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## Research Article

# Effects of 12 Weeks Aerobic Training in Hypoxia on Body Composition and Fat Metabolism in Obese Adults -

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## ABSTRACT

The purpose of this study was to investigate the effects of aerobic training in hypoxia on fat metabolism during resting and exercising and the body composition of people with obesity (body fat  $\geq 25\%$  for men and  $\geq 30\%$  for women). 18 males and females were randomly assigned to aerobic training under hypoxic (13.5% O<sub>2</sub>, n = 9) or normoxic (20.9% O<sub>2</sub>, n = 9) conditions. Subjects trained thrice weekly for 60 min over 12 weeks at 60-75% maximum heart rate (HRmax). Prior to and after training, body composition, venous blood parameters, and blood pressure were determined. Body fat percentage in the hypoxia group was significantly decreased, while it remained unchanged in the normoxia group. After 12 weeks, plasma albumin levels in the hypoxia group increased significantly immediately following exercise, when compared to resting, whereas it was decreased significantly in the normoxia group. Free Fatty Acid (FFA) and leptin were unchanged in both groups. When compared to resting after training, Hematocrit (Hct) and Hemoglobin (Hb) levels in the hypoxia group significantly increased immediately following exercise, whereas levels remained unchanged in the normoxia group. In the hypoxia group Red Blood Cells (RBC) increased immediately following exercise, when compared to resting both before and after training. High-Density Lipoprotein Cholesterol (HDL-C) in the blood of the hypoxia group was increased significantly, whereas it remained unchanged in the normoxia group. Thus, aerobic training in hypoxia reduces body fat and increases HDL-C more greatly than training in normoxia under the same exercise conditions.

**Keywords:** Aerobic; Hypoxia; Fat oxidation; Obesity; Body mass index

## INTRODUCTION

Recently, a study reported that living at high altitudes reduces body weight due to increased leptin secretion, which suppresses appetite [1] and increases the factors affecting fat metabolism [2,3]. Hypoxic exposure increases the density of capillaries [4], synthesis of mitochondria [5], plasma albumin levels [3], and secretion of hormones activating fat metabolism [2].

Intermittent hypoxic exposure induces hypoxia-inducible factor-1, which stimulates leptin gene expression, contributing to appetite suppression and reduced body weight [6,7]. Snyder et al. (2008) reported that plasma leptin concentration in healthy adults significantly increased after living for 17 h a day in a normobaric hypoxia chamber (~4,100 m) [8]. However, previous studies indicate conflicting results regarding plasma leptin levels during hypoxic exposure: increase [9,10], decrease [11-13], and no change [2,14,15].

Increased fat utilization through hypoxic exposure may be due to activation of the sympathetic nervous system [16]. Hypoxia induces adrenocorticotrophic hormone secretion and raises responsiveness between catecholamines and lipids in the adipose tissue [16], contributing to the activation of fat metabolism during rest and exercise [17-19]. Moreover, in hypoxic environments, plasma catecholamine levels during and after exercise are elevated for longer time periods than in normoxic environments [20,21].

Meanwhile reticulocyte, Hb, Hct, and erythropoietin concentration in blood increases even in short-term hypoxic exposure [22]. Improvement in oxygen transport capability is positively correlated with Basal Metabolic Rate (BMR) [16], and the increase in BMR during hypoxia contributes to reducing body fat [23,24]. In particular, improvement of oxygen-delivering ability to working muscle can contribute to fat oxidation [25].

Recently, exercise in hypoxic environments was a countermeasure suggested for treating obesity, patients suffering from musculoskeletal disorders, and the elderly who must perform low-intensity exercises because low-intensity exercise training in hypoxia generates training effects similar to those of middle- or high-intensity training in normoxia [26]. To date, most hypoxia training research focused on improving the performance of athletes or mountaineers, while few hypoxia studies studied obesity [26-29]. Few studies exist on the effects of long term exercise training in hypoxia on fat metabolism and oxygen transport ability during both resting and exercising, though

studies were conducted with obese people at moderate altitudes from 16% O<sub>2</sub>, (2,200m) to 15% O<sub>2</sub>, (2,800m) [26-29]. Therefore, the purpose of this study is to investigate the hypothesis that 12 weeks of aerobic training in normobaric hypoxia (13.5% O<sub>2</sub>, (3,500m)) will elicit further improvements in fat metabolism during resting and exercising and the body composition of obese individuals, when compared to training under normobaric normoxia. Additionally, we would like to ultimately provide a novel therapeutic strategy for optimizing body fat loss in obese.

