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Special Article - Intermittent Hypoxia

Intermittent Hypoxia on Anabolic/Catabolic Hormones and Muscular Enzymes in Athletes

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Abstract

This study investigates the effects of Acute Intermittent Hypoxia (IH) along 4 weeks training on anabolic/catabolic hormones and blood indicators of muscle damage. We studied professional male athletes exposed (PA) (n=12) or not (n=12) to IH, at three different moments: baseline (M1) (i.e., under resting conditions immediately before start the study); after two weeks of IH (M2); and at the end of the 4-week IH exposure period (M3).

We measured muscle damage biomarkers creatine kinase, aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase and total proteins; blood cell counts well as serum total Testosterone (T) and Cortisol (C) levels.

The main results were that, no overall IH effect was noted on muscle damage indicators. In CG, T and T/C showed a significant decrease ($p<0.05$). With respect physical performance test we don't have observed significant changes, but light increases around 1%, that is very important in professional sport exercise.

In conclusion, in this study we have observed that IH might potentially stimulate performance through an anabolic effect.

Keywords: Intermittent Hypoxia; Muscular enzymes; Testosterone; Cortisol; Physical performance

Introduction

The demands in the endurance sport high competition, leads to look systems that improve the results. From the decade of 60s the stimulus of hypoxia in athletes has been used as a method to improve athletic performance [1]. Continued exposure to hypoxia, typical of altitude training, involves a number of responses and physiological adaptations and which contribute to improved aerobic endurance [2].

However, from the last years, have been used new devices that aim to simulate the physiological effects of altitude. These methods have not the disadvantages of the difficulties of travel and expense associated; besides that altitude reduces the intensity training [3].

In this way hypoxic or hypobaric Intermittent Hypoxia Exposure (IHE) is an alternative. The option of IHE, in general is carried at rest in resting conditions, and training under normal conditions (normoxia) [4]. Hoppelerand Vogt [5], have informed that the training in hypoxia have specific effects on muscle tissue that not seen similar in normoxia at same intensity training. This group of researchers [6-8], have demonstrated that Intermittent Hypoxic Training (IHT) leads to muscular adaptations that either do not occur in normoxia conditions or, if they do so, do so a lesser degree. These muscular changes may have an origin at the molecular level, via the activation of a transcription factor, hypoxia inducible factor 1α (HIF-1), expressed en skeletal muscle [10].

From these data, Intermittent Exposure to Hypoxia (IHE) at rest has been supported as an ergogenic method to improve endurance performance at sea level [11]. Portable devices for IHE that are commercially available, such as the Altitrainer® or the GO_2 Altitude® Hypoxicator, appear more suitable and practical for applying IHE during cycling tour races.

On the other hand, hypoxia affects the function on the hypothamulus-pitutary-adrenal axis and increases the levels of plasma ACTH. Also, hypoxia stimulates the expression of the steroidogenic acute regulatory protein and enhances the secretion of glucocorticoids as cortisol [12]. In general, normoxia conditions, continuous and intensive exercise has been shown to induce a dysfunction of hypothalamic-pituitary-testicular axis, especially testicular impairment then causing a suppression of testosterone (T) secretion during the latter stages of exercise [13]. Galbo et al [14], have indicated that during intense prolonged exercise, Adrenocorticotropic Hormone (ACTH) concentrations increase, resulting in a significant release of cortisol (C). Hwang et al [12] have observed in rats, in hypoxia, an increase of testosterone production. In this same way we have observed similar effect and we have concluded that the hormone response to exercise is dependent on several factors, including the intensity, duration, mode of exercise, and the training status of the subject [15]. However, Hu et al [16] have informed testosterone decreased after exercise during normoxia and hypobaric hypoxia.

Also, the exercise represents a stress condition that alters metabolism, immunological process, increase muscle damage and inflammation and induces a powerful stimulus of the endocrine system, that generates a hormonal response and provokes changes to try and get homeostasis in the new circumstances, occasioned by the extreme physical effort [17,18].

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Therefore, potential applications of IHE in sport performance and health states are in study and require considerable research to develop protocols that optimize the balance between efficacy and safety on physiological effects of IHE but fundamentally in hormonal and muscular response [4,19].

