Main Text Article

# Hydrogen Gas Ameliorates Hepatic Reperfusion Injury After Prolonged Cold Preservation in Isolated Perfused Rat Liver

Shingo Shimada, Kenji Wakayama, Moto Fukai 🔀, Tsuyoshi Shimamura, Takahisa Ishikawa, Daisuke Fukumori, Maki Shibata, Kenichiro Yamashita, Taichi Kimura, Satoru Todo ... See all authors 🗸

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# Abstract

Hydrogen gas reduces ischemia and reperfusion injury (IRI) in the liver and other organs. However, the precise mechanism remains elusive. We investigated whether hydrogen gas ameliorated hepatic I/R injury after cold preservation. Rat liver was subjected to 48-h cold storage in University of Wisconsin solution. The graft was reperfused with oxygenated buffer with or without hydrogen at 37° for 90 min on an isolated perfusion apparatus, comprising the  $H_2(+)$  and  $H_2(-)$  groups, respectively. In the control group (CT), grafts were reperfused immediately without preservation. Graft function, injury, and circulatory status were assessed throughout the perfusion. Tissue samples at the end of perfusion were collected to determine histopathology, oxidative stress, and apoptosis. In the  $H_2(-)$  group, IRI was indicated by a higher aspartate aminotransferase (AST), alanine aminotransferase (ALT) leakage, portal resistance, 8-hydroxy-2-deoxyguanosine-positive cell rate, apoptotic index, and endothelial endothelin-1 expression, together with reduced bile production, oxygen consumption, and GSH/GSSG ratio (vs. CT). In the H<sub>2</sub>(+) group, these harmful changes were significantly suppressed [vs.  $H_2(-)$ ]. Hydrogen gas reduced hepatic reperfusion injury after prolonged cold preservation via the maintenance of portal flow, by protecting mitochondrial function during the early phase of reperfusion, and via the suppression of oxidative stress and inflammatory cascades thereafter.

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