Luminal Preloading with Hydrogen-Rich Saline Ameliorates Ischemia Reperfusion Injury Following Intestinal Transplantation in Rats

## ABSTRACT (249 WORDS)

**Background:** Prolonged intestinal cold storage causes considerable mucosal breakdown, which could bolster bacterial translocation and cause life-threatening infection for the transplant recipient. The intestine has an intraluminal compartment, which could be a target for intervention, but has not yet been fully investigated. Hydrogen gas exerts organ protection and has used been recently in several clinical and basic research studies on topics including intestinal transplantation. In this study, we aimed to investigate the cytoprotective efficacy of intraluminally-administered hydrogen-rich saline on cold ischemia reperfusion (IR) injury in intestinal transplantation.

**Methods:** Isogeneic intestinal transplantation with six hours of cold ischemia was performed on Lewis rats. Hydrogen-rich saline (H<sub>2</sub> concentration at 5 ppm) or normal saline was intraluminally introduced immediately before preservation. Graft intestine was excised three hours after reperfusion and analyzed.

**Results:** Histopathological analysis of control grafts revealed blunting of the villi and erosion. These mucosal changes were notably attenuated by intraluminal hydrogen. Intestinal mucosa damage caused by IR injury led to considerable deterioration of gut barrier function 3h post-reperfusion. However, this decline in permeability was critically prevented by hydrogen treatment. IR-induced upregulation of proinflammatory cytokine

mRNAs such as IL-6 were mitigated by hydrogen treatment. Western blot revealed that hydrogen treatment regulated loss of the transmembrane protein zonula occludens-1.

**Conclusions:** Hydrogen-rich saline intraluminally administered in the graft intestine modulated IR injury to transplanted intestine in rats. Successful abrogation of intestinal IR injury with a novel strategy using intraluminal hydrogen may be easily clinically applicable and will compellingly improve patient care after transplantation.