**Point Hypothesis:**

Epoetin (EPO), the synthetic form of erythropoietin, does increase the oxygen transport and performance in sporting events.

C-P: EPO does not increase oxygen transport and performance in sporting events.

*Use in the clinical setting:*

The loss of the erythropoietin production site in the kidneys leads to severe anemia, which was treated by blood transfusion until 1988 when EPO became available (1). Since then, EPO has been approved for the use in the clinical setting for treatment of anemia caused by renal failure, cancer, and various other types of anemia (1).

*Use in the non-clinical setting:*

EPO has been used for blood doping in endurance type sporting events; the infusion of blood into the body to increase red blood cell mass and hence, oxygen carrying capacity and VO2 maximum (1).

*Mechanism of action:*

EPO acts upon the cytokine erythropoietin receptor that is expressed on erythroid precursor cells (7). EPO binds to its receptor and activates a number of signalling pathways for the production of red blood cells. The most straightforward pathways is the JAK/STAT kinase pathway where JAK2 phosphorylates the EPO receptor allowing STATs to bind to phosphotyrosine residues on the receptor and become phosphorylated themselves. The STATs move into the nucleus, stimulating gene expression for increasing red blood cell number and thus, the oxygen carrying capacity of the blood (7).

*Recommended dose of drug and safe level of consumption:*

The administration of EPO is measured in terms of target blood hemoglobin levels and corresponds to the concentration of O2 in blood. There is no official RDA for EPO but it is recommended that an EPO dosage should be controlled as to not exceed resultant blood hemoglobin levels of 12g/dl (3).
Research outcomes supporting the ergogenic effect of this supplement:

EPO increases hematocrit, reticulocytes, macrocytes, serum EPO concentration, and sTfr concentration which all increase the oxygen carrying capacity of the blood to working muscles (1). Aerobic capacity improvements were displayed in participants as indicated by the 7% increase in $\text{VO}_{2\text{max}}$ observed after dose injections (4). 5 weeks of EPO treatment can increase red blood cell volume by 9.4%, ultimately increasing maximal oxygen transport (5). Increases in systemic oxygen delivery and cardiac output directed to the legs associated with EPO use leads to higher peak leg O$_2$ delivery and VO$_2$ (5). A lack in functional EPO results in a functional decrease in aerobic exercise tolerance. This decrease was seen to be associated with hematocrit, decreased oxygen supply to the muscles and a disruption of the energy pathway associated with glycolysis and oxidative phosphorylation (6).

Evidence to refute the purported ergogenic effect/lack of ergogenic effect of this supplement:

EPO may cause reduced physical pain or perceived effort in training leading athletes to exceed their limits during training, perhaps even leading to death for some (4). It may appear that oxygen transport is increased to working muscles but this could be due to the increase rate of exertion during exercise while supplementing EPO. EPO treatment can increase $\text{VO}_{2\text{max}}$ in both normoxic and hypoxic conditions, but will not have an effect on $\text{VO}_{2\text{max}}$ in severe hypoxic conditions equivalent to altitudes of 4500m (5). Increase in hematocrit results in an increase in blood viscosity. For every 20% increase in viscosity, blood pressure must increase by 20% or vasodilation must increase by around 5%. This is detrimental in vessels with little capacitive ability and may increase the risk for atherosclerosis progression (2). Although it is shown that EPO increases power output in humans by about 3-5%, however, the normal day-to-day variation in performance may be 3-6% so fluctuations in performance are not necessarily associated with doping as usually assumed (3).

Evidence to refute the purported lack of ergogenic effect of this supplement:
Perceived physical condition and physical strength, a prime motivator for intensive training, increased in the EPO group, in contrast to the placebo and control groups (4). Rather than reduced physical pain or perceived effort, EPO gave subjects the motivation to overtrain. EPO treatment is said to be associated with high blood pressure because of increased blood viscosity. Following EPO treatment, patients saw significant increases in plasma norepinephrine concentrations during peak exercise compared to those without EPO treatment (5). NE is a vasoconstrictor that may be the cause of elevated blood pressure, rather than increased blood viscosity (5). Very few sporting events take place in severely hypoxic environments yielding EPO’s lack of efficacy at high altitudes inconsequential. Furthermore, EPO was seen to increase performance from normoxic to mildly hypoxic conditions, which encompasses the majority of sporting environments (5).

Conclusion:

From the evidence noted above, it is clear that EPO does increase oxygen transport and performance in sporting events through a variety of mechanisms including, increased hematocrit blood levels, VO2 maximum, workload, condition and physical effort.
Bibliography


