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Changes in drug metabolism during hypoxia/reoxygenation in isolated perfused rat

Min-Young Seo°, Tai-Soon Cho and Sun-Mee Lee

Sung Kyun Kwan University

This study was done to investigate the effect of vitamin E on hypoxia/reoxygenation-induced hepatic injury in isolated perfused rat liver. Rats were pretreated with vitamin E or vehicle(soybean oil). Isolated livers from fasted 18 hours were subjected to 45min of low flow hypoxia or N_2 hypoxia followed by reoxygenation for 30min. The perfusion medium used was KHBB(pH 7.4) and 50 μmol/ ℓ of ethoxycoumarin was added to the perfusate to determine the ability of hepatic drug-metabolizing systems. In low flow hypoxia model, total glutathione and oxidized glutathione levels were significantly increased by hepoxia/reoxygenation with slight increase in LDH levels. These increases were prevented by vitamin E pretreatment. In N_2 hypoxia model, LDH, total glutathione and oxidized glutathione levels were increased significantly by hypoxia but restored to normal level by reoxygenation. Vitamin E had little effect on this hypoxic damage. There were no significant changes in the rate of hepatic oxidation of 7-EC to 7-HC in both hepoxic models. But, the subsequent conjugation of 7-HC by sulfate or glucuronic acid were significantly decreased by hypoxia, but restored by reoxygenation in both hypoxia models. As opposed to our expectation, treatment with vitamin E aggrevated the decrease of the rate of conjugation and even inhibited the restoration by reoxygenation. Our findings suggest that hypoxia/reoxygenation diminishes phase II drug metabolizing function and this is, in part, related to decreased energy level.