

Rapid Diffusion of Hydrogen Protects the Retina: Administration to the Eye of Hydrogen-Containing Saline in Retinal Ischemia-Reperfusion Injury

Hideaki Oharazawa,¹ Tsutomu Igarashi,² Takashi Yokota,³ Hiroaki Fujii,⁴ Hisaharu Suzuki,⁵ Mitsuru Machide,⁶ Hiroshi Takahashi,⁷ Shigeo Ohta,⁸ and Ikuroh Ohsawa⁹

¹Department of Ophthalmology, Musashikosugi Hospital, Nippon Medical School, Kawasaki, Japan ²Department of Ophthalmology, Nippon Medical School, Tokyo, Japan ³Department of Molecular Biology, Institute of Development and Aging Sciences, Nippon Medical School, Kawasaki, Japan ⁴Department of Ophthalmology, Musashikosugi Hospital, Nippon Medical School, Kawasaki, Japan ⁵Department of Ophthalmology, Nippon Medical School, Tokyo, Japan ⁶The Center of Molecular Hydrogen Medicine, Institute of Development and Aging Sciences, Nippon Medical School, Kawasaki, Japan ⁷Department of Ophthalmology, Nippon Medical School, Tokyo, Japan ⁸Department of Biochemistry and Cell Biology, Institute of Development and Aging Sciences, Nippon Medical School, Kawasaki, Japan ⁹The Center of Molecular Hydrogen Medicine, Institute of Development and Aging Sciences, Nippon Medical School, Kawasaki, Japan

Correspondence: Ikuroh Ohsawa, Email: iohsawa@nms.ac.jp

P<P, published online ahead of print October 15, 2009

(*Investigative Ophthalmology and Visual Science.*)

© 2009 by The Association for Research in Vision and Ophthalmology, Inc.

doi:10.1167/iovs.09-4089

Abstract

PURPOSE. Retinal ischemia-reperfusion (I/R) injury by transient elevation of intraocular pressure (IOP) is known to induce neuronal damage through the generation of reactive oxygen species. Previous studies indicate that molecular hydrogen (H₂) is an efficient antioxidant gas that selectively reduces the hydroxyl radical (OH) and suppresses oxidative stress-induced injury in

several organs. This study was conducted to explore the neuroprotective effect of H₂-loaded eye drops on retinal I/R injury.

METHODS. Retinal ischemia was induced in rats by raising IOP for 60 minutes. H₂-loaded eye drops were prepared by dissolving H₂ gas into a saline to saturated level and administered to the ocular surface continuously during the ischemia and/or reperfusion periods. One day after I/R injury, apoptotic cells in the retina were quantified and oxidative stress was evaluated by markers such as 4-hydroxynonenal and 8-hydroxy-2-deoxyguanosine. Seven days after I/R injury, retinal damage was quantified by measuring the thickness of the retina.

RESULTS. When H₂-loaded eye drops were continuously administered, H₂ concentration in the vitreous body immediately increased and I/R-induced OH level decreased. The drops reduced the number of retinal apoptotic and oxidative stress marker-positive cells, and prevented retinal

thinning with an accompanying activation of Müller glia, astrocytes, and microglia. The drops improved the recovery of retinal thickness by >70%.

CONCLUSIONS. H₂ has no known toxic effects on the human body. Thus, our study suggests that H₂-loaded eye drops will be a highly useful neuroprotective and anti-oxidative therapeutic treatment for acute retinal I/R injury.

Key Words: antioxidants • retinal ischemia • reperfusion • oxidative damage • intraocular pressure

Provided by www.LivingWaterUSA.com