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ORIGINAL ARTICLE

Effect of the aerobic power test performed at low-medium altitude on the myostatin, pgc-1 alpha and klotho levels

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ABSTRACT

BACKGROUND: The aim of this study was to investigate the influence of the aerobic power test on myostatin, PGC-1, and Klotho levels in athletes who had acclimatized to the altitude.

METHODS: A total of twenty athletes consisting of nine women and eleven men with an age average of 19.80±2.587 who were engaged in cross-country skiing at elite level participated in the study. The study was carried out at a ski center (altitude: 2000 m). The participants were measured for age, height, body mass (by standard methods), aerobic power test, blood lactate level after rest and aerobic power test. Blood was obtained from the (basal) antecubital vein in the fasting condition before to the aerobic power test. Two hours and 48 hours after the test, blood taking was repeated. Klotho, myostatin and PGC-1α levels were examined in the serum samples by the ELISA device and MicroELISA method.

RESULTS: As a result, the aerobic power test which lasted 15 minutes significantly increased the PGC-1α (31.2%) and Klotho (332.8%) levels ($P<0.016$). The serum, on the other hand, had no effect on the level of myostatin (7.2%) cheval ($P>0.016$).

CONCLUSIONS: Acute exercise (single repetition) was found to be effective even on elite athletes who had adapted to the altitude. Myostatin level did not change with the aerobic power test performed at low-mid altitude, but PGC-1α and Klotho levels increased.

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KEY WORDS: Klotho proteins; Myostatin; Peroxisome Proliferator-activated receptor gamma coactivator 1-alpha; Hypoxia.

General opinion in the sports community is that altitude exercises may enhance endurance performance. Traditional altitude exercise approaches, in which athletes live and train at middle elevations, are encouraged. Furthermore, it is believed that they may bring benefits in terms of performance enhancement for activities taking place at the sea level.[1] It is quite important at altitude camps to pay attention to particular parameters in a physiological manner in terms of acclimatization and erythrocytes; to spare sufficient time not to be less than two weeks; and to usually prefer low-medium (1000-2500 m) altitudes so that exposure to the relevant environment will be a pertinent state. Nevertheless, it has been stated that the altitude camps made 2-4 times a year will be quite beneficial for the competitive performance of the endurance athletes at

the sea level.[2] Altitude levels are categorized as close to sea level (0-500 m), low (500-2000 m), medium (2000-3000 m), high (3000-5000 m) and excessively high (>5000 m).[2, 3] The high-altitude environment is defined as locations where the proportion of oxygen (O_2) in the air begins to decrease as height rises, potentially limiting human survival. Myostatin, PDC-1α (gamma co-activator 1 alpha activated by peroxisome proliferator) and Klotho which particularly have significant effects on oxidative metabolism and mitochondrial density are rather new and even less known/unknown in the sports community. A member of the transforming growth factor beta (TGF-β) family, signal molecules of myostatin control the muscular growth in mammals.[4, 5] Myostatin is one of the molecules regulating the balance between the protein synthesis and state of deterioration in the skeletal muscle.[6, 7] Myostatin is synthesized as a proprotein composed of 376 amino acids (aa). Of this, 24 are aa's which are signal peptides; 243 are propeptide aa's and 109 are those aa's composed of a mature protein.[4] Myostatin strengthens the skeletal muscle with its highly oxidative capacity and lower fatigue effect. Therefore, it is the regulator of the sensitive balance between the muscular mass, muscular force, energy metabolism and endurance as well.[8] Myostatin (mouse myostatin) may cause excessive growth in the skeletal muscle in case of gene deletion or loss of function and lead to an enhancement of the muscular mass. Otherwise, *i.e.,* in case of excessive expression, it causes muscular atrophy (wasting, decrease).[4, 9, 10] As examining the study on myostatin at high altitude, it is discovered that there are no studies on the effects of physical activity on myostatin levels in hypobaric and hypoxic situations when compared to the known ones.[11] PGC-1α has been identified as a key regulator of energy metabolism.[12] Mitochondrial biogenesis including adaptable thermogenesis (process in which the body produces heat/keeping the body temperature constant) is a transcription coactivator which is involved in a variety of reactions such as glucose/fatty acid metabolism, coding of ligament type in the skeletal muscle, heart development, etc. and which interacts with a variety of transcription factors.[13] The *PGC-1* gene is found on the fourth chromosome in humans and the fifth chromosome in mice. It generates a protein-coding consisting of 798 amino acids (797 in mice). It is readily accessible in tissues where oxidative metabolism is occurring (brown fatty tissue, heart, skeletal muscle in which mitochondrion is intensive). This level is also high in brain and kidneys. However, it is expressed at a low level in the liver and at a much lower level in the white fatty tissue.[14] It is known that PGC-1α leads to reformation of the composition of the skeletal muscle. PGC-1α may be easily stimulated in the skeletal muscle both during the short-term and endurance-containing exercises on rodents and human beings.[15-18] The existence of the Klotho gene (*KL*) was first expressed in mice in 1997. Those mice that are deficient in terms of *KL* gene continue their normal development for a short time (3 weeks) and after which their development rate reduces. Immediately afterwards, they display signs of aging (8-9 weeks) and die. This state has been explained as a consequence of the fact that the *KL* gene displays some kind of aging phenotypes while it fails to display its normal function in the analyses carried out.[19] Klotho is an enzyme encoded by the *KL* gene in human beings (a protein composed of 1014 amino acids). The mutations in this property have also been associated with aging, bone loss and alcohol consumption. That is to say, the osteoporosis problem experienced at the old age phase and alcohol drinking mutates this protein and changes and alleviates its effect.[20, 21] S-Klotho (in soluble form) is considered to be a strong biomarker to be longevous. It has been observed that elevations in plasma Klotho concentrations caused by aerobic exercise improve vascular protection and may be responsible for the rehabilitation of arterial stiffness caused by endothelin.[22] The aim of this study was to see how the aerobic power test affected blood myostatin, PGC-1, and Klotho levels in athletes who had acclimatized to high altitude.