At now, not studies have investigated, in humans, the influence IHE regimens on hormonal response [testosterone (T) and cortisol (C)] and muscular activity enzymes (damage, inflammation, etc.), produced by acute exercise training program in these conditions. The purpose of the present study was investigating the effects of acute Intermittent Hypoxia (IH) 4 weeks training on anabolic/catabolic hormones and blood indicators of muscle damage. In this context we like to evaluate also the influence of IHE on specific test of performance and clarify if short duration intermittent hypoxia has additive effects on performance using this combination (IHE and normal training) to improve the endurance capacity in athletes.

Methods

We have studied the effect of IHE on the athletic sport performance in elite athletes undergoing training in the pre-competitive period. The protocol was approved by the local ethics committee at Valladolid University (Spain) and follows the recommendations of the Declaration of Helsinki. We have carried the analytical control in 3 moments: a) baseline at rest just before start the study (M1); b) after two weeks of the study (M2 - before start 14 day); c) at the end of 4th week of study (M3 - before start 28 day).

Subjects

Twelve Professional Male Athletes (PA) from the Soria High Training Center (CAEP) and the Spanish National Team have participated in the study. The volunteer athletes were informed about the research protocol. The physical characteristics of athletes as mean + standard deviation (X ± SD) are presented in (Table 1).

All subjects signed a written informed consent and completed a medical questionnaire and a cardiopulmonary and electrocardiographic examination before study entrance. None of the subjects smoked, drank alcohol, or were taking medication known to alter the hormonal response. Concomitant pathology was discarded by clinical rapport and medical examination. All subjects followed a similar diet throughout the season and, especially, the same diet during the study. The diet was constantly supervised by the medical group of the CAEP. The athletes followed the same training program. They trained daily in 2 sessions, from Monday to Saturday. The morning session consisted in specific workout (2-hour) and after which (1-hour) they did hypoxia session (see later). The afternoon session consisted in one hour of continuous and mixed workout. Sundays, they only did the morning training and hypoxia session. The duration of the study was 4 weeks, 3 of load (high intensity training) and one of discharge when where we performed the physical performance tests, the same that before start the hypoxia study.

Also were studied a control group (CG) (n=12), healthy, male, nonsmoking, moderately trained without hypoxia training (Table 1).

Blood collection and analysis

We have used the World Anti-Doping Agency (WADA) rules for collection and transport of samples (www.ama-wada.org). All samples were collected in basal conditions after an overnight fasting (at least 12 hours). All blood samples were taken at 8:30am with the subjects rested comfortably in a seated position, and with Vacutainer system (10mL to serum tubes, 5mL and 3mL tubes with EDTA).

Table 1: Physical and anthropometric characteristics.

	Mean ± SD	
	PA	CG
Age (ys)	26.12±2.90	25.31±4.40
Weight (kg)	63.37±9.72	79.00±4.53
Height (cm)	175.872±9.12	181.32±10.75
Body fat (%) (Yuhasz)	8.93±1.21	13.75±5.34
Max. oxygen uptake (ml. kg^{-1} min^{-1})	70.36±6.96	59.37±6.39

mean ± standard derivation (X ± SD). Group of Hypoxia (PA) and control group in normoxia (CG) athletes of study.

Immediately after drawing, tubes were inverted 10 times and stored in a sealed box at 4°C. Controlled temperature was assured during transportation: a specific tag (Libero Ti1, Elpro, Buchs, Switzerland) was used for temperature measurement and recording. Samples were transported in optimal conditions and the time to leave in the laboratory was 30min after extraction. The delays do not affect the analytical output for the measured parameters. The EDTA anticoagulated blood was homogenized for 15min prior to being analyzed, as recommend the WADA. The tube containing blood plus EDTA should be centrifuged at 2000rpm for 15 minutes. The plasma was extracted using a Pasteur pipette and transferred to a sterile storage tube and stored at -20ºC until by analyzed.

