic acid also stimulates the intramuscular receptors. The signals from these receptors cause the pituitary gland to secrete growth hormone, which increases metabolism and fat burning. These factors, i.e. the release of growth hormone and better contractile function of blood vessels, increase the production of nitric oxide (NO) and cause simultaneous activation of fast and slow tension fibers.

In the present study, because the blood lactate of adolescent males increased more during interval training with BFR than in the WFR, the increase in the use of fast twitch muscle fibers during interval training with BFR can be the reason for the increase in lactate in the group of interval training with BFR [18].

The results of this study also showed that two weeks of interval training with BFR caused a significant increase in GH level of active male adolescents. In this research, the main reason for the increase in growth hormone secretion may be associated with the increase in nitric oxide (NO) and lactate. As one of the most important intracellular and intercellular transmitters, nitric oxide plays an important role in controlling the release of growth hormone from the hypothalamus-pituitary axis [21]. Sharifi et al. (2020) stated that one of the reasons for the increase in GH secretion after moderate and high intensity exercises is the increase in the activity of the sympathetic nervous system. The increase in the activity of the sympathetic nervous system causes the release of epinephrine, norepinephrine and the stimulation of the activity of central adrenergic neurons, as a result of which the amount of GH secretion increases [22]. Growth hormone in the BFR group can be attributed to hypoxic conditions, which causes the accumulation of metabolites and, as a result, the increase in GH concentration to a greater amount compared to exercises without blood flow restriction [24,23]. However, the findings of the present study were not consistent with the results of Takano et al. [23] and Pullinen et al. [25].

Based on the results of many researches, it seems that the hormonal response and adaptability to it is highly dependent on the type of training program, which is also affected by the variables of training load, number of courses, number of repetitions, the time of rest between periods, the volume of muscles involved and the frequency of the number of sessions per week. This indicates that GH secretion depends on the intensity and volume of training, and on the type of contractile activity and the amount of motor unit recall [26]. Correa and Lengyel also stated the reasons for the reduction of GH in some studies, following the GH synthesis from a negative feedback, which means that the increase of GH reduces the stimulation of the synthesis of the hormone itself or it reduces the interaction with receptors in different tissues of the body[(27].

However, the restriction of blood flow alone does not increase the GH level in subjects, but training is needed to increase the secretion of this hormone. The higher level of this hormone during katsu exercises may be related to the afferents originating from the fast-twitch fibers of the skeletal muscle [28]. Also, exercises that cause more anaerobic needs may stimulate GH secretion to a greater extent [29]. In other words, it can be said that the limitation of blood flow causes a decrease in oxygen levels and ultimately increases the formation of lactate, as we found in our results. Lactate accumulates in the target muscle and blood flow restriction prevents the transfer of lactate to the liver and other tissues, as a result, lactate accumulation may increase GH secretion [30]. In general, findings indicate that low-intensity training with blood flow restriction increases GH as much as high-intensity training, while in our study [31], the results showed that high-intensity training increases GH. The stimulus for the hormonal response is through afferent feedback so that a relatively low mechanical stress is associated with a lower hormonal response [30].

Also, the absence of a significant change in the concentration of IGF-1 due to exercise in the BFR group was in line with the results of Fujita et al. [33], Beakley et al. (2005) and Ab et al. [23] . During exercise, the body is completely confused and many of the adjustments needed at this time are done with the nervous system and the endocrine system. A possible mechanism for creating an anabolic state is a hormonal response to exercise. Somatotropin (GH), somatomedins (insulin-like growth factor) increase acutely and chronically after a bout of strength training. These hormones have anabolic effects, but it is not clear whether the increase of these hormones in response to exercise is sufficient for the systemic and muscular adaptations observed after exercise.

