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ORIGINAL ARTICLE

Is an altitude below 1400 m above sea level sufficient to trigger an adaptive response?

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ABSTRACT

BACKGROUND: Over the past 2 decades, our studies have revealed that despite extensive research, many unanswered questions persist regarding hypoxic preparation and the resulting adaptive response. For these reasons, we believe it is essential to investigate the impact of environmental hypoxia at altitudes below 1500 m above sea level on the parameters monitored in the athlete's biological passport (ABP).

METHODS: The research was conducted as a pilot part of research on a group of seven Slovak endurance athletes (4 males, 3 females) aged 22-27 years who are active in athletics and cross-country skiing. All participants have extensive experience with hypoxic training (more than 5 years). As part of the research, we monitored their adaptive response to hypoxic conditions at altitudes up to 1350 m above sea level.

RESULTS: The findings from the study conducted on seven athletes affirm that, contrary to typical interpretations (such as those in the ABP sampling protocol), even hypoxic conditions at 1350 m above sea level can have a notable impact on the outcomes analyzed in the ABP. The results showed that exposure to hypoxia below 1350 m above sea level resulted in a reduction in hemoglobin levels, while a contrary trend was observed for reticulocytes. This trend was reflected in the Off-score, showing a decrease across all cases.

CONCLUSIONS: The data obtained confirmed the effect of hypoxic conditions at altitudes up to 1350 m above sea level on erythropoiesis.

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KEY WORDS: Altitude; Athletes biological passport; Reticulocytes.

Over the past 2 decades, our studies[1-4] have revealed that despite extensive research, many unanswered questions persist regarding hypoxic preparation and the resulting adaptive response. The results of several studies[5-7] suggest that various methods of hypoxic training lead to significant hematological changes. In this context, it is interesting that their findings suggest that the achieved adaptive response may indicate a violation of antidoping rules, considering how this is interpreted in the athlete's biological passport (ABP). It is worth noting that the ABP sampling protocol currently only regards staying at altitudes above 1500 m above sea level as a significant factor (this is to be reported by the athlete). However, there are studies[8, 9] suggesting that even altitudes of 1000-1200 m above sea level can have a significant

impact on the indicators monitored in the ABP. Certainly, it is crucial to recognize the variations in the adaptive response of each organism. Some studies[10-12] demonstrate a notable difference in the adaptive response to hypoxia, with certain individuals exhibiting minimal or no adaptive response at all. In recent years, several cases have sparked a society-wide debate about the reliability of the ABP, as some athletes have had abnormal ABP findings (in terms of how the ABP results are interpreted). The athletes were subsequently suspended, and in some cases, found not guilty after a long and costly process of proving their innocence. This situation may have involved training at altitudes below 1500 m above sea level, which the ABP sampling protocol does not consider as an important factor. For these reasons, we believe it is essential to investigate the impact of environmental hypoxia at altitudes below 1500 m above sea level on the parameters monitored in ABP. Additionally, we aim to clarify the specifics of the adaptive response in such conditions. As part of the research within the grant projects VEGA1/0707/22 (specifics of variability of hematological parameters monitored in the biological passport of an athlete) and VEGA (1/0547/22 The use of hypoxia and hyperoxia in sports preparation), we have also investigated the use of hypoxic training at altitudes up to 1500 m above sea level. This is because the protocol for sample collection for the biological passport of an athlete only considers training at altitudes above 1500 m above sea level as noteworthy.

Materials and methods

The research was conducted as a pilot part of a research on a group of seven Slovak endurance athletes (4 males, 3 females) aged 22-27 years who are active in athletics and cross-country skiing. All participants have extensive experience with hypoxic training (more than 5 years). As part of the research, we monitored their adaptive response to hypoxic conditions at altitudes up to 1350 m above sea level (Štrbské Pleso). Blood samples were taken before ascending to an altitude of approximately 1350 m above sea level and during the 6th day of their stay at this altitude. The sampling was conducted at 7:00 a.m. The analyzed parameters included those monitored in the ABP: hemoglobin and reticulocytes, from which the Off-score was calculated using the formula (Off-score=Hgb×10-60x (√reticulocytes). Additionally, the level of erythropoietin was monitored as a supplementary indicator. The sampling methodology used for the ABP sampling was adhered to. We used highly reliable analyzers: for reticulocytes Mindray BC 6200 (precision ≤15.0% [RBC ≥3×1012 $g.L^{-1}$; ≤1.0% RET% ≤4.0%]), for hemoglobin Mindray BC 6000 (Shenzhen Mindray Bio-Medical Electronics Co., Ltd, Shenzhen, China; precision ≤1.0% [110-180 $g.L^{-1}$]).