Materials and methods

Research ethics

This study has been upheld and unanimously accepted and approved in terms of the provi-

sions of the regulations concerning the "Scientific Research and Publication Ethics" by the "Ethical Committee for Clinical Research" of the Binali Yildirim University at Erzincan (protocol no. 33216249-903.99-E.14479, approval date: 20.03.2020). As the participants were professional (national) athletes, the necessary permission was obtained from the Turkish Skiing Federation as to the fact that there was not any obstacle for the athletes to participate in the research and that it was appropriate to carry out the research on athletes. At the same time, the "Voluntary Consent Forms" were caused to be signed by the athletes.

Group of participants

Research was carried out on a total of twenty athletes consisting of nine women and eleven men with an age average of 19.80±2.587 who were engaged in cross-country skiing at elite level participated in the study. Participants were selected by the cluster sampling method.

Place and time of research

Research was carried out at the ski center (altitude: 2000 m) as it was included in the low-medium altitude and was a place where athletes continuously camped.

Physical measurements

A Konscales-branded digital scale was used for the height (cm) and weight (kg) measurements of the athletes.

Information-notice

Participants were requested not to take any stimulants (caffeine, alcohol, drugs, etc.) and to avoid any severe physical activities prior to the test (24-48 hours).[23] It was confirmed that the participants did not have any diseases, that they did not use regular medicine nor smoke cigarettes, that they did not have any cardiovascular disorders and hormonal treatment in their medical histories, etc.[24]

Blood lactate concentration level measurement

A portable hand-held lactate measuring analyzer (THE EDGE-Lactate Analyzer) was used in order to measure the average lactate (fatigue marker) in the blood. Blood drop taken from the fingertip for measurement (0.7 μL) was dripped on strips and instantly analyzed in the blood lactate analyzer by using the lactate oxide technique. Measurements were taken in the following sequence: prior to the aerobic power test (5 minutes ago), during the test (4, 5 minutes), 2 minutes after the test and 5 minutes after the test.[25]

