

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 (P_{iO_2}) range minimally from 1520 Torr up to 2280 Torr, however, little is known about oxygen therapy below P_{iO_2} 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 P_{iO_2} 320 Torr.

Materials and Methods

Twelve, 10-week-old-Sprague-Dawley rats were randomly divided into two-groups. The treatment group exposed to P_{iO_2} 319 torr (41% O_2) 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+ ($p=0.99$). $TNF\alpha$ 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 P_{iO_2} 320 Torr. Previous research indicated HBOT mobilizes PSC's with P_{iO_2} 1520 Torr. Similar to this finding, our data demonstrates that a much smaller dose (P_{iO_2} 320 Torr), also mobilizes PSC's and additionally suggests a potential anti-inflammatory effect by reduction in $TNF\alpha$. 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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