The experiments reported in the manuscript were performed in accordance with the ethical standards of the Helsinki Declaration and that the participants signed an informed consent form.

Results

The research results suggest a decrease in hemoglobin levels associated with staying at an altitude of 1350 m above sea level, possibly linked to hemodilution due to induced erythropoiesis. As seen in Figure 1, all seven athletes experienced a decrease in hemoglobin levels.

Within the group, the mean hemoglobin before ascending to the altitude of 1350 m above sea level was 156.57 $g.L^{-1}$ and during the 6th day, the mean hemoglobin was recorded at 151.57 $g.L^{-1}$, resulting in an average decrease of 5 $g.L^{-1}$. The most notable decrease (2 $g.L^{-1}$) was observed in subjects 1 and 6, while the most significant in-

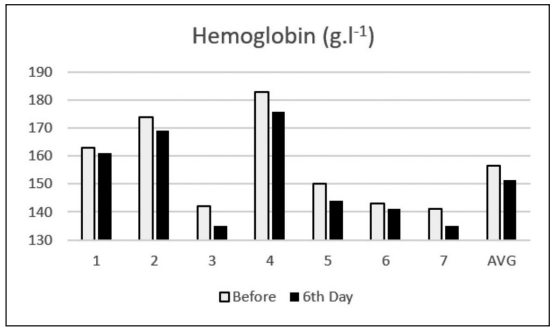

Figure 1.—Comparison of hemoglobin levels before staying at altitudes up to 1350 m above sea level and on the 6th day of staying at this altitude.

crease was observed in subjects 3 and 4, with a decrease of 7 g.L^{-1}.

For reticulocytes, all 7 subjects experienced an increase, with an average rise from 1.43% to 1.75%, reflecting an increase of 0.32% points. As shown in Figure 2, the smallest increase occurred for subject 7 (0.12% points). The most significant increase was observed in subject 5, by 0.52% points, while the second most notable difference was seen in subject 1 (0.44% points).

In terms of interpreting the results in the ABP, the correlation between hemoglobin levels and the proportion of reticulocytes defines the Off-score. As shown in Figure 3, the Off-score decreased for all seven subjects. The average decrease was from 85.25 to 72.80, with a lower difference in scores than 10 recorded for subjects 6 and 7, while the most significant decrease of 18.11 was achieved by subject 5 (decrease from 71.31 to 53.20). Other significant differences were recorded for subjects 3 and 4 (decreases of 15.01 and 13.99, respectively).

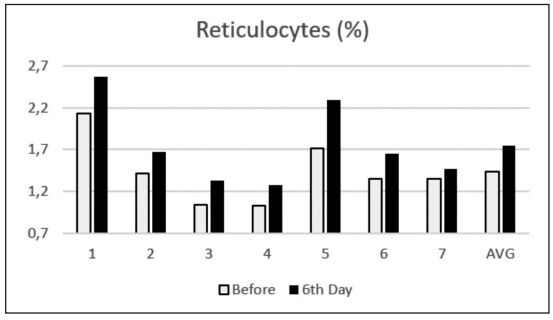

Figure 2.—Comparison of the proportion of reticulocytes before staying at altitudes up to 1350 m above sea level and on the 6th day of staying at this altitude.

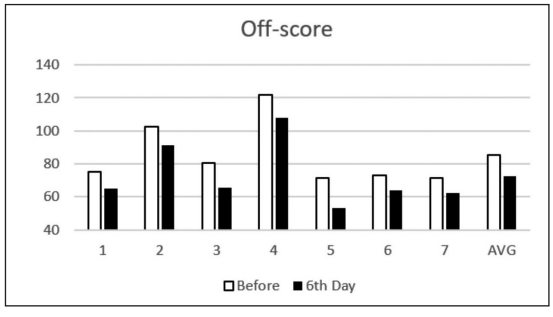

Figure 3.—Comparison of Off-score before staying at altitudes up to 1350 m above sea level and on the 6th day of staying at this altitude.