Taking blood samples and biochemical analyses

Blood was taken from the antecubital vein in the seated position by the medical personnel to determine the basal values of the subjects prior to the aerobic power test (in the fasted state between 08:00 and 09:00 AM) and then the test was performed (at 11:00 AM). Blood was taken from the subjects again to determine the early (2 hours afterward) and possible (48 hours afterwards) effects of the test. Serum and plasma were centrifugally segregated from the blood samples so taken and preserved (at +4°C). All samples were analyzed in one go. Klotho, myostatin and PGC-1α levels were studied on the serum samples by the enzyme-linked immunosorbent assay (ELISA) device and by the MicroELISA method in compliance with the manufacturer's instructions.[23, 24, 26-29] As far as hemogram test was concerned, the fluorescence flow cytometry method was used by an XN1000 Sysmex analyzer (SYSMEX, Norderstedt, Germany). Regarding PGC-1α by Elabscience (Elabscience, Houston, TX, USA) human peroxisome proliferator activated receptor gamma coactivator 1 alpha (PPARγC1α) ELISA kit (E-EL-H1359 96-Test) was used, and analyses was performed by the MicroELISA method. The myostatin used was by Elabscience (Elabscience) human myostatin (MSTN) ELISA Kit (E-EL-H1437 96-Test) was used, and analyses was performed by the MicroELISA method. Klotho was analyzed using Elabscience brand (Elabscience) Human KL (Klotho) ELISA Kit (E-EL-H5451 96-Test); furthermore, analyses was performed using the MicroELISA method. The Elisa device by Epoch Biotek Elisa Reader and Biotek (EL×50TM) automated strip washer (Agilent Technologies, Santa Clara, CA, USA) were used.

Aerobic power test

Åstrand-Ryhming (Å-R) bicycle ergometer test is an application serving to indirectly determine the O_2 consumption level of a person as a result of a submaximal test. The test started at 100W on women. 150W and 200W were applied after the 3rd and 6th minutes respectively. At the end of the 9th minute, the load was reset, and the subjects were requested to pedal idly (pedal speed: 50 rpm) for the purpose of regenerating/resting for 6 minutes. The test started at 150W on men. 200W and 250W were applied after the 3rd and 6th minutes respectively. At the end of the 9th minute, the load was reset, and the subjects were requested to pedal idly (pedal speed: 50 rpm) for the purpose of regenerating/resting for 6 minutes. HR measurements were taken during the last 15 seconds of each minute by the help of the polar watch available in the bicycle ergometer system.[30]

Statistical analysis

Data obtained from the research were analyzed by the IBM Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) 24.0 package program. Shapiro-Wilk Test was performed in the determination of the distribution of data; descriptive and frequency analysis in the determination of the averages; and one-way analysis of variance (ANOVA) in repeated measurements in the determination of the variances between measurements. Bonferroni adjustment was made to control the type I error. Results were provided as arithmetic average and standard deviation (X±SS), mean difference (MD), minimum observation value (minimum) and maximum observation value (maximum). Level of significance was considered to be P<0.016 in 3-repeat tests (for hemogram and markers) and P<0.012 in 4-repeat tests (for blood lactate).

Results

The findings of the study in which twenty athletes consisting of nine women (45%) and eleven men (55%) participated were presented and explained in the form of tables. In Table I, the age average of the participants was determined as 19.80±2.58 (years), sports age average as 8.20±2.82 (years), body mass average as 61.80±10.84 (kg), height average as 170.60±9.88 (cm), VO_{2max} average as 67.47±7.73 ($mL.dk^{-1}.kg^{-1}$), HR_{max} average as 75.26±3.26 (%). It was determined that an increase occurred in the WBC, RBC, HGB, HCT and PLT values prior to and after the aerobic power test (Table II). When looking at Figure 1, the following average values were discovered: serum Klotho (ng/mL) level was 1.25±0.35 prior to the test, 2.61±2.02 2 hours after the test and 5.41±5.67 48 hours after the test (increased by % 332.8), serum myostatin (ng/mL) level was 14.28±9.11 prior to the test, 13.85±5.42 2 hours after the test and 15.31±6.54 48 hours after the test (increased by % 7.2; serum PGC-1α (ng/mL) level was 4.70±0.99 prior to the test, 5.51±1.08 2 hours after the test and 6.17±1.03 48 hours after the test (increased by % 31.2). It was determined that the average of the blood lactate levels was 3.26±2.28mmol/L, 4.10±2.87mmol/L,

TABLE I.—*Distribution of some physical and physiological parameters.*

Variables	Min.	Max.	X±SS
Age (years)	16	25	19.80±2.58
Sports age (years)	3	13	8.20±2.82
Body mass (kg)	49	87	61.80±10.84
Height (cm)	156	187	170.60±9.88
VO_{2max} ($mL.dk^{-1}.kg^{-1}$)	56.56	83.11	67.47±7.73
HR_{max} (%)	68.80	81.00	75.26±3.26

HR_{max} (%): what percentage an individual uses of his maximum heart rate and at what rate during the test.

