

Impaired Erythropoietin Response to a Single Session of Intermittent Hypoxia in Patients with Type 2 Diabetes

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ABSTRACT

Patients with type 2 diabetes (T2D) exhibit, on average, a 20% decline in maximal oxygen consumption when compared to healthy adults. Hemoglobin mass strongly correlates to maximal oxygen consumption. A reduced total blood volume has been observed in patients with T2D, suggesting that a reduced hemoglobin mass contributes to the decreased maximal oxygen consumption in this population. Hypoxia stimulates the release of erythropoietin (EPO), the hormone regulating red blood cell production. We previously showed that intermittent hypoxia, consisting of alternating short bouts of breathing hypoxic and normoxic air, increases EPO levels. **PURPOSE:** To determine the effect of a single session of intermittent hypoxia on serum EPO levels and hemoglobin mass in patients with T2D. We hypothesized that a single session of intermittent hypoxia would raise serum EPO levels and lead to an increase in hemoglobin mass in patients with T2D. **METHODS:** Ten patients with T2D (4 women, age: 53 ± 10 years, body mass index: 36.2 ± 8.5 kg/m², HbA1c: $7.2 \pm 1.2\%$) were exposed to an intermittent hypoxia protocol consisting of eight 4-min cycles at a targeted oxygen saturation of 80% interspersed with normoxic cycles to resaturation. Air was made hypoxic by titrating nitrogen into a breathing circuit. Pulmonary gas exchange, oxygen saturation, and hemodynamics were continuously measured throughout the protocol. EPO levels were measured before and 4.5 hours after the beginning of the protocol. Hemoglobin mass was assessed via carbon monoxide rebreathing before and seven days following intermittent hypoxia. **RESULTS:** Intermittent hypoxia lowered oxygen saturation (97 ± 2 to $81 \pm 2\%$, $p < 0.01$), which resulted from a lower fraction of inspired oxygen (20.8 ± 0.1 to $11.1 \pm 1.0\%$, $p < 0.01$). There was no significant change in EPO levels following exposure to intermittent hypoxia (11.9 ± 5.3 to 12.1 ± 4.3 mU/ml, $p = 0.83$). There was also no change in hemoglobin mass in response to intermittent hypoxia (864 ± 152 to 850 ± 150 g, $p = 0.64$). Intermittent hypoxia did not affect mean arterial pressure (94 ± 5 to 97 ± 7 mmHg, $p = 0.18$) but increased cardiac output (9.1 ± 2.7 to 9.8 ± 2.8 L/min, $p = 0.03$) due to an increase in heart rate (78 ± 9 to 84 ± 10 bpm, $p < 0.01$). **CONCLUSION:** A single session of intermittent hypoxia did not increase serum EPO levels or hemoglobin mass in patients with T2D. These findings suggest an impaired EPO response to decreased oxygen levels in patients with T2D, which may contribute to the reduced hemoglobin mass and total blood volume observed in this population.