## MATERIALS AND METHODS

### Subjects

Study subjects included 18 adults (5men, 13 women) who are obese (body fat  $\geq 25\%$  for men and  $\geq 30\%$  for women), but have no musculoskeletal disorders that could limit walking or running. Subjects were randomly categorized into a hypoxia (13.5% O<sub>2</sub>, (3,500m)) group (n = 10), and a normoxia (20.9% O<sub>2</sub>, (0m)) group (n = 8). Subjects were not informed of which group belonged to (single blind assignment), and underwent exercise in the same indoor environment. All subjects were asked not to participate in additional physical activity throughout the study. Furthermore, subjects were required to continue their current, ongoing dietary behaviors. Prior to the subjects' participation, the study purpose was adequately explained and an experimental subject agreement was obtained. The study was performed in accordance with the recommendations of the Declaration of Helsinki. Additionally, the study was approved by the Korea National Sport University Institutional Review Board. Except the one subject abandoning the experiment from each group, a high blood pressure patient, and an amateur marathon participant, the 14 subjects' data were included in the results. The characteristics of the subjects are as on table 1.

The subjects in each experimental condition conducted 60minute treadmill exercises, including warm up (5 min) and cool down (3 min), 3 days per week for 12 weeks. Exercise intensity was gradually raised: week 1-4: 60-70% HRmax, week 5-6: 65-70% HRmax, and week 7-12: 70-75% HRmax. Target heart rate {THR = (HRmax - resting heart rate (HRrest))  $\times$  intensity (%) + HRrest} was calculated using HRmax obtained from the Graded Exercise Test (GXT). Using a HR monitor (Polar S610i, Finland) during exercise, HR was measured every 3 minutes to maintain a constant THR by adjusting the speed and treadmill gradient. According to the exercise groups, exercise

**Table 1:** Subject characteristics.

Variables	Hypoxia Group	Normoxia Group
Men/women (n)	2/6	1/5
Age (years)	38 ± 8.18	37.2 ± 13.1
Body weight (kg)	71.7 ± 19.7	73.2 ± 8.07
BMI (kg/m <sup>2</sup> )	26.3 ± 4.00	26.7 ± 1.46
Body fat percentage (%)	38.2 ± 4.92	40.0 ± 7.50
Resting heart rate (bpm)	70.9 ± 7.7	67.8 ± 8.71
Maximal heart rate (bpm)	180.1 ± 7.18	173.7 ± 13.98

Values are means ± SD.  
BMI: Body Mass Index; bpm: beats/min.

was conducted with hypoxic chamber oxygen concentration at 13.5% (3,500m) and 20.9% (0m). Indoor temperature and humidity were maintained at 22 ± 2°C and 50 ± 5%, respectively.

### Body Composition and Blood Pressure

During rest (8 hours without eating and 48 hours without exercise and alcohol), body fat percentage, fat mass, and muscle mass were measured using Dual-energy x-ray absorptiometry (DEXA; GE Lunar Prodigy, GE Lunar Corp) 4 times before training, 4 and 8 weeks into training, and after training completion. Blood pressure was measured using a mercury sphygmomanometer (Sankei, Japan) twice – before and after training.

### Blood variables

Blood was sampled 4 times by drawing 12 cc from the antecubital vein; at resting and immediately following exercise, both before and after the 12-week training period. Analysis categories included lipid metabolism-related factors such as FFA and albumin in blood, oxygen-carrying capacity factors such as RBC, Hct, and Hb, blood lipid factors such as TC, HDL-C, LDL-C, and TG, and a calorie intake factor, leptin hormone. Plasma FFA and albumin were determined using ACS-ACOD (colorimetry) and BCG Method (colorimetry) respectively (Modular Analytics, Roche). Measurements of RBC count and Hct were conducted by electronic impedance (XE 2100 D, Sysmex). Hb was determined using cyanide-free hemoglobin spectrophotometry (XE 2100 D, Sysmex). TC, HDL-C, LDL-C, and TG were measured with enzymatic colorimetric assay (Modular analytics, Roche). Leptin concentration was determined using radioimmunoassay (COBRA 5010 Quantum, Packard).

