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The Effects of Aerobic Exercise in Ski Beginners at Altitudes of 1250-2000m on Blood Oxygen Transport Parameters

Der aerobe Trainingseffekt auf Sauerstofftransportparameter bei Skianfängern in Höhenlagen zwischen 1250-2000m

ORIGINALIA

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Summary

- **Problem:** Lower altitude stay (1250m) and extensive recreational aerobic activity like skiing at lower to moderate altitude (1250-2000m) and its effect on oxygen transport parameters had not been thoroughly investigated.
- **Methods:** The experimental group (N=17) underwent an intervention, a typical 10-day ski-trip. They slept at 1250 m and performed 5-6 hours of aerobic activity (skiing) at 1250-2000m altitude. The control group (N=15) stayed at sea level and performed their regular activities. The ferritin levels, reticulocyte count, RBC parameters and erythropoietin before and 48 h after the trip were measured in both groups.
- **Results:** The reticulocyte count increased (44.5±16.6 to 67.9±19.18 G/L) and somewhat surprisingly erythropoietin decreased in experimental group (6.04±2.39 to 4.91±1.54 IU/L, ANOVA p=<0.001). Ferritin levels decreased and reticulocyte count increased in 88% of all experimental group subjects while in control group it changed in both directions. The initial erythrocyte concentration was found to be a good predictor of reticulocyte increase changes, while ferritin reserves was did not. No significant changes after intervention were observed in other parameters.
- **Discussion:** In recreational population, sleeping at lower altitudes in combination with aerobic activity of longer daily duration like skiing, elicits changes in erythropoiesis.

Zusammenfassung

- **Problemstellung:** Die Auswirkungen von Aufenthalten in relative niedriger Höhenlage (1250m) in Kombination mit aerober körperlicher Aktivität, wie z. B. Skifahren, auf die Sauerstofftransportparameter wurden in der Literatur kaum untersucht. Hierdurch hervorgerufene günstige Veränderungen könnten wiederum zu einer verbesserten Leistungsfähigkeit bzw. einer positiven Beeinflussung der Gesundheit führen.
- **Methodik:** Untersucht wurden 17 Personen während eines typischen Skiurlaubs von 10 Tagen mit täglicher aerober Aktivität zwischen 1250-2000m; Übernachtungshöhe: 1250m. Die Kontrollgruppe (n=15) blieb auf Meereshöhe und führte ihre übliche Aktivität aus. Die Konzentration von Ferritin, Retikulozyten, roter Blutbild-Parameter und Erythropoietin wurden vor und nach dem Skiurlaub im Blut beider Gruppen bestimmt.
- **Ergebnisse:** Erstaunlicherweise sank das Erythropoietin in der Versuchsgruppe (6.04±2.39 auf 4.91±1.54 IU/L), während die Retikulozytenzahl deutlich anstieg (44.5±16.6 bis 67.9±19.18 G/L; p<0.05), ANOVA p<0.001. Der Ferritinspiegel sank bei 88% der Probanden der Versuchsgruppe, in der Kontrollgruppe änderte er sich in beide Richtungen. Im Gegensatz zu Ferritin war die anfängliche Erythrozytenkonzentration ein aussagekräftiger Vorhersageparameter für höhen-und sportbedingte Veränderungen.
- **Diskussion:** Bei Freizeitsportlern führt das Schlafen in niedrigen Höhenlagen kombiniert mit länger andauernder aerober Aktivität tagsüber zu Veränderungen in der Erythropoese.

KEY WORDS:
Altitude, Training, Hypoxia, Ferritin, Reticulocyte, Erythropoietin

SCHLÜSSELWÖRTER:
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Introduction and Objective

In response to hypoxic stress, such as in an ascent to altitude or during exercise, the rate of erythropoiesis could be significantly increased. It is directly regulated through the activity of erythropoietin (EPO), hormone secreted by kidneys via activation of the hypoxia-inducible transcription factor complex (4). For organism to fully adapt to hypoxic stress, not only the appropriate kidney function and EPO secretion are needed, but also an adequate iron reserve, meaning serum ferritin (10, 23), is necessary.

In sports training methodology research, the positive effects of high-altitude stay on a sea-level performance are still a matter of debate (8, 14, 19) and several different training modalities such as "Live high-train high", "Live high-train low" or "Live low-train high" (11, 12, 21) are continuously being investigated. It is nowadays accepted that the athlete's stay at altitudes >2000m for a period of 3-4 weeks (6, 19) should be sufficient to cause the best possible improvements in hematological parameters ›

Table 1

The initial and final values of basic erythropoiesis variables for both groups and ANOVA* for repeated measures results between the experimental and control group. (*ANOVA=significance of interaction of time and intervention).