In the explanation of the results of these findings, it should be acknowledged that despite the general causes that are effective in reducing or not changing the resting levels of these hormones, following the training period, adaptability to exercise increases the amount of GH and insulin-like growth factor transporters (GHBP and IGFBPS). In addition, IGF-1-binding proteins (IGFBPs) and GHBP (GH) affect the function of these hormones. In such a way that, on the one hand, it increases the half-life of GH and 1-IGF in the blood, and on the other hand, it leads to a decrease of free IGF-1 and GH [36,35]. Therefore, GHBP and IGFBPs can play an effective role in regulating the amount of IGF-1 and GH during the day and night.

However, some studies reported a significant increase in IGF-1 concentration after flow-limiting exercise [37]. In explaining the observed differences between the previous studies and the current study, it seems that considering that the subjects participating in this research were active adolescents who are more active and agile than adults, perhaps one of the reasons for no significant change in the resting levels of IGF-1 after this training can be interpreted according to the hypothesis which indicates that the effect of exercise on the hormone secretion is inversely related to the level of physical activity

Conclusion

Based on the results of this research, the change in the levels of GH and lactate with blood flow restriction, which show more increase, it is suggested to use interval training to change the amount of growth hormone concentration. Considering that the presented training program is a simple, practical and useful for young and active people to increase growth hormone and lactate, so, it is suggested that this type of exercise is appropriate and desirable in the design and planning of training for young people.

References

1. Vilaça-Alves, J., Magalhães, P. S., Rosa, C. V., Reis, V. M., Garrido, N. D., Payan-Carreira, R., ... & Costa, P. B. (2022). Acute hormonal responses to multi-joint resistance exercises with blood flow restriction. Journal of Functional Morphology and Kinesiology, 8(1), 3.
2. Sundari, L. P. R., & Ar, N. L. K. A. (2022). Regular Physical Exercise Increase of Growth Hormone (GH) and Insulin-Like Growth Factor-1 (IGF-1) Activity in Elderly Improve the Aging Process and Quality of Life: A Mini Review. *Biomedical and Pharmacology Journal*, *15*(2), 883-890.
3. Sharifi, S., Monazzami, A., Nikousefat, Z., Heyrani, A., & Yari, K. (2020). The acute and chronic effects of resistance training with blood flow restriction on hormonal responses in untrained young men: A comparison of frequency. *Cellular and Molecular Biology*, *66*(1), 1-8.
4. Haj-Ahmad, L. M., Mahmoud, M. M., Sweis, N. W., Bsisu, I., Alghrabli, A. M., Ibrahim, A. M., & Zayed, A. A. (2023). Serum IGF-1 to IGFBP-3 molar ratio: a promising diagnostic tool for growth hormone deficiency in children. *The Journal of Clinical Endocrinology & Metabolism*, *108*(4), 986-994.
5. Teixeira, EL, Barroso, R., Silva-Batista, C., Laurentino, GC, Loenneke, JP, Roschel, H., ... & Tricoli, V. (2018). Blood flow restriction increases metabolic stress but decreases muscle activation during high-load resistance exercise. *Muscle & nerve*, *57* (1), 107-111.
6. Taylor, CW, Ingham, SA, & Ferguson, RA (2016). Acute and chronic effect of sprint interval training combined with postexercise blood-flow restriction in trained individuals. *Experimental physiology*, *101* (1), 143-154.
7. Moore, DR, Burgomaster, KA, Schofield, LM, Gibala, MJ, Sale, DG, & Phillips, SM (2004). Neuromuscular adaptations in human muscle following low intensity

resistance training with vascular occlusion. *European journal of applied physiology*, *92* (4-5), 399-406.

