3765

Inhibition of gamma-glutamyl transpeptidase ameliorates hepatic/reperfusion injury in rats with fatty liver

Ryuichi Kubota[1], Nobuhiko Hayashi[1], Mutsumi Tsuchishima[1], Mikihiro Tsutsumi[1], Joseph George[1]

[1]Kanazawa Medical University, Hepatology, Uchinada, Ishikawa, Japan

Email: georgej@kanazawa-med.ac.jp

Background and Aims: Fatty liver or steatosis is a condition of excessive fat deposition in the liver with increased γ-glutamyl transpeptidase (γ-GT) levels. Ischemia/reperfusion (IR) injury is a pathological condition with several deleterious effects. We evaluated the protective effects of a specific inhibitor of γ-GT in experimentally induced IR injury in rats with steatosis.

Methods: The portal vein and hepatic artery of left lateral and median lobes were clamped to induce ischemia. Before clamping, 1 ml of saline (IR group) or 1 ml saline containing 1 mg/kg body weight of GGsTop (γ-GT inhibitor) (IR- GGsTop group) was injected into the liver from inferior vena cava. The blood flow was restored at 30 min after the start of ischemia. Blood was collected before and at 30 min after ischemia, and at 2 h and 6 h after reperfusion. All the animals were euthanized at 6 h and the livers were collected.

Results: Treatment with GGsTop resulted in significant reduction of serum ALT, AST, and γ-GT levels and hepatic γ-GT, malondialdehyde, TNF-α, and 4-hydroxynonenal content at 6 h after reperfusion. Inhibition of γ-GT produced marked elevation of serum and hepatic glutathione levels. There was prominent hepatic necrosis in IR group, which is significantly reduced IR-GGsTop group.

Conclusions: Inhibition of γ-GT with GGsTop significantly increased serum and hepatic glutathione levels, reduced hepatic MDA and 4-HNE levels, and remarkably ameliorated hepatic necrosis after reperfusion. The results indicated that GGsTop might serve as an appropriate therapeutic agent to reduce IR-induced liver injury and related events in obesity.