### Graded Exercise Test

Through interviews, the existence of cardiovascular system irregularities was checked and GXT (Auto gas analyzer, Quinton Instrument Co, USA) was conducted before training. Using the Bruce protocol, the test was done until all-out state. The determination of “all-out” was when rating scales of perceived exertion (RPE) were over 17, when respiratory quotient was over 1.15, or when subjects raised their hand – signaling that they could not continue.

### Statistics

SPSS v20.0 was used to calculate the means and standard deviations of all variables. To compare interaction effects between groups and training periods, a two-way repeated measures ANOVA was conducted. When significant differences existed, post-verification (LSD) was completed. Statistical significance was set as  $P < 0.05$ .

## RESULTS

### Change of Body Composition

Regarding the change in body fat percentage, differences in interaction effect existed between group and training period ( $P = .040$ , Table 2). Body fat percentages significantly decreased in the hypoxia group ( $P = .000$ ) after 12 weeks of training, yet no differences existed in the normoxia group ( $P = .087$ ). In terms of change in body fat mass, differences in interaction effect existed between group and training period ( $P = .035$ , Table 2). Body fat mass significantly decreased in both groups (hypoxia group  $P = .000$ , normoxia group  $P = .035$ ) after 12 weeks of training. For change in muscle mass, no differences in interaction effect were observed between group and training period ( $P = .787$ , Table 2). Muscle mass remained unchanged in both groups after training (hypoxia group  $P = .271$ , normoxia group  $P = .345$ ).

### Change of Blood Variables

**FFA and Albumin:** For change in concentrations of FFA, no differences in interaction effect were observed between group and training period ( $P = .533$ , Table 3). Comparing before and after training for each group at resting and immediately after exercise, no significant differences at resting and immediately after exercise were observed in both groups, regardless of training period. However, in both groups FFA significantly increased immediately following exercise when compared to resting. For change in concentrations of albumin, differences in interaction effect was observed between group and training period ( $P = .001$ , Table 3). Comparing before and after training for each group at resting and immediately after exercise respectively, no significant differences were observed at resting after training in both groups. In the hypoxia group, albumin significantly increased immediately after exercise relative to before training ( $P = .028$ ), whereas it was significantly decreased in the normoxia group ( $P = .025$ ). Additionally, when comparing resting and immediately after exercise in the hypoxia group, no difference existed before training ( $P = .413$ ), and after training it increased immediately following exercise compared to resting ( $P = .010$ ). In the normoxia group, no significant differences were observed both before and after training ( $P = .519$  and  $P = .771$ , respectively).

**Leptin:** For change in concentrations of leptin, no differences in interaction effect were observed between group and training period ( $P = .607$ , Table 3). Comparing between, before, and after training for each group at resting and immediately after exercise, no significant differences were observed at resting and immediately following exercise in both groups.

**Oxygen Transport Capacity in Blood:** For change in RBC, no differences in interaction effect were observed between group and training period ( $P = .059$ , Table 4). Comparing between before and after training for each group at resting and immediately after exercise, no significant differences were observed at resting and immediately after exercise in both groups. However, comparing resting and immediately after exercise in the hypoxia group, RBC increased immediately after exercise when compared to resting both before and after training ( $P = .048$  and  $P = .001$ , respectively). In the normoxia group, no significant differences were observed before and after training ( $P = .851$  and  $P = .740$ , respectively).