TABLE II.—*Pretest and post-test average values in selected hemogram results.*

Variables	Test	Min.	Max.	X±SS
WBC (×10^3/µl)	Pretest	2.81	7.72	5.35±1.18
	After 2 hours	3.21	8.48	6.80±1.30
	After 48 hours	4.06	7.77	5.86±1.10
RBC (×10^3/µl)	Pretest	4.41	5.70	4.98±0.42
	After 2 hours	4.40	5.43	4.90±0.34
	After 48 hours	4.53	5.84	5.15±0.41
HGB (g/dL)	Pretest	12.60	17.00	14.94±1.17
	After 2 hours	12.10	16.10	14.70±1.06
	After 48 hours	12.40	17.40	15.38±1.17
HCT (%)	Pretest	46.70	60.00	52.48±3.67
	After 2 hours	46.00	56.40	51.20±2.74
	After 48 hours	47.70	60.40	53.69±3.25
PLT (×10^3/µl)	Pretest	108.00	287.00	189.60±62.11
	After 2 hours	100.00	283.00	193.05±61.14
	After 48 hours	131.00	285.00	205.63±55.51

Assessment of the samples taken prior to the aerobic power test and 2 hours and 48 hours after the test respectively.

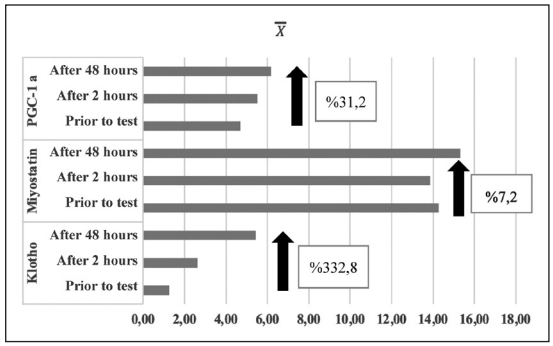


Figure 1.—Pretest and post-test average values in serum klotho, myostatin and pgc-1α levels.
Determination of serum klotho, myostatin and PGC-1α levels from the sample taken prior to the aerobic power test and 2 hours and 48 hours after the test respectively.

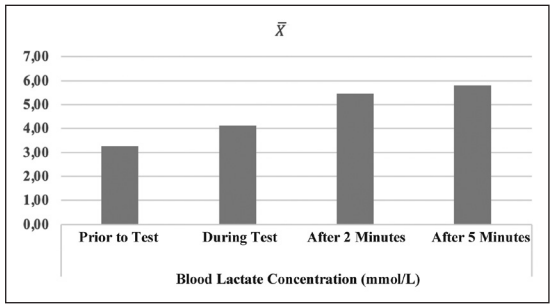


Figure 2.—Pretest and post-test average values in blood lactate levels.
Blood lactate levels measured prior to the aerobic power test, 2 minutes after the test and 5 minutes after the test.

5.45±2.39mmol/L and 5.79±3.81 mmol/L prior to the test, during the test 2 minutes after the test and 5 minutes after the test, respectively (Figure 2). In Table III, it was determined that there was a highly significant difference (P<0.016) in the serum Klotho and PGC-1α levels prior to the test, 2 hours after the test and 48 hours after the test but that there was not any significant difference in the serum myostatin level (P>0.016) prior to and after the test. As shown Table IV, it was determined that there was not any statistically significant difference (P>0.012) between the pretest and post-test blood lactate level measurements. As seen in Table V, it was determined that there was a significant difference (P<0.016) in the WBC, RBC, HGB and HCT parameters between the pretest and post-test values.

