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## Mitochondrial dysfunction in patients with carbon monoxide poisoning treated with hyperbaric oxygen

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**Background:** Carbon monoxide (CO) poisoning is the leading cause of poisoning mortality and morbidity in the United States. Carboxyhemoglogin (COHb) levels are not predictive of severity or prognosis of exposure. At this time the measurement of mitochondrial respiration may serve as a potential biomarker in CO poisoning and treatment. This is a preliminary study enrolling patients with confirmed CO poisoning treated with hyperbaric oxygen (HBO).

**Methods:** With informed consent we prospectively studied 6 patients >18 years of age having confirmed carbon monoxide exposure treated with HBO and 6 volunteers undergoing HBO as controls. A single venous blood sample was collected from each subject before and after HBO. Peripheral blood mononuclear cells (PBMCs) were placed in a 2-mL chamber at a final concentration of 3-4×$10^6$ cells/mL. Measurement of oxygen consumption were performed at 37°C in a high-resolution oxygraph (Oxygraph-2k Oroboros Instruments, Innsbruck, Austria). Oxygen flux (in pmol $O_2$/s/$10^6$ cells), which is directly proportional to oxygen consumption, was recorded continuously using DatLab software 6. Basal, ATP-linked, residual oxygen consumption (ROX) and maximal mitochondrial oxygen consumption rates along with specific complex-linked activity (in pmol/s/$10^6$ cells) were measured in permeabilized PBMCs using a standard series of substrates, inhibitor and uncoupler injections. Cell isolation and all metabolic measurements were performed within 2 hours.

**Results:** The range of COHb was 15-62% for patients with CO poisoning. There were differences in respiration before and after HBO in the CO group with a general increase in respiration. For routine respiration: 9.2 pmol $O_2$/s/$10^6$ cells; 95% CI 6.1 to 13.2, p<0.0001); Proton Leak: 0.83 pmol $O_2$/s/$10^6$ cells; 95% CI -0.23 to 1.9, p=0.157); Maximal respiration: 26.7 pmol $O_2$/s/$10^6$ cells; 95% CI 18.3 to 28.5, p<0.0001); ROX: 0.22 pmol $O_2$/s/$10^6$ cells; 95% CI -0.58 to 1.31, p=.557). There were no differences in the control group before and after HBO.

**Conclusions:** The key parameters of mitochondrial respiration was significantly lower in CO patients when compared to the control group with a significant increase in key parameters of mitochondrial respiration after HBO. This pilot clinical study demonstrates HBO treatment may result in improvement in mitochondrial respiration.