For change in Hct, differences in interaction effect were observed between group and training period ( $P = .001$ , Table 4). Comparing between before and after training for each group at resting and

**Table 2:** The change of body composition in each group.

Variables	Group	Baseline	4weeks	8weeks	12weeks
Body fat percentage (%)	Hypoxia	36.8 ± 4.92	35.9 ± 4.92	34.9 ± 4.58 <sup>a</sup>	33.5 ± 4.98 <sup>abc</sup>
	Normoxia	40.1 ± 7.50	39.9 ± 6.56	39.1 ± 7.07 <sup>b</sup>	38.8 ± 7.28
Body fat mass (kg)	Hypoxia	26.5 ± 7.36	25.2 ± 6.71 <sup>a</sup>	23.9 ± 6.75 <sup>ab</sup>	22.8 ± 7.21 <sup>abc</sup>
	Normoxia	26.7 ± 3.96	26.1 ± 3.17	25.0 ± 3.37 <sup>ab</sup>	24.8 ± 4.00 <sup>a</sup>
Muscle Mass (kg)	Hypoxia	45.8 ± 12.26	45.2 ± 11.92	44.6 ± 11.40	45.2 ± 12.18
	Normoxia	40.7 ± 9.83	40.1 ± 9.64	40.0 ± 10.24	39.9 ± 10.18

Values are means ± SD.  
a: significantly different from pre; b: significantly different from 4wk; c: significantly different from 8wk.  
*P* < 0.05.

**Table 3:** The change of FFA, Albumin and Leptin in each group.

Variables	Group	Baseline		12weeks	
		Rest	After exercise	Rest	After exercise
FFA (µEq/L)	Hypoxia	486.6 ± 197.2	1473.1 ± 405.8 <sup>a</sup>	571.0 ± 253.8	1419.4 ± 356.5 <sup>a</sup>
	Normoxia	699.3 ± 413.9	1445.5 ± 764.5 <sup>a</sup>	522.5 ± 349.3	1279.2 ± 627.6 <sup>a</sup>
Albumin (g/dL)	Hypoxia	4.50 ± 0.21	4.60 ± 0.26	4.64 ± 0.21	4.90 ± 0.21 <sup>ab</sup>
	Normoxia	4.60 ± 0.30	4.72 ± 0.33	4.47 ± 0.16	4.45 ± 0.24 <sup>b</sup>
Leptin (ng/mL)	Hypoxia	8.51 ± 3.62	7.86 ± 3.28	8.56 ± 3.85	8.30 ± 3.51
	Normoxia	15.95 ± 5.99	16.20 ± 9.22	15.57 ± 6.11	18.37 ± 10.34

Values are means ± SD.  
FFA: free fatty acid. a: significantly different from rest; b: significantly different from pre.  
*P* < 0.05.

**Table 4:** The change of oxygen transport capacity in each group.

Variables	Group	Baseline		12weeks	
		Rest	After exercise	Rest	After exercise
RBC (10 <sup>6</sup> ·µl <sup>-1</sup> )	Hypoxia	4.80 ± 0.61	4.94 ± 0.57 <sup>a</sup>	4.82 ± 0.45	4.97 ± 0.49 <sup>a</sup>
	Normoxia	4.53 ± 0.39	4.55 ± 0.52	4.41 ± 0.34	4.42 ± 0.35
Hct (%)	Hypoxia	42.40 ± 5.18	43.76 ± 4.95	43.61 ± 4.01	44.86 ± 4.28 <sup>a</sup>
	Normoxia	43.40 ± 6.53	43.25 ± 6.92	40.55 ± 4.48	41.02 ± 4.56
Hb (g/dL)	Hypoxia	14.24 ± 1.81	14.63 ± 1.96	14.38 ± 1.51	14.78 ± 1.56 <sup>a</sup>
	Normoxia	13.80 ± 2.04	13.85 ± 2.19	13.47 ± 1.51	13.52 ± 1.58

Values are means ± SD.  
RBC: Red Blood Cell; Hct: hematocrit; Hb: hemoglobin.  
a: significantly different from rest; b: significantly different from pre.  
*P* < 0.05.

immediately after exercise, no significant differences were observed at resting and immediately after exercise in both groups. Comparing resting and immediately after exercise in the hypoxia group, no significant differences were observed before training, yet after training Hct immediately increased following exercise when compared to resting (*P* = .011), while no significant differences were observed before and after training in the normoxia group.

