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Hydrogen Rich Solution Attenuates Cold Ischemia-Reperfusion Injury in Rat Liver Transplantation

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Introduction: Liver transplantation (LT) is considered as the standard treatment for end stage liver disease. However, there is a problem of donor shortage, and the need of grafts from marginal donors has increased. Attenuation of ischemia and reperfusion injury (IRI) in such marginal donors is crucial for less possibility of primary non-function and the graft loss. There have been some reports that hydrogen (H₂) shows the antioxidant and anti-inflammatory effects, and eventually prevents IRI, in some non-hepatic transplant models^{[1][2]}. Therefore, we investigated whether the H₂ attenuates IRI in LT model using rats.

Methods: We made and used the H₂ rich water bath (HRWB), in which the H₂ ion was dissolved in the UW solution. Isogenic LT model of Lewis rats was used. Without arterial reconstruction, orthotopic LT was performed according to Kamada's cuff method. The animals were divided into four groups; sham operation (Sham), not preserved (NP), preserved 12 hours in UW solution (UW), preserved 12 hours in H₂ rich UW solution (UW+H₂). H₂ ion solution in the graft liver was measured every hour after preservation in the preliminary study. Blood and tissue samples were corrected 6 hours after the reperfusion. Hepatic enzymes in serum were measured. Pathological findings including the expressions of cytokines and heme oxygenase-1 (HO-1) in liver tissues were evaluated.

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[Figure](#)

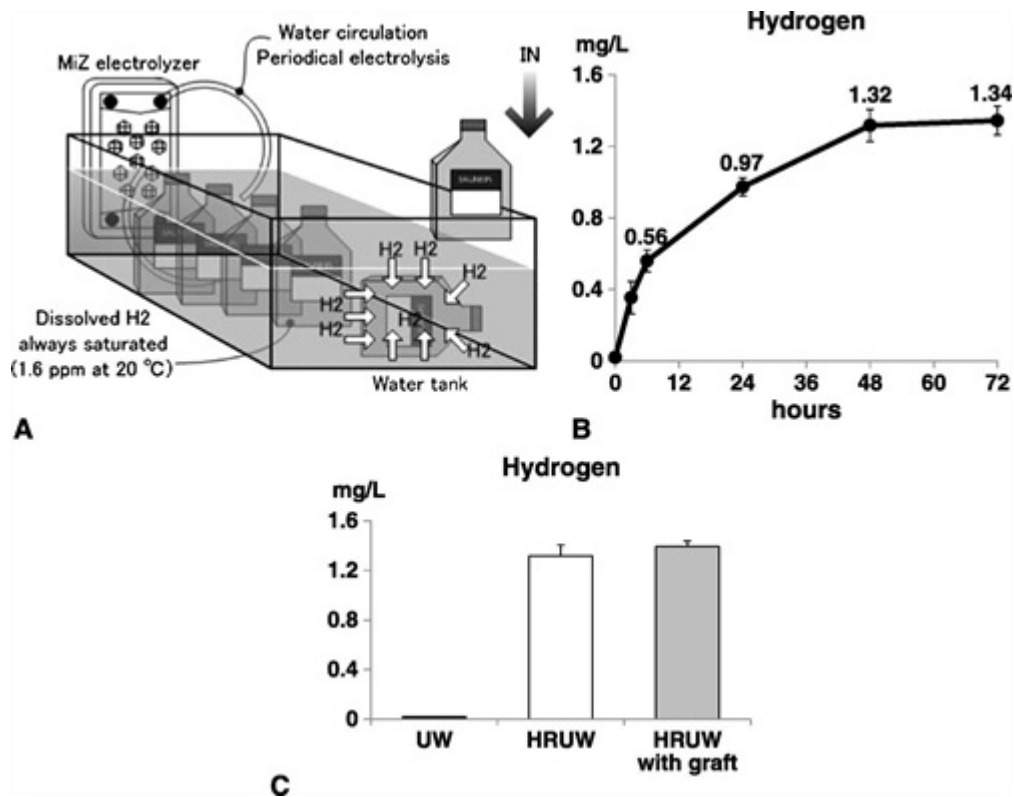
Result: H₂ concentration of graft tissue increased depending on the storing time in the HRWB, and it became plateau after 1 hour. AST, ALT, and LDH levels of serum showed significantly lower in UW+H₂ groups. In the UW group, liver histology showed focal hemorrhage, cell ballooning, and infiltration of neutrophils and macrophages, and those findings were much attenuated in the UW+H₂ group. UW+H₂ group also showed less oxidative damage and hepatocyte apoptosis. UW+H₂ groups tended to have lower proinflammatory cytokines and higher HO-1 levels in mRNA expressions, and protein levels of HO-1 increased significantly.

