

RhEPO improves time to exhaustion by non-hematopoietic factors in humans

It is still unclear by which mechanism recombinant human erythropoietin (rhEPO) improves endurance performance. The common belief that it acts by increasing oxygen delivery is rather unlikely. Therefore, we investigated several exercise-relevant variables in healthy, very active men with and without rhEPO. The most intriguing result was that the rhEPO-induced endurance prolongation was not due to higher oxygen consumption.

In more details, we investigated the effects of different doses of rhEPO [placebo (*P*), low (*L*), medium (*M*), and high (*H*) dosage] given during 4 weeks in 40 subjects. As expected, rhEPO improved the maximum oxygen consumption by about 6% independent of the rhEPO doses. However, normal endurance competitions last more than just a few minutes. This means that 1) most endurance competitions are below the intensity of maximum oxygen consumption, and 2) the active muscles cannot use the entire available oxygen provided by the blood. Therefore, it is questionable that the EPO-induced increase in red blood cell, which brings more oxygen to the active muscle, is of any benefit in normal endurance competitions. Our results showed that *L* prolonged intense constant-load exercise (85% of the intensity of maximum oxygen consumption) after 4 weeks of rhEPO administration by about 30%, *M* by about 63%, and *H* by about 73%. On average, we could not find any higher oxygen consumption during submaximal exercise with or without rhEPO in the many tests performed.

We conclude that submaximum oxygen consumption did not increase with rhEPO administration, which shows that the active muscle cannot benefit from the higher oxygen carrying capacity of the blood except for maximum oxygen consumption after rhEPO. This indicates for the first time that other, non-hematopoietic factors must play a crucial role for the impressive, dose-dependent prolongation of intense endurance exercise. We think that direct effects of rhEPO on skeletal muscle (e.g. increased fat oxidation) mainly contributed to the prolongation of intense endurance exercise.

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