For change in Hb, no differences in interaction effect were observed between group and training period (*P* = .119, Table 4). Comparing between before and after training for each group at resting and immediately after exercise, no significant differences were observed at resting and immediately after exercise in both groups. Comparing resting and immediately after exercise in the hypoxia group, no significant differences were observed before training,

yet after training Hb immediately increased after exercise when compared to resting (*P* = .007), while no significant differences were observed both before and after training in the normoxia group.

**Blood Lipid Component:** For TC, HDL-C, LDL-C, and TG, no differences in interaction effect were observed between group and training period (Table 5). Comparing before and after training for each group at resting and immediately after exercise for TC, LDL-C, and TG, no significant differences were observed at resting and immediately after exercise in both groups. However, in the hypoxia group, TC increased immediately following exercise when compared to resting after training (*P* = .004).

For HDL-C, comparing before and after training for each group at resting and immediately after exercise, after training HDL-C increased both at resting and immediately following exercise in the

**Table 5:** The change of blood lipid component in each group.

Variables	Group	Baseline		12weeks	
		Rest	After exercise	Rest	After exercise
TC (mg/dL)	Hypoxia	188.3 ± 29.9	192.9 ± 27.2	188.0 ± 34.3	198.1 ± 35.8 <sup>a</sup>
	Normoxia	202.3 ± 42.3	208.5 ± 60.2	181.2 ± 24.6	184.5 ± 31.3
HDL-C (mg/dL)	Hypoxia	47.8 ± 14.7	53.8 ± 15.4 <sup>a</sup>	56.8 ± 14.5 <sup>b</sup>	60.5 ± 15.6 <sup>ab</sup>
	Normoxia	55.7 ± 5.2	57.0 ± 6.1	62.3 ± 6.4	61.2 ± 5.4 <sup>b</sup>
LDL-C (mg/dl)	Hypoxia	106.4 ± 21.8	110.3 ± 19.6	112.3 ± 32.8	118.4 ± 32.3 <sup>a</sup>
	Normoxia	114.3 ± 29.9	119.3 ± 36.7	110.0 ± 20.2	109.5 ± 22.8
TG (mg/dL)	Hypoxia	166.3 ± 78.4	150.9 ± 72.0	145.4 ± 83.6	161.9 ± 87.1
	Normoxia	154.8 ± 124.6	147.5 ± 134.6	138.3 ± 109.4	193.8 ± 181.3

Values are means ± SD.

TC: Total Cholesterol; HDL-C: High-Density Lipoprotein Cholesterol; LDL-C, Low-Density Lipoprotein Cholesterol; TG: Triglyceride.

a: significantly different from rest; b: significantly different from pre.

*P* < 0.05.

**Table 6:** The change of blood pressure in each group.

Variables	Group	Baseline	12weeks
SBP (mm Hg)	Hypoxia	130.5 ± 12.4	123.1 ± 10.6
	Normoxia	128.3 ± 22.5	123.3 ± 22.5
DBP (mm Hg)	Hypoxia	83.9 ± 11.8	73.1 ± 8.7*
	Normoxia	80.8 ± 11.6	74.5 ± 12.1*

Values are means ± SD.

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure.

\* *P* < 0.05.

hypoxia group (*P* = .008 and *P* = .014, respectively). No difference at resting (*P* = .073) was observed in the normoxia group, yet HDL-C increased immediately after exercise when compared to before training (*P* = .003). In the hypoxia group, HDL-C increased immediately following exercise when compared to resting before and after training (*P* = .009, *P* = .015, respectively). Following training, LDL-C increased immediately when compared to resting in the hypoxia group (*P* = .021).

**Change in Blood Pressure:** For reduction in SBP, no differences in interaction effect were detected between group and training period (*P* = .708, Table 6). For reduction in DBP, no differences in interaction effect were observed between group and training period (*P* = .366). DBP significantly decreased in both groups (hypoxia group *P* = .023, normoxia group *P* = .030), yet no significant differences existed in both groups after 12 weeks of training.

