
Abstract
Objectives: To determine whether administration of glycine, a nonessential amino acid, early after the onset of polymicrobial sepsis has any beneficial effects on hepatocellular function and the survivability of septic animals and, if so, whether the beneficial effects of glycine are associated with down-regulation of proinflammatory cytokine tumor necrosis factor-α production.
Design: Prospective, controlled, and randomized animal study.
Setting: A university research laboratory.
Subjects: Male adult rats were subjected to polymicrobial sepsis by cecal ligation and puncture or sham operation followed by the administration of normal saline solution.
Measurements and Main Results: At 1 hr after cecal ligation and puncture, glycine (0.6 mmol/kg) or vehicle (normal saline solution) was administered intravenously over 15 mins. At 5 hrs after cecal ligation and puncture (i.e., early stage of sepsis), hepatocellular function (i.e., the maximal velocity and efficiency of in vivo indocyanine green clearance) was determined and hepatocyte injury was assessed by measuring plasma concentrations of α-glutathione S-transferase. Serum tumor necrosis factor-α was measured by enzyme-linked immunosorbent assay. In additional animals, the necrotic cecum was excised at 20 hrs after cecal ligation and puncture, the peritoneal cavity was irrigated with saline, and the midline incision was closed in layers. Mortality was monitored for 10 days thereafter. The results indicate that hepatocellular function was depressed in the early stage of sepsis (i.e., 5 hrs after cecal ligation and puncture) as indicated by significant decreases in both maximal velocity and transport efficiency of in vivo indocyanine green clearance. Plasma concentrations of α-glutathione S-transferase and tumor necrosis factor-α were elevated significantly at that interval after cecal ligation and puncture. Administration of glycine 1 hr after cecal ligation and puncture, however, increased maximal velocity and maximal efficiency by 60% and 101% (p < .05), respectively. Glycine administration in septic animals decreased α-glutathione S-transferase and tumor necrosis factor-α by 43% and 80% (p < .05). In addition, glycine treatment decreased the mortality rate from 50% to 0% (p < .05) at 10 days after cecal ligation and puncture and cecal excision.
Conclusions: It appears that the beneficial effect of glycine on hepatocyte function and integrity in sepsis may be mediated via down-regulation of tumor necrosis factor-α. Because administration of glycine attenuated hepatocellular depression and injury during early sepsis and decreased sepsis-induced mortality rates, this amino acid appears to be a useful adjunct for maintaining cellular functions and preventing lethality from polymicrobial sepsis.