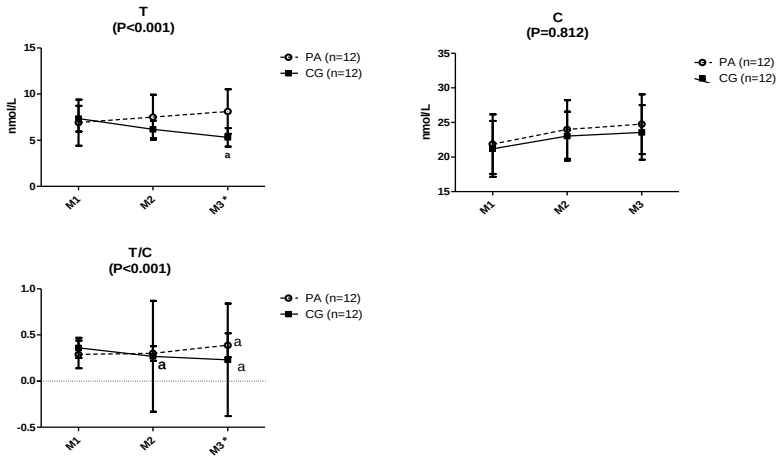
Red Blood Cell (RCB), White Blood Cell (WBC), Lymphocytes (LYM), Monocytes (MON), Hemoglobin (Hb), and Hematocrit (Hct) were determined on a Coulter Counter (model MAX-M).

Biochemical serum markers of muscular behavior [(Creatín Kinase (CK), Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Lactate Dehydrogenase (LDH) and Total Proteins (TP)] were measured by mean an automatic auto analyzer (Hitachi 917, Japan). Mioglobin (Mb) was assessed by chemiluminescence reaction enzyme immunoassay "sandwich" of two points (Myoglobin ELISA Kit, MEXLAB. Zapopan, Jalisco, Mexico).

Serum total testosterone (TT) levels were measured by ELISA (DRG testosterone ELISA kit®, DRG Instruments GmbH, Marburg/Lahn, Germany. Cortisol (C) levels were determined by an enzyme-linked fluorescent assay with the aid of a multiparametric analyzer (Minividas®, Biomerieux, Marcyl'Etoile, France), using as substrate 4 methylumbelliferone capable of a fluorescent emission at 450nm, after stimulation at 370nm. TT and cortisol were expressed in nmol•L^{-1}. TT/C ratios were calculated from TT and cortisol molar concentrations. Percent changes of plasma volume (%ΔPV) were calculated using Van Beaumont's equation [20].

Hypoxia protocol

The athletes (PA), while seated comfortably at rest, received a daily session of IHE for 4 weeks, breathing through a hand-held face mask for a total of 90min per day. The intermittent breathing was administered in a ratio of 5min hypoxic conditions followed by 5min ambient air (IHE 5min on, 5min off). They received either a normobaric hypoxic gas via a GO_2 Altitude hypoxicator device



Data are expressed as mean ± standard deviation (SD). P: Two-factor repeated-measures ANOVA (time x Group). *Significant differences between groups in that specific control point by independent t-test. Significant differences among period of study by Scheffé test [a]p<0.05: [a]vs. M1.T: Testosterone ; C: Cortisol ; T/C: Testosterone/Cortisol ratio.

Figure 1: Hormonal response along the different moment of the study (M1: Baseline M2: before start 14rd day M3: before start 28rd day) on the Professional Athletes (PA) in hypoxia and athletes Control Group (CG) in normoxia.

(Biomedtech, Victoria, Australia). To allow sufficient time for adaptation and in accordance with the manufacturer's instructions, the oxygen concentration in the hypoxic gas was progressively reduced in the experimental condition (FIO_2: 13%, SaO_2: 84-88% in week 1; FIO_2: 12%, SaO_2: 80-84% in week 2; FIO_2: 11%, SaO_2: 77-80% in week 3; FIO_2: 10%, SaO_2: 74-76% in week 4). Peripheral oxygen saturation for each individual was monitored either automatically by the hypoxicator device or manually by a research assistant (Sport-Stat, Nonin Medical, Minneapolis, MN). None of the subjects were acclimated or exposed with recent anteriority to altitude or hypoxia, except that they live in Soria (1.100m). Since the present study was conducted during the subjects' important pre-competitive period of the season. The IHE was administered during recovery hours.