Discussion

It has been reported that while the workouts performed in hypoxic conditions improved performance, they also exhibited signs of a larger rise in capacity after the activities.[31] The lack of a change in myostatin levels was due to the test failing to promote protein synthesis since it was not resistance exercise-oriented, and the oxidative metabolism not being particularly active in-

TABLE IV.—*Inter-test comparison of blood lactate levels.*

Test		Blood lactate concentration (mmol/L)		
		MD	±SS	P
Prior to test	During test	-0.84	0.70	1.00
	After 2 min.	-2.19*	0.67	0.02
	After 5 min.	-2.53	1.03	0.14
During test	Prior to test	0.84	0.70	1.00
	After 2 min.	-1.34	0.77	0.60
	After 5 min.	-1.69	0.91	0.47
After 2 min.	Prior to test	2.19*	0.67	0.02
	During test	1.34	0.77	0.60
	After 5 min.	-0.34	0.99	1.00
After 5 min.	Prior to test	2.53	1.03	0.14
	During test	1.69	0.91	0.47
	After 2 min.	0.34	0.99	1.00

Comparison of the blood lactate levels measured prior to and during the aerobic power test, 2 minutes after the test and 5 minutes after the test.

TABLE III.—*Intertest comparison of serum klotho, myostatin and pgc-1α levels.*

Test		PGC-1α (ng/mL)			Myostatin (ng/mL)			Klotho (ng/mL)		
		MD	±SS	P	*MD*	±SS	P	*MD*	±SS	P
Prior to Test	After 2 hours	-0.83*	0.20	0.00*	-0.02	2.57	1.00	-1.47*	0.44	0.01*
	After 48 hours	-1.50*	0.23	0.00*	-1.51	2.42	1.00	-4.20*	1.26	0.01*
After 2 hours	Prior to Test	0.83*	0.20	0.00*	0.02	2.57	1.00	1.47*	0.44	0.01*
	After 48 hours	-0.67	0.28	0.09	-1.49	1.72	1.00	-2.73	1.19	0.10
After 48 hours	Prior to Test	1.50*	0.23	0.00*	1.51	2.42	1.00	4.20*	1.26	0.01*
	After 2 hours	0.67	0.28	0.09	1.49	1.72	1.00	2.73	1.19	0.10

Comparison of the klotho, myostatin and PGC-1α levels from the samples taken prior to the aerobic power test, 2 hours after the test and 48 hours after the test.
*Statistically significant.

TABLE V.—*Inter-test comparison of selected hemogram values.*

	WBC (×10^3/µl)					
	1st test		2nd test		3rd test	
	2nd test	3rd test	1st test	3rd test	1st test	2nd test
MD	-1.41*	-0.49	1.41*	0.91*	0.49	-0.91*
±SS	0.25	0.29	0.25	0.23	0.29	0.23
P	0.00*	0.32	0.00*	0.00*	0.32	0.00*
	RBC (×10^3/µl)					
	1st test		2nd test		3rd test	
	2nd test	3rd test	1st test	3rd test	1st test	2nd test
MD	0.08	-0.14*	-0.08	-0.22*	0.14*	0.22*
±SS	0.04	0.03	0.04	0.03	0.03	0.03
P	0.14	0.00*	0.14	0.00*	0.00*	0.00*
	HGB (g/dL)					
	1st test		2nd test		3rd test	
	2nd test	3rd test	1st test	3rd test	1st test	2nd test
MD	0.23	-0.35*	-0.23	-0.58*	0.35*	0.58*
±SS	0.10	0.10	0.10	0.10	0.10	0.10
P	0.11	0.01*	0.11	0.00*	0.01*	0.00*
	HCT (%)					
	1st test		2nd test		3rd test	
	2nd test	3rd test	1st test	3rd test	1st test	2nd test
MD	1.31*	-0.96*	-1.31*	-2.27*	0.96*	2.27*
±SS	0.39	0.31	0.39	0.29	0.31	0.29
P	0.01*	0.02	0.01*	0.00*	0.02	0.00*
	PLT (×10^3/µl)					
	1st test		2nd test		3rd test	
	2nd test	3rd test	1st test	3rd test	1st test	2nd test
MD	-3.00	-15.42	3.00	-12.42	15.42	12.42
±SS	7.74	8.78	7.74	7.84	8.78	7.84
P	1.00	0.29	1.00	0.39	0.29	0.39

Comparison of the results of the samples taken prior to the aerobic power test (1st test) 2 hours after the test (2nd test) and 48 hours after the test (3rd test).
*Statistically significant.

