Nrf2 activation in the liver of rats subjected to a preconditioning sub-chronic iron protocol

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Sub-chronic iron (Fe) administration induces liver oxidative stress upregulating cytoprotective mechanisms that may involve redox-sensitive nuclear factor erythroid 2-related factor 2 (Nrf2). We aimed to investigate whether Fe activates Nrf2, in relation to its negative regulator Kelch-like ECH associated protein 1 (Keap1), with consequent antioxidant enzyme induction. Sprague-Dawley rats received six Fe doses (50 mg kg-1) on alternate days or saline (controls), a protocol that abrogates ischemia-reperfusion liver injury. Liver reduced glutathione (GSH) content and Nrf2 (Western blot) were measured 24 h after each Fe dose. Increased hepatic Fe deposition (Perls staining) was paralleled by reversible GSH depletion and enhancements in nuclear Nrf2 content and in nuclear/cytosolic Nrf2 ratios. A similar profile was observed for heme oxygenase-1 (HO-1) and NADPH-quinone oxidoreductase 1 (NQO-1) contents, antioxidant enzymes that significantly correlated with nuclear/cytosolic Nrf2 ratios.