Carbamylated form of human erythropoietin normalizes cardiorespiratory disorders triggered by intermittent hypoxia mimicking sleep apnea syndrome

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Abstract
BACKGROUND AND OBJECTIVE: Chronic intermittent hypoxia (CIH), one of the main features of obstructive sleep apnea (OSA), enhances carotid body-mediated chemoreflex and induces hypertension and breathing disorders. The carbamylated form of erythropoietin (cEpo) may have beneficial effects as it retains its antioxidant/anti-inflammatory and neuroprotective profile without increasing red blood cells number. However, no studies have evaluated the potential therapeutic effect of cEpo on CIH-related cardiorespiratory disorders. We aimed to determine whether cEpo normalized the CIH-enhanced carotid body ventilatory chemoreflex, the hypertension and ventilatory disorders in rats. METHODS: Male Sprague-Dawley rats (250 g) were exposed to CIH (5% O2, 12/h, 8 h/day) for 28 days. cEPO (20 µg/kg, i.p) was administrated from day 21 every other day for one more week. Cardiovascular and respiratory function were assessed in freely moving animals. RESULTS: Twenty-one days of CIH increased carotid body-mediated chemoreflex responses as evidenced by a significant increase in the hypoxic ventilatory response (FiO2 10%) and triggered irregular eupneic breathing, active expiration, and produced hypertension. cEpo treatment significantly reduced the carotid body--chemoreflex responses, normalizes breathing patterns and the hypertension in CIH. In addition, cEpo treatment effectively normalized carotid body chemosensory responses evoked by acute hypoxic stimulation in CIH rats. CONCLUSION: Present results strongly support beneficial cardiorespiratory therapeutic effects of cEpo during CIH exposure.