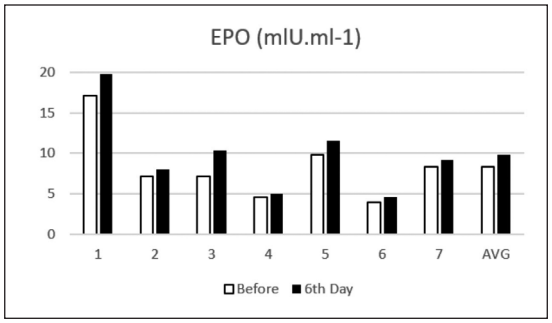

Figure 4.—Comparison of erythropoietin levels before staying at altitudes up to 1350 m above sea level and on the 6th day of staying at this altitude.

The assumption that even an altitude of 1350 m above sea level can induce a significant adaptive response is supported by changes in erythropoietin levels. As can be seen in Figure 4, all 7 subjects showed an increase in erythropoietin levels, with an average increase of 1.49 mLU.mL^{-1} (from 8.30 to 9.79 mLU.mL^{-1}). Subjects 2, 4, 6, and 7 showed an increase in erythropoietin levels of up to 1 mLU.mL^{-1}, but subject 3 showed an increase of 3.29 mLU.mL^{-1} (from 7.12 to 10.41 mLU.mL^{-1}). A consistent trend observed in all seven subjects suggests stimulation of erythropoiesis even at an altitude of 1350 m above sea level.

The research findings clearly confirm the positive effect of altitudes below 1350 m above sea level on the organism of the athletes studied. Based on the conducted research, it is important to note that these findings are somewhat specific, as they apply to the seven subjects studied in this research. To achieve a broader generalization, it is necessary to conduct research involving a larger group of athletes. However, the consistent trend observed in this study provides insight into the changes that can be expected.

Discussion

As stated by Čillík *et al.*,[4] the interpretation of the body's response to hypoxia typically implies that hypoxic conditions stimulate erythropoiesis and enhance athletic performance.[5-7, 13, 14] However, it is important to note that the interpreted data cannot be generalized. Our research highlights the fact that even altitudes below 1500 m

above sea level can affect erythropoiesis, which is particularly significant given the sample submission protocol for the ABP. This finding corresponds to studies[8, 9] indicating an adaptive response even at altitudes below 1500 m. Our research results confirm the positive impact of hypoxic exposure at altitudes up to 1350 m on a group of athletes (3 women and 4 men). These changes demonstrate that such exposure can also influence results in the ABP. This factor must be considered, especially in further research aimed at optimizing the data interpretation for ABP purposes. Čillík *et al.*[4] point out the need to consider the fact that there are studies[10-12] that show a significant difference in the adaptive response to hypoxia, while some individuals are described as having little or no adaptive response. Taking into account that in the interpretation of the ABP, a variance of approximately 29 $g.L^{-1}$ for hemoglobin,[15] *i.e.*, a variance from the mean predicted value of less than 15 $g.L^{-1}$, the most significant difference we observed was 7 $g.L^{-1}$, which is almost half of this value. This cannot be considered negligible. This is similar for reticulocytes, where the ABP calculates a variance of about 1% point,[15] *i.e.*, half a percentage point from the mean. For this reason, it is important to note that for one subject, the change was as much as 0.52% points, while the average difference was 0.32% points, which is more than half the variance from the mean. Respecting the predicted variance of the Off-score, approximately 45 (*i.e.*, 22.5 from the mean),[15] we can consider a significant difference greater than 5, which was achieved by all observed subjects. For these reasons, we consider it essential to verify on a larger group the impact of environmental hypoxia at altitudes below 1500 m above sea level on the parameters monitored in the ABP. Additionally, at higher altitudes and with other methods, it is necessary to verify the specifics of the adaptive response in a larger group of elite athletes.

Conclusions

The findings from the study conducted on seven athletes affirm that, contrary to typical interpretations (such as those in the ABP sampling protocol), even hypoxic conditions at 1350 m above sea level can have a notable impact on the outcomes analyzed in the ABP. The results showed that exposure to hypoxia below 1350 m above sea level resulted in a reduction in hemoglobin levels, while a contrary trend was observed for reticulocytes. This trend was reflected in the Off-score, showing a decrease across all cases. The data obtained confirm the effect of hypoxic conditions at altitudes up to 1350 m above sea level on erythropoiesis. Monitoring changes in erythropoietin levels, which increased in all subjects, was also conducted to objectify the data. For these reasons, it is considered necessary to further expand our understanding of hypoxic preparation and the data analyzed in the ABP. Taking fair play principles into account is essential when interpreting results in an ABP. Inaccurate or inconsistent data interpretation may lead to unjust accusations against innocent athletes. This not only violates fair play principles but also undermines the core values of sports and the primary goal of the anti-doping system, which is to detect doping violations and not to unfairly penalize honest athletes.

