Blood Doping

Effect of pre-competition and altitude training on blood models used to detect erythropoietin abuse by athletes

This study reports blood model scores used for detection of recombinant human erythropoietin (rHuEPO) abuse by athletes. Elite female rowers were monitored prior to their World Championships, including a period spent training at moderate altitude. In contrast to previous results, no substantial increase in model scores was found following altitude exposure.

haematologica 2004; 89:1019-1020
(*http://www.haematologica.org/2004/8/1019*)

One of the challenges of blood models is to differentiate between changes in erythropoietic rates caused by (illegal) rHuEPO use and those induced by (legal) altitude training. Previous research reported elite male cyclists training 2690 m above sea level demonstrated marked increases in blood model scores, influenced primarily by increases in hemoglobin concentration (Hb) which is a key variable in algorithms that reflect either accelerated (ON models) or decelerated (OFF models) erythropoiesis.[1]

Table 1. Hematologic parameters (mean±SD) for 18 elite female rowers in the weeks preceeding the 2003 World Championships. Post-altitude values (collected 18 days before the World Championships) were obtained 10 days after returning from a 3-week altitude training sojourn at St Moritz (2440 m).

	Pre 1	*Pre 2*	*Pre 3*	*Post-Altitude*
Hb	134±5	139±7	131±7	132±8
Retic	0.8±0.4	1.3±0.3	1.0±0.3	0.8±0.3
EPO	10.9±4.5	11.4±4.0	13.7±3.3	12.5±6.2
sTfr*	1.42±0.26	1.52±0.30	1.33±0.20	1.40±0.17
ON-he	156.3±6.2	161.6±6.2	156.3±6.6	155.5±7.9
ON-hes*	154.6±7.2	161.8±11.5	153.3±9.0	154.7±8.2
OFF-hr	80.7±15.7	70.8±10.5	72.4±10.4	79.2±13.2
OFF-hre	73.3±14.2	65.5±10.5	64.0±9.9	70.9±13.7

Values were collected as follows: Pre 1 – eight weeks prior to altitude training; Pre 2 – two weeks prior to altitude training; Pre 3 – one week prior to altitude training; Post-Altitude – 10 days after returning to sea level. Abbreviations (and units): Hb, hemoglobin concentration (g/L); Retic, percent reticulocytes; EPO, erythropoietin concentration (mU/mL); sTfr, serum transferrin receptor (mg/L). Denotes n=15 due to missing data points.*

