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The effects of supraphysiological doses of erythropoietin in healthy young men

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Abstract

The use of recombinant erythropoietin (rhEPO) by athletes (1) has been prohibited by the International Olympic Committee since 1990 (2), although no analytical method is currently in use in doping control laboratories to disclose its misuse (3). One of the physiological responses to rhEPO administration is an increase in serum levels of soluble transferrin receptor (sTfR) (4). In the present study, we wanted to assess the possibility to use sTfR as a marker of doping with rhEPO. We therefore performed a double blind, placebo-controlled study with the administration of 5000 U of rhEPO or placebo three times weekly for four weeks to 20 healthy male athletes. We measured haematocrit (hct) and levels of hemoglobin (hgb), sTfR, ferritin, erythropoietin (EPO) and quantified the effects on performance by measuring time to exhaustion and maximal oxygen uptake (VO_2 max) on a cycle ergometer.

Haematocrit increased from 42.1 ±1.7% to 50.8 ±2.0% in the EPO-group, and peaked one day after treatment was stopped. Haematocrit did not change in the placebo-group. Treatment was stopped before day 30 in two athletes as they reached the pre-determined hct cut-off level of 50%. Mean levels of sTfR and the ratio between sTfR and ferritin (sTfR/ferritin) increased in the EPO-group during treatment from 3.1 ±0.9 to 6.3 ± 2.3 mg/l and from 3.2 ± 1.6 to 11.8 ± 5.1, respectively, and did not change in the placebo-group. The increase in sTfR was significant after one week of treatment, and remained so for one week after treatment was stopped. Individual values for sTfR throughout the study period showed that 8/10 subjects receiving rhEPO, but none receiving placebo, had sTfR-levels that exceed baseline mean level +2SD for the whole population (4.6 mg/l) when stopping treatment. The mean level of VO_2-max at

baseline was 63.3 ±4.5 ml/kg/min in the EPO group, increasing to 68.1 ± 5.4 ml/kg/min one day post-treatment ($p<0.01$) (5). Baseline serum levels of EPO were 13.7 ±7.7 U/l in the EPO-group and 9.7 ±6.2 U/l in the control group (p=ns) (6). Twenty-four hours after the last injection, the level of EPO was 41.8 ±9.8 U/l and it was reduced to pre-treatment levels 48-72h after the last injection.

In conclusion, serum levels of sTfR might be used as an indirect marker of supranormal erythropoiesis during and one week after the administration of rhEPO. Maximal oxygen consumption and time to exhaustion were enhanced for three weeks post treatment. Hence there was a two week "open window" where athletic performance was enhanced, but in which this indirect marker of rhEPO doping was negative.

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A full length paper of this lecture has been submitted for publication.