	UNIT	MEAN EXPERIMENTAL	MEAN CONTROL	ANOVA
Erythrocytes 1 **Erythrocytes 2**	T/L	5.13±0.29 5.20±0.29	5.32±0.29 5.34±0.22	F(1.30)=0.525;p=0.474
Haemoglobin 1 **Haemoglobin 2**	g/L	152.4±9.57 154.5±8.77	155.6±6.30 156±5.82	F(1.30)=1.197;p=0.283
Hematocrit 1 **Hematocrit 2**	%	0.45±0.03 0.45±0.02	0.46±0.02 0.45±0.02	F(1.30)=1.554;p=0.222
MCV 1 **MCV 2**	fL	88.3±1.67 86.5±1.65	86.2±3.20 83.9±3.03	F(1.30)=2.498;p=0.124
MCH 1 **MCH 2**	pg	29.7±0.66 29.7±0.63	29.3±0.94 29.2±0.85	F(1.30)=0.258;p=0.615
MCHC 1 **MCHC 2**	g/L	336.6±6.49 343.4±6.51	340.0±8.26 348.3±7.96	F(1.30)=0.794;p=0.379
Reticulocytes % 1 **Reticulocytes % 2**	G/L	8.6±2.75 12.9±3.22	10.3±2.40 9.4±2.48	F(1.30)=46.37;p<0.001
Reticulocytes N 1 **Reticulocytes N 2**	G/L	44.5±16.16 67.9±19.18	54.7±13.52 50.2±13.73	F(1.30)=55.51; p<0.001
Erythropoietin 1 **Erythropoietin 2**	IU/L	6.05±2.40 4.91±1.54	5.99±2.60 6.31±3.04	F(1.30)=4.75; p<0.05
Ferritin 1 **Ferritin 2**	µg/L	84.1±54.09 64.3±40.24	103.4±45.74 91.7±44.50	F(1.30)=0.97; p=0.330

and consequently improve their sea-level performance. In recreational population, the goal would not be to improve the results at sea level, but rather the hematological benefits might at least temporary improve their everyday tasks performance and that had rarely been studied (2).

There are 115 million skiers in the world according to the 2013 International report on Snow and Mountain Tourism, 40 million of those in US (3). Therefore, it is of interest to determine whether the stay at lower altitude in combination with an extensive daily workout like skiing might elicit the positive effects on oxygen-transport system.

Consequently, the aim of the study was to search for changes in blood oxygen transport parameters and early signs of accelerated erythropoiesis such as reticulocyte increase and ferritin decrease after 9 days/10 nights long intermittent hypoxia above 1250m combined with several hours of skiing activity up to 2000m.

Material and Methods

The experimental group consisted of young able-bodied male students (n=17, age=21.5±1.07 years, no professional athletes included) who attended the ski school classes in Sappada, Italy (1250 m altitude of sleeping). As this was the case-control study, their counterparts, the students of the same age and similar physical activity level (n=15, age=21.5±1.06 years) volunteered to form the control group. The control group stayed at 120m altitude (which was also the home living altitude of the experimental group), did not attend ski-classes and continued their normal daily activities. This design with two factors combined in the intervention (skiing and altitude) was supposed to mimic typical winter ski trip situation in which otherwise sedentary individuals go for a skiing holiday once a year. Each participant signed a written consent and the study was approved by Ethics Committee of the Faculty of Kinesiology at University of Zagreb. The study was conducted in concordance with Declaration of Helsinki.

The ski-classes were held for 9 days (while the duration of whole stay was 10 nights) at Sappada ski region that has a skiing altitude range from 1250 to 2000 m above sea level. The subjects were all ski beginners or maybe had a few days of skiing previously in childhood. Each day the lessons were conducted from 9 AM to 3.30 PM with an effective duration of intermittent skiing activity of 5h and 30min. All participants went through the same ski school program under the supervision of the licensed ski instructors of Croatian association of ski teachers (HZUTS) licensed by ISIA or IVSI federations.

The venous blood samples were taken at two time points, at the same time for the experimental and the control group. The initial measurements were performed 30 hours before the ski-classes started (day 0) and the final 48 hours after the last class was held (day 14). Both groups were asked to refrain from physical activity 48h before the initial testing. The measurements were conducted at the licensed biochemistry laboratory "Breyer" in a seated position, in which participants were resting for 10 minutes prior to testing. The parameters that were analyzed were: erythrocytes count (T/L), reticulocytes count (G/L) and percentage (%), hemoglobin (g/L), hematocrit (%), RBC indices, ferritin concentration (µg/L) and EPO (IU/L).

The statistical analysis was performed with Statistica 12 software (Dell, USA) licensed to the Faculty of Kinesiology, University of Zagreb. The significance of the pre- and post-intervention results were determined with ANOVA for repeated measures. Finally, the regression analysis was used to determine the relations between initial ferritin levels and erythrocyte count and relative reticulocyte increase (expressed in percentage of change)). The level of significance was set at $p<0.05$. G*Power free software was used for post hoc power and effect size analysis.

