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Molecular hydrogen ameliorates several characteristics of preeclampsia in the Reduced Uterine Perfusion Pressure (RUPP) rat model

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Abstract

Oxidative stress plays an important role in the pathogenesis of preeclampsia. Recently, molecular hydrogen (H_2) has been shown to have therapeutic potential in various oxidative stress-related diseases. The aim of this study is to investigate the effect of H_2 on preeclampsia. We used the reduced utero-placental perfusion pressure (RUPP) rat model, which has been widely used as a model of preeclampsia. H_2 water (HW) was administered orally ad libitum in RUPP rats from gestational day (GD) 12-19, starting 2 days before RUPP procedure. On GD19, mean arterial pressure (MAP) was measured, and samples were collected. Maternal administration of HW significantly decreased MAP, and increased fetal and placental weight in RUPP rats. The increased levels of soluble fms-like tyrosine kinase-1 (sFlt-1) and diacron reactive oxygen metabolites as a biomarker of reactive oxygen species in maternal blood were decreased by HW administration. However, vascular endothelial growth factor level in maternal blood was increased by HW administration. Proteinuria, and histological findings in kidney were improved by HW administration. In addition, the effects of H_2 on placental villi were examined by using a trophoblast cell line (BeWo) and villous explants from the placental tissue of women with or without preeclampsia. H_2 significantly attenuated hydrogen peroxide-induced sFlt-1 expression, but could not reduce the expression induced by hypoxia in BeWo cells. H_2 significantly attenuated sFlt-1 expression in villous explants from women with preeclampsia, but not affected them from normotensive pregnancy. The prophylactic administration of H_2 attenuated placental ischemia-induced hypertension, angiogenic imbalance, and oxidative stress. These results support the theory that H_2 has a potential benefit in the prevention of preeclampsia.

Keywords: Angiogenic factors; Antioxidants; Hydrogen peroxide; Molecular hydrogen; Oxidative stress; Preeclampsia.

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