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**LS-11-P-3533 Hepatocytes and liver hemopoietic cells responses to mild and severe hyperoxia in newborn rats**

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Premature newborns are frequently exposed to both mild and severe hyperoxia and experimental data indicate modulation of liver metabolism by hyperoxia in the first postnatal period. Conversely, nothing is known about possible modulation of growth factors and signaling molecules involved in other hyperoxic responses and no data are available about the effects of hyperoxia in postnatal liver haematopoiesis.

The aim of this study is to analyse the effects of hyperoxia in neonatal liver tissue, focusing the attention on the responses shown by hepatocytes and haemopoietic cells in terms of Vascular Endothelial Growth Factor (VEGF), Matrix Metalloproteinase 9 (MMP-9), Hypoxia-Inducible Factor-1α (HIF-1α), endothelial Nitric Oxide Synthase (eNOS), and Nuclear Factor-kB (NF-kB), expression along with apoptotic event occurrence.

Exposure of newborn rats to room air (controls), 60% O2 (mild hyperoxia), or 95% O2 (severe hyperoxia) was performed for the first two postnatal weeks. The results were obtained by means of immunohistochemical, TUNEL and Western blot analyses.

Severe hyperoxia increases hepatocyte apoptosis and MMP-9 expression and decreases VEGF expression. Reduced content in reticular fibers is found in moderate and severe hyperoxia. Moderate hyperoxia specifically induces in hepatocytes upregulation of HIF-1α and downregulation of eNOS and NF-kB expression. Postnatal hyperoxia exposure upregulates VEGF (both moderate and severe hyperoxia) and eNOS (severe hyperoxia) expression in haemopoietic cells.

In conclusion, our study reveals different effects of hyperoxia on hepatocytes and haemopoietic cells, with growth factors and intracellular mechanisms being differently involved. Postnatal hyperoxia shows detrimental action on hepatic tissue. Decreased VEGF expression may play a role in severe hyperoxia whereas some other changes seem to drive response to moderate hyperoxia, such as increased HIF-1α expression, and decreased expression of eNOS and NF-kB. Conversely, postnatal hyperoxia exposure increases liver haemopoiesis and upregulates VEGF and eNOS expression. Thus, it may be hypothesized the involvement of VEGF and eNOS in the liver haemopoietic response to hyperoxia.