Results

The mean values of measured parameters in experimental and control group before and after the intervention together with the results of ANOVA for repeated measures (significance of interaction of time and intervention) are presented in Table 1.

The experimental group had a significant absolute and relative reticulocyte increase (Fig. 1). The mean increase in absolute reticulocyte count in experimental group was 23.4±10.5. The calculated effect size of intervention was 0.57, suggesting a large effect size (Cohen's f larger than 0.40 is a large effect for within factors ANOVA for repeated measures and the post hoc Power=0.95). The difference in erythropoietin change between the groups was also significant (Fig. 2). There was a significant drop of 1.13 IU/L or 19% in EPO in experimental group (Cohen's f=0.499; Power=0.88)

Regarding the individual iron status, only 4 out of 32 participants had ferritin levels lower than recommended (reference 30.00-400.00 μg/L). A larger decrease in ferritin reserves was observed in experimental group, but that effect was not significant when the intervention effects were compared between the groups (Table 1).

In order to test the hypothesis that the ferritin reserves might have decreased while the reticulocyte count could have increased, the direction of changes was analyzed. In 88% of all experimental group subjects the ferritin reserves decreased and reticulocyte count increased while in control group the values changed in both directions. The significance in proportion of subjects with those changes between the groups was confirmed by chi-square test with Yates correction (chi-squared= 7.971; p=0.005).

The final analysis included searching for the relations between the initial ferritin and erythrocyte counts and the relative reticulocyte increase. For that purpose, the whole sample was included and the model was found to be significant (R=0.38, R^2=0.14). The significant predictive parameter was found to be the initial erythrocyte concentration, though it could explain only 13.8% of the factors that influenced the increase and it implicated that those with lower erythrocyte count at the beginning might have stronger reticulocyte response. The initial ferritin reserves were not a good predictor of reticulocyte response. A simple regression analysis revealed that the decrease in EPO was also a good predictor for increase in reticulocytes (b=-0.42; R=0.43; R^2=0.18; p<0.001).

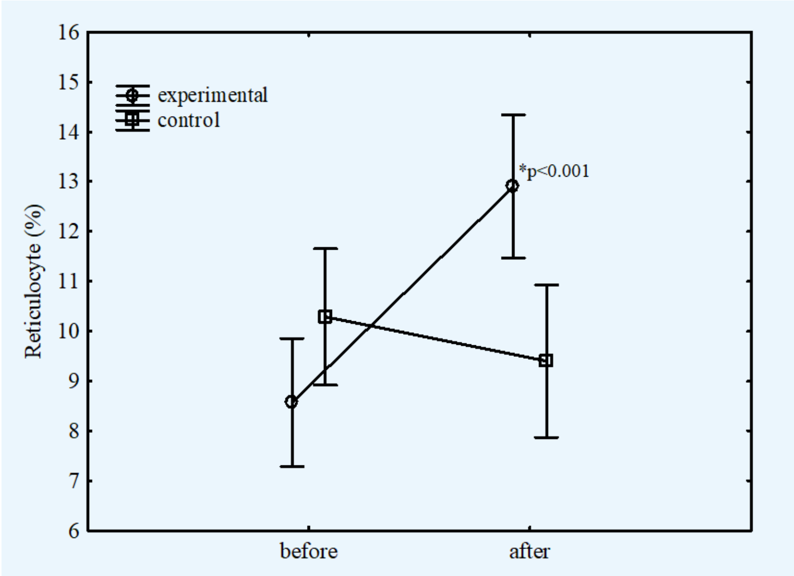

Figure 1

The change in relative reticulocyte count before and after intervention.

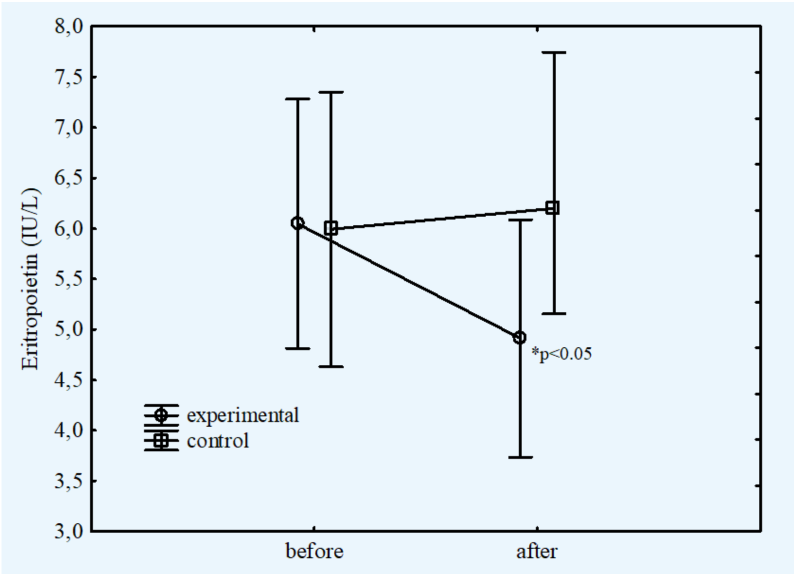

Figure 2

EPO change before and after intervention.