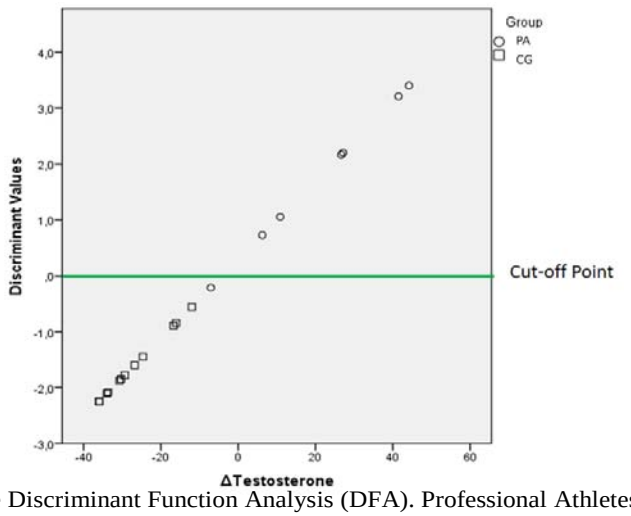
Performance test

As both groups (PA and CG) trained together, with the same program (appropriate to each physical level), the same physical controls were established. Physical performance was assessed by individual test: aerobic power, lactic power and speed were performed in the athletics track, over distances of 1000 meters (m), 400m and 60m respectively. For the strength test, force of the quadriceps with a dynamometer was measured (Leg Jamar, USA). The tests were performed on baseline (M1: day 1rd of the study), without hypoxia treatment, and the final day of the study, (M3: before start 28 day) after 4 weeks of hypoxic exposure.

Statistical analyses

Statistical analyses were performed using the IBM Statistical Package (SPSS Version 22) and Graph pad Prism (Graph pad Software Version 6. San Diego, CA). Data were expressed as mean ± standard deviation (SD). Significant differences were considered for $p < 0.05$. Differences between groups in each control point in all blood samples and performance tests were assessed by an independent Student's t test or Mann–Whitney U-test, after normality of the data had been confirmed with the Shapiro-wilk test, to decide parametric or non-parametric analysis. Additionally, a two factor repeated measure analysis of variance (ANOVA) was carried out by Greenhouse-geisser test to check the existence of an interaction effect (time x group) between PA and CG in anabolic/catabolic hormones, muscular enzymes and performance tests along the different phases of the study (M1, M2 and M3).

On the other hand, an one-way repeated measure (ANOVA) was carried out for hormone, biochemical and hematological parameters by wilks´s Lambda test to check if there were significant variations between all parameters along the different phases of the study (M1, M2 and M3). Post hoc Scheffé multiple comparisons test was applied to determine differences between periods of study. On the other hand, a paired t-test or wilcoson tests was used in performance tests to identify significant differences between M1 and M3 in each group independently. We lastly performed stepwise, discriminant function analysis (DFA) for building a multivariate model that predicted group membership (i.e., hypoxia group) in M1, M3 and Δ (M1-M3). The discriminant function maximally and parsimoniously differentiates groups based on a linear combination of variables (i.e., T, C, CK, Mb, AST, ALT, LDH, TP and T/C ratio). The F-value for entry of a variable into the discriminant function was set as 3.84 and the F-value for removal as 2.71 (i.e., default values). Wilks' Lambda and F-values were examined per stage of the stepwise DFA for identifying the significance of separation of cases into groups, and expressed the overall strength of the association between variables and group membership in the final model based on the canonical correlation and its square (i.e., variance explained). We provided Wilks' Lambda and the associated chi-square for establishing the overall significance of the final model. We inspected the standardized discriminant function coefficients (i.e., comparable with beta weights) for identifying the relative importance of the variables for predicting group membership. We inspected centroids (i.e., multivariate group means) for interpreting the discriminant profile per group.



Data are expressed by the Discriminant Function Analysis (DFA). Professional Athletes (PA) in hypoxia and athletes control group (CG) in normoxia.

Figure 2: Stepwise discriminant function analysis resulted in a final model that included one variable (Δ Testosterone).