8. Uchida, MC, Bacurau, RFP, Navarro, F., Pontes Jr, FL, Tessuti, VD, Moreau, RL, ... & Aoki, MS (2004). Alteration of testosterone: cortisol ratio induced by resistance training in women. *Revista Brasileira de Medicina do Esporte* , *10* (3), 165-168.
9. Zaravar, L., Nemati, J., Rezaei, R., Jahromi, M. K., & Daryanoosh, F. (2021). Effect of eight weeks water exercise with blood flow restriction on growth hormone, insulin-like growth factor-1 and bone metabolism in elderly women. *Sport Physiology*, *13*(51), 69-92.
10. Reeves, GV, Kraemer, RR, Hollander, DB, Clavier, J., Thomas, C., Francois, M., & Castracane, VD (2006). Comparison of hormone responses following light resistance exercise with partial vascular occlusion and moderately difficult resistance exercise without occlusion. *Journal of applied physiology*, *101* (6), 1616-1622.
11. Yinghao, L., Jing, Y., Yongqi, W., Jianming, Z., Zeng, G., Yiting, T., & Shuoqi, L. (2021). Effects of a blood flow restriction exercise under different pressures on testosterone, growth hormone, and insulin-like growth factor levels. *Journal of International Medical Research*, *49*(9), 03000605211039564.
12. Madarame, H., Sasaki, K., & Ishii, N. (2010). Endocrine responses to upper- and lower-limb resistance exercises with blood flow restriction. *Acta Physiologica Hungarica* , *97* (2), 192-200.
13. Neto, GR, Novaes, JS, Dias, I., Brown, A., Vianna, J., & Cirilo-Sousa, MS (2017). Effects of resistance training with blood flow restriction on hemodynamics: a systematic review. *Clinical physiology and functional imaging* , *37* (6), 567-574.
14. Shimizu, R., Hotta, K., Yamamoto, S., Matsumoto, T., Kamiya, K., Kato, M., & Tanaka, S. (2016). Low-intensity resistance training with blood flow restriction improves vascular endothelial function and peripheral blood circulation in healthy elderly people. *European journal of applied physiology*, *116* (4), 749-757.
15. Heydari., F. (2012). Acute response of lactate, GH and IGF-1 to two exercise protocols with blood flow restriction in adolescent men, Master's Thesis, Faculty of Physical Education and Sports Sciences, Ferdowsi University of Mashhad.
16. Matin Homai et al. (2012). The effect of eight weeks of intermittent and continuous training on the resting levels and response to single-session activity of GH and IGF-1 in the serum of active adolescent men, master's thesis, Tehran Azad University, Faculty of Sports Sciences.
17. Borland, R. L., Cameron, L. A., Tonge, B. J., & Gray, K. M. (2022). Effects of physical activity on behaviour and emotional problems, mental health and psychosocial well-being in children and adolescents with intellectual disability: A systematic review. Journal of Applied Research in Intellectual Disabilities, 35(2), 399-420.
18. basereh, a., ebrahim, kh, hovanloo, f., dehghan, p., & khoramipour, k. (2017). Effect of blood flow restriction deal during isometric exercise on growth hormone and testosterone active males.