hibiting protein synthesis. As a result, it is assumed that myostatin did not show any diminution. It is believed that their PGC-1 expression did not decrease and that there was no decrease in mitochondrial intensity because the participants who had acclimatized to the hypoxic environment were not exposed to excessive and long-term hypoxia because they continued their training, living, and competing processes at low-medium altitudes. It is thought that the increase in the Klotho level stemmed from the cell proliferation and inflammatory effect. The high blood lactate level is assumed to have stemmed from the fact that the participants were elite athletes, that they were in competition, and that their resting periods were insufficient owing to strenuous activities. The fact that the subjects were acclimatized is likely to have caused the increases in erythrocyte, leucocyte, and HGB levels. It is believed that there are no deceptive aspects in the blood values of participants who are known not to have dehydration problems and who do not have any modifications in their food habits as a result of their camps at high elevations. In research conducted at an altitude of 2350m, twenty-four top athletes (six women and eighteen men) with an average age of 21.5±3.3 who engaged in endurance workouts were tested at various times during the day to allow the athletes to become used to the environment and exercise program. During the test, a treadmill was used, and physical and physiological measurements were obtained through incremental exercises. As a result of the exercise, HRmax average was de-

termined as 191.5±8.3 (bpm) and VO_{2max} average as 60.0±5.8 ($mL \cdot kg^{-1} \cdot dk^{-1}$).[32] When these results are compared with those of this study, it is observed that the VO_{2max} level (67.47±7.73 $mL \cdot kg^{-1} \cdot dk^{-1}$) is lower and the HR average is higher. The disparity is assumed to be due to the varied test protocols utilized and the lack of acclimatization. Studies carried out on lactate threshold have reported that the lactate threshold as $\%VO_{2max}$ does not change. However, it has further been determined that the lactate level is higher at submaximal exercise intensities. As significant reductions will be observed in the VO2max level as the altitude level increases, a reduction is also observed in the existing lactate threshold value. Therefore, the intensity in the maximal exercise reduces as well.[33] In a research, the effect of acute exercise on the S-Klotho levels in sedentary youth and sedentary adults were examined. A one-hour walk of a treadmill in which VO_{2max} was 55% was preferred for the young group (16 weeks). And a one-hour bicycle ergometer workout in which VO_{2max} was 45% was preferred for the adult group (14 weeks). While any significant change was not observed in the S-Klotho levels of the young individuals prior to and after the initial program, significant increase was achieved in the S-Klotho levels of both young individuals (more effect) and adult individuals (less effect) at the end of the 16-weeks' program.[34, 35] In a study that looked at serum Klotho levels in well-trained athletes, the experimental group included thirty well-trained male soccer players (18-22 years old), whereas the control group included twenty-eight healthy individuals (18-27 years of age). The control group consisted of people who went about their daily lives and exercised but were not athletes, and no physical activity level measurements were recorded. And the experimental group proceeded with their regular workout routines. It was found in the measurement results that the plasma Klotho level was 3.375±1.48 ng/mL in the experimental group and 1.39±0.43 ng/mL in the control group. As a result, it was reported that the exercises taken at an aerobic level led to an increase in the plasma Klotho levels and that the acute effects should be neglected.[24] The effect of acute and chronic exercise on the S-Klotho level in women who exercised and those who did not was explored in a research. S-Klotho levels were found to be greater in women who exercised than in those who did not in measures made prior to the exercise test. In consideration of this fact, it was stated that regular exercise might regularly keep the Klotho level at high levels. According to the study's results, acute exercise generated a significant increase in plasma Klotho levels in both women who exercised and those who did not, however chronic exercise only had a stimulating impact on Klotho in women who exercised on a regular basis.[36] Bai *et al.* aimed to investigate the influence of 4-week hypoxic resistance workouts on myostatin and follistatin gene expression in rat skeletal muscles in their study. The study utilized 24 8-week-old male rats separated into random groups. The groups were established as normoxic control group (N. 6 rats), normoxic exercise group (N. 6 rats), hypoxic control group n:6 rats) and hypoxic exercise group (N. 6 rats). After 4-week hypoxic intervention and hypoxic resistance exercise, the relation of Myostatin mRNA showed changes in a different manner in the muscles of each group. Myostatin mRNA expression in the soleus muscle of the hypoxic control group was found to be 37.2% higher than that of the normoxic control group. In the soleus and biceps brachii muscles of the hypoxic exercise group, the myostatin mRNA expression (591.1%) was found to be lower than that of the hypoxic exercise group (478.4%).[37] In the results, when the myostatin mRNA expression was reviewed, it was observed that it was found to be higher in hypoxic conditions than in normoxic conditions, but that in the case where any exercise was not taken in hypoxic conditions, it was higher. The importance of maintaining a balance between muscle mass, muscular force, energy metabolism, and endurance capacity to adapt to the hypoxic environment is assumed to be the cause of this rise. In the study of Śliwicka *et al.,* eight male participants between the ages of 23-31 made the 4000 m summit climb. The participants had not exposed to high altitude during the past 6 months prior to the climb. In a period 14 days, starting from 1000 m, they reached an altitude of 3000 m within the initial 24 hours and set the base camp at which they would acclimatize for 24 hours. The next day,