Results

Biochemical parameters

Figure 1 show hormone levels and tendency of T, C and T/C. Significant differences were observed throughout the study (M1 to M3) in T and T/C between groups. In PA group T increase significantly (P<0.001), however the tendency of cortisol was to increase but no significantly. With respect T/C ratio increase (p<0.01) along of study (M1 to M3). In CG both, T and T/C were showed a significant decrease along the study (p<0.05), and T/C ratio decrease significantly in M2 and M3 with respect baseline (M1).

The stepwise discriminant function analysis resulted in a final model that included one variable, the T. The overall model was statistically significant (Wilks' Lambda = 0.235, p < 0.001), and the canonical correlation was 0.874. The centroids indicated athletes who use hypoxia (centroid = 1,793) had higher Δ Testosterone values, whereas the athletes who use Normoxia (centroid = -1,569) had lower Δ Testosterone values (Table 2). This model overall correctly classifies 94.7% of cases into groups, with the classification rates of 85,7% and 100% for the groups of hypoxia and normoxia, respectively (Figure 2).

The stepwise DFA in M1 produce a final model with 3 variables (CK, GPT and Mb). However, the stepwise DFA in M3 and in Δ (M1-M3) included one variable, T (Table 2). The overall models were statistically significant (Wilks' Lambda: M1: 0.182 (p<0.001); M3: 0.564 (p<0.005) and Δ (M1-M3): 0.235 (p < 0.001)), and the canonical correlation were 0.904, 0.661 and 0.874 respectively. The centroids indicated athletes who use hypoxia had higher CK, GPT and Mb values in M1 (centroid = 2.502) and T values in M3 (centroid = 1.040) and Δ (M1-M3) (centroid = 1,793), whereas the CG had lower CK, GPT and Mb values in M1 (centroid = -1.592) and T values in M3 (centroid = -0.662) and Δ (M1-M3) (centroid = -1,569). In M1 and M3 the models classified 94.4% and 84.2% of cases into groups. On the other hand, the model in Δ (M1-M3) correctly classifies 94.7% of cases into groups, with the classification rates of 85, 7% and 100% for the groups of hypoxia and normoxia, respectively (Figure 1).

Table 2: Summary of stepwise discriminant analysis of the professional athletes (PA) in hypoxia and athletes control group (CG) in normoxia.

	Lambda de Wilks	Canonical Correlation	Group centroids	
			PA	CG
M1				
CK	0.182 (p<0.001)	0.904	2.502	-1.592
ALT				
Mb				
M3				
T	0.564 (p<0.005)	0.661	1.04	-0.662
Δ (M1-M3)				
T	0.235 (p<0.001)	0.874	1.793	-1.569

Data are expressed by the discriminant function analysis (DFA). CK: Creatine Kinase; ALT: Alanine Transaminase; Mb: Myoglobin; T: Testosterone.

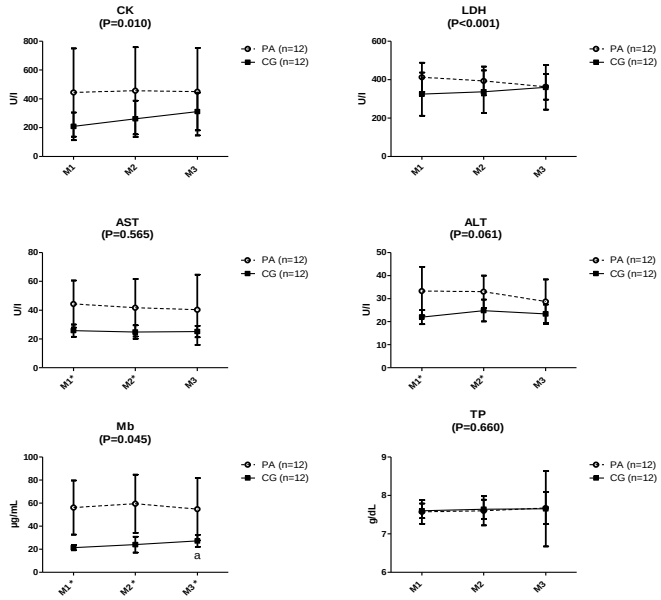
With respect, the muscular enzymes levels (Figure 3) significant differences were observed between groups in CK, LDH and Mb. In PA group CK remain constant, however, the other markers of muscular damage (AST, Mb, ALT and LDH) it showed a downward trend. On the other hand in CG group significant increases were observed in Mb concentrations (p<0.05) at M3 with respect M1, and an upward trend in the other enzymes.