Conclusion: By using the HRWB, sufficient H₂ distribution in the liver graft was obtained. Storage of the liver grafts in H₂ rich UW solution presented superior functional and morphologic protection for IRI. Up-regulation of HO-1 was suggested as one mechanism of this effect. Result of our present study demonstrated that H₂ rich solution decrease oxidative stress and inflammatory changes by IRI in rat LT model.

References:

1. Abe et al. Hydrogen-Rich University of Wisconsin Solution Attenuates Renal Cold Ischemia–Reperfusion Injury. *Transplantation*. 2012; 94: 14-21.
2. Noda et al. A novel method of preserving cardiac grafts using a hydrogen-rich water bath. *The Journal of Heart and Lung Transplantation*. 2013; 32: 241-250.

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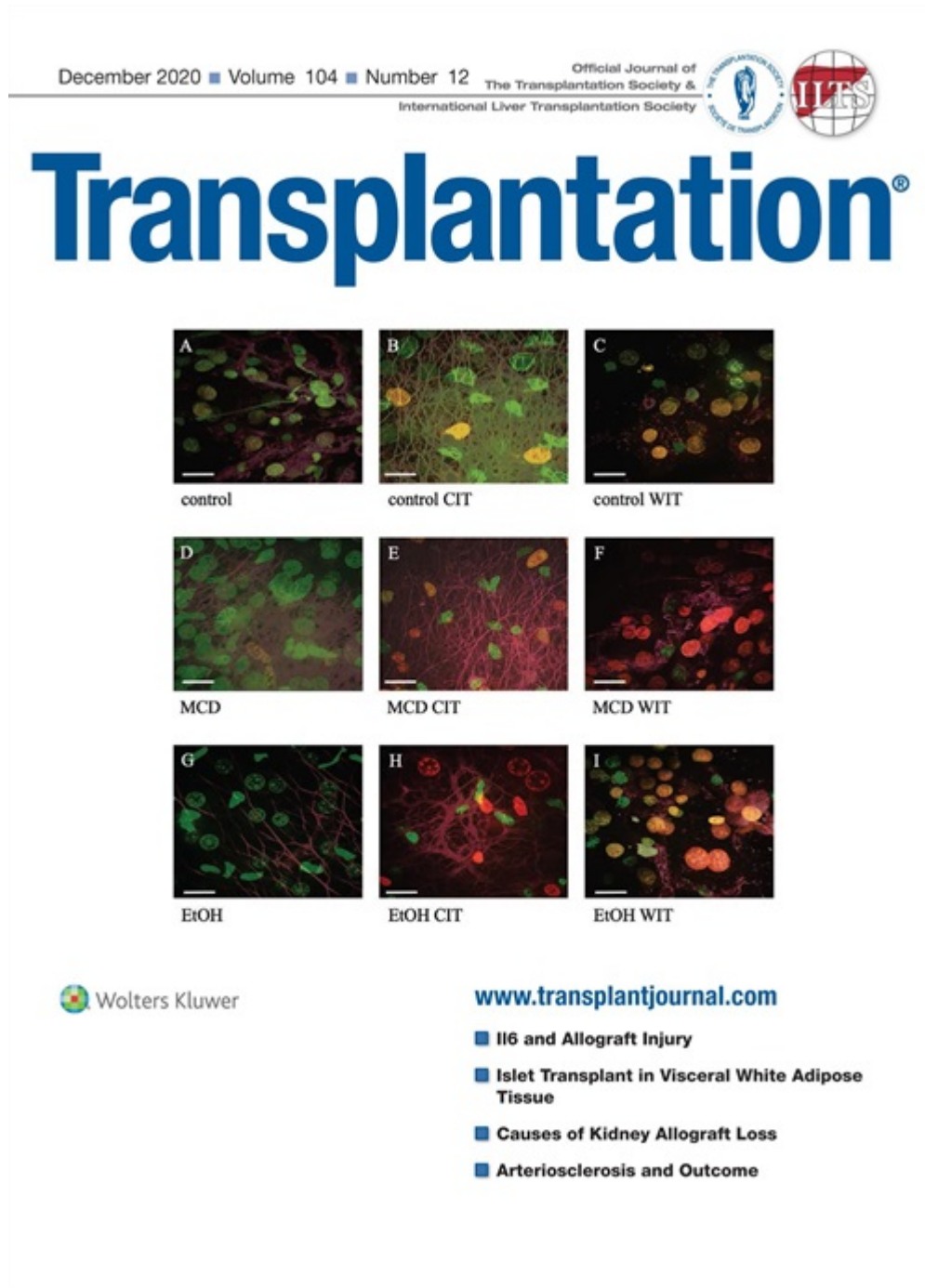
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Score	Vacuolization	Cortical damage	Necrosis
0	None	None	None
1	Minimal	-10%	Individual cells necrosis
2	Mild	-20%	-30%
3	Moderate	-30%	-60%
4	Severe	>30%	>60%

