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HYPOTHERMIC OXYGENATION OF THE RAT LIVER AFTER COLD STORAGE PREVENTS REPERFUSION INJURY

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Introduction : The role of Kupffer cells as important source of reactive oxygen species upon liver ischemia reperfusion injury was often pointed out especially after a preservation time of ³ 24 hours when endothelial cell structure already is altered. Nevertheless a recent study suggested a different mechanism of rat liver reperfusion injury after shorter periods of preservation (10h), reflecting more the role of hepatocyte intracellular integrity : hepatocyte mitochondrial electron transfer was correlated with the release of reactive oxygen species as well as with the induction of apoptosis. This study should investigate the possibility of short termed hypothermic oxygenation following cold storage prior to reperfusion with respect on reperfusion injury.

Methods : Rat livers (Brown norway) were either preserved by cold storage (4°C) in UW solution (CS) for 10 hours or perfused for 3 hours (oxygenated modified UW solution) after 10h CS (CS+HOPE). After preservation the livers were analysed for Lipidperoxidation, total glutathione, Energy charge, glycogen and expressions of TNFa, bad, bax, bid, c-jnk, MIP-2 and hgf (RT PCR). Addidtional experiments were performed with isolated normothermic liver perfusion for 90 minutes after preservation (10h CS, 10h CS+HOPE) and investigation of LDH release, superoxide anion formation, bile flow, Lipidperoxidation and expressions of TNFa, bad, bax, bid, c-jnk, MIP-2 and hgf (RT PCR). During preservation and reperfusion transhepatic light absorption (400–600 nm) was detected to analyse mitochondrial cytochrome redox state. Before and after reperfusion electron microscopy of liver samples was performed.

Results : After 10h cold storage mitocondrial cytochrome redox state was completely reduced and the livers were metabolically depressed. PCR analysis showed no expression of mediators, Electron micoscopy showed no signs of morphological alterations. Nevertheless cold stored livers (CS) showed during reperfusion formation of reactive oxygen species, expression of mediators (TNFa, c-jnk, MIP-2) and induction of apoptosis. All of these events could be prevented by hypothermic oxygenation over 3 hours after cold storage (CS+HOPE). Those livers showed prior to reperfusion a restored cellular energy charge and oxidized mitochondrial cytochromes which resulted in significant less cell death, less oxidative stress, decreased mediator and apoptosis expression during reperfusion.

Conclusions : Ischemia reperfusion injury after short periods of reperfusion is suggested to be related with intact hepatocyte mitochondrial function and can be effectively decreased by methods of hypothermic oxygenation prior to transplantation.