Hematological parameters

In table 3 are showed the hematological data for both groups (PA and CG). No statistical differences were presented neither in each group throughout the study nor between both groups between groups along the study in white series (WBC, LYM and MON) and red series (RBC, Hb and Hct). On the other hand, statistical differences were observed (p<0.05) between groups in WBC in M2 and M3.

Physical performance test

At the end of study was evaluated again the physical performance parameters (Table 4). In general, all physical parameters studied have improved in both groups. Also the results were better in PA group that in CG, being significant the differences in anaerobic (P=0.003)



Data are expressed as mean ± Standard Deviation (SD). P: Two-factor repeated-measures ANOVA (time x Group). *Significant differences between groups in that specific control point by independent t-test. CK: Creatine Kinase; LDH: Lactate Dehydrogenase; AST: Aspartate Transaminase; ALT: Alanine Transaminase; Mb: Myoglobin; TP: Total Proteins.

Figure 3: Biochemical serum markers of muscular behavior along the different moment of the study (M1: Baseline M2: before start 14rd day M3: before start 28rd day) on the professional athletes (PA) in hypoxia and athletes Control Group (CG) in normoxia.

and aerobic (P>0.001) power between both groups. In PA group anaerobic and aerobic power was significantly improved at the end of study. The differences represent around 1-2%

Discussion

The main results were that, no overall IH effect was noted on muscle damage indicators. Also physical performance test we don't have observed significant changes, but light increases around 1% that is very important in professional sport exercise.

Before starting the discussion we must consider that our athletes habitually live in moderate hypoxia (1,100-1,200 m) so the physiological (hematological, enzymes and hormones) response must be placed in the context of performing intermittent hypoxia within a situation of moderate hypoxia.

During the last few decades, the athletes have increased the time spent to train and the accumulative training effect is extremely important [21]. Along of this study, the preparatory period training involves high training load phases in both, volume and intensity. With respect the training under hypoxia conditions, are used two types of intermittent hypoxia stimuli: a) Intermittent Hypoxic Exposure (IHE)- passive exposure to hypoxia lasting from a few minutes to hours that is usually repeated over several days, b) Intermittent Hypoxic Training (IHT) consists on physical activity under hypoxic conditions (during short periods) and remaining at normoxia conditions for the rest of the time [22]. The performance on IHT supposes greater wear, fatigue, immunosuppression, muscular catabolism, in short a high organic stress than the one performed in normoxia. In Theory the periods of recovery would be greater

Table 3: Hematological data along the different moment of the study (M1: Baseline M2: before start 14rd day M3: before start 28rd day) on the professional athletes (PA) in hypoxia and athletes control group (CG) in normoxia.

Test	Group	Moment of control			P
		M1	M2	M3	
WBC (x10³/mL)	PA	5.32±0.94	5.06±0.87	4.6±1.14	0.804
	CG	6.50±1.54	6.69±1.41*	6.42±1.39*	
MON (%)	PA	8.44±1.12	8.04±1.26	8.21±1.14	0.592
	CG	7.60±1.47	7.32±1.43	8.30±2.09	
LYM(%)	PA	38.95±9.54	37.10±9.31	35.8±8.36	0.813
	CG	37.30±8.50	37.14±7.45	37.77±7.73	
RBC (10⁶ µL⁻¹)	PA	5.11±0.33	5.18±0.34	5.01±0.20	0.66
	CG	5.13±0.40	5.40±0.49	5.15±0.33	
Hb (g.dL⁻¹)	PA	15.67±1.11	15.81±0.97	15.27±0.65	0.232
	CG	15.61±0.72	16.43±0.85	15.25±0.92	
Htc (%)	PA	45.42±2.79	45.65±2.53	45.39±2.22	0.908
	CG	46.45±2.46	47.32±2.25	46.72±2.51	

Data are expressed as mean ± standard deviation (SD). Data are expressed as mean ± standard deviation (SD). P: Two-factor. Repeated-measures ANOVA (time x Group). *Significant differences between groups in that specific control point by independent t-test.WBC: White bloodcells; MON: Monocytes; LYM: Lymphocytes; RBC: Redbloodcells; Hb: Hemoglobin; Htc: Hematocrit.

