Is Erythropoietin (EPO) Useful For High Altitude Acclimatization?

Background

Erythropoietin (EPO) is a glycoprotein, which stimulates red blood cell (RBC) production. It is produced primarily in the kidney in response to hypoxia and/or endurance training. During ascent to moderate (>5,000 ft) or higher altitudes, endogenous EPO levels rise rapidly peaking in the first 48 hours of altitude exposure. An increase in RBC mass is measurable after 3-4 weeks and further increases have been reported for up to 9 months of continuous altitude residence. Several recombinant EPOs are marketed under various FDA approvals for the treatment of chronic anemias associated with renal failure, HIV infection, and cancer. Depending on the specific recombinant EPO, dosages and frequency of administration varies, but in general require injection(s) on a weekly basis for a month or more. The maximal rate of RBC expansion is ~50 ml/wk. Emerging data also supports a role for EPO as a neuroprotectant against ischemia, anoxia and severe hypoxia. A few human clinical trials have reported improved outcomes following stroke and other neurodegenerative disorders following administration of very large doses of EPO.

Myths and/or Claims

Weeks to months of EPO injections do increase RBC mass and have been demonstrated to increase aerobic exercise performance at low altitudes. An increase in RBC mass is a natural feature of altitude acclimatization, and does increase arterial oxygen content. This increase in arterial oxygen content should improve one's aerobic endurance performance and reduce fatigue at high altitude.

Facts

The natural increase in EPO is <u>only one</u> of many adaptations the body undergoes to improve work performance and reduce susceptibility to altitude sickness during high altitude exposure. In fact, the increase in RBC mass is one of the last adaptations to be manifest at high altitude. By far, increased ventilation (ventilatory acclimatization) is the most significant component of altitude acclimatization. Upon ascent to high altitude, ventilation increases immediately and achieves near maximal increase in a few days to a week. Furthermore, adaptations in body fluid regulation, acid-base balance, and metabolic pathways all contribute to improved physical function and decreased susceptibility to altitude sickness. To determine if a rapid increase in RBC mass would facilitate altitude acclimatization, SF volunteers were either blood-doped or received plain saline prior to ascending to 14,100 ft. No differences in performance or altitude illness were observed between the two groups.

Cautions

Most recombinant EPOSs are contraindicated in individuals with: uncontrolled hypertension, known hypersensitivity to mammalian cell-derived products, or known hypersensitivity to Albumin (Human). An excessive increase in RBC mass (hematocrit >50%) can potentially cause a "thickening" of the blood and possible thrombogenic events.

Summary

Several weeks to months of high altitude exposure, or regular injections of recombinant EPO's are proven ways to increase RBC mass. However, no improvement in physical work performance nor decreased susceptibility to altitude sickness at high altitudes (>8000 ft) has been demonstrated by increasing RBC mass alone. Other features of altitude acclimatization (e.g., increased ventilation, glucose transport, etc.) are essential to mitigating the effects of hypoxia, and are only attainable by exposure to high altitude.

Recommendation

The HPRC does not recommend use of recombinant EPOs to induce or enhance altitude acclimatization. If a Warfighter chooses to use these products, they should do so under appropriate medical supervision and with the understanding that use of these products does not induce most of the key physiological adaptations comprising altitude acclimatization.

Resources

1. **Sawka MN, Muza SR and Young AJ**. Erythrocyte volume expansion and human performance. In: Pharmacology, Doping and Sports: A scientific guide for athletes, coaches, physicians, scientists and administrators, edited by Fourcroy JL. London: Routledge, 2009, p. 125-134.

2. **Young AJ and Reeves JT**. Human adaptation to high terrestrial altitude. In: Medical aspects of harsh environments, edited by Lounsbury DE, Bellamy RF and Zajtchuk R. Washington, D.C.: Office of the Surgeon General, Borden Institute, 2002, p. 647-691.

3. **Young AJ, Sawka MN, Muza SR, Boushel R, Lyons T, Rock PB, Freund BJ, Waters R, Cymerman A, Pandolf KB and Valeri CR**. Effects of erythrocyte infusion on VO2max at high altitude. *J Appl Physiol* 81: 252-259, 1996.