Discussion

This study shows that even such a short stay of 10 days at low to moderate altitude might induce some changes in erythropoiesis. The before after differences in reticulocyte count were significant and the before after differences in ferritin were not significant but the intervention lead to the individual reticulocyte increase and concurrent ferritin decrease in almost 90% of the subjects of the experimental group which was not the case in the control group.

There was a somewhat surprising, but explainable, a slight significant decrease in EPO concentration in experimental group. It was not expected as it was previously reported that the highest EPO response usually occurs after 48h and is very apparent in higher altitudes and at low SpO_2. The explained probable mechanism in that study was the HIF-1α stabilization and progressive acclimatization (13). The participants in our study were not exposed to such high altitude and strong hypoxia, but the significant EPO changes still occurred. There was probably a slight increase in plasma EPO after approximately two days at moderate altitude and, as a reaction to a slightly higher erythropoiesis, a suppression of EPO production 48h after the return to sea level. Those EPO changes cannot be attributed to endurance exercise alone with certainty, as it was proven previously that during the endurance exercise a small decrease in PO_2 happens but probably not sufficient to elicit a significant EPO response (15). Montero et al. (16) observed only a mild, transient increases in circulating EPO › concentration after endurance training. The overnight decrease in SpO_2 does induce EPO responses (1) but in our study the altitude of sleep at 1250m was probably not inducing major SpO_2 changes. SpO_2 measurements in experimental group were performed only occasionally, not in all subjects, and with great variance (91-97% at 2000m) so those are not reported in results. Still, it could be mentioned that the saturations were not nearly as low as in a study on skiers skiing at 2800-3440m (22). Conclusively, as it will be stated later in discussion, it seems that the combined effect of activity and altitude determined the outcomes, not one of them exclusively.

The differences were not observed in RBC and hemoglobin concentration. That might be due to the early control measurement and the lack of follow up after 3 weeks but also due to low to moderate altitude. A significant increase in erythrocyte count could usually be noticed after approximately 21 days, but additional measurement at that time point would be compromised as in this study there was no mechanism to control the participant's activities after the return.

Although the hemoglobin mass was not measured per se, it might be interesting to mention that a few studies reported a small increase in hemoglobin mass at altitudes lower than 2000m (5, 18) like a study conducted on runners at 1800m in which a 3% increase in hemoglobin mass after only 2 weeks of exposure was observed (7).

An iron-supplementation, which our participants did not receive, seems to be necessary to fulfill prerequisites for successful erythropoiesis (20). Govus et al. (9) had shown that in athletes with adequate ferritin reserves but who had not received the iron supplementation, the hemoglobin mass had not significantly increased. Despite initial ferritin levels higher than 100µg/l, the participant's iron delivery to the erythron might for some reason be impaired (17). Still, since almost all of the subjects had the initial iron stores in reference range, and as the results had shown no predictive power of ferritin for reticulocyte increase, it seems that their initial iron stores did not influence the outcome to a large extent. The relation that was confirmed though, was that those with a lower initial erythrocyte count had a stronger reticulocyte response which was an expected adaptation mechanism.

The main concern originating from the proposed study design is that the observed effects of the intervention could not easily be attributed to either altitude or aerobic exercise alone, as the intervention had those two components. That is why this study design might seem to be lacking an experimental group, which would be active in similar volume and intensity as the experimental group. There were many studies published previously that investigated these two effects separately and the goal of this project was different. This study aimed to mimic the situation of many recreational skiers, who are not active at all during the year and then go for their annual skiing trip. Usually, during that trip they perform skiing activities at moderate altitude while staying at a lower altitude. After the return, they become sedentary again, just like the control group participants.

In conclusion, this study shows that the combined effect intervention (comprising of aerobic activity like recreational alpine skiing in low skilled skiers and low to moderate altitude effect), might lead to some changes in blood-oxygen transport system. The EPO decrease and the reticulocyte increase were of large effect sizes and the decrease in ferritin with reticulocyte increase occurred in 88% of experimental group subjects. Those changes are not easily explained by only low to moderate altitude or low to moderate exercise intensity either, so it seems that these two factors might have had enhanced each other's subtle effects.

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Conflict of Interest

The authors have no conflict of interest.

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