[7,23,24]. Moreover, hypoxic exercise may increase the training stimulus, thus magnifying the effects of endurance training [25].

The training model used in this work was the intermittent hypoxic exposure out training. Some authors suggest that IHT may improve

Table 4: Performance tests along the different moment of the study (M1: Baseline M3: before start 28rd day) on the professional athletes (PA) in hypoxia and athletes control group (CG) in normoxia.

Test	Condition	Moment of control		P	Improvement %
		M1	M3		
Strength (gr.cm/s²)	PA	50.75±19.26	51.63±20.04	0.283	2.91
	CG	41.13±15.58	42.00±13.90		2.11
Speed 60m (seg)	PA	8.04±0.97	7.89±1.01	0.923	1.86
	CG	8.39±0.98	8.32±0.69		0.83
Anaerobic power	PA§	55.05±5.78	53.94±5.84	0.003	2.01
400m (seg)	CG	61.65±5.57	60.80±5.13		1.37
Aerobic power	PA§	155.50±10.88	152.37±9.42	<0.001	2.02
1000m (seg)	CG	159.12±12.67	158.75±12.32*		0.23

Data are expressed as mean ± standard deviation (SD). P: Two-factor repeated-measures ANOVA (time x Group). *Significant differences between groups y that specific control point by independent t-test. §Significant differences between M1 and M3 in each group by dependent t-test. The improvement is expressed in percent (%).

anaerobic exercise performance [26], possibly via increases in muscle buffering capacity [27], and increased glycolytic enzyme activity [28]. In our study we are not observed significant differences in the test results (Strength, Speed, anaerobic power and aerobic power), remaining in the same level in the PA group. But similar results were obtained in the CG group. However, was observed an increase around of 1% (of course non significant) that in high level athletes is important because is know that when increase de performance between 0.5-1%, for example in an athletic international test of 1500m represent the possibility to be winner. This effect is easy to corroborate if is analyzed the different results of international championships.

Other authors have reported also improvements in anaerobic capacity and performance [29]. However, Ventura et al. [30] did not observed improvements of performance in athletes training in hypoxia (3-5 weeks at a simulated height of 2300 to 4000) than that achieved with the same training program in athletes at sea level. However as have concluded Millet el al [10] overall, in studies with control groups, IHE does not induce any substantial change in either hematological parameters or in endurance performance.

The steroid hormones TT and C, has been used as an indicator of physical activity [31]. The T/C ratio is an indicator of anabolic and catabolic balance and is with the fatigue state. This relation is used to detect the overtraining and/or for preventing excessive activity derived from training and competition [15]. As have informed Vingren et al [32] in review, various studies have demonstrated that resistance exercise increases circulating T concentrations. In our study the main finding was that, under hypoxic conditions (PA) increase the T levels with respect the CG.

These data suggest that depending on the altitude and training program can modify the physiological response, and on the other hand, the influence of hypoxia is low or that the adaptation of athletes were good. We think that this last condition is more close to the reality because the behavior in the hormones and muscular markers of damage are in this line.

But, independent of ambient conditions (hypoxia or no), it same clear that the endogenous T levels may affect training adaptations by mechanisms other than the direct anabolic effect on protein synthesis. T controls many physiological processes and, therefore, acts on neural tissue via different mechanisms. These include neurotransmitter synthesis and release to development and remodeling of synaptic circuitry [33]. It has also have been reported that T indirectly stimulates secretion of IGF-1 and GH [34]. Furthermore, T may act as an antiglucocorticoid to suppress protein degradation, by blocking the effects of C, and it may be involved in the exercise-induced glycogen super compensation [35]. In addition, T exerts some influence on satellite cells [36,37]. These changes in skeletal muscle lead to improved muscle strength and leg power.