## DISCUSSION

The results of this study have demonstrated that 12 weeks of aerobic training in hypoxia results in increased reduction of body fat percentage and body fat mass in obese subjects compared to training in normoxia, while increasing blood HDL-C concentration. These results are consistent with the findings of which demonstrated that 60 minutes of training 3 days a week for 4 weeks in normobaric hypoxia (15% = 2,740m) reduced more body fat mass in obese subjects than training in normoxia [26]. The results are also consistent with a study by Netzer et al. (2008) that demonstrated 90-minutes of training 3 days a week for 8 weeks in normobaric hypoxia (15% = 2,740m) resulted in more body weight reduction in obese subjects than training in normoxia [29].

The current study suggests that lipolysis may not be promoted on acute and long-term intermittent hypoxic exposure, since plasma FFA levels in the hypoxia group remained unchanged. Previous studies provided controversial results regarding lipolysis during hypoxia. Strobel, et al. (1996) reported that lipolysis decreases during hypoxia due to increased catecholamine levels [21], whereas Barnholt, et al. (2006) reported that lipolysis increases during hypoxia by a greater autonomic neuroendocrine stimulation [2]. In this study, the increase in lipid oxidation likely explains increased body fat reduction in the hypoxia group instead of lipolysis promotion.

Firstly, in the hypoxia group, increased plasma albumin concentration after training can deliver FFA produced by lipolysis during exercise to working muscle more effectively, allowing it play a critical role in producing energy via β-oxidation [30], which contributes to a reduction of body fat. Nearly all FFA released into blood plasma from adipose tissue is transported by plasma albumin [31]. Imoberdorf, et al. (2001) investigated the variation in plasmatic quantity and plasma albumin concentration by dividing mountain climbers into groups – a group walking to 4,559m in altitude and a group ascending by helicopter [3]. The walking group exhibited a significant increase in plasmatic quantity and in plasma albumin concentration, indicating aerobic exercise increased plasma albumin levels. Alternatively, the group ascending by helicopter displayed a tendency to increase plasma albumin concentration, indicating that hypoxia has an independent effect on the increase of plasma albumin. Mcnurlan, et al. (1996) reported that albumin synthesis increases due to the effect of catecholamine [32]. Therefore, it is possible that epinephrine and nor epinephrine increase during exposure to hypoxia-promoted albumin synthesis, potentially improving the transport and metabolism of FFA.





As the results of this study indicate, no change of plasma albumin concentration is observed immediately following a one-time aerobic exercise in hypoxia. However, the concentration significantly increases immediately following exercise when compared with to resting after 12 weeks of training, indicating that aerobic training in hypoxia for more than a certain period increases albumin synthesis during exercise. Conversely, after training in normoxia, no significant change in plasma albumin concentration is observed immediately following exercise compared to that at resting, indicating that long-term aerobic training in normoxia has no effect on albumin synthesis during exercise.

Secondly, to promote the efficiency of body fat reduction in hypoxia, it may be necessary to improve oxygen-delivering ability to working muscle [22,25]. This study indicates that there are significant differences in training effects on RBC concentration between the two experimental groups. The normoxia group displayed no changes between resting and during exercise. However, in the hypoxia group, both before and after the training, RBC concentration increased during exercise than resting. The results suggest that although aerobic training in intermittent hypoxia does not increase RBC during resting and exercising compared to before training, a prompt increase in RBC during exercise is a temporary adaptation for delivering insufficient oxygen to working muscle cells more effectively. In hypoxia, the higher use of oxygen may play a crucial role in enhancing fat oxidation, since oxygen is the final acceptor of electron transport [25]. However, this theory remains controversial. Chia, et al. (2013) suggested that decreased body fat following hypoxia training may not be related to increased fat metabolism due to relatively lower oxygen availability [27]. Since most existing studies investigated hypoxia training effects for hours or a few weeks, long-term studies are necessary to clarify the differences.