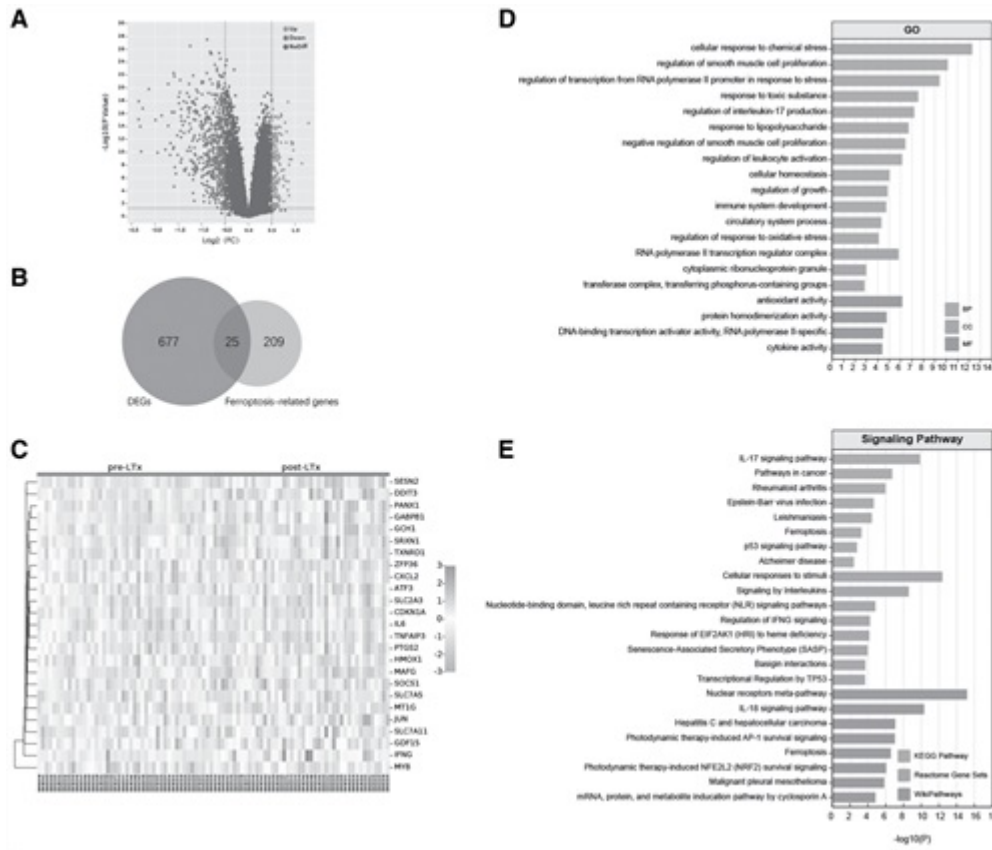
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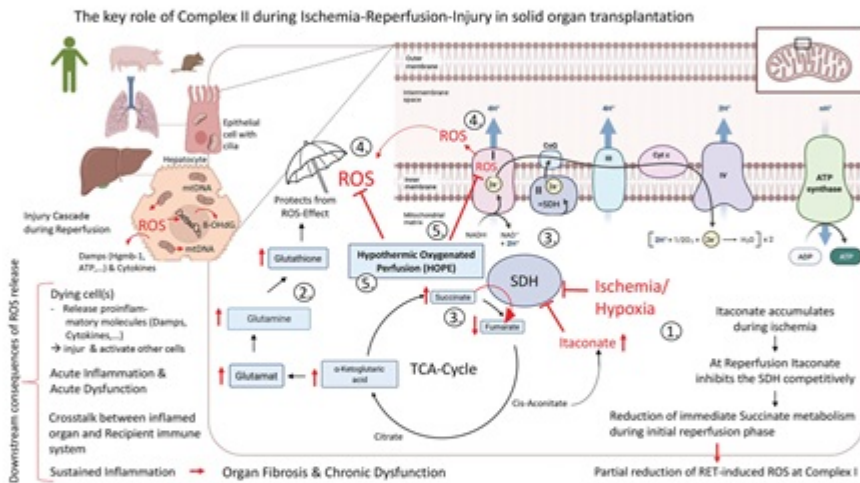


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