19. Takarada, Y., Nakamura, Y., Aruga, S., Onda, T., Miyazaki, S., & Ishii, N. (2000). Rapid increase in plasma growth hormone after low-intensity resistance exercise with vascular occlusion. *Journal of Applied Physiology, 88* (1), 61-65.
20. Christiansen, D., Eibye, K., Hostrup, M., & Bangsbo, J. (2021). The effect of blood-flow-restricted interval training on lactate and H+ dynamics during dynamic exercise in man. *Acta Physiologica*, *231*(3), e13580.
21. Sharifi, S., Monazzami, A., Nikousefat, Z., Heyrani, A., & Yari, K. (2020). The acute and chronic effects of resistance training with blood flow restriction on hormonal responses in untrained young men: A comparison of frequency. *Cellular and Molecular Biology*, *66*(1), 1-8.
22. Abe, T., Yasuda, T., Midorikawa, T., Sato, Y., Inoue, K., Koizumi, K., & Ishii, N. (2005). Skeletal muscle size and circulating IGF-1 are increased after two weeks of twice daily "KAATSU" resistance training. *International Journal of KAATSU Training Research, 1* (1), 6-12.
23. Takano, H., Morita, T., Iida, H., Asada, KI, Kato, M., Uno, K., & Eto, F. (2005). Hemodynamic and hormonal responses to a short-term low-intensity resistance exercise with the reduction of muscle blood flow. *European journal of applied physiology, 95* (1), 65-73.
24. Sharifi, S., Monazzami, A., Nikousefat, Z., Heyrani, A., & Yari, K. (2020). The acute and chronic effects of resistance training with blood flow restriction on hormonal responses in untrained young men: A comparison of frequency. *Cellular and Molecular Biology*, *66*(1), 1-8.
25. Kraemer, WJ, Staron, RS, Hagerman, FC, Hikida, RS, Fry, AC, Gordon, SE, & Newton, RU (1998). The effects of short-term resistance training on endocrine function in men and women. *European Journal of Applied Physiology and Occupational Physiology, 78* (1), 69-76.
26. Correa-Silva, SR, & Lengyel, AMJ (2003). Influência dos glicocorticoids sobre o eixo somatotrófico. *Arquivos Brasileiros de Endocrinologia & Metabologia* .
27. Takano, H., Morita, T., Iida, H., Kato, M., Uno, K., Hirose, K., & Eto, F. (2005). Effects of low-intensity "KAATSU" resistance exercise on hemodynamic and growth hormone responses. *International Journal of KAATSU Training Research, 1* (1), 13-18.
28. Takano, H., Morita, T., Iida, H., Asada, KI, Kato, M., Uno, K., & Eto, F. (2005). Hemodynamic and hormonal responses to a short-term low-intensity resistance exercise with the reduction of muscle blood flow. *European Journal of Applied Physiology and Occupational Physiology, 95* (1), 65-73.
29. Ahtiainen, JP, Pakarinen, A., Kraemer, WJ, & Häkkinen, K. (2003). Acute hormonal and neuromuscular responses and recovery to forced vs. maximum repetitions multiple resistance exercises. *International Journal of Sports Medicine, 24* (06), 410-418.
30. 3 1. Wideman, L., Weltman, JY, Hartman, ML, Veldhuis, JD, & Weltman, A. (2002). Growth hormone release during acute and chronic aerobic and resistance exercise. *Sports Medicine*, *32* (15), 987-1004.

31. Sato, Y., & Abe, T. (2005). KAATSU-walk training increases serum bone-specific alkaline phosphatase in young men. *International Journal of KAATSU Training Research, 1* (2), 77-81.
32. Abe, T., Kearns, CF, & Sato, Y. (2006). Muscle size and strength are increased following walk training with restricted venous blood flow from the leg muscle, Kaatsu-walk training. *Journal of Applied Physiology, 100* (5), 1460-1466.
33. Fujita, S., Abe, T., Drummond, MJ, Cadenas, JG, Dreyer, HC, Sato, Y., & Rasmussen, BB (2007). Blood flow restriction during low-intensity resistance exercise increases S6K1 phosphorylation and muscle protein synthesis. *Journal of Applied Physiology, 103* (3), 903-910.
34. Cuneo, RC, Salomon, FRANC, Wiles, CM, Hesp, R., & Sonksen, PH (1991). Growth hormone treatment in growth hormone-deficient adults. I. Effects on muscle mass and strength. *Journal of Applied Physiology, 70* (2), 688-694.
35. Hansen, S., Kvorning, T., Kjaer, M., & Sjøgaard, G. (2001). The effect of short-term strength training on human skeletal muscle: the importance of physiologically elevated hormone levels. *Scandinavian Journal of Medicine & Science in Sports, 11* (6), 347-354.
36. Reeves, GV, Kraemer, RR, Hollander, DB, Clavier, J., Thomas, C., Francois, M., & Castracane, VD (2006). Comparison of hormone responses following light resistance exercise with partial vascular occlusion and moderately difficult resistance exercise without occlusion. *Journal of Applied Physiology, 101* (6), 1616-1622.