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Protective effect of Betaine against Galactosamine-induced acute hepatic injury in rats

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Statement of the Problem: Galactosamine (GalN) is a potent hepatotoxicant that inhibits RNA and protein synthesis via depletion of uridine nucleotide in the liver. Earlier studies suggested that some endogenous sulfur-containing substances, particularly glutathione (GSH) and/or S-adenosylmethionine (SAM), might antagonize the induction of liver injury by GalN. In this study, we determined the effect of betaine, a methyl donor used for remethylation of homocysteine to methionine, against GalN-induced acute liver injury in association with alterations in the metabolomics of sulfur-containing amino acids and related substances in the liver.

Methodology: Male Sprague-Dawley rats received betaine (1% in drinking water) for 2 wk prior to GalN challenge (400 mg/kg, ip). Rats were sacrificed 24 h later for the assay.

Findings: GalN treatment elevated serum alanine transaminase (ALT), aspartate transaminase (AST), and sorbitol dehydrogenase (SDH) activities significantly, and these changes were blocked by betaine supplementation. Histopathological examination revealed extensive multifocal necrosis with macrophage infiltration in liver of the GalN-treated rats, which was also inhibited by betaine supplementation. GalN treatment increased methionine, but not SAM levels in the liver. Betaine supplementation further increased the hepatic levels of methionine, SAM, and methionine adenosyltransferase (MAT) activity. Hepatic GSH contents were not altered by betaine or GalN. GalN treatment elevated ornithine and spermidine, but decreased putrescine levels in the liver, suggesting that the metabolic conversion of ornithine to putrescine was impaired. Betaine supplementation increased hepatic putrescine and spermidine significantly, but ornithine levels were unaltered. LDH leakage increased progressively for 24 h after GalN treatment in H4IIE cells, which was inhibited almost completely by betaine or SAM addition.

Conclusion & Significance: The results suggest that the hepatoprotective effect of betaine against GalN-induced liver injury may be associated with an enhancement of polyamine biosynthesis via induction of MAT activity and SAM availability in the liver.

Biography

Young C Kim is a Professor of Toxicology at Seoul National University, College of Pharmacy, since 1986. He received his MS and PhD from Purdue University and completed Post-doctoral research at the National Institute of Environmental Health Sciences (NIEHS), NIH, USA. He has published more than 100 papers in reputed journals. He is a recipient of several prestigious international and national awards including the Thieme Most Innovative Original Paper Award at GA, Society for Medicinal Plant and Natural Product Research, and the Korean Teachers' Award.

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