특 강 V.

간장내 허혈 및 재순환에 있어 α-tocopherol이 약물대사 효소계에 미치는 영향

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The purpose of this study was to determine the relationship between microsomal lipid peroxidation during hepatic ischemia/reperfusion and alteration in cytochrome P-450 dependent drug metabolism. Rats were pretreated with α-tocopherol to inhibit lipid peroxidation or with vehicle (soybean oil) and then subjected to 60 min no-flow hepatic ischemia in vivo. Controls were time-matched sham-ischemic animals. Following 1, 5 or 24 hrs of reperfusion, liver microsomes were isolated and cytochrome P-450 content and mixed function oxidases were studied. In vehicle-treated ischemic rats, serum transaminase (ALT) levels peaked at 5 hrs (5242±682 U/L) and were significantly reduced by α-tocopherol pretreatment (1854±229 U/L, $p<0.01$). Similarly, microsomal cytochrome P-450 content and aminopyrine-N-demetylase activity were both decreased in vehicle-treated ischemic rats to 60% and 70% of sham-ischemic control levels, respectively. Although α-tocopherol restored cytochrome P-450 content to the level of sham-ischemic controls, aminopyrine-N-demethylase activity remained at 76% of control with α-tocopherol treatment ($p<0.01$ compared to sham-ischemic control). In contrast to what was seen with cytochrome P-450 and aminopyrine-N-demethylase, aniline p-hydroxylase activity was elevated in the vehicle-treated ischemic rats compared to sham-ischemia. These increases were prevented by α-tocopherol pretreatment. Our findings suggest that pretreatment with α-tocopherol reduces hepatocellular damage as indicated by abnormalities in microsomal drug metabolizing function during ischemia/reperfusion and that this protection is, in major part, caused by decreased lipid peroxidation.