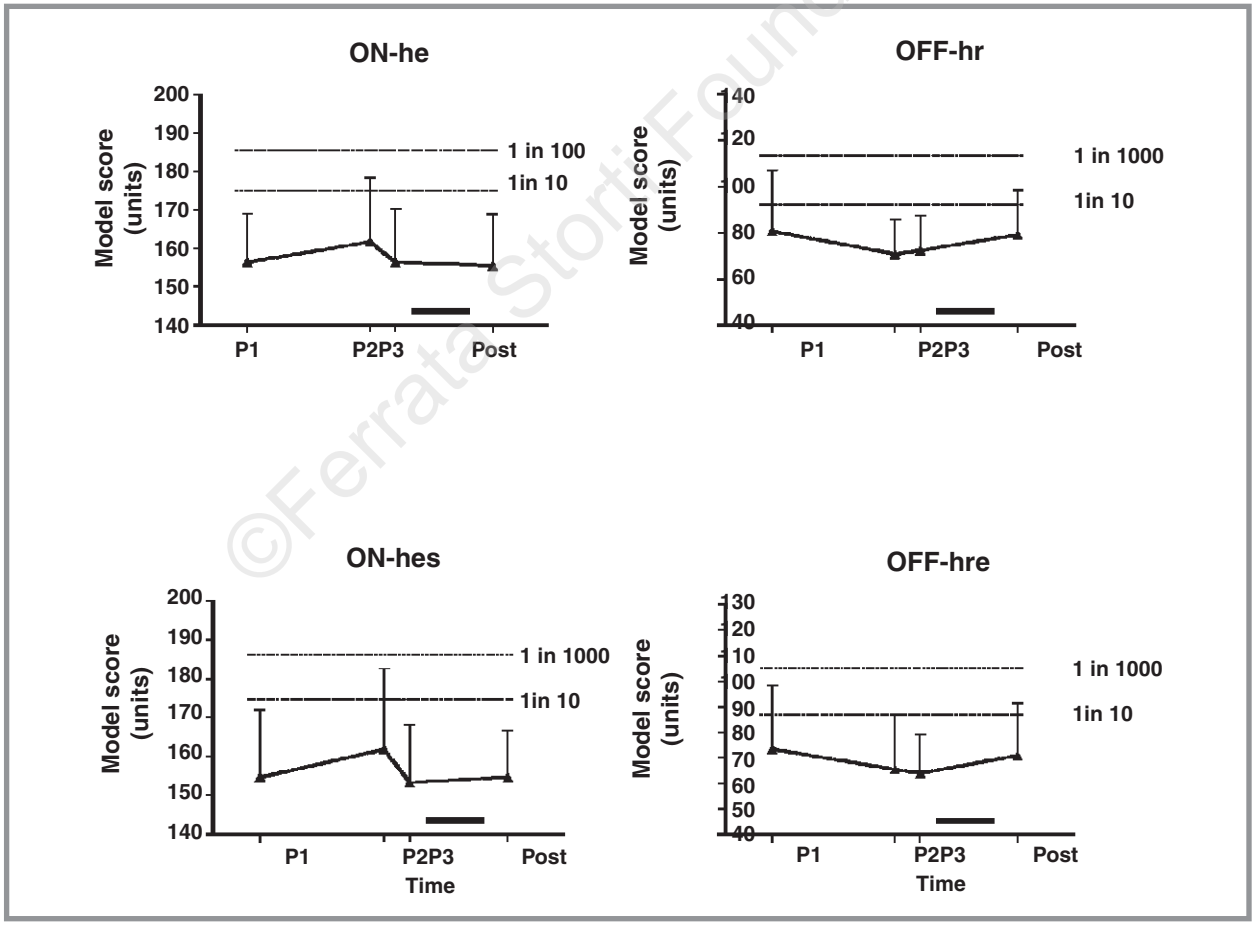

Figure 1. Mean ON (left hand column) and OFF (right hand column) model scores for 18 elite female rowers in the weeks preceeding the 2003 FISA World Championships. The error bars depict the highest score recorded at each timepoint. P1 – eight weeks prior to altitude; P2 – two weeks prior to altitude; P3 – one week prior to altitude; Post – 10 days after returning to sea level. The solid horizontal line depicts the 3-weeks spent training at an altitude 2440 m above sea level. The 1 in 10 (ON-he 175.0; ON-hes 174.6; OFF-hr 92.2; OFF-hre 86.8), 1 in 100 (ON-he 185.3; ON-hes 186.3) and 1:1000 (OFF-hr 113.5; OFF-hre 105.2) cut-off scores correspond to selected false-positive rates for *worst-case* female endurance athletes.[2] ON-hes represents n=15 due to missing data points.

Because rHuEPO must be injected for several weeks preceeding competition to facilitate the necessary substantial elevation of red cell mass, this period is also typically when athletes will face out-of-competition blood testing by anti-doping authorities. Therefore the aim of this study was two-fold. First, to quantify normal fluctuations of blood values in elite female athletes in the weeks preceeding a major competition, and second to report changes associated with a *bona fide* altitude training regimen.

Eighteen female rowers chosen to represent Australia provided blood samples on four separate occasions: 8, 2 and 1 week(s) prior to a 3-week altitude training sojourn, as well as 10 days after returning to sea level (the final collection was 18 days prior to the World Championships).

The first two samples were collected in Australia and measured in Canberra, the latter two samples were collected after the rowers had relocated to Europe and were measured in Freiburg (the same set of assays were used in both locations). Hemoglobin concentration (Hb) and percentage reticulocytes (Retic) were derived from EDTA samples measured on an ADVIA 120 Hematology Analyzer. Erythropoietin (EPO) and transferrin receptor (sTfr) concentration were measured from serum samples using commercial assay kits (Diagnostic Products Corporation USA, and Dade Behring Germany, respectively).

