Intermittent Hypoxia Increases Erythropoietin Levels in Healthy Individuals

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ABSTRACT

Few minutes of hypoxic exposure stabilizes hypoxia-inducible factor-1a, resulting in erythropoietin (EPO) gene transcription and production. PURPOSE: The objective of this study was to identify the shortest intermittent hypoxia protocol necessary to increase serum EPO levels in healthy individuals. We hypothesized that two separate intermittent hypoxia protocols would significantly increase EPO levels in healthy individuals. METHODS: A total of seven individuals (4 women and 3 men, age: 28±7 years, height: 177±9 cm, weight: 79.7±18.4 kg) participated in the study. In Experiment 1, the spontaneous EPO changes under normoxia (NORM) and the EPO response to five 4-minute cycles of intermittent hypoxia (IH5) were determined in six individuals. In Experiment 2, the EPO response to eight 4-minute cycles of intermittent hypoxia (IH8) and 120 minutes of continuous hypoxia (CONT) was determined in six individuals. All hypoxic protocols were performed at a targeted arterial oxygen saturation of 80%. Air was made hypoxic by titrating nitrogen into a breathing circuit. Pulmonary gas exchange, arterial oxygen saturation, and hemodynamics obtained by finger plethysmography were continuously monitored throughout all hypoxic protocols. In Experiment 1, EPO levels were measured before, 2.5 and 4.5 hours after the beginning of the IH5 and NORM protocols. In Experiment 2, EPO levels were measured before, 4.5 and 6 hours after the beginning of the IH8 and CONT protocols. **RESULTS**: There was no significant change in EPO levels in response to normoxia or in response to five cycles of intermittent hypoxia (NORM: 9.5±1.8 to 10.5±1.8, IH5: 11.4±2.3 to 13.4±2.1 mU/ml, main effect for time p=0.35). There was an increase in EPO levels in response to eight cycles of intermittent hypoxia and 120 minutes of continuous hypoxia, with peak levels observed 4.5 hours after the onset of hypoxia (IH8: 11.2±2.0 to 16.7±2.2, CONT: 11.1±3.8 to 19.4 \pm 3.8 mU/ml, main effect for time p<0.01). Eight cycles of intermittent hypoxia increased EPO levels to a similar extent as 120 minutes of continuous hypoxia (main effect for condition p=0.36). Intermittent hypoxia did not affect mean arterial pressure (IH5: 88±7 to 87±7, IH8: 90±7 to 88±7 mmHg, p>0.05). **CONCLUSION**: Eight 4-minute cycles of intermittent hypoxia represent the shortest protocol to increase serum EPO levels in healthy individuals.