



ISCHAEMIA REPERFUSION INJURY IN LIVER TRANSPLANTATION: EFFECT OF HYPERBARIC OXYGEN

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Liver Transplantation (LT) is the only effective therapy for patients with end stage liver disease and specific liver malignancies. The development of donor organ dysfunction due to Ischaemia, Preservation and Reperfusion Injury (IPRI) is the major factor contributing to morbidity and mortality of LT. IPRI is a complex process that involves donor and recipient immune cells interacting with the parenchymal and non parenchymal cells (NPC) of the donor liver. One of the NPCs that play an integral role in the development of IPRI are the Liver Sinusoidal Endothelial Cells (LSEC). They are also a major target for injury. Hyperbaric Oxygen Therapy (HBO) has been shown to inhibit a number of processes that are integral to IPRI with improvement in the severity of IPRI in a

number of experimental models and some clinical situations. Our preliminary data indicates that HBO influences both the innate and acquired immune response as well as the patho-physiological changes of IPRI. Using a well established rat model of LT we have demonstrated that HBO applied after LT results in a significant reduction in hepatocyte necrosis and apoptosis while stimulating liver regeneration. This proposal investigates the potential applicability of HBO therapy in LT focussing on its impact on LSEC. We will characterise the pattern and the mechanisms of injury to LSECs from IPRI following liver transplantation. We also aim to determine the effect of HBO on LSEC exposed to IPRI.

Techniques:

Histopathology
Stereology
Immunohistochemistry
Animal models of disease
In vivo confocal microscopy
Biochemical assays
RT-PCR

Projects

1. Determination of the temporal sequence of hepatocyte and LSEC injury that occurs after LT due to IPRI.
2. Investigation of the effect of HBO on hepatocyte and LSEC injury after LT
3. Evaluation of the underlying mechanisms of action of HBO on LSEC injury after LT.
4. Determine the effect of HBO on LSEC independent to that on neutrophils and Kupffer cell

Publications:

Fink MA, Angus PW, Gow PJ, Berry SR, Wang BZ, Muralidharan V, Christophi C, Jones RM. Liver transplant recipient selection – MELD versus clinical acumen. *Liver Transpl*, 11(6): 621-6, 2005.

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