Effect of increased cardiac output on hepatic and intestinal microcirculatory blood flow, oxygenation, and metabolism in hyperdynamic murine septic shock.


From Sektion Anasthesiologische Pathophysiologie und Verfahrensentwicklung, Universitätsklinikum, Ulm, Germany.

OBJECTIVE:: Septic shock-associated organ dysfunction is attributed to derangements of microcirculatory perfusion and/or impaired cellular oxygen utilization. The hepatosplanchnic organs are regarded to play a pivotal role in the pathophysiology of sepsis-related organ failure. In a murine model of septic shock, we tested the hypothesis whether achieving normotensive, hyperdynamic hemodynamics characterized by a sustained increase in cardiac output would allow maintenance of regional microvascular perfusion and oxygenation and, thus, hepatic metabolic capacity. DESIGN:: Prospective, controlled, randomized animal study. SETTING:: University animal research laboratory. SUBJECTS:: Male C57Bl/6 mice. INTERVENTIONS:: Fifteen hours after sham operation (n = 11) or cecal ligation and puncture (CLP) (n = 9), mice were anesthetized, mechanically ventilated, and instrumented (central venous and left ventricular pressure-conductance catheter, portal vein and superior mesenteric artery ultrasound flow probes). Animals received continuous intravenous hydroxyethylstarch and norepinephrine to achieve normotensive and hyperdynamic hemodynamics, and glucose was infused to maintain normoglycemia.

MEASUREMENTS AND MAIN RESULTS:: Measurements were recorded 18, 21, and 24 hrs post-CLP. In CLP mice, titration of hemodynamic targets were affiliated superior mesenteric artery and portal vein flow. Using a combined laser-Doppler flowmetry and remission spectrophotometry probe, we found well-maintained gut and liver capillary perfusion as well as intestinal microcirculatory hemoglobin oxygen saturation, whereas hepatic microcirculatory hemoglobin oxygen saturation was even increased. At 24 hrs post-CLP, the rate of de novo gluconeogenesis as derived from hepatic C-glucose isotope enrichment after continuous intravenous 1,2,3,4,5,6-C6-glucose infusion (condensation biosynthesis modeling after gas chromatography-mass spectrometry isotope measurements) was similar in the two experimental groups. CONCLUSIONS:: During murine septic shock achieving normotensive hyperdynamic hemodynamics with fluid resuscitation and norepinephrine, exogenous glucose requirements together with the lack of norepinephrine-induced increase in the rate of gluconeogenesis mirror impaired metabolic capacity of the liver despite well-maintained hepatosplanchnic microvascular perfusion and oxygenation.

PMID: 16215389 [PubMed - in process]