References

1. Pupiš M, Švantner R, Barthová M, Líška D. Môže nadmorská výška nižšia ako 1350 m.n.m. ovplyvniť výsledky v biologickom pase športovca? [Can an altitude lower than 1350 m above sea level affect the results in an athlete's biological passport?] In: Pupiš M, Pupišová Z, editors. Kyslík, krv a šport: vedecký recenzovaný zborník vydaný za podpory GÚ [Oxygen, blood and sport: a peer-reviewed scientific collection published with the support of the General Institute]. Banská Bystrica: Slovenská Asociácia Kondičných Trénerov; 2023. p.41–50. [Slovak].

2. Pupiš M. Hypoxický tréning: vysokoškolská učebnica [Hypoxic training: a university textbook]. Bratislava: Slovenský Atletický Zväz; 2021. [Slovak].

3. Pupiš M, Korčok P. Hypoxia ako súčasť športovej prípravy [Hypoxia as part of sports training]. Banská Bystrica: Univerzita Mateja Bela; 2007. [Slovak].

4. Čillík I, Pupiš M. Training in high altitude environments and its influence on the changes in selected physiological indicators of a Slovak Republic representative in walking. Acta Univ Palacki Olomuc Gymn 2005;35:43–9.

5. Rusko HK, Tikkanen HO, Peltonen JE. Altitude and endurance training. J Sports Sci 2004;22:928–44.

6. Wilber RL, Stray-Gundersen J, Levine BD. Effect of hypoxic "dose" on physiological responses and sea-level performance. Med Sci Sports Exerc 2007;39:1590–9.

7. Nummela A, Eronen T, Koponen A, Tikkanen H, Peltonen JE. Variability in hemoglobin mass response to altitude training camps. Scand J Med Sci Sports 2021;31:44–51.

8. Al-Sweedan SA, Alhaj M. The effect of low altitude on blood count parameters. Hematol Oncol Stem Cell Ther 2012;5:158–61.

9. Singh K, Gupta RK, Soree P, Rai L, Himashree G. Long-term stay at low altitude (1,200 m) promotes better hypoxia adaptation and performance. Indian J Physiol Pharmacol 2014;58:376–80.

10. Hamlin MJ, Manimmanakorn A, Creasy RH, Manimmanakorn N. Live high-train low altitude training: responders and non-responders. J Athl Enhancement 2015;4:1–8.

11. Chapman RF, Stray-Gundersen J, Levine BD. Individual variation in response to altitude training. J Appl Physiol 1998;85:1448–56.

12. Lippi G, Franchini M, Salvagno GL, Guidi GC. Intermittent hypoxic training: doping or what? Eur J Appl Physiol 2006;108:411–2.

13. Ashenden MJ, Gore CJ, Parisotto R, Sharpe K, Hopkins WG, Hahn AG. Effect of altitude on second-generation blood tests to detect erythropoietin abuse by athletes. Haematologica 2003;88:1053–62.

14. Garvican L, Martin D, Quod M, Stephens B, Sassi A, Gore C. Time course of the hemoglobin mass response to natural altitude training in elite endurance cyclists. Scand J Med Sci Sports 2012;22:95–103.

15. Mørkeberg J. Athlete biological passport. Best Anti-Doping Program Implementation Models; 2016 [Internet]. Available from: https://nada.by/en/education/mezhdunarodnyy_seminar_effektivnye_modeli_realizatsii_antidopingovykh_programm/ [cited 2025, Mar 27].

Conflicts of interest
Martin Pupiš received research grants from the VEGA 1/0707/22 – Specifics of Variability of Haematological Parameters Monitored in the Biological Passport of an Athlete and VEGA 1/0547/22 – The Use of Hypoxia and Hyperoxia in Sports Preparation.

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Authors' contributions
All authors read and approved the final version of the manuscript.

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