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Protective effect of molecular hydrogen against oxidative stress caused by peroxynitrite derived from nitric oxide in rat retina

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Abstract

Background: Oxidative and nitrative processes have an important role in the pathogenesis of glaucomatous neurodegeneration. Oxidative stress occurs when cellular production of reactive oxygen species outweighs the protective capacity of antioxidant defences. Reactive oxygen species are generated as by-products of cellular metabolism, primarily in the mitochondria. Herein, we present a novel investigation of the effects of molecular hydrogen (H₂) on retinal cells exposed to oxidative stress.

Methods: We cultured adult rat retinal tissues in an organotypic culture system with a nitric oxide donor, S-nitroso-N-acetylpenicillamine, in the presence or absence of H₂. Loss of mitochondrial membrane potential and apoptosis of retinal cells were analysed using a MitoTMRE detection kit and TdT-mediated dUTP nick end labeling (TUNEL) assay, respectively. Tyrosine nitration levels and oxidative stress damage in the retina were evaluated using immunohistochemical staining. Retinal damage was quantified by measuring the numbers of cells in the ganglion cell and inner nuclear layers and the thickness of the retina.

Results: H₂ suppressed loss of mitochondrial membrane potential and apoptosis in retinal cells. Moreover, H₂ decreased the tyrosine nitration level and suppressed oxidative stress damage in retinal cells. S-nitroso-N-acetylpenicillamine treatment decreased the cell numbers in the ganglion cell layer and inner nuclear layer, but the presence of H₂ inhibited this reduction. These findings suggest that H₂ has a neuroprotective effect against retinal cell oxidative damage, presumably by scavenging peroxynitrite.

Conclusions: H₂ reduces cellular peroxynitrite, a highly toxic reactive nitrogen species. Thus, H₂ may be an effective and novel clinical tool for treating glaucoma and other oxidative stress-related diseases.

Keywords: antioxidant; molecular hydrogen; oxidative stress; retina.

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