According with Guilhem et al [31], the increases observed in our study respect the T could reflect the high training level of PA. Also, the increase of testosterone (T) in M2 and M3 could indicate a better capacity for performance. In this same sense, Hwang et al [38] have observed also an increase in testosterone levels in intermittent hypoxia in rats. However, Hu et al [39], showed that testosterone secretion could be suppressed during exercise under hypoxic conditions. They suggest that the rest time in between the periods of intermittent exercise during hypoxia might have been insufficient to restore normal testicular function due to slow recovery after exercise during hypobaric hypoxia. However these authors have studied the behavior of testosterone after a short period (24h) of hypoxia. An optimized endocrine response to resistance training and/or the hypoxia is of great importance for muscular adaptations.

The cortisol (C)/T ratio may indicate the catabolic/anabolic environment of an organism due to their roles in protein degradation and protein synthesis, respectively. The morning elevated T level (seen as beneficial to achieve muscle hypertrophy) may be counteracted by the morning elevated C level and, therefore, protein degradation [40]. Cortisol is released from the adrenal cortex in response to the stresses during exercise. Many studies have been showed significant increases in cortisol after resistance exercise [41].

Significant greater increase of T/C in PA group compared with CG group was observed at the end of the experimental protocol. The results suggested that the PA group was in a potential better anabolic environment at the end of the protocol, which was not observed in the beginning. We can speculate that the preferable anabolic environment in PA group was induced by the accumulation of additional hypoxia stimulus, which might partly contribute to the greater strength.

In the present study, the C increase, but without significantly changes, showing a similar behavior in both groups, after a period of exercise during in PA and CG. This might be explained as an adaptation to the exercise after training both during normoxia and intermittent hypoxia. In base of this, as some studies have assumed that glucocorticoid hormones might be the reason for lower T during endurance exercise, as remaining the C concentrations don't affect to T behavior.

Some muscular enzymes and proteins are considered as markers of muscle metabolism intensity and damages. Previously, we observed that muscle damage is associated with increase in plasma CK, ALT, and Aldolase (ALD) levels, which is a routine biochemical evaluation in the diagnosis of muscle disease [42]. This study supports that IHE, when the training is adequate and well programme, may prevent or

regulate the level of biochemical muscular markers. These phenomena are in the way mentioned before respect the testosterone. That is to say, the endogenous T levels may affect training adaptations by mechanisms other than the direct anabolic effect on protein synthesis, as the antiglucocorticoid effect to suppress protein degradation, the stimulation of IGF-1 and GH secretion and also by it influence on satellite cells [33-37].

On the other hand, the effect of exposure to altitude on different hematological variables has been of great interest for researchers. The increase in the secretion of erythropoietin (EPO) and hematocrit and hemoglobin are the most significant hematological changes in relation to hypoxia [43]. The explanation for the greater number of red blood cells could be given by an action of EPO. However, Bóning et al [44,45] in both men and women, report non-significant hormone differences between sea-level residents and intermediate-height residents.

Other authors [46], have develop a mathematical model where they demonstrate that the man in altitude does not need a high hematocrit for the transport of maximum oxygen, and that the erythrocytosis should be considered as an adaptation limited to moderate altitudes.

In this study the levels of red blood parameters (Hct, Hb and RBC) at the different time points analyzed don't have showed significantly differences, both in PA and CG groups. Neither was observed significant differences in the white cells. Exist a light decrease in mean levels of Hb, Hct, and erythrocytes from M1 to M3 that were more pronounced in the PA, but it is not apparent. Previously in our work group [46] we have observed an increase in the hormone erythropoietin following the application of a program in cyclists along the cycle tour to Spain 2001, but did not observe changes in hematocrit, hemoglobin or erythrocytes. With this knowledge in the present study we did not do the EPO determination because it could not contribute anything new that we no longer know. As shown Millet et al [10] in a review the behavior of hematological parameter in hypoxia and exercise are contradictories and it depends on protocol oh intermittent hypoxia used.

Conclusion

This study we have observed that IH might potentially stimulate performance through an anabolic effect. On the other hand the testosterone is a determinant informative to evaluate the answer to exercise in PA (Hypoxia). Also, no overall IH effect was noted on muscle damage indicators. For all this we recommended performing the resistance training under the intermittent hypoxia to induce anabolic hormone responses and after improve the physical performances.

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