Letter To The Editor

No proof for augmented arterial oxygen content as only factor influencing exercise capacity after Epo doping

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TO THE EDITOR: In their paper, Lundby et al. (3) state that “the ergogenic effect of rHuEpo on VO2max can entirely be explained through the enhancement of the O2-carrying capacity of blood.” The main cause is assumed to be the increased hemoglobin concentration, since the blood volume was not raised and isovolemic hemodilution to control [Hb] decreased VO2max markedly. After carefully reading the paper, we have some concerns to fully follow this conclusion. After 13 wk of erythropoietin (Epo) application with an increase in hemoglobin concentration from 142 ± 4 to 156 ± 4 g/l at rest, eight physically active men underwent a graded cycle test to exhaustion. Following Epo application (Post-rHuEpo measurements) maximal work rate and oxygen uptake increased significantly by 9% (337 to 368 W) and 8% (3,950 to 4,255 ml/min) respectively. Then the extra red cell volume was withdrawn and replaced by a 5% albumin solution. After only 2 h, the cycle test with all measurements was repeated. The performance decreased to 339 W (not significant) and maximal oxygen uptake to 4,060 ml/min (P < 0.05). This result is not convincing evidence for a pure effect of Hb concentration. Can the authors exclude remaining fatigue or decreasing motivation at the end of a long experiment? Interestingly the lactate concentrations after hemodilution are the lowest in all tests including the pre-Epo values, whereas arterial norepinephrine concentrations are the highest, hinting at reduced glucose availability or increased strain but lower exhaustion. Also the arrangement of the experiment relative to circadian rhythm has to be considered; in early afternoon the intention to work hard is reduced. Might blood loss for the measurements have influenced maximal work rate? Very problematic is the fact that the experiments were not blinded. The subjects as well as the scientists knew when the Epo-induced increase in [Hb] was present.

In addition, some data in Table 1 apparently supporting the main effect of hemoglobin concentration seem to imply calculation errors. One-leg maximal oxygen delivery is not significantly decreased from the Post-rHuEpo value of 2,080 to 1,710 ml/min after hemodilution (pre-Epo 1,777 ml/min), as the table states. From the mean values given for arterial oxygen content and leg blood flow we calculate instead 2,047 ml/min. Correspondingly leg maximal oxygen uptake amounts to 1,710 (only 110 ml/min smaller than Post-rHuEpo) instead of 1,428 ml/min. The cause for the only small decreases is the slightly higher leg blood flow (corresponding to a significantly higher cardiac output) after hemodilution compared to Post-rHuEpo, which compensates largely the decrease in arterial oxygen content caused by the lower [Hb]. When calculating whole body oxygen delivery, the difference between Post-rHuEpo (5,365 ml/min) and hemodilution (5,188 ml/min) is also modest. Lundby et al. also argue that the enlarged heart work because of rising blood viscosity does not limit maximal cardiac output and thus exercise capacity. They derive this conclusion from the values of the heart rate pressure product RPP, which is clearly greater in the Post-rHuEpo measurement (25,027 mmHg·beats/min) than in both other conditions (21,150 mmHg·beats/min). A better measure of mechanical work of the heart, however, is cardiac power estimated as the product of stroke volume times pressure times heart rate. It increases from Pre-rHuEpo (6.66 W) to Post-rHuEpo (7.84 W) but tends also to slightly higher values after hemodilution (6.94 W). In the latter case the stroke volume is clearly higher and the blood pressure lower than Post-rHuEpo (blood pressures at maximal performance are surprisingly low in this investigation). One might speculate that a fully compensating increase of the stroke volume is restricted mechanically during the diastole (e.g., by heart wall stiffness or by too low filling pressure).

If these hemodilution experiments do not give the final answer about the nondisputable Epo-doping effects, what can be the causes? The following mechanisms might play a role (2): increased diffusion capacity for O2 in the lungs as well as in O2-consuming tissues because of the enlarged red cell surface, increased proportion of young erythrocytes with optimal functional properties, increased amount of non-bicarbonate buffers because of rising Hb mass, vasoconstriction in some organs that might improve filling of the circulation, increased binding or liberating of NO by Hb, improved scavenging in erythrocytes, increased growing of vessels, brain protection against hypoxia, improvement of mood, and placebo effects. A blood volume increase, however, has not been detected in contrast to altitude training. The importance of the placebo effect is unknown. Astonishingly there are only few true double-blind investigations (e.g., Refs. 1, 4). Thus it remains to be elucidated, how much of the 5–10% improvement in VO2peak found in most studies can be ascribed to any single factor.

REFERENCES