Hct and Hb were compared between before and after training, and the results of this study were consistent with the results of research by Koistinen, et al. (2000), which indicated no significant changes in Hct and Hb following exposure for 12 hours per day for seven days in normobaric hypoxia (15.4%, ~2,500m) [33]. However, the hypoxia group in this study exhibited an increasing tendency both at resting and during exercise, whereas the normoxia group exhibited a reduced tendency. Following 12 weeks training, Hct and Hb levels in the hypoxia group increased more during exercise than rest. In a hypoxic environment, increased Hct and Hb, as well as RBC, may contribute to fat oxidation by effectively delivering oxygen to working muscle [25]. That aerobic training in normoxia reduced Hct and Hb is an unexpected result. To clarify changes of Hct and Hb in hypoxia related to obesity, it is necessary to perform follow-up studies which vary the training (duration, frequency and intensity) and hypoxic environment (oxygen concentration and air pressure).

Additionally, hypoxia promotes efficiency in body fat reduction, as there is an increase in leptin, which is a dietary control hormone [34,35]. However, the relationship between hypoxia and leptin varies depending on the study. Wiesner et al. (2010) conducted 60-minute aerobic training with 65% VO<sub>2</sub>max (maximal oxygen consumption) 3 days per week for 4 weeks in hypoxia (15% = 2,740m) for men and women with obesity [26]. The results indicated no change in leptin. Haufe, et al. (2008) conducted 60-minute aerobic training 3 days per week for 4 weeks in hypoxia (15% = 2,740m) for healthy men [36]. The results indicated that leptin was reduced. Lippl, et al. (2010) exposed participants with obesity to high altitude (2,650m)

for 1 week [28]. The results indicated an increase in leptin. In this study, both groups failed to indicate any significant change in leptin. Conflicting results from these studies resulted from differences in applied air pressure, length of hypoxia exposure, and the degree of a subject's obesity. In this study, body fat loss through long-term aerobic training in intermittent hypoxia may not be related with the involuntary reduction of caloric intake by appetite suppression, given that there was no change in leptin concentration after training, and subjects were asked to maintain their normal diet and nutrition throughout the study.

TC, LDL-C, and TG between the two groups failed to indicate significant differences before and after training, and HDL-C significantly increased in the hypoxia group only. However, TG decreased in both groups. TC failed to indicate any change following training in the hypoxia group, yet decreased in the normoxia group. LDL-C increased in the hypoxia group, yet decreased in the normoxia, which is contrary to initial expectations. The results are somewhat in contrast to a report by Netzer, et al. (2008) [29], yet Wiesner et al. (2010) reported that TC, HDL-C, LDL-C and TG did not exhibit significant changes [26]. Lippl, et al. (2010) reported that HDL-C significantly decreased without significant changes to TC and TG in a hypoxia group, yet LDL-C significantly increased, indicating different results, thus it is necessary to conduct follow-up studies.

Regarding changes in blood pressure, both groups exhibited a significant reduction in DBP only, yet no difference in training effects between the two groups. The hypoxia group exhibited a tendency to decrease more both SBP and DBP compared to the normoxia group, which might be due to greater decrease in body weight. On the other hand, the study of Wiesner, et al. (2010) didn't show a significant improvement in both SBP and DBP [26]. Since this study didn't investigate vascular system we are uncertain why our intervention lowered DBP, but not SBP. Further research is warranted.

This is the first time that a study has investigated fat metabolism during both resting and exercising for long-term hypoxia training. Additionally, this study was conducted with obese people at a significant lower oxygen level (13.5% O<sub>2</sub>, (3,500m)) compared to previous studies, at 15% O<sub>2</sub>, (2,800m) to 16% O<sub>2</sub>, (2,200m) [26-29]. Therefore, this study provides a novel therapeutic strategy for optimizing body fat loss, as individuals of the hypoxia group didn't report any serious illness and showed significant body fat reduction. However, the small number of subjects could have affected statistical power. Moreover, the subjects' diets were not directly supervised, and some subjects may have altered their diet even though they were required to continue their current, ongoing dietary behavior.

## CONCLUSIONS

In conclusion, aerobic training in hypoxia reduces body fat and increases HDL-C in obese more greatly than training in normoxia under the same exercise conditions. Body fat reduction appears to be primarily due to promoted fat metabolism. The increase of albumin, RBC, Hct, and Hb during exercise may indirectly contribute to improving the efficiency of fat oxidation. Further studies are necessary to optimize fat loss with exercise in various hypoxic environments.

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