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Molecular hydrogen alleviates asphyxia-induced neuronal cyclooxygenase-2 expression in newborn pigs

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Abstract

Cyclooxygenase-2 (COX-2) has an established role in the pathogenesis of hypoxic-ischemic encephalopathy (HIE). In this study we sought to determine whether COX-2 was induced by asphyxia in newborn pigs, and whether neuronal COX-2 levels were affected by H₂ treatment. Piglets were subjected to either 8 min of asphyxia or a more severe 20 min of asphyxia followed by H₂ treatment (inhaling room air containing 2.1% H₂ for 4 h). COX-2 immunohistochemistry was performed on brain samples from surviving piglets 24 h after asphyxia. The percentages of COX-2-immunopositive neurons were determined in cortical and subcortical areas. Only in piglets with more severe HIE, we observed significant, region-specific increases in neuronal COX-2 expression within the parietal and occipital cortices and in the CA3 hippocampal subfield. H₂ treatment essentially prevented the increases in COX-2-immunopositive neurons. In the parietal cortex, the attenuation of COX-2 induction was associated with reduced 8'-hydroxy-2'-deoxyguanosine immunoreactivity and retained microglial ramification index, which are markers of oxidative stress and neuroinflammation, respectively. This study demonstrates for the first time that asphyxia elevates neuronal COX-2 expression in a piglet HIE model. Neuronal COX-2 induction may play region-specific roles in brain lesion progression during HIE development, and inhibition of this response may contribute to the antioxidant/anti-inflammatory neuroprotective effects of H₂ treatment.

Keywords: 8'-hydroxy-2'-deoxyguanosine; COX-2; hypoxic-ischemic encephalopathy; microglia; molecular hydrogen; neuroprotection; newborn pigs.

Figures

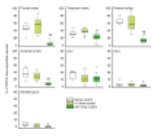


Figure 1 The ratio of neocortical COX-2-immunopositive...

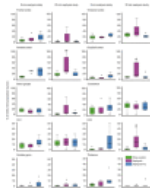


Figure 2 The effect of perinatal asphyxia...

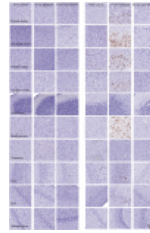


Figure 3 Representative photomicrographs (x20) showing cyclooxygenase-

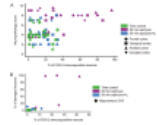


Figure 4 High ratios of COX-2-immunopositive neurons/total...

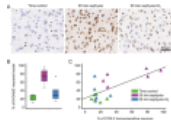


Figure 5 8-OHdG immunopositivity in the parietal...

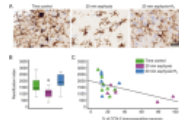


Figure 6 Iba-1 immunopositivity and microglial ramification...

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