they climbed up to an altitude of 3800m and then returned to 3616 m. They pitched camps at an altitude between 3200m and 3600m per 2-3 days. Body mass, body mass index and free fat mass of the participants substantially reduced after the exercise. A positive relation was found between the myostatin and IL-6 levels of the participants and myostatin and CRP after returning from the climb. It was reported that this relation might be one of the factors which prevent the restoration of the inflammatory effect and damaged muscular tissue.[38] The effects of 1200 mg/day alpha lipoic acid (-LA) supplementation and 3 sessions/week faradic (an electrical stimulating system) application on anthropometric parameters, body composition, vascular endothelial growth factor (VEGF), sirtuin-1, nitric oxide (NO), and PGC-1 were studied in obese individuals who were on a diet for weight loss. Randomized clinical study was carried out on one-hundred obese adults. Subjects were arbitrarily assigned to four groups of twenty-five individuals on diet and physical activity basis as follows: faradic, α-LA, αLA + faradic and control groups. A bioelectric impedance analyzer was used to estimate the anthropometric measurements including body weight, body mass index, fat mass and fat-free mass and the serum levels of the sirtuin-1, PGC-1α, VEGF and NO levels were measured. Measurements were obtained before and after the application, which lasted 8 weeks. At the conclusion of the trial, it was found that the average blood sirtuin-1 and PGC-1α levels in the -LA and -LA + faradic groups were significantly higher than in the control group. When the average serum PGC-1α levels (ng/mL) in this study were reviewed, the levels were fond out to be 7.88±3.58 in α-LA, 7.81±3.63 in faradic, 6.68±2.36 in α-LA + faradic and 7.25±3.23 in control group in the measurements taken prior to the application and 10.65±4.64 in α-LA, 8.41±3.94 in faradic, 11.09±5.57 in α-LA + faradic and 6.84±2.63 in control group in the measurements taken after the application.[39] In another study, Edgett *et al.* used eight healthy and slender (lean) men in research to separate increases in PGC-1α and regulators from exercise intensity and muscle activation following acute exercise. The individuals did three distinct high-intensity interval training (HIIT) sessions that targeted 73 percent, 100 percent, and 133 percent of their maximal aerobic capacity to explore the acute effects of varied intensity workouts on the mRNA expression of PGC-1α and its regulators. PGC-1α mRNA expression rose after all HIITs, according to the findings of the study. Surprisingly, it was discovered that when HIITs were performed at 100% effort, an increase of 790% was attained, which was significantly larger than the gains seen at other intensities (+432% in 73% intensity; +424% in 133% intensity).[40]

Conclusions

Acute exercise (single repetition) was found to be effective even on elite athletes who had adapted to the altitude. Myostatin level did not change with the aerobic power test performed at low-mid altitude, but PGC-1α and Klotho levels increased. According to the results, myostatin can be supportive and stabilizer of oxidative metabolism in aerobic exercises. With exercise, PGC-1α can be rapidly stimulated in skeletal muscle. It may have important effects on mitochondrial biogenesis and rapid adaptation to exercise. Klotho can be rapidly stimulated by exercise, resulting in cell proliferation and inflammatory effects. With both acute and chronic exercises, it can delay senescence phenotypes with their anti-aging effect, thus prolonging the lifespan. Klotho is a real justification for getting people to exercise. Klotho is the unknown, hidden, the truest reason for the phrase "exercise is beneficial."

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