Mean blood parameters measured 10 days after return from altitude training were less than the highest mean values encountered during the weeks preceeding the altitude sojourn (Table 1). It was therefore not surprising that post-altitude blood model scores were also below peak pre-altitude scores (Figure 1). Of particular interest is the OFF-hr model since this has already been adopted by some sport federations. The highest OFF-hr score of 107.1 (Hb=145 g/L, Retic 0.4%) was measured during the first collection, which was unexpected but not due to any traceable methodological/technical anomalies. In total six different individuals exceeded the 1:10 cut-off for OFF-hr on one occasion each (four during the first collection, and two post-altitude); from 72 readings it would be expected that 7.2 would exceed a 1:10 cut-off.

Notwithstanding the absence of a control group, the ~7 unit increase in OFF-hr model score post-altitude could be attributed to the effect of altitude training. This represents approximately one quarter of the ~27 unit increase found in two groups of elite male cyclists in earlier research.[1] Several differences can be identified between the two studies. In addition to the gender and sport differences between cohorts, samples were collected at different intervals post-altitude. The rowers were measured 10 days after returning from altitude. At a comparable timepoint the OFF-hr score of one group of cyclists had decreased substantially (*Toluca 199*6 had scores 12 units higher nine days after returning from altitude), however, results from the *Toluca 2000* group were inconsistent with both scenarios in that the values of these athletes were still 17 units above baseline 14 days after an altitude sojourn.[1]

Published data on the effect of altitude on blood model scores seems inconclusive; two groups of male cyclists have shown marked increases in OFF-hr model scores (albeit with different temporal characteristics) whilst the response in female rowers was greatly attenuated. Three groups of male athletes exposed to simulated altitude also failed to show the marked response found in the male cyclists.[1] Whilst it seems clear that OFF-hr model scores are elevated post-altitude, at least to some extent, the magnitude of these increases should be placed in perspective. No athlete has exceeded the 1:1000 threshold either during or after altitude training, whilst it has been shown that 20-80% of athletes exceed this level after ceasing treatment with various doses of rHuEPO.[2] Introduction of an OFF-hr rule would have a considerable deterrent effect against rHuEPO doping and thereby protect the rights of *clean* athletes. In weighing the risk to an individual athlete being falsely suspected of blood doping, consideration should also be given to the utilitarian principle that gives precedence to the *greatest good to the greatest number of people*.

Michael J. Ashenden, Ken Sharpe,° Christian Schoch,# Yorck Olaf Schumacher#*

**Science and Industry Against Blood doping (SIAB) research consortium, Gold Coast, Australia; °Department of Mathematics and Statistics, The University of Melbourne, Melbourne, Australia. #Medizinische Universitätsklinik, Abteilung Sportmedizin, Freiburg, Germany*

Funding: this project was carried out with the support of the World Anti-Doping Agency.

Acknowledgments: we wish to thank Hannah Hroens, Ted Polglaze, Tony Rice and Bill Webb for supporting this research initiative and Sally Wright and Graeme Allbon for their technical support. Special recognition is due to the rowers who volunteered for this study in the midst of their championship preparations. We are grateful for the encouragement provided by FISA.

Key words: recombinant human erythropoietin, altitude, athletes, blood tests, doping, erythropoiesis

Correspondence: Michael J. Ashenden, Science and Industry Against Blood doping (SIAB), P.O. Box 572, Gold Coast QLD 4217, Australia. Phone: international +61.7.5570 3713. Fax: international +61.7.55703713. E-mail: heyasho@hotmail.com

References

1. Ashenden MJ, Gore CJ, Parisotto R, Sharpe K, Hopkins W, Hahn AG. Effect of altitude on second-generation blood tests to detect erythropoietin abuse by athletes. Haematologica 2003;88:1028-37.
2. Gore CJ, Parisotto R, Ashenden MJ, Stray-Gundersen J, Sharpe K, Hopkins W, et al. Second-generation blood tests to detect erythropoietin abuse by athletes. Haematologica 2003;88:333-44.