The Effect of Intermittent Normobaric Hyperoxia on Stem Cell Mobilization and Cytokine Expression

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Introduction/Background

Mechanisms of Hyperbaric Oxygen Therapy (HBOT) putatively include inducing transduction cascades that modulate cytokine expression and mobilize proangiogenic stem/progenitor cells (PSC). Accepted clinical HBOT inhaled oxygen tensions (PiO2) range minimally from 1520 Torr up to 2280 Torr, however, little is known about oxygen therapy below PiO2 760torr. A central dogma in contemporary oxygen therapy research asserts low values of hyperoxia are benign and a useful sham. In this experiment we measure inflammatory cytokine expression and PSC mobilization at PiO2 320 Torr.

Materials and Methods

Twelve, 10-week-old-Sprague-Dawley rats were randomly divided into two-groups. The treatment group exposed to PiO2 319 torr (41%O2) and the control group exposed to room air. Treatments were administered 5 days/week, 2 hours/day, totaling 20hrs. After sacrifice, monocytes/cells harvested from venous blood were prepared for flow cytometry using antibodies for CD45+, CD34+ and CD133+. Flow cytometry using the BDLSRII/DIVA was analyzed with FlowJo software. Statistics performed using a non-parametric unpaired t-test (Mann-Whitney) with a p<0.05 to indicate significance. Cytokine survey was performed on blood plasma using the Signosis Rat Cytokine ELISA Plate Array per manufacturers instructions.

Results

Treated animals showed an increase in mobilized CD45+/133+/34- PSC’s (p=0.009) compared to controls, but no difference in CD45+/133-/34+ (p=0.99). TNFα was significantly decreased in treated animals compared to controls (p=0.004).

Summary/Conclusions

To our knowledge, this is the first study to demonstrate biologic activity at PiO2 320 Torr. Previous research indicated HBOT mobilizes PSC’s with PiO2 1520 Torr. Similar to this finding, our data demonstrates that a much smaller dose (PiO2 320 Torr), also mobilizes PSC’s and additionally suggests a potential anti-inflammatory effect by reduction in TNFα. Together these findings support the likelihood of biologic activity, consubstantial with HBOT, being activated at much lower dose of hyperoxia than previously postulated. Future research examining oxygen/dose relationship will further elucidate the biological effect of various doses of hyperoxia, and establish differences between concentration and pressure, along with establishing basal active levels.
Bio – Kent MacLaughlin is a 4th year PhD graduate student in the Physiology Graduate Training program at the University of Wisconsin – Madison’s Eldridge lab.

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References;


